Drugs and Cosmetics Rules, 1945

[21st December 1945]

Notificaiton: No. F. 28-10/45-H (1). _In exercise of the powers conferred by [1][sections 6(2), 12, 33 and 33N] of the Drugs and Cosmetics Act, 1940 (XXIII of 1940), the Central Government is pleased to make the following Rules:-

PART I
PRELIMINARY

1. ***Short title, extent and commencement***. *(1)* These Rules may be called the Drugs [9][and Cosmetics] Rules, 1945.

(2) They extend to the whole of India. [2][***]

[10][***]

2. *Definitions*. In these Rules, unless there is anything repugnant in the subject or context

(a) ―the Act‖ means the Drugs and Cosmetics Act, 1940 (XXIII of 1940) as amended from time to time;

[3][*(b)* ―Central Licence Approving Authority‖ means the Drugs Controller, India, or the Joint Drugs Controller (India) or the Deputy Drugs Controller (India) appointed by the Central Government;]

(c) ―Director‖ means the Director of the Central Drugs Laboratory;

(d) ―Form‖ means a form set forth in Schedule A;

[4][*(dd)* Homoeopathic medicines include any drug which is recorded in Homoeopathic provings or therapeutic efficacy of which has been established through long clinical experience as recorded in authoritative Homoeopathic literature of India and abroad and which is prepared according to the techniques of Homoeopathic pharmacy and covers combination of ingredients of such Homoeopathic medicines but does not include a medicine which is administered by parenteral route;]

(*e)* ―Laboratory‖ means the Central Drugs Laboratory;

[5][*(ea)* ―registered Homoeopathic medical practitioner‖ means a person who is registered in the Central Register or State Register of Homoeopathy;]

[8][(eb)―Phytopharmaceutical drug‖ includes purified and standardised fraction with defined minimum four bio-active or phyto-chemical compounds (qualitatively and quantitatively assessed) of an extract of a medicinal plant or its part, for internal or external use of human beings or animals for diagnosis, treatment, mitigation or prevention of any disease or disorder but does not include administration by parenteral route.]

[6][*(ee)* ―Registered medical practitioner‖ means a person

(i) holding a qualification granted by an authority specified or notified under section 3 of the Indian Medical Degrees Act, 1916 (7 of 1916), or specified in the Schedules to the Indian Medical Council Act, 1956 (102 of 1956); or

(ii) registered or eligible for registration in a medical register of a State meant for the registration of persons practising the modern scientific system of medicine [7][excluding the Homoeopathic system of medicine]; or

1. Subs. by G.S.R. 370(E), dt. 7-4-1994.
2. Omitted by G.S.R. 358, dt. 15-3-1975.
3. Sub. by GSR. 579(E), dt. 20-9-2006, earlier Ins. by G.S.R. 923(E), dt. 14-12-1992.
4. Ins. by Notfn. No. F. 1-59 / 68-D, dt. 19-11-1969.
5. Ins. by G.S.R 680 (E), dt. 5-12-1980.
6. Ins. by Notfn. F. 1-22 / 59-D, dt. 9-4-1960. 7. Ins. by S.O. 2139, dt. 15-6-1972.
8. Ins. By G.S.R 918(E), dt. 30-11-2015.
9. Ins. by GSR 1183(E), dt 17-8-1964.
10. Sub-rule (3) omitted by GSR 19, dt. 15-12-1977.

(iii) registered in a medical register, [1][other than a register for the registration of Homoeopathic practitioner], of a State, who although not falling within sub-clause (i) or sub-clause (ii) is declared by a general or special order made by the State Government in this behalf as a person practising the modern scientific system of medicine for the purposes of this Act; or

(iv) registered or eligible for registration in the register of dentists for a State under the Dentists Act, 1948 (16 of 1948); or

(v) who is engaged in the practice of veterinary medicine and who possesses qualifications approved by the State Government;]

[2][*(f)* —retail sale‖ means a sale [3][whether to a hospital, or dispensary, or a medical, educational or research institute or to any other person] other than a sale by way of wholesale dealing];

[4][*(g)* —sale by way of wholesale dealing‖ means sale to a person for the purpose of selling again and includes sale to a hospital, dispensary, medical, educational or research institution;]

[5][*(h)* —Schedule‖ means a Schedule to these Rules;]

[6][*(i)* State Government in relation to a Union Territory means the Administrator thereof;

[9][***]

PART II

THE CENTRAL DRUGS LABORATORY

3. *Functions*. It shall be the function of the Laboratory

(*i*) to analyse or test such samples of drugs as may be sent to it under sub- section (2) of section 11, or under sub-section (4) of section 25 of the Act;

[7][* * * * *]

(iii) to carry out such other duties as may be entrusted to it by the Central Government or, with the permission of the Central Government, by a State Government after consultation with the Drugs Technical Advisory Board.

[8][**3A.** *(1)*The functions of the Laboratory in respect of the following drugs or classes of drugs shall be carried out at the Central Research Institute, Kasauli, and the functions of the Director in respect of the said drugs or classes of drugs shall be exercised by the Director of the said Institute :

(1) Sera.

(2) Solution of serum proteins intended for injection.

(3) Vaccines.

(4) Toxins.

(5) Antigens.

1. Ins. by S.O. 2139, dt. 5-6-1972.
2 Subs. by Notfn. No. F. 1-3/51-DS., dt. 15-11-1954.
3. Ins. by G.S.R 681 (E), dt. 6-6-1988.
4. Subs. by Notfn. F-1-16/57, dt. 15.6.1957.
5. Subs. by Notfn. No. F. 28-10/45-H (1), dt. 31-3-1957.
6. Subs. by Notfn. No. F-1-16/57-D, dt. 15-6-1957.
7. Cl. (ii) omitted, by Notfn. No. F-1-16/57-D, dt. 15-6-1957.
8 Ins. by Notfn. No. F. 4-1 / 60-D, dt. 15-5-1961.
9. Cl. (j) omitted by GSR 592(E), dt. 13-08-2008

(7) Sterilized surgical ligature and sterilised surgical suture.

(8) Bacteriophages:

[1][Provided that the functions of the Director in respect of Oral Polio Vaccine shall be exercised by the Deputy Director and Head of the Polio Vaccine Testing Laboratory in case of Central Research Institute, Kasauli only.]

[2][*(1A)* The functions of the Laboratory in respect of Oral Polio Vaccine shall be carried out by the following Institutes and the functions of the Director in respect of the said drugs shall be exercised by the Director of the respective Institutes :-

(a) Pasteur Institute of India, Coonoor.

(b) Enterovirus Research Centre (Indian Council of Medical Research), Haffkin Institute Compound, Parel, Bombay-400012.]

[3][*(c)* The National Institute of Biologicals, NOIDA.]

[4][*(2)* The functions of the Laboratory in respect of the following drugs or classes of drugs shall be carried out at the Indian Veterinary Research Institute, Izatnagar or Mukteshwar and the functions of the Director in respect of the said drugs or classes of drugs shall be exercised by the Director of either of the said institutes.

(1) Anti-sera for veterinary use.

(2) Vaccines for veterinary use.

(3) Toxoids for veterinary use.

(4) Diagnostic Antigens for veterinary use.]

[5][*(3)* The functions of the laboratory in respect of testing of condoms shall be carried out at the Central Drugs Testing Laboratory, Chennai, and the functions of the Director in respect of the said products shall be exercised by the Director of the said Laboratory.]

[6][*(4)*] The functions of the Laboratory in respect of the following drug shall be carried out at the Laboratory of the Serologist and Chemical Examiner to the Government of India, Calcutta and the functions of the Director in respect of the said drug shall be performed by the Serologist and Chemical Examiner of the said Laboratory :

VDRL Antigen.

[7][*(5)* The function of the Laboratory in respect of Intra-Utrine Devices and Falope Rings shall be carried out at the Central Drugs Testing Laboratory, Thane, Maharashtra and the functions of the Director in respect of the said devices shall be exercised by the Director of the said Laboratory.]

1. Subs. by G.S.R.445(E), dt. 30-4-1992. Earlier Ins. by G.S.R.62(E), dt. 15-2-1982.
2. Ins. by G.S.R. 445(E), dt. 30-4-1992.
3. Ins. by G.S.R.249(E), dt. 4-4-2002.
4. Ins. by Notfn. No. F.-1-6/62-D, dt. 2-7-1969.
5. Sub. By G.S.R. 651(E), dt. 9-9-2009, earlier Ins. by S. O. No. 2139, dt. 12-8-1972.
6. Sub-rule (4) omitted and sub-rule (5) renumbered as sub-rule (4) by Notfn. No. G.S.R. 62(E), dt. 15-2-1982.
7. Subs. by G.S.R 242(E), dt. 18-3-1998. Earlier Ins. by G.S.R. No. 865 (E), dt. 25-10-1990.

[1][*(6)* The functions of the Laboratory in respect of human blood and human blood products including components, to test for freedom of HIV antibodies, shall be carried out by the following Institutes/Hospitals and the functions of the Director in respect of the above mentioned products shall be exercised by the head of the respective Institute, namely:-

(a) National Institute for Communicable Disease, Department of Microbiology, Delhi.

(b) National Institute of Virology, Pune

(c) Centre of Advanced Research in Virology, Christian Medical College, Vellore.]

[2][*(7)* The functions of the Laboratory in respect of Homoeopathic medicines shall be carried out at the Homoeopathy Pharmacopoeia Laboratory, Ghaziabad and the functions of the Director in respect of the Homoeopathic medicines shall be exercised by the Director of the laboratory.]

[3][(8) (a) The functions of the Laboratory in respect of the following kits or class of drugs shall be carried out at the National Institute of Biologicals, Noida and the functions of the Director in respect of the said drugs or class of drugs shall be exercised by the Director of the said institute.

(b) The kits or class of drugs referred to in clause (a) are- (1)

Blood grouping reagents.

(2) Diagnostic kits for human immunodeficiency virus, Hepatitis B Surface Antigen and Hepatitis C Virus.

(3) Blood products-

(a) Human Albumin;

(b) Human Normal Immunoglobulin (intramuscular and intravenous); (c) Human Coagulation Factor VIII;

(d) Human Coagulation Factor IX;

(e) Plasma Protein Fractionation;

(f) Fibrin Sealant Kit;

(g) Anti Inhibitor Coagulation complex.

(4) Recombinant products such as-

(a) Recombinant insulin and insulin analogue;

(b) r-erythropoietin (EPO);

(c) r-Granulocyte Colony stimulating Factor (G-CSF).

(5) Biochemical kits-

(a) Glucose Test Strips;

(b) Fully Automated analyzer based glucose reagents.]

4. *Despatch of samples for test or analysis*.- (*1)* Samples for test or analysis under sub-section (4) of section 25 of the Act shall be sent by registered post in a sealed packet, enclosed, together with a memorandum in

Form 1, in an outer cover addressed to the Director.

(2) The packet as well as the outer cover, shall be marked with a distinguishing number.

(*3*) A copy of the memorandum in

Form 1 and a specimen impression of the seal used to seal the packet shall be sent separately by registered post to the Director.

5. *Recording of condition of seals*.

On receipt of the packet, it shall be opened by an officer authorised in writing in that behalf by the Director who shall record the condition of the seal on the packet. 1. Ins. by G.S.R 16(E), dt. 10-1-1990. 2. Ins. by G.S.R 246(E), dt. 1-5-1991.

3. Sub. by G.S.R. No. 908(E), dt. 4-4-2014. Earlier Ins. by G.S.R. No. 249 (E), dt. 4-4-2002.

6. *Report of result of test or analysis*. After test or analysis the result of the test or analysis, together with full protocols of the tests applied, shall be supplied forthwith to the sender in

Form 2.

7. *Fees*. The fees for test and analysis shall be those specified in Schedule B.

8. *Signature of certificates*. Certificates issued under these Rules by the Laboratory shall be signed by the Director or by an officer authorised by the Central Government by Notification in the Official Gazette to sign such certificates.

[1][PART III

[RULES 9 to 20- omitted by SRO. 2136 dated 15-06-1957]

PART IV

[2][IMPORT AND REGISTRATION]

21. In this Part.–

[3][*(a)* ―import licence‖ means either a licence in Form 10 to import drugs [4][* * *]; excluding those specified in Schedule X, or a licence in Form 10-A to import drugs specified in Schedule X;]

(b) ―licensing authority‖ means the authority appointed by the Central Government to perform the duties of the licensing authority under these Rules and includes any person to whom the powers of a licensing authority may be delegated under Rule 22;

(c) ―licence for examination, test or analysis‖ means a licence in Form 11 to import small quantities of drugs the import of which is otherwise prohibited, for the purpose of examination, test or analysis;

[5][*(d)* ―manufacturer‖ includes a manufacturer of drugs, who may be a Company or a unit or a body corporate or any other establishment in a country other than India, having its drugs manufacturing facilities duly approved by the National Regulatory Authority of that country, and who also has a free sale approval of the drugs approved by the said authority in the concerned country, and /or in other major countries;

(e) ―Registration Certificate‖ means a certificate issued under Rule 27A by the licensing authority in

Form 41 for registration of the premises and the drugs manufactured by the manufacturer meant for import into and use in India.]

22. The licensing authority may with the approval of the Central Government by an order in writing delegate the [2][power to sign licences and Registration Certificate and] such other powers as may be specified in the order to any other person under his control.

1. Part III (Rules 9 to 20) omitted by Notfn. No. F. 1-16/57-D (SRO 2136), dt. 15-6-1957.
2. Sub. by G.S.R 604 (E), dt. 24-8-2001.
3. Subs. by G.S.R 462 (E),dt. 22-6-1982.
4. Omitted by G.S.R 604 (E), dt. 24-8-2001.
5. Ins. by G.S.R 604 (E), dt. 24-8-2001.

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[1][**23**. *Import licences*.–An import licence in Form 10 shall be required for [2] [import of drugs], excluding those specified in Schedule X, and an import licence in Form 10- A shall be required for the import of drugs specified in Schedule X.]

[2][**24.** *Form and manner of application for import licence*.– *(1)* An application for an import licence shall be made to the licensing authority in

Form 8 for drugs excluding those specified in Schedule X, and in Form 8A for drugs specified in Schedule X, either by the manufacturer himself having a valid wholesale licence for sale or distribution of drugs under these Rules, or by the manufacturer‘s agent in India either having a valid licence under the Rules to manufacture for sale of a drug or having a valid wholesale licence for sale or distribution of drugs under these Rules, and shall be accompanied by a licence fee of one thousand rupees for a single drug and an additional fee at the rate of one hundred rupees for each additional drug and by an undertaking in Form 9 duly signed by or on behalf of the manufacturer:

Provided that in the case of any subsequent application made by the same importer for import licence for drugs manufactured by the same manufacturer, the fee to accompany each such application shall be one hundred rupees for each drug:

(2) Any application for import licence in Form 8 or Form 8-A, as the case may be, shall be accompanied by a copy of Registration Certificate issued in Form 41 under Rule 27A:

Provided that in case of emergencies the licensing authority may, with the approval of the Central Government, issue an import licence in

Form 10 or 10A, as the case may be, without the issuance of Registration Certificate under Rule 27A, for reasons to be recorded in writing.

[3][Provided further that Registration certificate shall not be required to be accompanied with an application for an import licence under the Rules for the import of in-vitro diagnostic kits and regents, except for the diagnostic kits notified from time to time under sub-clause (iv) of clause (b) of section 3.]

(3) A fee of two hundred and fifty rupees shall be paid for a duplicate copy of the licence issued under this Rule, if the original is defaced, damaged or lost.]

4[**24A.** *Form and manner of application for Registration Certificate.—(1)* An application for issue of a Registration Certificate shall be made to the licensing authority in

Form 40, either by the manufacturer himself, having a valid wholesale licence for sale or distribution of drugs under these rules, or by his authorised agent in India, either having a valid licence under the rules to manufacture for sale of a drug or having a valid wholesale licence for sale or distribution of drugs under these rules, and shall be accompanied by the fee specified in sub-rule *(3)* and the informations and undertakings specified in Schedules D-I and D-II duly signed by or on behalf of the manufacturer.

1. Subs. by G.S.R. 462 (E), dt. 22-6-1982.
2. Subs. by G.S.R 604 (E), dt. 24-8-2001.
3. Ins. by G.S.R. 35(E), dt. 20.1.2005.
4. Ins. by G.S.R 604 (E), dt. 24-08-2001.

(2) The authorisation by a manufacturer to his agent in India shall be documented by a power of attorney executed and authenticated either in India before a First Class Magistrate, or in the country of origin before such an equivalent authority, the certificate of which is attested by the Indian Embassy of the said country, and the original of the same shall be furnished along with the application for Registration Certificate.

(3) (i) A fee of one thousand and five hundred US dollars [1][or its equivalent in Indian rupees] shall be paid along with the application in

Form 40 as registration fee for his premises meant for manufacturing of drugs intended for import into and use in India

(ii) A fee of one thousand US dollars [1][or its equivalent in Indian rupees] shall be paid along with the application in

Form 40 for the registration of a single drug meant for import into and use in India and an additional fee at the rate of one thousand US dollars for each additional drug:

Provided that in the case of any subsequent application for registration of additional drugs by the same manufacturer, the fee to accompany shall be one thousand US dollars [1][or its equivalent in Indian rupees] for each drug.

(4) The fees shall be paid through a Challan in the Bank of Baroda, Kasturba Gandhi Marg, New Delhi-110001 or any other branch or branches of Bank of Baroda, or any other bank, as notified, from time to time, by the Central Government, to be credited under the Head of Account ―0210-Medical and Public Health, 04-Public Health, 104-Fees and Fines‖:

Provided that in the case of any direct payment of fees by a manufacturer in the country of origin, the fees shall be paid through Electronic Clearance System (ECS) from any bank in the country of origin to the Bank of Baroda, Kasturba Gandhi Marg, New Delhi, through the Electronic Code of the bank in the Head of Account ―0210- Medical and Public Health, 04- Public Health, 104-Fee and Fines‖, and the original receipt of the said transfer shall be treated as an equivalent to the bank challan, subject to the approval by the Bank of Baroda that they have received the payment.

(5) The applicant shall be liable for the payment of a fee of five thousand US dollars [1][or its equivalent in Indian rupees] for expenditure as may be required for inspection or visit of the manufacturing premises or drugs, by the licensing authority or by any other persons to whom powers have been delegated in this behalf by the licensing authority under Rule 22.

(6) The applicant shall be liable for the payment of testing fees directly to a testing laboratory approved by the Central Government in India or abroad, as may be required for examination, tests and analysis of drug.

(7) A fee of three hundred US dollars [1][or its equivalent in Indian rupees] shall be paid for a duplicate copy of the Registration Certificate, if the original is defaced, damaged or lost.

(8) No Registration Certificate shall be required under these Rules in respect of an inactive bulk substance to be used for a drug formulation, with or without pharmacopoeial conformity.]

1. Ins. by G.S.R. 35(E), dt. 20.1.2005.

25. *Licences for import of drugs manufactured by one manufacturer*.– *(1)* A single application may be made, and a single licence may be issued, in respect of the import of more than one drug or class of drugs manufactured by the same manufacturer:

[1][Provided that the drugs or classes of drugs are manufactured at one factory or more than one factory functioning conjointly as a single manufacturing unit:

Provided further that if a single manufacturer has two or more factories situated in different places manufacturing the same or different drugs a separate licence shall be required in respect of the drugs manufactured by each such factory.]

[2][* * * * *]

[3][**25A**. *Condition to be satisfied before a licence in Form 10 or Form 10-A is granted*.–*(1)* A licence in Form 10 or in Form 10-A shall be granted by the licensing authority having regard to–

(i) the premises, where the imported substances will be stocked, are equipped with proper storage accommodation for preserving the properties of the drugs to which the licence applies; and

(ii) the occupation, trade or business ordinarily carried out by the applicant:

Provided that the licensing authority may refuse to grant a licence in

Form 10-A in respect of any applicant where he is satisfied,--

(a) that the applicant has not complied with the provisions of the Act or these rules; or

(b) that by reasons of—

4[*(i)* his conviction under the Act or these Rules or the Narcotic Drugs and Psychotropic Substances Act, 1985 (61 of 1985) or the rules made thereunder;]

(ii) previous suspension or cancellation of the licence granted to him;

he is not a fit person to whom licence shall be granted.

(2) Any person who is aggrieved by the order passed by the licensing authority under this Rule may, within thirty days of the receipt of the order, appeal to the Central Government and the Central Government may after such enquiry into the matter as it considers necessary and after giving the appellant an opportunity for making a representation in the matter, make such orders in relation thereto as it thinks fit.]

1. Ins. by Notfn. No. F. 1-19/48-D, dt. 27-10-1949.
2. Omitted Notfn. No.F. 1-16/57-D, dt. 15-6-1957.
3. Subs. by G.S.R 462(E), dt. 22-6-1982. Earlier Ins. by Notfn. No. F. 1-9/52-D. dt. 3-11-1958.
4. Subs. by G.S.R 604 (E), dt. 24-8-2001.

1[**25B.** *Registration Certificate for import of drugs manufactured by one manufacturer.--(1)* A single application may be made, and a single Registration Certificate in Form 41 may be issued in respect of the import of more than one drug or class of drugs, manufactured by the same manufacturer:

Provided that the drug or classes of drugs, are manufactured at one factory or more than one factory functioning conjointly as a single manufacturing unit:

Provided further that if a single manufacturer has two or more factories situated in different places manufacturing the same or different drugs, separate Registration Certificates shall be required in respect of the drugs manufactured by each such factory.]

26. *Conditions of import licence.* An import licence shall be subject to the following conditions:

(i) the manufacturer shall at all times observe the undertaking given by him or on his behalf in

Form 9;

(ii) the licensee shall allow any Inspector authorised by the licensing authority in that behalf to enter with or without notice any premises where the imported substance is stocked, to inspect the means, if any, employed for testing the substance and to take samples;

(iii) the licensee shall on request furnish to the licensing authority from every batch of each substance or from such batch or batches as the licensing authority may from time to time specify a sample of such amount as the licensing authority may consider adequate for any examination required to be made, and the licensee shall, if so required, furnish full protocols of the tests, if any, which have been applied;

(iv) if the licensing authority so directs the licensee shall not sell or offer for sale any batch in respect of which a sample is or protocols are furnished under the last preceding sub-rule until a certificate authorising the sale of the batch has been issued to him by or on behalf of the licensing authority;

(v) the licensee shall, on being informed by the licensing authority that any part of any batch of the substance has been found by the licensing authority not to conform with the standards of strength, quality and purity prescribed by Chapter III of the Act, or the rules thereunder and on being directed so to do, withdraw the remainder of that batch from sale and, so far as may in the particular circumstances of the case be practicable, recall the issues already made from that batch;

(vi) the licensee shall maintain a record of all sales by him of substances for the import of which a licence is required, showing particulars of the substance and of the person to whom sold and such further particulars, if any, as the licensing authority may specify and such record shall be open to the inspection of any Inspector authorised in that behalf by the licensing authority:

1. Ins. by G.S.R. No. 604(E), dt. 24-8-2001.

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1[Provided that in respect of the sale or distribution of drugs specified in Schedule X, the licensee shall maintain a separate record or register showing the following particulars, namely:

1. Name of the Drug,

2. Batch number,

3. Name and address of the manufacturer,

4. Date of transaction,

5. Opening stock on the business day,

6. Quantity of drug received, if any, and the source from which received,

7. Name of the purchaser, his address and licence number,

8. Balance quantity of drug at the end of the business day,

9. Signature of the person under whose supervision the drugs have been supplied.]

(vii) the licensee shall comply with such further requirements, if any, applicable to the holders of import licenses, as may be specified in any rules, subsequently made under Chapter III of the Act and of which the licensing authority has given to him not less than four months‘ notice.

27. *Grant of import licence*. On receipt of an application for an import licence in the form and manner prescribed in Rule 24, the licensing authority shall, on being satisfied that, if granted, the conditions of the licence will be observed, issue an import licence in

Form 10 [1][or From 10A, as the case may be].

[2][**27A** *Grant of Registration Certificate.* (*1)* On receipt of an application for Registration Certificate in the Form and manner specified in Rule 24A, the licensing authority shall, on being satisfied, that, if granted, the conditions of the Registration Certificate will be observed, issue a Registration Certificate in

Form 41:

Provided further that if the application is complete in all respects and informations specified in Schedules D-I and D-II are in order, the licensing authority shall, within nine months from the date of receipt of an application, issue such Registration Certificate, and in exceptional circumstances and for reasons to be recorded in writing, the Registration Certificate may be issued within such extended period, not exceeding three months, as the licensing authority may deem fit.

(2) If the applicant does not receive the Registration Certificate within the period as specified in the proviso to sub-rule (1), he may appeal to the Central Government and the Central Government may after such enquiry into the matter, as it considers necessary, may pass such orders in relation thereto as it thinks fit.]

1. Ins. by G.S.R 462 (E), dt. 22-6-1982.

2. Ins. by G.S.R 604 (E), dt. 24-8-2001.

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1[**28.** *Duration of import licence.* A licence unless, it is sooner suspended or cancelled, shall be 2[valid for a period of three years from the date of its issue:]

Provided that if application for a fresh licence is made three months before the expiry of the existing licence the current licence shall be deemed to continue in force until orders are passed on the application.]

3[**28A**. *Duration of Registration Certificate.*— A Registration Certificate, unless, it is sooner suspended or cancelled, shall be valid for a period of three years from the date of its issue:

Provided that if the application for a fresh Registration Certificate is made nine months before the expiry of the existing certificate, the current Registration Certificate shall be deemed to continue in force until orders are passed on the application.]

4[**29.** *Suspension and cancellation of import licence*. If the manufacturer or licensee fails to comply with any of the conditions of an import licence, the licensing authority may after giving the manufacturer or licensee an opportunity to show cause why such an order should not be passed, by an order in writing stating the reasons therefor, suspend or cancel it for such period as it thinks fit, either wholly or in respect of some of the substances to which it relates:

Provided that a person, who is aggrieved by the order passed by the licensing authority under this rule may, within thirty days of the receipt of the order, appeal to the Central Government, and the Central Government may, after such enquiry into the matter as it considers necessary and after giving the appellant an opportunity for representing his views in the matter, pass such orders in relation thereto as it thinks fit.]

3[**29A**. *Suspension and cancellation of Registration Certificate.* —If the manufacturer fails to comply with any of the conditions of the Registration Certificate, the licensing authority may after giving him an opportunity to show cause why such an order should not be passed, by an order in writing stating the reasons therefor, suspend or cancel the Registration Certificate for such period as it thinks fit either wholly or in respect of some of the substances to which it relates:

Provided that a person, who is aggrieved by the order passed by the licensing authority under this rule may, within thirty days of the receipt of the order, appeal to the Central Government, and the Central Government may, after such enquiry into the matter as it considers necessary and after giving the appellant an opportunity for representing his views in the matter, pass such orders in relation thereto as it thinks fit.]

1. Amended by Notfn. No. F. 1-10/62-D, dt. 19-4-1964.

2. Subs. by G.S.R 604 (E), dt. 24-8-2001.

3. Ins. by G.S.R 604 (E), dt. 24-8-2001.

4. Subs. by G.S.R 604 (E), dt. 24-8-2001.

30. *Prohibition of import after expiry of potency.* —No biological or other special product specified in Schedule C or C (I) shall be imported after the date shown on the label, wrapper or container of the drug as the date up to which the drug may be expected to retain a potency not less than, or not to acquire a toxicity greater than, that required, or as the case may be, permitted by the prescribed test.

[1][* * * * *]

[2][**30AA.** *Import of new Homoeopathic medicine.—(1)* No new Homoeopathic medicine shall be imported except under and in accordance with the permission in writing of the Licensing Authority.

(2) The importer of a New Homoeopathic medicine when applying for permission shall produce before the Licensing Authority such documentary and other evidence as may be required by the Licensing Authority for assessing the therapeutic efficacy of the medicine including the minimum provings carried out with it.]

[3][*Explanation.* —For the purpose of this rule, ‗New Homoeopathic Medicine' means—

(*i*) a Homoeopathic medicine which is not specified in the Homoeopathic Pharmacopoeia of India or United States of America or of the United Kingdom or the German Homoeopathic Pharmacopoeia; or

(*ii*) which is not recognized in authoritative Homoeopathic literature as efficacious under the conditions recommended; or

(iii) a combination of Homoeopathic medicines containing one or more medicines which are not specified in any of the Pharmacopoeias referred to in clause *(i)* as Homoeopathic medicines and also not recognized in authoritative Homoeopathic literature as efficacious under the conditions recommended.]

[4][**30B.** *Prohibition of import of certain drugs*. No drug, the manufacture, sale or distribution of which is prohibited in the country of origin, shall be imported under the same name or under any other name except for the purpose of examination, test or analysis.]

[5][**31.** *Standard for certain imported drugs*.—No drug shall be imported unless it complies with the standard of strength, quality and purity, if any, and the test prescribed in the Rules shall be applicable for determining whether any such imported drug complies with the said standard:

Provided that the drugs intended for veterinary use, the standards of strength, quality and purity, if any, shall be those that are specified in Schedule F(1) and the test prescribed in that Schedule shall be applicable for determining whether any such imported drug complies with the said standards and where no standards are specified in Schedule F(1) for any veterinary drug, the standards for such drug shall be those specified in the current edition, for the time being in force, of the British Pharmacopoeia Veterinary:

1. Rule 30A omitted by G.S.R.944 (E), dt. 21-9-1988. Earlier rules 30A and 30AA ins. by Notfn. F. 1-30/48-G, Dt. 14.4.1952.

2. Ins. by notification No. F 1-30/48, dt. 14-01-1952.

3. Subs. G.S.R. 680 (E) ,dt. 5-12-1980.

4. Ins. by Notfn. No. F. 1-45 4-1-1951.

5. Subs. G.S.R. 604 (E), dt. 24-8-2001.

Provided further that the licensing authority shall not allow the import of any drug having less than sixty per cent residual shelf-life period as on the date of import:

Provided also that in exceptional cases the licensing authority may, for reasons to be recorded in writing, may allow, the import of any drug having lesser shelf-life period, but before the date of expiry as declared on the container of the drug.]

[1][**32.** *Packing and labelling of imported drugs.* No drug shall be imported unless it is packed and labelled in conformity with the Rules in Parts IX and X [2][* * *] and further conform to the standards laid down in Part XII provided that in the case of drugs intended for veterinary use, the packing and labelling shall conform to the rules in Parts IX and X and Schedule F(1)].

[3][**32A** *Packing and Labelling of Homoeopathic medicine*. No Homoeopathic medicine shall be imported unless it is packed and labelled in conformity with the rules in Part IX-A.]

33. *Import of drugs for examination, test or analysis* Small quantities of drugs the import of which is otherwise prohibited under section 10 of the Act may be imported for the purpose of examination, test or analysis subject to the following conditions:

(*a*) No drug shall be imported for such purpose except under a licence in Form 11;

(*b*) the licensee shall use the substances imported under the licence exclusively for purposes of examination, test or analysis and shall carry on such examination, test or analysis in the place specified in the licence, or in such other places as the licensing authority may from time to time authorise;

(*c*) the licensee shall allow any Inspector authorized by the licensing authority in this behalf to enter, with or without prior notice, the premises where the substances are kept, and to inspect the premises, and investigate the manner in which the substances are being used and to take samples thereof;

(*d*) the licensee shall keep a record of, and shall report to the licensing authority, the substances imported under the licence, together with the quantities imported, the date of importation and the name of the manufacturer;

(*e*) the licensee shall comply with such further requirements, if any, applicable to the holders of licences for examination, test or analysis as may be specified in any rules subsequently made under Chapter III of the Act and of which the licensing authority has given to him not less than one month‘s notice.

1. Subs. by Notfn. No. F. 1-6/62-D (SO 2889), dt. 2-7-1969.
2. Certain words omitted by G.S.R. 661(E), dt. 3-7-1992.
3. Ins. by S. O. No. 2139, dt. 5-6-1972.

[1][**33A** *Import of drugs by a Government Hospital or Autonomous Medical Institution for the treatment of patients.*—Small quantities of new drug, as defined in Rule 122-E, the import of which is otherwise prohibited under section 10 of the Act, may be imported for treatment of patients suffering from life threatening diseases, or diseases causing serious permanent disability, or such disease requiring therapies for unmet medical needs, by a Medical Officer of a Government Hospital or an Autonomous Medical Institution providing tertiary care, duly certified by the Medical Superintendent of the Government Hospital, or Head of the Autonomous Medical Institution, subject to the following conditions, namely:-

(a) no new drug shall be imported for the said purpose except under a licence in

Form 11-A, and the said drug has been approved for marketing in the country of origin;

(b) the licensee shall use the substances or drugs imported under the licence exclusively for the purpose of treatment of patients suffering from life threatening diseases, or diseases causing serious permanent disability, or such diseases requiring therapies for unmet medical needs, under the supervision of its own Medical Officers at the place, specified in the licence or at such other places, as the licensing authority, may from time to time authorise;

(c) the licensee shall allow an Inspector authorised by the licensing authority in this behalf to enter, with or without prior notice, the premises where the substances or drugs are stocked, and to inspect the premises and relevant records and investigate the manner in which the substances or drugs are being used and to take, if necessary, samples thereof ;

(d) the licensee shall keep a record of, and shall submit the said report half yearly to the licensing authority, the substances or drugs imported under the licence, together with the quantities imported and issued to the patients, the date of importation, the name of the manufacturer, the name and address of the patient for whom the drug is prescribed and the name of disease;

(*e*) the licensee shall comply with such other requirements, if any, applicable to the holders of import licences for import of new drugs for treatment of patients by Government Hospitals, as may be specified from time to time in any rule subsequently made under Chapter III of the Act and of which the licensing authority has given to him not less than one month‘s notice;

(*f*) the drug shall be stocked under proper storage conditions and shall be dispensed under the supervision of a registered pharmacist;

(*g*) the quantity of any single drug so imported shall not exceed 100 average dosages per patient:

Provided that the licensing authority may, in exceptional circumstances, sanction the import of drug of a larger quantity.]

34. *Application for licence for examination, test or analysis.(1)* An application for a licence for examination, test or analysis shall be made in Form 12 and shall be made or countersigned by the head of the institution in which, or by a proprietor or director of the company or firm by which the examination, test or analysis will be conducted.

1. Ins. by G.S.R 604 (E), dt. 24-8-2001.

(2) The licensing authority may require such further particulars to be supplied as he may consider necessary.

1[*(3)* Every application in Form 12 shall be accompanied by a fee of one hundred rupees for a single drug and an additional fee of fifty rupees for each additional drug.

(4) The fees shall be paid through a challan in the Bank of Baroda, Kasturba Gandhi Marg, New Delhi-110001 or any other branch or branches of Bank of Baroda, or any other Bank, as notified, from time to time, by the Central Government, to be credited under the Head of Account 0210-Medical and Public Health, 04- Public Health, 104- Fees and Fines.]

[2][**34A**. *Application for licence to import small quantities of new drugs by a Government Hospital or Autonomous Medical Institution for the treatment of patients.(1)* An application for an import licence for small quantities of a new drug, as defined in Rule 122-E for the purpose of treatment of patients suffering from life threatening diseases, or diseases causing serious permanent disability, or such diseases requiring therapies for unmet medical needs, shall be made in

Form 12-AA, by a Medical Officer of the Government Hospital or Autonomous Medical Institution, which shall be certified by the Medical Superintendent of the Government Hospital or Head of the Autonomous Medical Institution, as the case may be.

(2) The licensing authority may require such further particulars to be supplied, as he may consider necessary.

(3) Every application in Form 12-AA shall be accompanied by a fee of one hundred rupees for a single drug and an additional fee of fifty rupees for each additional drug.

(4) The fees shall be paid through a challan in the Bank of Baroda, Kasturba Gandhi Marg, New Delhi-110001 or any other branch or branches of Bank of Baroda, or any other Bank, as notified, from time to time, by the Central Government, to be credited under the Head of Account 0210- Medical and Public Health, 04- Public Health, 104- Fees and Fine.]

35. *Cancellation of licence for examination, test or analysis.(1)* A licence for examination, test or analysis may be cancelled by the licensing authority for breach of any of the conditions subject to which the licence was issued.

(2) A licensee whose licence has been cancelled may appeal to the Central Government within three months of the date of the order.

1. Subs. by G.S.R 604 (E), dt. 24-8-2001.

2. Ins. by G.S.R 604 (E), dt. 24-8-2001.

1[**35A.** *Cancellation of licence for import of small quantities of new drugs.(1)* A licence for import of small quantities of a new drug, defined in Rule122E, for the purpose of the treatment of patients suffering from life threatening diseases, or diseases causing serious permanent disability, or such diseases requiring therapies for unmet medical needs, by a Government Hospital or an Autonomous Medical Institution may be cancelled by the licensing authority for breach of any of the conditions subject to which the licence was issued or for contravention of any of the provisions of the Act and rules made thereunder.

(2) A licensee whose licence has been cancelled may appeal to the Central Government within three months from the date of the receipt of the order, and the Central Government may after such enquiry into the matter, as it considers necessary and after giving the appellant an opportunity for representing his views, may pass such orders in relation thereto, as it thinks fit.]

36. *Import of drugs for personal use*.-Small quantities of drugs, the import of which is otherwise prohibited under section 10 of the Act, may be imported for personal use subject to the following conditions:

(i) the drugs shall form part of a passenger's *bona fide* baggage and shall be the property of, and be intended for, the exclusive personal use of the passenger;

(ii) the drugs shall be declared to the Customs authorities if they so direct;

(iii) the quantity of any single drug so imported shall not exceed one hundred average doses :

Provided that the licensing authority may in an exceptional case in any individual case sanction the import of a larger quantity:

2[Provided further that any drug, imported for personal use but not forming part of *bona fide* personal baggage, may be allowed to be imported subject to the following conditions, namely:

(i) the licensing authority, on an application made to it in

Form 12A is satisfied that the drug is for *bona fide* personal use;

(ii) the quantity to be imported is reasonable in the opinion of the licensing authority and is covered by prescription from a registered medical practitioner ; and

(iii) the licensing authority grants a permit in respect of the said drug in

Form 12B.]

[3][**37.** *Packing of patent or proprietary medicine.* —Patent or proprietary medicines shall be imported in containers intended for retail sale:

[4][Provided that such medicines may be imported in bulk containers by any person who holds a licence to manufacture, if such person has obtained permission in writing to import such medicines from the licensing authority at least three months prior to the date of import and the imports are made within a period of twelve months from the date of issue of such permission].]

38. *Statement to accompany imported drugs.*All consignments of drugs sought to be imported shall be accompanied by an invoice or other statement showing the name and address of the manufacturer and the name and quantities of the drugs.

39. *Documents to be supplied to the Customs Collector.*Before drugs for the import of which a licence is not required are imported a declaration signed by or on behalf of the manufacturer or by or on behalf of the importer that the drugs comply with the provisions of Chapter III of the Drugs and Cosmetics Act, 1940 and the Rules thereunder shall be supplied to the Customs Collector.

1. Ins. by G.S.R 604 (E), dt. 24-8-2001.

2. Ins. by Notfn. No.F-1-36/54-D.S., (SRO 560), dt. 3-3-1955. 3. Ins. by Notfn. No.F-1-3/51-D.S., (SRO 3262), dt. 15-10-1954. 4. Ins. by Notfn. No.F-1-45/58-D, (SO 115), dt. 4-1-1961.

[1][**40.** *Procedure for the import of drugs.*—*(1)* If the Customs Collector has reason to doubt whether any drugs comply with the provisions of Chapter III of the Act and Rules thereunder he may, and if requested by an officer appointed for this purpose by the Central Government shall, take samples of any drugs in the consignment and forward them to the Director of the laboratory appointed for this purpose by the Central Government and may detain the drugs in the consignment of which samples have been taken until the report of the Director of the said laboratory or any other officer empowered by him on this behalf, subject to the approval of the Central Government, on such samples is received:

Provided that if the importer gives an undertaking in writing not to dispose of the drugs without the consent of the Customs Collector and to return the consignment or such portion thereof as may be required, the Customs Collector shall make over the consignment to the importer.

(2) If an importer who has given an undertaking under the proviso to sub-rule *(1)* is required by the Customs Collector to return the consignment or any portion thereof he shall return the consignment or portion thereof within ten days of receipt of the notice.]

[2][**41.** *(1)* If the Director of the laboratory appointed for the purpose by the Central Government or any other officer empowered by him on this behalf, subject to the approval of the Central Government, reports to the Customs Collector that the samples of any drug in a consignment are not of standard quality, or that the drug contravenes in any other respect the provisions of Chapter III of the Act or the Rules thereunder and that the contravention is such that it cannot be remedied by the importer, the Customs Collector shall communicate the report forthwith to the importer who shall, within two months of his receiving the communication either export all the drugs of that description in the consignment, to the country in which they were manufactured or forfeit them to the Central Government which shall cause them to be destroyed :

Provided that the importer may within fifteen days of receipt of the report make a representation against the report to the Customs Collector, and the Customs Collector shall forward the representation with a further sample to the licensing authority, who after obtaining, if necessary, the report of the Director of the Central Drugs Laboratory, shall pass orders thereon which shall be final.

[3][*(2)* If the Director of the laboratory appointed for the purpose by the Central Government or any other officer empowered by him on this behalf, subject to the approval

of the Central Government reports to the Customs Collector that the samples of any drug contravene in any respect the provisions of Chapter III of the Act or the Rules thereunder and that the contravention is such that it can be remedied by the importer, the Customs Collector shall communicate the report forthwith to the importer and permit him to import the drug on his giving an undertaking in writing not to dispose of the drug without the permission of the officer authorised in this behalf by the Central Government.]]

4[* * * * *]

1. Subs. by Notifn. 1-99/52-D.S., dated 3-11-1953.

2. Subs. by Notfn. No. F. 7-7/47-D, dt. 5-1-1954.

3. Ins. by Notfn. No. 7-11/47-D, dt. 5-10-1951.

4. Rule 42 omitted by Notfn. No. F. 1-9/52-DS., dt. 3-11-1953.

43. The drugs specified in Schedule D shall be exempt from the provisions of Chapter III of the Act and of the Rules made thereunder to the extent, and subject to the conditions specified in that Schedule.

1[**43A**. No drug shall be imported into India except through one of the following places, namely:

Freozepore Cantonment and Amritsar Railway Stations:

In respect of drugs imported by rail across the frontier with Pakistan.

Ranaghat, Bongaon and Mohiassan Railways Stations:

In respect of drugs imported by rail across the frontier with Bangladesh.

5[Petrapole Road in West Bengal, Sutarkandi in Assam, Old Raghna Bazar and Agartala in Tripura :

In respect of drugs imported by Road from Bangladesh;]

2[Raxaul:
In respect of drugs imported by road and railway lines connecting Raxaul in India and Birganj in Nepal;]

4[Chennai, Kolkata, Mumbai, Cochin, Nhava Sheva, Kandla and Inland Container Depots at Tuglakabad and Patparganj in Delhi and Tuticorin in Tamil Nadu and Marmugao port in Goa and Visakhapatnam in Andhra Pradesh:
In respect of drugs imported by sea into India;

Chennai, Kolkata, Mumbai, Delhi,Ahmedabad, Hyderabad, Goa, Bengaluru and Visakhapatnam:
in respect of drugs imported by air into India.]

4[**43-B**. Drugs, consignments of which are in transit through India to foreign countries and which shall not be sold or distributed in India shall be exempted from the requirements of Chapter III of the Drugs and Cosmetics Act, 1940 (23 of 1940) and the Rules made thereunder:

Provided that if the Government of the countries to which the drugs are consigned regulate their import by the grant of import licences, the importer shall at the time of import into India, produce such import licences.]

1. Subs. by G.S.R 478 (E), dt. 6-8-1981. Earlier Ins. by Notfn No. F.7/7/47-D. dt. 5-1-1954.

2. Ins. by G.S.R 120 (E), dt. 5-3-1998.

3. Sub. by G.S.R 532 (E), dt. 18-05-2016. Earlier sub. by G.S.R 575 (E), dt. 17-11-2012, G.S.R 101 (E), dt. 18-2-2011, G.S.R 45 (E), dt. 21-1-2010, G.S.R 504 (E), dt. 18-7-2002, G.S.R 647 (E), dt. 28-10-1998.

4. Added by Notfn. No. E. 1-60/D, (SO 1056) dt. 19-3-1964.

5. Ins. by G.S.R. 116 (E), 24-01-2009.

PART V

1[GOVERNMENT ANALYSTS, INSPECTORS, LICENSING AUTHORITIES AND CONTROLLING AUTHORITIES]

[2][**44. *Qualifications of Government Analyst*.** A person appointed as a Government Analyst under the Act shall be a person who

(a) is a graduate in medicine or science or pharmacy or Pharmaceutical Chemistry of a [3][University established in India by law or has an equivalent qualification recognized and notified by the Central Government for such purpose] and has had not less than five years' post-graduate experience in the testing of drugs in a laboratory under control of *(i)* a Government Analyst appointed under the Act, or *(ii)* the head of an Institution or testing laboratory approved for the purpose by the appointing authority, [4][or has completed two years' training on testing of drugs, including items stated in Schedule C, in Central Drugs Laboratory], or

(b) possesses a post-graduate degree in medicine or science or pharmacy or Pharmaceutical chemistry of a [3][University established in India by law or has an equivalent qualification recognized and notified by the Central Government for such purpose] or possesses the Associateship Diploma of the Institution of Chemists (India) obtained by passing the said examination with ‗Analysis of Drugs and Pharmaceuticals' as one of the subjects and has had after obtaining the said post-graduate degree or diploma not less than three years' experience in the testing of drugs in a laboratory under the control of *(i)* a Government Analyst appointed under the Act, or *(ii)* the head of an Institution or testing laboratory approved for the purpose by the appointing authority [4][or has completed training on testing of drugs, including items stated in Schedule C, in Central Drugs Laboratory]:

Provided that-

[4][*(i)* for purpose of examination of items in Schedule C,-

(ia) the persons appointed under clause *(a)* or *(b)* and having degree in Medicine, Physiology, Pharmacology, Microbiology, Pharmacy should have experience or training in testing of said items in an institution or laboratory approved by the appointing authority for a period of not less than six months;

(ib) the person appointed under clause*(a)* or *(b)* but not having degree in the above subjects should have experience or training in testing of said Schedule C drugs for a period of not less than three years in an institution or laboratory approved by the appointing authority or have completed two years training on testing of drugs including items stated in Schedule C in Central Drugs Laboratory;]

1. Subs. by G.S.R 443 (E), dt. 12-4-1989.
2. Subs. by G.S.R. No. 1427, dt. 22-10-1977.
3. Subs. by G.S.R. 71(E), dt 30.1.1987.
4. Ins. by G.S.R 697(E) dt. 26-10-1995.

(ii) for a period of four years from the date on which Chapter IV of the Act takes effect in the States, persons whose training and experience are regarded by the appointing authority as affording, subject to such further training, if any, as may be considered necessary, a reasonable guarantee of adequate knowledge and competence, may be appointed as Government Analysts. The persons so appointed may, if the appointing authority so desires, continue in service after the expiry of the said period of four years;

(iii) no person who is engaged directly or indirectly in any trade or business connected with the manufacture of drugs shall be appointed as a Government Analyst for any area:

Provided further that for the purpose of examination of Anti-sera, Toxoid and Vaccines and Diagnostic Antigens for Veterinary use, the person appointed shall be a person who is a graduate in Veterinary Science, or general science, or medicine or pharmacy and has had

not less than five years‘ experience in the standardization of biological products or person holding a post-graduate degree in Veterinary Science, or general science, or medicine or pharmacy or pharmaceutical chemistry with an experience of not less than three years in the standardization of biological products :

Provided also that persons, already appointed as Government Analysts may continue to remain in service, if the appointing authority so desires, notwithstanding the fact that they do not fulfil the qualifications as laid down in clause *(a),* clause *(b)* or the preceding proviso.

45. *Duties of Government Analysts*.–*(1)*The Government Analyst shall cause to be analysed or tested such samples or drugs [1][and cosmetics] as may be sent to him by Inspectors or other persons under the provisions of Chapter IV of the Act and shall furnish reports of the results of test or analysis in accordance with these Rules.

(2) A Government Analyst shall from time to time forward to the Government reports giving the result of analytical work and research with a view to their publication at the discretion of Government.

46. *Procedure on receipt of sample*.–On receipt of a package from an Inspector containing a sample for test or analysis, the Government Analyst shall compare the seals on the packet [2][or on portion of sample or container] with the specimen impression received separately and shall note the condition of the seals on the [3][packet or on portion of sample or container]. After the test or analysis has been completed, he shall forthwith supply to the Inspector a report in triplicate in

Form 13 of the result of the test or analysis, together with full protocols of the tests or analysis applied:

1. Ins. by S.O. 2139 dt. 5-6-1972.
2. Ins. by G.S.R. 59(E), dt. 7-2-1995.
3. Subs.by G.S.R. 59(E),dt. 7-2-1995.

[1][*Explanation*.-It shall be deemed to be full and sufficient compliance with the requirement of the rule in respect of the supply of ―protocols of the tests or analysis applied‖, if

(*1*) for pharmacopoeial drug, where the tests or methods of analysis prescribed in the official pharmacopoeia are followed, references to the specific tests or analysis in the pharmacopoeias are given in the report;

(2) for patent or proprietary medicines for which the tests and methods prescribed in any of the official pharmacopoeias are applicable and are followed, references to the specific tests or analysis in the pharmacopoeias are given in the report;

*(3)*for patent or proprietary medicines containing pharmacopoeial drugs for which the official tests or analysis or methods of assays are modified and applied, a description of the actual tests or, as the case may be, analysis or methods of assays so applied is given in the report;

(4) for patent or proprietary medicines for which no pharmacopoeial tests or methods of analysis are available or can be applied but for which tests or methods of analysis given in standard books or journals are followed, a description of such tests or methods of analysis applied together with the reference to the relevant books or journals from which the tests or methods of analysis have been adopted, is given in the report;

(5) for those drugs for which methods of test are not available and have been evolved by the Government Analyst, a description of tests applied is given in the report.]

47. *Report of result of test or analysis*. An application from a purchaser for test or analysis of a drug under section 26 of the Act shall be made in

Form 14 A and the report of test or analysis of the drug made on such application shall be supplied to the applicant in Form 14B.

48. *Fees*. The fees to be paid by a person submitting to the Government Analyst under section 26 of the Act for test or analysis of a drug [3][or cosmetic] purchased by him shall be those specified in Schedule B.

[2][**49.** *Qualifications of Inspectors*. —A person who is appointed an Inspector under the Act shall be a person who has a degree in Pharmacy or Pharmaceutical Sciences or Medicine with specialisation in Clinical Pharmacology or Microbiology from a University established in India by law:

Provided that only those Inspectors: —

1. Ins. by No. F. 1-60/61-D, dt. 12-7-1962 (G.S.R 984 (E), dt. 12-7-1962).

2. Subs. by No. G.S.R 658 (E), dt. 19-10-1993.

3. Ins. by No. G.S.R 1140 (E), dt. 26-8-1978.

(i) Who have not less than 18 months' experience in the manufacture of at least one of the substances specified in Schedule C, or

(ii) Who have not less than 18 months' experience in testing of at least one of the substances in Schedule C in a laboratory approved for this purpose by the licensing authority, or

(iii) Who have gained experiences of not less than three years in the inspection of firms manufacturing any of the substances specified in Schedule C during the tenure of their services as Drugs Inspectors;

shall be authorised to inspect the manufacture of the substances mentioned in Schedule C:]

[1][Provided further that the requirement as to the academic qualification shall not apply to persons appointed as Inspectors on or before the 18th day of October, 1993.]

[2][**49A.** *Qualification of a Licensing Authority*.—No person shall be qualified to be a Licensing Authority under the Act unless:-

(i) he is a graduate in Pharmacy or Pharmaceutical Chemistry or in Medicine with specialization in clinical pharmacology or microbiology from a University established in India by law; and

(ii) he has experience in the manufacture or testing of drugs or enforcement of the provisions of the Act for a minimum period of five years:

[3][Provided that the requirements as to the academic qualification shall not apply to those inspectors and the Government Analysts who were holding those positions on the 12th day of April,1989.]]

[4][**50.** *Controlling authority.–(1)* All Inspectors appointed by the Central Government shall be under the control of an officer appointed in this behalf by the Central Government.

(2) All Inspectors appointed by the State Government shall be under the control of an officer appointed in this behalf by the State Government.

(3) For the purposes of these rules an officer appointed by the Central Government under sub-rule (1), or as the case may be, an officer appointed by the State Government under sub-rule (2), shall be a controlling authority.]

1. Ins. by G.S.R 552 (E), dt. 4-12-1996.

2. Ins. by G.S.R 443 (E), dt. 12-4-1989.

3. Subs. by G.S.R. 532 (E), dt. 14.8.1991.

4. Subs. by S.O. 2139, dt. 5-6-1972.

[1][**50A.** Qualification *of a Controlling Authority*. *(1)* No person shall be qualified to be a Controlling Authority under the Act unless

(i) he is a graduate in Pharmacy or Pharmaceutical Chemistry or in Medicine with specialization in Clinical Pharmacology or Microbiology from a University established in India by law; and

(ii) he has experience in the manufacture or testing of drugs or enforcement of the provisions of the Act for a minimum period of five years:

2[Provided that the requirements as to the academic qualifications shall not apply to those Inspectors and the Government Analysts who were holding those positions on the 12th day of April, 1989.]

51. *Duties of Inspectors of premises licensed for sale*. Subject to the instructions of the controlling authority, it shall be duty of an Inspector authorized to inspect premises licensed for the sale of drugs

(1) to inspect 3[not less than once a year] all establishments licensed for the sale of drugs within the area assigned to him;

(2) to satisfy himself that the conditions of the licences are being observed;

(3) to procure and send for test or analysis, if necessary, imported packages which he has reason to suspect contain drugs being sold or stocked or exhibited for sale in contravention of the provisions of the Act or Rules thereunder;

(4) to investigate any complaint in writing which may be made to him;

(5) to institute prosecutions in respect of breaches of the Act and Rules thereunder;

(6) to maintain a record of all inspections made and action taken by him in the performance of his duties, including the taking of samples and the seizure of stocks, and to submit copies of such record to the controlling authority;

(7) to make such enquiries and inspections as may be necessary to detect the sale of drugs in contravention of the Act;

1. Ins. by G.S.R 443 (E), dt. 12-04-1989.
2. Subs. by G.S.R 532 (E), dt. 14-8-1991.
3. Subs. by G.S.R. 700 (E), dt. 28-9-2001.

(8) when so authorized by the State Government, to detain imported packages which he has reason to suspect contain drugs, the import of which is prohibited.

52. *Duties of Inspectors specially authorized to inspect the manufacture of* 1[*drugs or cosmetics*].-Subject to the instructions of the controlling authority it shall be the duty of an Inspector authorized to inspect the manufacture of drugs

(*1*) to inspect 2[not less than once a year], all premises licensed for manufacture of 1[drugs or cosmetics] within the area allotted to him to satisfy himself that the conditions of the licence and provisions of the Act and Rules thereunder are being observed;

(*2*) in the case of establishments licensed to manufacture products specified in Schedules C and C(1) to inspect the plant and the process of manufacture, the means employed for standardizing and testing the 2[drugs or cosmetics], the methods and place of storage, the technical qualifications of the staff employed and all details of location, construction and administration of the establishment likely to affect the potency or purity of the product;

(*3*) to send forthwith to the controlling authority after each inspection a detailed report indicating the conditions of the licence and provisions of the Act and rules thereunder which are being observed and the conditions and provisions, if any, which are not being observed;

(*4*) to take samples of the 1[drugs or cosmetics] manufactured on the premises and send them for test or analysis in accordance with these Rules;

(*5*) to institute prosecutions in respect of breaches of the Act and Rules thereunder.

53. *Prohibition of disclosure of information*. Except for the purposes of official business or when required by a Court of Law, an Inspector shall not, without the sanction in writing of his official superior, disclose to any person any information acquired by him in the course of his official duties.

54. *Form of order* not *to dispose of stock*. An order in writing by an Inspector under clause *(c)* of section 22 of the Act requiring a person not to dispose of any stock in his possession shall be in

Form 15.

1. Subs. by G.S.R 504 (E), dt. 18-7-2002.

2. Subs. by G.S.R 700 (E), dt. 28-9-2001.

[1][**54A**. *Prohibition of sale*.-No person in possession of a drug [2][or cosmetic] in respect of which an Inspector has made an order under clause *(c)* of sub-section *(1)* of section 22 of the Act shall in contravention of that order sell or otherwise dispose of any stock of such drug [2][or cosmetic].

[3][**55.** *Forms of receipts for seized drug, cosmetic, record register, document or any other material object*.-- A receipt by an Inspector for the stock of any drug or cosmetic or for any record, register, document or any other material object seized by him under clause *(c)* or clause *(cc)* of sub-section *(1)* of section 22 of the Act shall be in

Form 16.]

[4][**55A.** *Manner of certifying copies of seized documents.*—The Drugs Inspector shall return the documents , seized by him under clause *(cc)* or produced before him under clause *(cca),* of sub-section *(1)* of section 22 of the Act, within a period of twenty days of the date of such seizure or production, to the person from whom they have seized or, as the case may be, the person who produced them, after copies thereof of extracts therefrom have been signed by the concerned Drug Inspector and the person from whom they have seized , or, as the case may be , who produced such records.]

56. *Form of intimation of purpose of taking samples*.-When an Inspector takes a sample of a drug for the purpose of test or analysis, he shall intimate such purpose in writing in

Form 17 to the person from whom he takes it.

[5][**56A.** *Form or receipt for samples of drugs where fair price tendered is refused.*— Where the fair price, for the samples of drugs taken for the purpose of test or analysis, tendered under sub-section *(1)* of section 23 has been refused, the Inspector shall tender a receipt therefor to the person from whom the said samples have been taken as specified in

Form 17A.]

57. *Procedure for despatch of sample to Government Analyst.(1)* The portion of sample or the container sent by an Inspector to the Government Analyst for test or analysis under sub-section *(4)* of section 23 of the Act shall be sent by registered post or by hand in a sealed packet, enclosed together with a memorandum in

Form 18, in an outer cover addressed to the Government Analyst.

(2) A copy of the memorandum and a specimen impression of the seal used to seal the packet shall be sent to the Government Analyst separately by registered post or by hand.

1. Ins. by No. F. 1-19/59-D, dt. 13-6-1961.
2. Ins. by G.S.R 850(E), dt. 07-12-1994.
3. Subs. by G.S.R. No. 926 dt. 16-7-1977.
4. Ins. by G.S.R 89 (E), dt. 16-2-1985.
5. Ins. by G.S.R 292 (E), dt. 29-5-1997.

1[**58.** *Confiscation of drugs, implements, machinery etc*. (*1*) Where any person has been convicted for contravening any of the provisions of Chapter IV of the Act or any Rule made thereunder, the stock of the drug in respect of which the contravention has been made shall be liable to confiscation.

(*2*) Where any person has been convicted for the manufacture of any drug deemed to be misbranded under clause *(a),* clause *(b),* clause *(c),* clause *(d),* clause *(f)* or clause *(g)* of section 17 of the Act, or adulterated drug under section 17B of the Act, or for manufacture for sale, or stocking or exhibiting for sale or distribution of any drug without a valid licence as required under clause *(c)* of section 18 of the Act, any implements or machinery used in such manufacture, sale or distribution and any receptacle, packages, or coverings in which such drug is contained and the animals, vehicles, vessels or other conveyances used in carrying such drug shall also be liable to confiscation.]

2[**58A.** *Procedure for disposal of confiscated drugs. (1)* The Court shall refer the confiscated drugs to the Inspector concerned for report as to whether they are of standard quality or contravene the provisions of the Act or the Rules in any respect.

(2) If the Inspector, on the basis of Government Analyst‘s report finds the confiscated drugs to be not of standard quality or to contravene any of the provisions of the Act or the Rules made thereunder, he shall report to the Court accordingly. The Court shall thereupon order the destruction of the drugs. The destruction shall take place under the supervision of the Inspector in the presence of such authority, if any, as may be specified by the Court.

(3) If the Inspector finds that the confiscated drugs are of standard quality and do not contravene the provisions of the Act or the Rules made thereunder, he shall report to the Court accordingly. 3[The Court may then order the Inspector to give the stocks of confiscated drugs to hospital or dispensary maintained or supported by the Government or by Charitable Institutions].]

1. Subs. by S. O. 289, dt. 3-2-1973.
2. Ins. by No. F. 1-9/62-D (GSR 6), dt. 2-12-1964.
3. Subs. by G.S.R 59 (E), dt. 7-2-1995.

PART VI

SALE OF DRUGS OTHER THAN HOMOEOPATHIC MEDICINES

59. *(1)* The State Government shall appoint Licensing Authorities for the purpose of this Part for such areas as may be specified.

[1][*(2)* Applications for the grant or renewal of a licence [2][to sell, stock, exhibit or offer for sale or distribute] drugs, other than those included in Schedule X, [3][shall be made in

Form 19 accompanied by a fee of rupees one thousand and five hundred or Form 19A accompanied by a fee of rupees five hundred, as the case may be, or in the case of drugs included in Schedule X shall be made in Form 19C accompanied by a fee of rupees five hundred, to the licensing authority:]

Provided that in the case of an itinerant vendor or an applicant who desires to establish a shop in a village or town having population of 5,000 or less, the application in

Form 19-A shall be accompanied by a fee of rupees ten .

(3) [3][A fee of rupees one hundred and fifty] shall be paid for a duplicate copy of a licence [2][to sell, stock, exhibit or offer for sale or distribute] drugs, other than those included in Schedule X, or for a licence [2][to sell, stock, exhibit or offer for sale or distribute] drugs, included in Schedule X, if the original is defaced, damaged or lost:

Provided that in the case of itinerant vendor or an applicant who desires to establish a shop in a village or town having a population of 5,000 or less, the fee for a duplicate copy of a licence if the original is defaced, damaged or lost, shall be rupees two.

(4) Application for renewal of a licence [2][to sell, stock, exhibit or offer for sale or distribute] drugs, after its expiry but within six months of such expiry [3][shall be accompanied by a fee of rupees one thousand and five hundred plus an additional fee at the rate of rupees five hundred per month or part thereof in

Form 19, rupees five hundred plus an additional fee at the rate of rupees two hundred and fifty per month or part thereof in Form 19-A and rupees five hundred plus an additional fee at the rate of rupees two hundred and fifty per month or part thereof in Form 19C:]

Provided that in the case of an itinerant vendor or an applicant desiring to open a shop in a village or town having a population of 5,000 or less the application for such renewal shall be accompanied by a fee of rupees ten, plus an additional fee at the rate of rupees eight per month or part thereof.]

1. Subs. by G.S.R 462 (E), dt. 22-6-1982.
2. Subs. by G.S.R 788 (E), dt. 10-10-1985.
3. Subs. by G.S.R 601 (E), dt. 24-08-2001.

[1][**60.** A licensing authority may with the approval of the State Government by an order in writing delegate the power to sign licences and such other powers as may be specified in the order to any other person under his control.]

[2][**61.** *Forms of licences to sell drugs*. *(1)* a licence [3][to sell, stock, exhibit or offer for sale or distribute] drugs other than those specified in Schedules C, C (1) and X and by retail on restricted licence or by wholesale, shall be issued in

Form 20, Form 20A or Form 20B, as the case may be:

Provided that a licence in Form 20A shall be valid for only such drugs as are specified in the licence.

(2) A licence [3][to sell, stock, exhibit or offer for sale or distribute] drugs specified in Schedule C and C (1) excluding those specified in Schedule X, by retail on restricted licence or by wholesale shall be issued in

Form 21, Form 21A or Form 21B, as the case may be:

4[Provided that a licence in Form 21A shall not be granted for drugs specified in Schedules C and shall be valid for only such Schedule C (1) drugs as are specified in the licence.]

*(3)*A licence [3][to sell, stock, exhibit or offer for sale or distribute] drugs specified in Schedule X by retail or by wholesale shall be issued in

Form 20F or Form 20G as the case may be.]

62. *Sale at more than one* place. If drugs are sold or stocked for sale at more than one place, separate application shall be made, and a separate licence shall be issued, in respect of each such place:

5[Provided that this shall not apply to itinerant vendors who have no specified place of business and who will be licensed to conduct business in a particular area within the jurisdiction of the licensing authority.]

1. Amended by F. 1-16/57-D, dt. 15-6-1957.
2. Subs. by G.S.R 462 (E), dt. 22-6-1982.
3. Subs. by G.S.R 788 (E), dt. 10-10-1985.
4. Subs. by G.S.R 487 (E), dt. 2-7-1984.
5. Added by Notfn. No. F. 10-21/49-D, dt. 10-3-1953.

1[**62A.** *Restricted licences in Forms 20A and 21A*. *(a)* Restricted licences in Forms 20A and 21A shall be issued subject to the discretion of the Licensing Authority, to dealers or persons in respect of drugs whose sale does not require the supervision of a qualified person.

(b) Licences to itinerant vendors shall be issued only in exceptional circumstances for *bona fide* travelling agents of firms dealing in drugs or for a vendor who purchases drugs from a licensed dealer for distribution in sparsely populated rural areas where other channels of distribution of drugs are not available.

(c) The licensing authority may issue a licence in

Form 21A to a travelling agent of a firm but to no other class of itinerant vendors for the specific purpose of distribution to medical practitioners or dealers, samples of biological and other special products specified in Schedule C:

Provided that travelling agents of licensed manufacturers, agents, of such manufacturers and importers of drugs shall be exempted from taking out licence for the free distribution of samples of medicines among members of the medical profession, hospitals, dispensaries and the medical institution or research institutions.

1[**62-B**. *Conditions to be satisfied before a licence in Form 20A or Form 21A is granted*.

(1) A licence in Form 20A or Form 21A shall not be granted to any person, unless the authority empowered to grant the licence is satisfied that the premises in respect of which the licence is to be granted are adequate and equipped with proper storage accommodation for preserving the properties of drugs to which the licence applies:

Provided that this condition shall not apply in the case of licence granted to itinerant vendors.

(2) In granting a licence under Rule 62A the authority empowered to grant it shall have regard to:

(i) the number of licences granted in the locality during one year immediately preceding; and

(ii) the occupation, trade or business carried on by such applicant :

1. Ins. by Notfn. No. F. 1-9/60-D, dt. 3-7-1961.

Provided that the licensing authority may refuse to grant or renew a licence to any applicant or licensee in respect of whom it is satisfied that by reason of his conviction of an offence under the Act or these Rules or the previous cancellation or suspension of any licence granted thereunder, he is not a fit person to whom a licence should be granted under this rule.

(3) Any person who is aggrieved by the order passed by the licensing authority in sub-rule *(1)* may, within 30 days from the date of the receipt of such order appeal to the State Government and the State Government may, after such enquiry into the matter as it considers necessary and after giving the appellant an opportunity for representing his views in the matter make such order in relation thereto as it thinks fit.]

[1][**62C**. *Application for licence to sell drugs by wholesale or to distribute the same from a motor vehicle.(1)* Application for the grant or renewal of a licence to sell by wholesale or to distribute from a motor vehicle shall be made to the Licensing Authority in

Form 19AA and shall be accompanied by [2][a fee of rupees five hundred]:

Provided that if the applicant applies for the renewal of a licence after its expiry but within six months of such expiry , the fee payable for renewal of such licence shall be [2][rupees five hundred plus an additional fee at the rate of rupees two hundred and fifty per month or part thereof].

(2) A fee of [2][rupees one hundred and fifty] shall be paid for a duplicate copy of a licence issued under this rule, if the original is defaced, damaged or lost.]

[3][**62D.** *Form of licences to sell* drugs *by wholesale or distribute drugs from a motor vehicle*.-A licence shall be issued for sale by wholesale or for distribution from a motor vehicle of drugs other than those specified in Schedule and Schedule C(1) in

Form 20BB and of drugs specified in Schedule C and Schedule C(1) in Form 21BB :

Provided that such a licence shall not be required in a case where a public carrier or a hired vehicle is used for transportation or distribution of drug.]

3[**63.** *Duration of licence*. An original licence or a renewed licence to sell drugs, unless sooner suspended or cancelled, shall be 2[valid for a period of five years on and from the date on which] it is granted or renewed:

1. Ins. by Notfn. No. 1-9/60-D dt. 3-7-1961.
2. Subs. by Notfn. No. G.S.R 601 (E), dt. 24-8-2001.
3. Amended by Notfn. No. F. 1-10/62-D, dt. 10-4-1964.

1[Provided that if the application for renewal of licence in force is made before its expiry or if the application is made within six months of its expiry, after payment of additional fee, the licence shall continue to be in force until orders are passed on the application. The licence shall be deemed to have expired if application for its renewal is not made within six months after its expiry].]

[2][**63A**. *Certificate of renewal of a sale licence*.-The certificate of renewal of a sale licence in Forms 20, 20A, 20B,[3][20F, 20G], 21, 21A and 21B shall be issued in

Form 21C.]

4[**63B.** *Certificate of renewal of licence*.-A certificate of renewal of a licence in Form 20BB or Form 21BB shall be issued in Form 21CC.]

5[**64.** *Conditions to be satisfied before a licence in Form* 8[20, 20B, 20F,20G, 21 or 21B] *is granted* . *(1)*A licence in Form 3[20, 20B, 20F, 20G, 21 or 21B] 6[to sell, stock, exhibit or offer for sale or distribute] drugs shall not be granted 7[or renewed] to any person unless the authority empowered to grant the licence is satisfied that the premises in respect of which the licence is to be granted 7[or renewed] are adequate, equipped with proper storage accommodation for preserving the properties of the drugs to which the licence applies and are in charge of a person competent in the opinion of the licensing authority to supervise and control the sale, distribution and preservation of drugs :

Provided that in the case of a pharmacy a licence in

Form 20 or 21 shall not be granted [7][or renewed] unless the licensing authority is satisfied that the requirements prescribed for a pharmacy in Schedule N have been complied with:

[3][Provided further that licence in Form 20F shall be granted [7][or renewed] only to a pharmacy and in areas where a pharmacy is not operating, such licence may be [7][granted or renewed] to a chemist and druggist.]

Explanation.-For the purpose of this rule the term ‗Pharmacy' shall be held to mean to include every store or shop or other place : (1) where drugs are dispensed, that is, measured or weighed or made up and supplied ; or (2) where prescriptions are compounded; or (3) where drugs are prepared; or (4) which has upon it or displayed within it, or affixed to or used in connection with it, a sign bearing the word or words ―Pharmacy‖, ―Pharmacist‖, ―Dispensing Chemist‖ or ―Pharmaceutical Chemist‖; or (5) which, by sign, symbol or indication within or upon it gives the impression that the operations mentioned at (1), (2) and (3) are carried out in the premises; or (6) which is advertised in terms referred to in (4) above.

1. Amended by S. O. No. 2139, dt. 12-8-1972.
2. Ins. by Notfn. No. F. 1-10/62-D, dt. 10-4-1964.
3. Ins. by G.S.R 462 (E), dt. 22-6-1982.
4. Ins. by Notfn. No. F.1-10/62-D,dt. 10-4-1964.
5. Subs. by Notfn. No.F.1-16/57-D,dt. 15-6-1957 and No. F. 1-19/59-D, dt. 13-6-1961.
6. Subs. by G.S.R 788 (E), dt. 10-10-1985.
7. Subs. by No. G.S.R 681(E), dt. 6-6-1988.
8. Subs. by G.S.R 462 (E), dt. 22-6-1982.

(2) In granting [1][or renewing] a licence under sub-rule *(1)* the authority empowered to grant it shall have regard

[2][*(i)* to the average number of licences granted [1][or renewed] during the period of 3 years immediately preceding, and]

(ii) to the occupation, trade or business ordinarily carried on by such applicant during the period aforesaid:

Provided that the licensing authority may refuse to grant or renew a licence to any applicant or licensee in respect of whom it is satisfied that by reason of his conviction of an offence under the Act or these rules, or the previous cancellation or suspension of any licence granted [1][or renewed] thereunder, he is not a fit person to whom a licence should be granted [1][or renewed] under this rule. Every such order shall be communicated to the licensee as soon as possible:

[3][Provided further that in respect of an application for the grant of a licence in

Form 20B or Form 21B or both, the licensing authority shall satisfy himself that the premises in respect of which a wholesale licence is to be granted [1][or renewed] are:-

(i) of an area of not less than ten square meters; and]

[4][*(ii)* in the charge of a competent person, who—

(*a*) is a Registered Pharmacist, or

(*b*) has passed the matriculation examination or its equivalent examination from a recognised Board with four years' experience in dealing with sale of drugs, or

(*c*) holds a degree of a recognised University with one year's experience in dealing with drugs:]

[5][Provided also that,-

(i) in respect of an application for the grant of a licence in

Form 20 or Form 21 or both, the licensing authority shall satisfy itself that the premises are of an area] of not less than 10 square meters, and

(ii) in respect of an application for the grant of a licence

(A) In Form 20 or Form 21 or both, and

(B) In Form 20 B or Form 21B or both,

the licensing authority shall satisfy itself that the premises are of an area not less than 15 square meters:

1. Ins. by G.S.R 681(E), dt. 6.6.1988.
2. Subs. by Notfn. No. F. 1-19/59-D, dt. 13-6-1961.
3. Ins. by G.S.R 681(E), dt. 6.6.1980.
4. Substituted. G.S.R 351(E), dt. 26-4-2000.
5. Ins. by G.S.R 91(E), dt. 25-2-1997.

Provided also that the provisions of the preceding proviso shall not apply to the premises for which licences have been issued by the licensing authority before the commencement of the Drugs and Cosmetics (1st Amendment) Rules, 1997.]

[1][(3) Any person who is aggrieved by the order passed by the licensing authority in sub-Rule (1) may, within 30 days from the date of receipt of such order, appeal to the State Government and the State Government may, after such enquiry into the matter as it considers necessary and after giving the appellant an opportunity for representing his views in the matter, make such an order in relation thereto as it thinks fit.]

65. *Condition of licences.* Licences in [2][Forms 20, 20-A, 20-B, 20-F, 20-G, 21 and 21-B] shall be subject to the conditions stated therein and to the following general conditions

[2][*(1)* Any drug shall, if compounded or made on the licensee's premises be compounded or made by or under the direct and personal supervision of a [3][registered Pharmacist].]

(2) The supply, otherwise than by way of wholesale dealing, [4][* * *] of any drug supplied on the prescription of a Registered Medical Practitioner shall be effected only by or under the personal supervision of a [3][registered Pharmacist].

[5][*(3) (1)* The supply of any drug [6][other than those specified in Schedule X] on a prescription of a Registered Medical Practitioner shall be recorded at the time of supply in a prescription register specially maintained for the purpose and the serial number of the entry in the register shall be entered on the prescription. The following particulars shall be entered in the register:_

(a) serial number of the entry,

(b) the date of supply,

(c) the name and address of the prescriber,

[7][*(d)* the name and address of the patient, or the name and address of the owner of the animal if the drug supplied is for veterinary use,

(e) the name of the drug or preparation and the quantity or in the case of a medicine made up by the licensee, the ingredients and quantities thereof,

(f) in the case of a drug specified in [2][Schedule C or [8][Schedule H and Schedule H1]] the name of the manufacturer of the drug, its batch number and the date of expiry of potency, if any,

(g) the signature of the [3][registered Pharmacist] by or under whose supervision the medicine was made up or supplied:

1. Amended by F.1-9/60-D dt. 3-7-1961.
2. Subs. by G.S.R 462 (E), dt. 22-6-1982.

3. Subs. by G.S.R 676 (E), dt. 6-9-1994.
4. Omitted by No. G.S.R 462(E), dt. 22-6-1982.
5. Subs. by S. O. 2139, dt. 5-6-1972.
6. Ins. by G.S.R. 462(E), dt. 22-6-1982.
7. Subs. by G.S.R. 926 dt. 16-7-1977.
8. Subs. by G.S.R 588 (E), dt. 30-08-2013.

Provided that in the case of drugs which are not compounded in the premises and which are supplied from or in the original containers, the particulars specified in items *(a)* to *(g)* above may be entered in a cash or credit memo book, serially numbered and specially maintained for this purpose:

Provided further that if the medicine is supplied on a prescription on which the medicine has been supplied on a previous occasion and entries made in the prescription register, it shall be sufficient if the new entry in the register includes a serial number, the date of supply, the quantity supplied and a sufficient reference to an entry in the register recording the dispensing of the medicine on the previous occasion:

Provided also that it shall not be necessary to record the above details in the register or in the cash or credit memo particulars in respect of−

(i) any drugs supplied against prescription under the Employees State Insurance Scheme if all the above particulars are given in that prescription, and

(ii) any drug other than that specified in [1][Schedule C or [4][Schedule H and Schedule H1]] if it is supplied in the original unopened container of the manufacturer and if the prescription is duly stamped at the time of supply with the name of the supplier and the date on which the supply was made and on condition that the provisions of sub-rule *(4)(3)* of this rule are complied with.

[5][(h) the supply of a drug specified in Schedule H1 shall be recorded in a separate register at the time of the supply giving the name and address of the prescriber, the name of the patient, the name of the drug and the quantity supplied and such records shall be maintained for three years and be open for inspection.]

(2) The option to maintain a prescription register or a cash or credit memo book in respect of drugs and medicines which are supplied from or in the original container, shall be made in writing to the Licensing Authority at the time of application for the grant or renewal of the licence to sell by retail:

Provided that the Licensing Authority may require records to be maintained only in prescription register if it is satisfied that the entries in the carbon copy of the cash or credit memo book are not legible.]

[2][*(4) (1)* The supply by retail, otherwise than on a prescription of a drug specified in Schedule C [3][* * *] shall be recorded at the time of supply either−

1. Subs. by G.S.R 462 (E), dt. 22-6-1982.
2. Ins. by Notfn. No. 1-63/61-D, dt. 17-7-1963.
3. Omitted by G.S.R 462 (E), dt. 22-6-1982.
4. Subs. by G.S.R 588 (E), dt. 30-08-2013.
5. Ins. by G.S.R 588 (E), dt. 30-08-2013.

(i) in a register specially maintained for the purpose in which the following particulars shall be entered :

(a) serial number of the entry,

(b) the date of supply,

(c) the name and address of the purchaser,

(d) the name of the drug and the quantity thereof,

(*e*) in the case of a drug specified in Schedule C, the name of the manufacturer, the batch number and the date of expiry of potency,

(*f*) the signature of the person under whose supervision the sale was effected, or

(ii) in a cash or credit memo book, serially numbered containing all the particulars specified in items *(b)* to *(f)* of sub-clause *(i)* above.

NOTE:-The entries in the carbon copy of the cash or credit memo which is retained by the licensee shall be maintained in a legible manner.

(2) The option to maintain a register or a cash or credit memo book shall be made in writing to the Licensing Authority at the time of application for the grant or renewal of a licence to sell by retail:

Provided that the Licensing Authority may require records to be maintained in a register if it is satisfied that the entries in the carbon copy of the cash/credit memo book are not legible.

(3)(i) The supply by retail of any drug shall be made against a cash/credit memo which shall contain the following particulars :

(a) Name, address and sale licence number of the dealer,

1[*(b)* Serial number of the cash/credit memo,

(c) the name and quantity of the drug supplied.]

(ii) Carbon copies of cash/credit memos shall be maintained by the licensee as record.

1. Ins. by G. S. R. No. 245, dt. 21-2-1976.

1[*(4)(i)* Records of purchase of a drug intended for sale or sold by retail shall be maintained by the licensee and such records shall show the following particulars, namely:

(*a*) the date of purchase,

(*b*) the name and address of the person from whom purchased and the number of the relevant licence held by him,

(*c*) the name of the drug, the quantity and the batch number, and

(*d*) the name of the manufacturer of the drug.

(ii) Purchase bills including cash or credit memo shall be serially numbered by the licensee and maintained by him in a chronological order.]

2[*(5)(1)* Subject to the other provisions of these Rules the supply of a drug by wholesale shall be made against a cash or credit memo bearing the name and address of the licensee and his licence number under the Drugs and Cosmetics Act in which the following particulars shall be entered

(*a*) the date of sale,

(*b*) the name, address of the licensee to whom sold and his sale licence number. In case of sale to an authority purchasing on behalf of Government, or to a hospital, medical, educational or research institution or to a Registered Medical Practitioner for the purpose of supply to his patients the name and address of the authority, institution or the Registered Medical Practitioner as the case may be,

(*c*) the name of the drug, the quantity and the batch number,

(*d*) the name of the manufacturer,

3[*(e)* the signature of the competent person under whose supervision the sale was effected.]

(2) Carbon copies of cash or credit memos specified in clause (1) shall be preserved as records for a period of three years from the date of the sale of the drug.

1. Subs. by G.S.R 1242 (E), dt. 17-9-1979.

2. Amended by F. 1-63/62-D, dt. 17-7-1963.

3. Ins. by G.S.R 496 (E), dt. 9-6-1995.

1[*(3) (i)* Records of purchase of a drug intended for resale or sold by wholesale shall be maintained by the licensee and such records shall show the following particulars, namely:-

(*a*) the date of purchase,

(*b*) the name, address and the number of the relevant licence held by the person from whom purchased,

(*c*) the name of the drug, the quantity and the batch number, and

(*d*) the name of the manufacturer of the drug.

(ii) Purchase bills including cash or credit memos shall be serially numbered by the licensee and maintained by him in a chronological order.]

(6) The licensee shall produce for inspection by an Inspector appointed under the Act on demand all registers and records maintained under these Rules, and shall supply to the Inspector such information as he may require for the purpose of ascertaining whether the provisions of the Act and Rules thereunder have been observed.

(7) Except where otherwise provided in these Rules, all registers and records maintained under these Rules shall be preserved for a period of not less than two years from the date of the last entry therein.

(8) Notwithstanding anything contained in this Rule it shall not be necessary to record particulars in a register specially maintained for the purpose if the particulars are recorded in any other register specially maintained under any other law for the time being in force.

2[*(9) (a)* Substances specified in 3[Schedule H and Schedule H1] or Schedule X shall not be sold by retail except on and in accordance with the prescription of a Registered Medical Practitioner and in the case of substances specified in Schedule X, the prescriptions shall be in duplicate, one copy of which shall be retained by the licensee for a period of two years.

(b) The supply of drugs specified in 3[Schedule H and Schedule H1] or Schedule X to Registered Medical Practitioners, Hospitals, Dispensaries and Nursing Homes shall be made only against the signed order in writing which shall be preserved by the licensee for a period of two years.]

1. Subs. by G.S.R 1242(E), dt. 17-9-1979.

2. Subs. by G.S.R 462(E), dt. 22-6-1982.

3. Subs. by G.S.R 588(E), dt. 30-8-2013.

(10) For the purposes of clause *(9)* a prescription shall

(a) be in writing and be signed by the person giving it with his usual signature and be dated by him;

1[*(b)* specify the name and address of the person for whose treatment it is given, or the name and address of the owner of the animal if the drug is meant for veterinary use;]

(c) indicate the total amount of the medicine to be supplied and the dose to be taken.

(11) The person dispensing a prescription containing a drug specified in 5[Schedule H and Schedule H1] 2[and Schedule X] shall comply with the following requirements in addition to other requirement of these rules.

(a) the prescription must not be dispensed more than once unless the prescriber has stated thereon that it may be dispensed more than once;

(b) if the prescription contains a direction that it may be dispensed a stated number of times or at stated intervals it must not be dispensed otherwise than in accordance with the directions;

(c) at the time of dispensing there must be noted on the prescription above the signature of the prescriber the name and address of the seller and the date on which the prescription is dispensed.

[4][*(11-A)* No person dispensing a prescription containing substances specified in [3][[5][Schedule H and Schedule H1] or X], may supply any other preparation, whether containing the same substance or not, in lieu thereof.

[3][*(12)* Substances specified in Schedule X kept in retail shop or premises used in connection therewith shall be stored—

(*a*) under lock and key in cupboard or drawer reserved solely for the storage of these substances; or

(*b*) in a part of the premises separated from the remainder of the premises and to which only responsible persons have access;]

1. Subs. by G. S. R. No. 926, dt. 24-6-1977.
2. Ins. by G.S.R 462 (E), dt. 22-6-1982.
3. Subs., by G.S.R 462 (E), dt. 22-6-1982.
4. Ins. by SO 2139, dt. 5-6-1972.
5. Subs. by G.S.R 588(E), dt. 30-8-2013.

[1][* * * * *]

[2][*(15)(a)* The description ―Drugstore‖ shall be displayed by such licensees who do not require the services of a [3][Registered Pharmacist].

(b) The description ―Chemists and Druggists‖ shall be displayed by such licensees who employ the services of a [3][Registered Pharmacist] but who do not maintain a ―Pharmacy‖ for compounding against prescriptions.

(c) The description ―Pharmacy‖, ―Pharmacist‖, ―Dispensing Chemist‖ or ―Pharmaceutical Chemist‖ shall be displayed by such licensees who employ the services of a [3][Registered Pharmacist] and maintain a ―Pharmacy‖ for compounding against prescriptions:

[3][*Explanation:*- For the purpose of this rule,-

(i) ―Registered Pharmacist‖ means a person who is a registered Pharmacist as defined in clause *(i)* of section (2) of the Pharmacy Act, 1948 (Act No. 8 of 1948):

Provided that the provisions of sub-clause (i) shall not apply to those persons who are already approved as ―qualified person‖ by the licensing authority on or before 31st December, 1969:

(ii) ―Date of Expiry of potency‖ means the date that is recorded on the container, label or wrapper as the date up to which the substance may be expected to retain a potency not less than or not to acquire a toxicity greater than that required or permitted by the prescribed test].]

[4][*(16)* The licensee shall maintain an Inspection Book in

Form 35 to enable an Inspector to record his impressions and the defects noticed.]

1. Sub-Rules (13) and (14) omitted by G.S.R 462 (E), dt. 22-6-1982. 2.
Subs. by Notfn. No. F. 1-16/57-D, dt. 15-6-1957.
3. Subs. by G.S.R 676 (E), dt. 6-9-1994.
4. Subs. by Notfn. No. F. 1-14/68-D dt. 26-10-1968.

1[*(17)* No drug shall be sold or stocked by the licensee after the date of expiration of potency recorded on its container, label or wrapper, or in violation of any statement or direction recorded on such container, label or wrapper:

Provided that any such drugs in respect of which the licensee has taken steps with the manufacturer or his representative for the withdrawal, reimbursement or disposal of the same, may be stocked after the date of expiration of potency pending such withdrawal, reimbursement or disposal, as the case may be, subject to the condition that the same shall be stored separately from the trade stocks 2[and all such drugs shall be kept in packages or cartons, the top of which shall display prominently, the words ―Not for sale‖].]

3[*(18)* No drug intended for distribution to the medical profession as free sample which bears a label on the container as specified in clause 4[(ix)] of sub-rule (1) of rule 96, and no drug meant for consumption by the Employees' State Insurance Corporation, the Central Government Health Scheme, the Government Medical Stores Depots, the Armed Forces Medical Stores or other Government institutions, which bears a distinguishing mark or any inscription on the drug or on the label affixed to the container thereof indicating this purpose shall be sold or stocked by the licensee on his premises:]

5[Provided that this sub-rule shall not be applicable to licensees who have been appointed as approved chemists, by the State Government in writing, under the employees' State Insurance Scheme, or have been appointed as authorised agent or distributor, by the manufacturer in writing, for drugs meant for consumption under the Central Government Health Scheme, the Government Medical Stores Depots, the Armed Forces Medical Stores or other Government Institutions for drugs meant for consumption under those schemes 6[or have been appointed as authorised Depots or Carrying and Forwarding agent by the manufacturer in writing, for storing free samples meant for distribution to medical profession] subject to the conditions that the stock shall be stored separately from the trade stocks and shall maintain separate records of the stocks received and distributed by them.]

1. Ins. by Notfn. No. F. 1-55/61-D, dt. 22-8-1964.
2. Ins. by S. O. No. 903, dt. 28-2-1976.
3. Ins. by Notfn. No. 1-113/69-D, dt. 23-12-1969.
4. Subs. by G.S.R. 676(E) dt. 6-9-1994.
5. Subs. by G.S.R. 496(E) dt. 9-6-1995.
6. Ins. by G.S.R 352(E), dt. 26-4-2000.

1[*(19)* The supply by retail of any drug in a container other than the one in which the manufacturer has marketed the drug, shall be made only by dealers who employ the services of a 2[Registered Pharmacist] and such supply shall be made under the direct supervision of the 2[Registered Pharmacist] in an envelope or other suitable wrapper or container showing the following particulars on the label:

(a) name of the drug,

(b) the quantity supplied,

(c) the name and address of the dealer.]

3[*(20)* The medicines for treatment of animals kept in a retail shop or premises shall be labelled with the words ―Not for human use and shall be stored for treatment of animals only'

(a) in a cupboard or drawer reserved solely for the storage of veterinary drugs, or

(b) in a part of the premises separated from the remainder of the premises to which customers are not permitted to have access.]

4[*(21) (a)* The supply of drugs specified in Schedule X shall be recorded at the time of supply in a register (bound and serially page numbered) specially maintained for the purpose and separate pages shall be allotted for each drug.

(b) The following particulars shall be entered in the said register, namely:-- (*i)* Date of transaction;

(ii) Quantity received, if any, the name and address of the supplier and the number of the relevant licence held by the supplier;

(iii) Name of the drug;

(iv) Quantity supplied;

(v) Manufacturer‘s name;

(vi) Batch No. or Lot No;

(vii) Name and address of the patient/purchaser;

(viii) Reference Number of the prescription against which supplies were made;

(ix) Bill No and date in respect of purchases and supplies made by him; (x) Signature of the person under whose supervision the drugs have been supplied.]

1. Ins. by G. S. R. 444 dt. 28-4-1973.
2. Subs. by G.S.R 676 (E), dt. 6-9-1994.
3. Added by G. S. R. No. 926 dt. 16-7-1977.
4. Ins. by G.S.R 462 (E), dt. 22-6-1982.

1[**65A.** *Additional information to be furnished by an applicant for liscence or a licensee to the Licensing Authority.* The applicant for the grant of a licence or any person granted a licence under this Part shall, on demand, furnish to the licensing authority, before the grant of the licence or during the period the licence is in force, as the case may be, documentary evidence in respect of the ownership of occupation or rental or other basis of the premises, specified in the application for licence or in the licence granted, constitution of the firm, or any other relevant matter which may be required for the purpose of verifying the correctness of the statements made by the applicant or the licensee, while applying for or after obtaining the licence, as the case may be.]

66. *Cancellation and suspension of licences*. *(1)* The Licensing Authority may, after giving the licensee an opportunity to show cause why such an order should not be passed by an order in writing stating the reasons therefor, cancel a licence issued under this Part or suspend it for such period as he thinks fit, either wholly or in respect of some of the substances to which it relates, if in his opinion, the licensee has failed to comply with any of the conditions of the licence or with any provisions of the Act or Rules thereunder:

1[Provided that, where such failure or contravention is the consequence of an act or omission on the part of an agent or employee, the licence shall not be cancelled or suspended if the licensee proves to the satisfaction of the licensing authority−

(a) that the act or omission was not instigated or connived at by him or, if the licensee is a firm or company, by a partner of the firm or a director of the company, or

(*b*) that he or his agent or employee had not been guilty of any similar act or omission within twelve months before the date on which the act or omission in question took place, or where his agent or employee had been guilty of any such act or omission the licensee had not or could not reasonably have had, knowledge of that previous act or omission, or

(*c*) if the act or omission was a continuing act or omission, he had not or could not reasonably have had knowledge of that previous act or omission, or

(d) that he had used due diligence to ensure that the conditions of the licence or the provisions of the Act or the Rules thereunder were observed.]

[2][*(2)* A licensee whose licence has been suspended or cancelled may, within three months of the date of order under sub-rule *(1)*, prefer an appeal against that order to the State Government, which shall decide the same.]

[3][**66A.** *Procedure for disposal of drugs in the event of cancellation of licence.— (1)* In case a licensee, whose licence has been cancelled, desires to dispose of the drugs he has in his possession in the premises in respect of which the licence has been cancelled, he shall apply in writing to the licensing authority for this purpose, giving the following particulars, namely:—

1. Ins. by S. O. 2139, dt. 12-8-1972.
2. Subs. by G. S. R. 926 dt. 16-7-1977.
3. Ins. by G.S.R 1242 (E), dt. 17-9-1979.

(*a*) the name and address of the person to whom the drugs are proposed to be sold or supplied together with the number of the licence for sale or manufacture, as the case may be, held by him,

(*b*) the names of drugs together with their quantities, batch numbers, the names and addresses of their manufacturers and the dates of their expiry, if any, proposed to be sold to the person mentioned in clause *(a)*.

(2) The licensing authority may, after examination of the particulars referred to in sub-rule *(1)* and, if necessary, after inspection by an Inspector of the premises where the drugs are stocked, grant the necessary permission for their disposal.]

[6][****]

[1][PART VIA

SALE OF HOMOEOPATHIC MEDICINES

67A. *(1)* The State Government shall appoint Licensing Authorities for the purpose of this Part for such areas as may be specified.

(2) Application for the grant or renewal of a licence [2][to sell, stock or exhibit or offer for sale or distribute] Homoeopathic medicines shall be made in

Form 19-B to the Licensing Authority and shall be accompanied by a [3][fee of rupees two hundred and fifty]:

[4][Provided that if the applicant applies for renewal of licence after its expiry but within six months of such expiry the fee payable for renewal of such licence shall be [3][rupees two hundred and fifty plus an additional fee at the rate of rupees fifty or part thereof].

[5][(3) If the original licence is either defaced, damaged or lost, a duplicate copy thereof may be issued on payment of a [3][fee of rupees fifty].]

67B. A Licensing Authority may, with the approval of the State Government, by an order in writing, delegate the power to sign licences and such other powers, as may be specified, to any other person under his control.

67C. *Forms of licences to sell drugs.-(1)* A licence [2][to sell, stock or exhibit or offer for sale or distribute] Homoeopathic medicines by retail or by wholesale shall be issued in Form 20C or 20D as the case may be.

1. Added by Notfn. No. F. 1-35/64-D, dt. 18-8-1964.
2. Subs. by G.S.R 788(E) dt. 10-10-1985.
3. Subs. by G.S.R 601 (E), dt. 24-8-2001.
4. Amended by S. O. 2139 dt. 12-8-1972.
5. Added by G. S. R. 665, dt. 28-5-77.
6. Rule 67 omitted by SO 289 (E), dt. 20-12-1972.

67D. *Sale at more than one place*. If drugs are sold or stocked for sale at more than one place, a separate application shall be made and a separate licence shall be obtained in respect of each place.

67E. *Duration of licences*. An original licence or a renewed licence unless it is sooner suspended or cancelled shall be [1][valid for a period of five years on and from the date on which] it is granted or renewed :

[2][Provided that if the application for renewal of a licence in force is made before its expiry or if the application is made within six month of its expiry, after payment of additional fee, the licence shall continue to be in force until orders are passed on the application and the licence shall be deemed to have expired if application for its renewal is not made within six months after its expiry.]

[3][**67EE.** *Certificate of renewal*. The certificate of renewal of a sale licence in Forms 20C and 20D shall be issued in

Form 20E.]

67F. *Condition to be satisfied before a licence in Form 20C or Form 20D is granted.-* *(1)* A licence in Form 20C or Form 20D to [4][to sell, stock or exhibit or offer for sale or distribute] Homoeopathic medicines shall not be granted to any person unless the authority empowered to grant the licence is satisfied that the premises in respect of which the licence is to be granted are clean and in the case of a licence in Form 20C the sale premises is in charge of a person who is or has been dealing in Homoeopathic medicines and who is in the opinion of the Licensing Authority competent to deal in Homoeopathic medicines:

[5][Provided that no registered Homoeopathic medical practitioner who is practising Homoeopathy in the premises where Homoeopathic medicines are sold shall deal in Homoeopathic medicines.]

(2) Any person who is aggrieved by the order passed by the Licensing Authority under sub-rule *(1)* may within 30 days from the date of the receipt of such order appeal to the State Government and the State Government may, after such enquiry into the matter as it considers necessary and after giving the appellant an opportunity for representing his case, make such order in relation thereto as it thinks fit.

1. Subs. by G.S.R 601 (E), dt. 24-8-2001.
2. Subs. by S. O. 2139 dt. 5-6-1972.
3. Added by Notfn. No. F. 1-14/67-D, dt. the 3-2-1969.
4. Subs. by G.S.R 788 (E), dt. 10-10-1985.
5. Ins. by Notfn. No. G.S.R 680 (E), dt. 5-12-1980.

67G. *Conditions of licence*. Licence in Form 20C or 20D shall be subject to the conditions stated therein and to the following further conditions, namely:

(1) The premises where the Homoeopathic medicines are stocked for sale or sold are maintained in a clean condition.

(2) The sale of Homoeopathic medicines shall be conducted under the supervision of a person, competent to deal in Homoeopathic medicines.

(3) The licensee shall permit an Inspector to inspect the premises and furnish such information as he may require for ascertaining whether the provisions of the Act and the Rules made thereunder have been observed.

(4) The licensee in

Form 20D shall maintain records of purchase and sale of Homoeopathic medicines containing alcohol together with names and addresses of parties to whom sold.

[1][*(5)* The licensee in

Form 20C shall maintain records of purchase and sale of Homoeopathic medicines containing alcohol. No records of sale in respect of Homoeopathic potentised preparation in containers of 30 ml. or lower capacity and in respect of mother tinctures made up in quantities up to 60 ml.

need be maintained.]

[2][*(6)* The licensee shall maintain an Inspection Book in

Form 35 to enable an Inspector to record his impressions and the defects noticed.]

3[**67GG.** *Additional information to be furnished by an applicant for licence or a licensee to the Licensing Authority.* The applicant for the grant of a licence or any person granted a licence under this Part shall, on demand furnish to the Licensing Authority, before the grant of the licence or during the period the licence is in force as the case may be, documentary evidence in respect of the ownership or occupation or rental or other basis of the premises, specified in the application for licence or in the licence granted, constitution of the firm, or any other relevant matter, which may be required for the purpose of verifying the correctness of the statements made by the applicant or the licensee, while applying for or after obtaining the licence, as the case may be.]

1. Ins. by Notfn. No. F. 1-59/68-D, dt. the 19-11-1969.

2. Ins. by G.S.R 331 (E), dt. 8-5-1984.

3. Ins. by S. O. 2139 dt. 5-6-1972.

67-H. *Cancellation and suspension of licences.(1)* The Licensing Authority may, after giving the licensee an opportunity to show cause why such an order should not be passed by an order in writing stating the reasons therefor, cancel a licence issued under this Part or suspend it for such period as he thinks fit, if in his opinion, the licensee has failed to comply with any of the conditions of the licence or with any provisions of the Act or Rules made thereunder:

1[Provided that, where such failure or contravention is the consequence of an act or omission on the part of an agent or employee, the licence shall not be cancelled or suspended if the licensee proves to the satisfaction of the Licensing Authority–

(a) that the act or omission was not instigated or connived at by him or, if the licensee is a firm or company, by a partner of the firm or a director of the company, or

(b) that he or his agent or employee had not been guilty of any similar act or omission within twelve months before the date on which the act or omission in question took place, or where his agent or employee had been guilty of any such act or omission, the licensee had not or could not reasonably have had, knowledge of that previous act or omission, or

(c) if the act or omission was a continuing act or omission that he had not or could not reasonably have had knowledge of that previous act or omission, or

(d) that he had used due diligence to ensure that the conditions of the licence or the provisions of the Act or the Rules thereunder were observed.]

2[*(2)* A licensee whose licence has been suspended or cancelled may, within three months of the date of the order under sub-rule *(1)*, prefer an appeal against that order to the State Government, which shall decide the same.]

1. Ins. by S. O. 2139 dt. 5-6-1972.

2. Amended by G.S.R. 926 dt. 16-7-1977.

PART VII

1[MANUFACTURE FOR SALE OR FOR DISTRIBUTION] OF DRUGS OTHER THAN HOMOEOPATHIC MEDICINES

68. *Manufacture on more than one set of premises*. If drugs are manufactured on more than one set of premises a separate application shall be made and a separate licence shall be issued in respect of each such set of premises.

2[**68-A.** *Grant or Renewal of Licences by the Central Licence Approving Authority.—(1)* Notwithstanding anything contained in this Part, on and from the commencement of the Drugs and Cosmetics (Amendment) Rules,1992, a licence for the manufacture for sale or distribution of drugs as specified from time to time by the Central Government by

notification in the Official Gazette, for the purpose of this rule, shall be granted or renewed, as the case may be, by the Central Licence Approving Authority (appointed by the Central Government):]

Provided that the application for the grant or renewal of such licence shall be made to the Licensing Authority.

(2) On receipt of the application for grant or renewal of a licence, the licensing authority shall,-

(i) verify the statement made in the application form;

(ii) cause the manufacturing and testing establishment to be inspected in accordance with the provisions of rule 79; and

(iii) in case the application is for the renewal of licence, call for the information(s) of the past performance of the licensee.

(3) If the licensing authority is satisfied that the applicant is in a position to fulfil the requirements laid down as in these Rules, he shall prepare a report to that effect and forward it along with the application [3][and the licence (in triplicate) to be granted and renewed, duly completed] to the Central Licence Approving Authority:

Provided that if the licensing authority is of the opinion that the applicant is not in a position to fulfil the requirements laid down in these Rules, he may, by order, for reasons to be recorded in writing, refuse to grant or renew the licence, as the case may be.

(4) If on receipt of the application and the report of the licensing authority referred to in sub-rule *(3)* and after taking such measures including inspection of the premises by the Inspector, appointed by the Central Government under section 21 of the Act, with or without an expert in the concerned field if deemed necessary, the Central Licence Approving Authority, is satisfied that the applicant

1. Subs. by G.S.R 788 (E), dt. 10-10-1985.
2. Ins. by G.S.R 923 (E), dt. 14-12-1992.
3. Subs. by G.S.R 89 (E), dt. 14-2-1996.

is in a position to fulfil the requirements laid down in these Rules, he may grant or renew the licence, as the case may be:

Provided that if the Central Licence Approving Authority is of the opinion that the applicant is not in a position to fulfil the requirements laid down in these rules, he may, notwithstanding the report of the licensing authority, by order, for reasons to be recorded in writing, reject the application for grant or renewal of licence, as the case may be.]

[1][**68B.** *Delegation of Powers by the Central Licence Approving Authority.*—The Central Licence Approving Authority may with the approval of the Central Government, by notification delegate his powers of signing licences and any other powers under the rules to any person under his control having same qualifications as prescribed for controlling authority under Rule 50A for such areas and for such periods as may be specified.]

[2][**69.** *Application for licence to manufacture drugs other than those specified in Schedules C and C(I) to the Drugs and Cosmetics Rules*.—[3][*(1)* Application for grant or renewal of [4][licence to manufacture for sale or for distribution] of drugs, other than those specified in Schedules C and C(I)shall be made to the licensing authority appointed by the State Government for the purpose of this Part (hereinafter in this Part referred to as the licensing authority) and shall be made

(a) in the case of repacking of drugs excluding those specified in Schedule X for sale or distribution in,

Form 24B;

(b) in the case of manufacture of drugs included in Schedule X, in

Form 24F;

(c) in any other case, in Form 24.]

5[(2)*(a)* Every application in Form 24B shall be made up to ten items for each category of drugs categorised in Schedule M and shall be accompanied by a licence fee of rupees five hundred plus and an inspection fee of rupees two hundred for every inspection or for the purpose of renewal of the licence.

1. Ins. by G.S.R 89 (E), dt. 14-02-1996.

2. Amended by Notfn. F. 1-22/59-D, dt. 9-4-1960.

3. Subs. by G.S.R 462 (E), dt. 22-06-1982.

4 Subs. by G.S.R.788 (E), dt. 10-10-1985.

5. Subs. by G.S.R 601(E), dt. 21-8-2001.

(b) Every application in Form 24F shall be made up to ten items for each category of drugs categorised in Schedule M and shall be accompanied by a licence fee of rupees six thousand and an inspection fee of rupees one thousand and five hundred for every subsequent inspection or for the purpose of renewal of licence.

(c) Every application in Form 24 shall be made up to ten items for each category of drugs 3[referred to in Schedule M relating to pharmaceuticals products and Schedule MIII relating to medical devices and *in-vitro* diagnostics] and shall be accompanied by a licence fee of rupees six thousand and an inspection fee of one thousand and five hundred for every inspection or for the purpose of renewal of the licence.]

1[*(3)* If a person applies for the renewal of a licence after the expiry thereof but within six months of such expiry the fee payable for the renewal of such licence shall be–]

[2][*(i)* in the case of

Form 24B a licence fee of rupees five hundred plus an additional fee at the rate of rupees two hundred and fifty per month or part thereof in addition to an inspection fee of rupees two hundred;

(ii) in the case of

Form 24F a licence fee of rupees six thousand plus an additional fee at the rate of rupees one thousand per month or part thereof in addition to an inspection fee of rupees one thousand;

(iii) in the case of

Form 24 a licence fee of rupees six thousand plus an additional fee at the rate of rupees one thousand per month or part thereof in addition to an inspection fee of rupees one thousand and five hundred.]

[1][*(4)* A fee [2][rupees one thousand shall be paid] for a duplicate copy of the licence issued under clause *(a)*, clause *(b)* or clause *(c)* of sub-Rule *(1)* if the original is defaced, damaged or lost.]

[2][*(5)* Applications for manufacture of more than ten items of each category of drugs as categorized under Schedule M and M-III or for manufacture of additional items of drugs by licensees in

Form 24 or Form 24F shall be accompanied by an additional fee at the rate of rupees three hundred for each additional item of drug. Applications in Form 24B for licence to manufacture for sale and distribution for repacking for more than 10 items of each category or for manufacture of additional item of drug shall be accompanied by additional fee of rupees one hundred for each additional item of drugs as cetegorized in Schedule M and M-III].

1. Subs. by G.S.R 462 (E), dt. 22-6-1982.
2. Subs. by G.S.R 26 (E), dt. 19-1-2006.
3. Subs. by G.S.R 640 (E), dt. 29-6-2016.

[1][*(6)* Where an application under this Rule is for the manufacture of drug formulations falling under the purview of new drug as defined in rule 122E, such application shall also be accompanied with approval, in writing in favour of the applicant, from the licensing authority as defined in clause *(b)* of rule 21.]

[2][**69A**. *Loan Licences*.—[3][*(1)* Application for the grant or renewal of loan licences to manufacture for sale or for distribution of drugs other than those specified

in Schedule C, Schedule C (1) and Schedule X shall be made up to ten items for each category of drugs [5][referred to in Schedule M relating to pharmaceuticals products and Schedule M-III relating to medical devices and *in-vitro* diagnostics] and shall be made in

Form 24A accompanied by a licence fee of rupees six thousand and an inspection fee of rupees one thousand and five hundred to the licensing authority:

Provided that if the applicant applies for the renewal of a licence after its expiry but within six months of such expiry, the fee payable for renewal of such licence shall be accompanied by a licence fee of rupees six thousand and an inspection fee of rupees one thousand and five hundred plus an additional fee at the rate of rupees one thousand per month or part thereof.]

[4][*Explanation*.- For the purpose of this rule a loan licence means a licence which the Licensing Authority may issue to an applicant who does not have his own arrangements for manufacture but who intends to avail himself of the manufacturing facilities owned by a licensee in

Form 25.]

(2) The Licensing Authority shall, before the grant of a loan licence, satisfy himself that the manufacturing unit has adequate equipment, staff, capacity for manufacture, and facilities for testing, to undertake the manufacture on behalf of the applicant for a loan licence.

3[*(3)* Subject to the provisions of sub-rule *(2)*, application for manufacture of more than ten items for each category of drug on a loan licence shall be accompanied by an additional fee of rupees three hundred per additional item specified 5[referred to in Schedule M relating to pharmaceuticals products and Schedule MIII relating to medical devices and *in-vitro* diagnostics].

1. Ins. by G.S.R 311 (E), dt. 1-5-2002.
2. Amended by Notfn. No. F. 1-16/57-D, dt. 15-6- 1957.
3. Subs. by G.S.R 601(E) dt. 24-8-2001.
4. Subs. by G.S.R 724(E) dt. 07-11-2013.
5. Subs. by G.S.R 640 (E), dt. 29-6-2016.

1[(4) If the Licensing Authority is satisfied that a loan licence is defaced, damaged or lost or otherwise rendered useless, he may, on payment of a 2[fee of rupees one thousand] issue a duplicate licence.]

3[* * * * *]

4[**70.** *Form of licence to repack or manufacture drugs other than those specified in Schedules C and C(1).-*

Licences for repacking of drugs against application in Form 24-B shall be granted in Form 25-B, licences for manufacture of drugs included in Schedule X and against application in Form 24-F shall be granted in Form 25-F and licences for manufacture of drugs against application in Form 24 shall be granted in Form 25.]

5[**70A.** *Form of loan* 6[*licence to manufacture for sale or for distribution*] *of drugs other than those* 7[*specified in Schedules C, C(1) and X*].—

A loan[6] [licence to manufacture for sale or for distribution] or drugs other than those [7][specified in Schedules C, C(1) and X] shall be issued in

Form 25A.]

[8][**71.** *Conditions for the grant or renewal of a licence in*

Form 25 [9][*or Form 25F*].—

Before a licence in Form 25 [9][or Form 25F] is granted or renewed, the following conditions shall be complied with by the applicant.-

(*1*) The manufacture shall be conducted under the active direction and personal supervision of competent technical staff consisting at least of one person who is a whole-time employee and who is

(*a*) a graduate in Pharmacy or Pharmaceutical Chemistry of [10][a University established in India by law or has an equivalent qualification recognised and notified by the Central Government for such purpose] and has had at least eighteen months practical experience after the graduation in the manufacture of drugs. This period of experience may, however, be reduced by six months if the person has undergone training in manufacture of drugs for a period of six months during his University course; or

(*b*) a graduate in Science of [10][a University established in India by law or has an equivalent qualification recognized and notified by the Central Government for such purpose] who for the purpose of his degree has studied Chemistry as a principal subject and has

1. Ins. by Notfn. No. F.1-20/64-D, dt. 26.10.1968.
2. Subs. by Notfn. No. G.S.R. 601 (E), dt. 24.8.2001.
3. Rule 69 omitted by G.S.R. 944 (E), dt. 21-9-1988.
4. Subs. by Notfn. No. G.S.R. 462 (E), dt. 22.6.1982.
5. Ins. by Notfn. No. F.1-16/57 D, 15-6-1957 & No. F.1/22/59-D, dt. 9.4.1960.
6. Subs. by Notfn. No. G.S.R. 788 (E), dt. 10-10-1985.
7. Subs. by Notfn. No. G.S.R. 462 (E), dt. 22-6-1982.
8. Subs. by Notfn. No. F.1-16/57-D, dt. 15-6-1957.
9. Ins. by G.S.R. 462(E), dt. 22-6-1982.
10. Subs. by Notfn. No. G.S.R. 71 (E), dt. 30-1-1987.

had at least three years practical experience in the manufacture of drugs after his graduation; or

(c) a graduate in Chemical Engineering or Chemical Technology or Medicine of [1][a University established in India by law or has an equivalent qualification recognised and notified by the Central Government for such purpose] with general training and practical experience, extending over a period of not less than three years in the manufacture of drugs, after his graduation; or

[2][(d) holding any foreign qualification the quality and content of training of which are comparable with those prescribed in clause (a), clause (b) or clause (c) and is permitted to work as competent technical staff under this Rule by the Central Government:]

Provided that any person who was immediately before the 29th June, 1957, actively directing and personally supervising the manufacture of drugs and whose name was accordingly entered in any licence granted in

Form 25 [3][or Form 25F] as it existed before the date shall be deemed to be qualified for the purposes of this rule:

[4][Provided further that for drugs other than those specified in Schedules C, C(1) and X and meant for veterinary use, the whole-time employee under whose supervision the manufacture is conducted shall be a graduate in Veterinary Science or Pharmacy or General Science or Medicine of a University recognized by the Central Government and who has had at least three years practical experience in the manufacture of drugs excluding graduate in Pharmacy who shall have at least eighteen months practical experience in the manufacture of drugs:]

[5][Provided [6][also] that the Licensing Authority may, in the matter of manufacture of disinfectant fluids, insecticides, liquid paraffin, medicinal gases, non-chemical contraceptives, plaster of Paris and surgical dressings, for the manufacture of which the knowledge of Pharmaceutical Chemistry or Pharmacy is not essential, permit the manufacture of the substance under the active direction and personal supervision of the competent technical staff, who, although not having any of the qualifications included in clause (a), (b) or (c) of this rule, has, in the opinion of the Licensing Authority, adequate experience in the manufacture of such substance.]

1. Subs. by G.S.R. 71(E), dt. 30-1-1987.
2. Added by Notfn. NO. F. 1-19/59-D, dt. 13-6-1961.
3. Ins. by. G.S.R. 462 (E), dt. 22-6-1982.
4. Ins. by. G.S.R. 93 (E), dt. 24-2-1999.
5. Added Notfn. No. F. 1-14/68-D, dt. the 26-10-1968.
6. Sub. by. G.S.R. 93 (E), dt. 24-2-1999.

(2) The factory premises shall comply with the conditions prescribed in Schedule M.

(3) The applicant shall provide adequate space, plant and equipment for the manufacturing operations; the space, plant and equipment recommended for various operations are given in Schedule M.

[1][(4) The applicant shall provide and maintain adequate staff, premises and laboratory equipment for carrying out tests of the strength, quality and purity of the substances at a testing unit, which shall be separate from the manufacturing unit and the head of the testing unit shall be independent of the head of the manufacturing unit :

Provided that the manufacturing units, which, before the commencement of the Drugs and Cosmetics (Amendment) Rules, 1977, were making arrangements with institutions approved by the Licensing Authority for such tests to be carried out on their behalf may continue such arrangements up to the 30th June, 1977 :

Provided further that for tests requiring sophisticated instrumentation techniques or biological or microbiological methods other than sterility the Licensing Authority may permit such tests to be conducted by institutions approved by it [4][under Part XV(A) of these rules] for this purpose.]

[2][(4A) The head of the testing unit referred to in condition (4) shall possess a degree in Medicine or Science or Pharmacy or Pharmaceutical Chemistry of a University recognized for this purpose and shall have experience in the testing of drugs, which in the opinion of the licensing authority is considered adequate.]

(5) The applicant shall make adequate arrangements for the storage of drugs manufactured by him.

[3][(6) The applicant shall, while applying for a licence to manufacture patent or proprietary medicines, furnish to the Licensing Authority evidence and data justifying that the patent or proprietary medicines

(i) contain the constituent ingredients in therapeutic/prophylactic quantities as determined in relation to the claims or conditions for which the medicines are recommended for use or claimed to be useful;

1. Subs. by G.S.R. 926 dt. 16-7-1977.
2. Ins. by G.S.R. 681(E), dt. 5-12-1980.
3. Ins. by G.S.R. 515 dt. 10-4-1976.
4. Ins. by G.S.R. 1172 dt. 23-8-1977.

(ii) are safe for use in the context of the vehicles, excipients, additives and pharmaceutical aids used in the formulation and under the conditions in which the formulation for administration and use are recommended;

(iii) are stable under the conditions of storage recommended;

(iv) contain such ingredients and in such quantities for which there is therapeutic justification; and]

[1][(v) have the approval, in writing, in favour of the applicant to manufacture drugs formulations falling under the purview of new drug as defined in Rule 122-E, from the Licensing Authority as defined in clause (b) of rule 21.]

[2][(7) The licensee shall comply with the requirements of Good Manufacturing Practices as laid down in Schedule M.]

[6][(8) The applicant shall make application for grant of licence for a drug formulation containing single active ingredient only in proper name.]

[3][**71A**. Conditions for the grant or renewal of a licence in

Form 25B. Before a licence in Form 25B is granted or renewed the following conditions shall be complied with by the applicant :-

(1) the repacking operation shall be carried out under hygienic conditions and under the supervision of a competent person;

[4][(2) the factory premises shall comply with the conditions prescribed in Schedule M; and]

[5][(3) the applicant shall have adequate arrangements in his own premises for carrying out tests for the strength, quality and purity of the drugs at a testing unit which shall be separate from the repacking unit:]

[6][(4) The application for grant of licence for a drug formulation containing single active ingredient shall be made only in proper name:]

Provided that the repacking units, which before the commencement of the Drugs and Cosmetics (Second Amendment) Rules, 1977, were making arrangements with institutions approved by the licensing authority for such tests to be carried out on their behalf, may continue such arrangements up to the 31st July, 1977:

1. Ins. by G.S.R. 311 (E), dt. 1-5-2002.
2. Ins. by G.S.R. 735 (E), dt. 24-6-1988.
3. Ins. by No. F.1-22/59-D, dt. 9-4-1960.
4. Amended by S.O. 2139 dt. 12-8-1972.
5. Amended by G.S.R. 926 dt. 16-7-1977.
6. Ins. by G.S.R. 570 (E), dt. 7-8-2014.

Provided further that for tests requiring sophisticated instrumentation techniques or biological or microbiological methods the licensing authority may permit such test to be conducted by institutions approved by it under Part XV(A) of these Rules for this purpose.]

Explanation.−A person who satisfies the following minimum qualifications shall be deemed to be a ―competent person‖ for the purposes of rule 71A or 74A of these rules, namely: −

(a) a person who holds the Diploma in Pharmacy approved by the Pharmacy Council of India under the Pharmacy Act, 1948 (VIII of 1948) or a person who is registered under the said Act, or

(b) a person who has passed the Intermediate examination with Chemistry as one of the principal subjects or an examination equivalent to it or an examination recognized by the Licensing Authority as equivalent to it; or

(c) a person who has passed the Matriculation examination or an examination recognized by the Licensing Authority as equivalent to it and has had not less than four years‘ practical experience in the manufacture, dispensing or repacking of drugs.]

[1][**71B. Conditions for the grant of renewal of a licence in**

Form 25A.− Before a licence in Form 25A is granted or renewed, the applicant shall, while applying for a licence to manufacture patent or proprietary medicines, furnish to the Licensing Authority evidence and data justifying that the patent or proprietary medicines:-

(i) contain the constituent ingredients in therapeutic/prophylactic quantities as determined in relation to the claims or conditions for which the medicines are recommended for use or claimed to be useful;

(ii) are safe for use in the context of the vehicles, recipients, additives and pharmaceutical aids used in the formulations and under conditions in which the formulations for administration and use are recommended;

(iii) are stable under the conditions of storage recommended; and

(iv) contain such ingredients and in such quantities for which there is therapeutic justification.

2[Provided that the application for grant of a licence for a drug formulation containing single active ingredient shall be made only in proper name.]

1. Ins. by G.S.R. 515 (E), dt. 24-3-1976.
2. Ins. by G.S.R. 570 (E), dt. 7-8-2014.

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1[**72**. ***Duration of licence***.–An original licence or a renewed licence in Form 25, 2[Form 25B or Form 25F] unless sooner suspended or cancelled shall be 3[valid for a period of five years on and from the date on which] it is granted or renewed:

4[Provided that if the application for the renewal of a licence is made before its expiry, or if the application is made within six months of its expiry, after payment of additional fee, the licence shall continue to be in force until orders are passed on the application and the licence shall be deemed to have expired if the application for its renewal is not made within six months of its expiry.]

[2][**73.** *Certificate of renewal.*– The certificate of renewal of a licence in

Form 25 or Form 25F shall be issued in Form 26 or Form 26E respectively].

[5][**73A.** *A certificate of renewal of loan licence.*- The certificate of renewal of a loan licence in

Form 25A shall be issued in Form 26A.]

5**[73AA.** *Duration of loan licence.*– An original loan licence in Form 25A or a renewed loan licence in Form 26A, unless sooner suspended or cancelled, shall be 3[valid for a period of five years on and from the date on which] it is granted or renewed:]

6[Provided that if the application for the renewal of a licence is made before its expiry, or if the application is made within six months of its expiry, after payment of additional fee, the licence shall continue to be in force until orders are passed on the application and the licence shall be deemed to have expired if the application for its renewal is not made within six months of its expiry.]

7**[73B.** *Certificate of renewal of licence in Form 25B.*–The certificate of renewal of a licence in Form 25B shall be issued in Form 26B.]

1. Subs. by Notfn. No. F.1-10/62-D, dt. 10-4-1964.
2. Subs. by G.S.R. 462 (E), dt. 22-6-1982.
3. Subs. by G.S.R. 601 (E), dt. 24-8-2001.
4. Amended by S.O. 2139 dt. 12-8-1972.
5. Amended by Notfn. No. F.1-10/62-D, dt. 10-4-1964.
6. Amended by S.O. 2139 dt. 12-8-1972.
7. Ins. by S.O. 1196, dt. 6-5-1960.

1[**74.** ***Conditions of licence in Form 25.***−A licence in 2[Form 25 and Form 25F] shall be subject to the conditions stated therein and to the following further conditions, namely :

(*a*) the licensee shall provide and maintain staff, premises and the equipment as specified in rule 71;

(*b*) the licensee shall comply with the provisions of the Act and of these rules and with such further requirements, if any, as may be specified in any rules subsequently made under Chapter IV of the Act; provided that where such further requirements are specified in the Rules, these would come into force, four months after publication in the Official Gazette;

(*c*) the licensee shall either in his own laboratory or in any other laboratory approved by the Licensing Authority 4[under Part XV (A) of these rules] test each batch or lot of the raw material used by him for the manufacture of his products and also each batch of the final product and shall maintain records or registers showing the particulars in respect of such tests as specified in Schedule U. The records or registers shall be retained for a period of 5 years from the date of manufacture;

(*d*) the licensee shall keep records of the details of manufacture as per particulars given in Schedule U of each batch of the drugs manufactured by him and such records shall be retained for a period of five years;

(*e*) the licensee shall allow an 3[Inspector appointed under the Act], to enter, with or without prior notice, any premises and to inspect the plant and the process of manufacture and the means employed in standardizing and testing the drugs;

(*f*) the licensee shall allow an 3[Inspector appointed under the Act] to inspect all registers and records maintained under these rules and to take samples of the manufactured drugs and shall supply to such Inspector such information as he may require for the purpose of ascertaining whether the provisions of the Act and the rules thereunder have been observed;

(*g*) the licensee shall, from time to time, report to the Licensing Authority any changes in the expert staff responsible for the manufacture or testing of the drugs and any material alterations in the premises or plant used for the purpose which have been made since the date of the last inspection made on behalf of the licensing authority;

1. Subs. by Notfn. No. F. 1-20/64-D (S.O. 3868), dt. 26-10-1968. 2.
Subs. by G.S.R. 462 (E), dt. 22-6-1982.
3. Amended by G.S.R. 444 dt. 28-4-1973.
4. Ins. by G.S.R. 1172 (E), dt. 23-8-1977.

[1][(h) the licensee shall, on request, furnish to the Licensing Authority, the Controlling Authority or to such authorities as the Licensing Authority or the Controlling Authority may direct from every batch, or batches of drugs as the Licensing Authority or the Controlling Authority may from time to time specify, a sample of such quantity as may be considered adequate by such authority for any examination and, if so required, also furnish full protocols of tests which have been applied;]

(i) if the Licensing Authority [2][or the Controlling Authority] so directs and if requested by the licensee who had also furnished *prima facie* reasons for such directions, the licensee shall not sell or offer for sale any batch in respect of which a sample is or protocols are furnished under clause (h) until a certificate authorizing the sale of the batch has been issued to him by or on behalf of the Licensing Authority [2][or the Controlling Authority;

(j) the licensee shall on being informed by the Licensing Authority [2][or the Controlling Authority] that any part of any batch of the drug has been found by the Licensing Authority [2][or the Controlling Authority]not to conform with the standards of strength, quality or purity specified in these rules and on being directed so to do, withdraw the remainder of the batch from sale, and, so far as may in the particular circumstances of the case be practicable, recall all issues already made from that batch;

(k) the licensee shall maintain an Inspection Book in

Form 35 to enable an Inspector to record his impressions and the defects noticed;

[1][(l) the licensee shall maintain reference samples from each batch of the drugs manufactured by him in a quantity which is at least twice the quantity of the drug required to conduct all the tests performed on the batch. In case of drugs bearing an expiry date on the label, the reference samples shall be maintained for a period of three months beyond the date of expiry or potency. In case of drugs where no date of expiry of potency is specified on the label, the reference samples shall be maintained for a period of three years from the date of manufacture;]

[2][(m) the licensee, who has been granted a licence in

Form 25F, shall-

(i) forward to the licensing authority of the concerned States of manufacture and supply of the drug a statement of the sales effected to manufacturers, wholesalers, retailers, hospitals, dispensaries and nursing homes and Registered Medical Practitioners every three months;

(ii) maintain accounts of all transactions giving details as indicated below in a register bound and serially page numbered and such records shall be retained for a period of five years or one year after the expiry of potency, whichever is later:-

1. Subs. by G.S.R. No. 444 dt. 31-3-1973.
2. Ins. by G.S.R. No. 444 dt. 31-3-1973.
3. Ins. by G.S.R. 462 (E), dt. 22-6-1982.

A. Accounts of the drugs specified in Schedule X used for the manufacture:

1. Date of issue.
2. Name of the drug.
3. Opening balance of stock on the production day.
4. Quantity received, if any, and source from where received. 5. Quantity used in manufacture.
6. Balance quantity on hand at the end of the production day. 7. Signature of the person in charge.

B. Accounts of production:

1. Date of manufacture.
2. Name of the drug.
3. Batch Number.
4. Quantity of raw material used in manufacture.
5. Anticipated yield.
6. Actual yield,
7 Wastage,
8. Quantity of the manufactured goods transferred.

C. Accounts of the manufactured drugs:

1. Date of manufacture.
2. Name of the drug.
3. Batch Number.
4. Opening Balance.
5. Quantity manufactured.
6. Quantity sold.
7. Name of the purchaser and his address.
8. Balance quantity at the end of the day.
9. Signature of the person in charge.

(n) the licensee shall store drugs specified in Schedule X in bulk form and when any of such drug is required for manufacture in a place other than its place of storage it shall be kept in a separate place under the direct custody of a responsible person;]

[1][(o) the licensee shall comply with the requirements of [2][Good Laboratory Practices as laid down in Schedule L-I and] _Good Manufacturing Practices' as laid down in Schedule M.]

[3][(p) No advertisement of the drugs specified in Schedule H, Schedule H1 and Schedule X shall be made except with the previous sanction of the Central Government.]

1. Ins. by G.S.R. 735 (E), dt. 24-6-1988.
2. Ins by G.S.R. 780 (E), dt. 10-11-2008.
3. Ins by G.S.R. 289 (E), dt. 15-04-2015.

74A. *Conditions for licence in Form 25B*._ A licence in Form 25B shall be subject to the conditions stated therein and to the following conditions:_

(a) the repacking of drugs shall at all times be conducted under the personal supervision of at least one person who is approved as a competent person by the Licensing Authority;

(b) the licensee shall either provide and maintain adequate arrangements in his own premises for carrying out tests of the strength, quality and purity of the drugs repacked or make arrangements with some institution approved by the Licensing Authority [3][under Part XV (A) of these rules] for such tests to be regularly carried out on his behalf by the institution;

(c) the licensee shall make adequate arrangements for the storage of drugs;

[2][(d) the licensee shall comply with the provisions of the Act and of these rules and with such further requirements, if any, as may be specified in any rules subsequently made under Chapter IV of the Act:

Provided that where such further requirements are specified in the Rules, these would come into force four months after publication in the Official Gazette.]

(e) the licensee shall allow any [4][Inspector appointed under the Act] to enter with or without notice, any premises where the packing of drugs in respect of which the licence is issued is carried on, to inspect the premises and to take samples of repacked drugs;

[2][(f) the licensee shall, either in his own laboratory or, in any other laboratory approved by the Licensing Authority, test each batch or lot of raw material used by him for repacking and also each batch of the product thus repacked and shall maintain records or registers showing the particulars in respect of such tests as specified in Schedule U. The records or registers shall be retained for a period of five years from the date of repacking. The licensee shall allow the Inspector to inspect all registers and records maintained under these rules and shall supply to the Inspector such information as he may require for the purpose of ascertaining whether the provisions of the Act and these rules have been observed;]

1. Ins. by G.S.R. 735 (E), dt. 24-6-1988.
2. Subs. by Notfn. No. F.1-20/64-D, dt. 26-10-1968.
3. Ins. by G.S.R. 1172 (E), dt. 23-8-1977.
4. Subs. by G.S.R. 444 (E), dt. 31-3-1973.

[1][(g) the licensee shall maintain an Inspection Book, in

Form 35, to enable an Inspector to record his impressions and the defects noticed;]

[2][(h) the licensee shall maintain reference samples from each batch of the drugs manufactured by him in a quantity which is at least twice the quantity of the drug required to conduct all the tests performed on the batch. In case of drugs bearing an expiry date on the label, the reference sample shall be maintained for a period of three months beyond the date of expiry of potency. In case of drugs where no date of expiry of potency is specified on the label, the reference samples shall be maintained for a period of three years from the date of manufacture.

[4][(i) No advertisement of the drugs specified in Schedule H, Schedule H1 or Schedule X shall be made except with the previous sanction of the Central Government.]

[3][**74B**.*Conditions of licence in Form 25A*. (*1*) The licence in Form 25A shall be deemed to be cancelled or suspended, if the licence owned by the licensee in Form 25, whose manufacturing facilities have been availed of by the licensee, is cancelled or suspended, as the case may be, under these rules.

(2) The licensee shall comply with the provisions of the Act and of these rules and with such further requirements if any, as may be specified in any rules subsequently made under Chapter IV of the Act; provided that where such further requirements are specified in the rules, these would come into force four months after publication in the Official Gazette.

(3) The licensee shall test each batch or lot of the raw material used by him for the manufacture of his products and also each batch of the final product and shall maintain records or registers showing the particulars in respect of such tests as specified in Schedule U. The records or registers shall be retained for a period of five years from the date of manufacture. The licensee shall allow an Inspector to inspect all registers and records maintained under these rules and shall supply to the Inspector such information as he may require for the purpose of ascertaining whether the provisions of the Act and these rules have been observed.

1. Ins. by Notfn. No. 1-14/68-D, dt. 26-10-1968.
2. Ins. by G.S.R. 444 (E) dt. 31-3-1973 .
3. Subs. by Notfn. No. F. 1-14/68-D, dt. the 26-10-1968.
4. Ins. by G.S.R. 289 (E) dt. 15-4-2015.

(4) The licensee shall either-

(i) provide and maintain to the satisfaction of the Licensing Authority adequate staff and adequate laboratory facilities for carrying out test of the strength, quality and purity of the substances manufactured by him, or

(ii) make arrangements with some institution approved by the Licensing Authority [7][under Part XV (A) of these rules] for such tests to be regularly carried out on his behalf by the institution.

[1][(5) The licensee shall maintain reference samples from each batch of the drugs manufactured by him in a quantity which is at least twice the quantity of the drug required to conduct all the tests performed on the batch. In case of drugs bearing an expiry date on the label the reference samples shall be maintained for a period of three months beyond the date of expiry of potency. In case of drugs where no date of expiry of potency is specified on the label, the reference samples shall be maintained for a period of three years from the date of manufacture.]

[2][(6) The licensee shall maintain an Inspection Book in

Form 35 to enable an Inspector to record his impressions and the defects noticed.]

[8][(7) No advertisement of the drugs specified in Schedule H, Schedule H1 or Schedule X shall be made except with the previous sanction of the Central Government.]

[3][**75**. *Form of application for licence to manufacture for sale or distribution of drugs specified in Schedules C and C(1) and X* [4][*excluding those specified in Part XB and Schedule X*]. (1) Applications for the grant or renewal of licence to manufacture for sale or distribution of drugs specified in Schedules C and C(1) [4][excluding those specified in Part X-B and Schedule X], shall be made to the Licensing Authority in

Form 27 and [5][shall be made up to ten items for each category of drugs [6][referred to in Schedule M relating to pharmaceuticals products and Schedule M-III relating to medical devices and *in-vitro* diagnostics] and shall be accompanied by a licence fee of rupees six thousand and an inspection fee of rupees one thousand and five hundred for every inspection or for the purpose of renewal of licences:]

Provided that if the applicant applies for renewal of licence after its expiry but within six months of such expiry, the fee payable for renewal of the licence shall be [5][a licence fee of rupees six thousand plus an additional fee of rupees one thousand per month or a part thereof in addition to an inspection fee of rupees one thousand and five hundred.]

(2) Application for grant or renewal of licence to manufacture for sale or distribution of drugs specified in Schedules C, C(1) and X shall be made to the licensing authority in

Form 27-B, and [5][shall be made up to ten items for each category of drugs [6][referred to in Schedule M relating to pharmaceuticals products and Schedule M-III relating to medical devices and *in-vitro* diagnostics] and shall be accompanied by a licence fee of rupees six thousand and an inspection fee of rupees one thousand five hundred for every inspection or for the purpose of renewal of licences]:

1. Ins. by G.S.R.. No. 444, dt. 28-4-1973. 7. Subs. by G.S.R. 1172(E), dt. 23-8-1977. 2. Ins. by G.S.R. 331 (E), dt. 8-5-1984. 8. Ins. by G.S.R. 289(E), dt. 15-4-2015. 3. Subs. by G.S.R. 462 (E), dt. 22-6-1982.
4. Subs. by G.S.R. 28(E), dt. 22-1-1993.
5. Subs. by G.S.R. 601(E), dt. 24-8-2001.
6. Subs. by G.S.R. 640(E), dt. 29-6-2016.

Provided that the applicant shall possess a licence in

Form 28 to manufacture such drugs:

Provided further that if the application for renewal of a licence is made after its expiry but within six months of such expiry, the fee payable for renewal of the licence shall be [1][rupees six thousand plus an additional fee of rupees one thousand per month or part thereof in addition to an inspection fee of rupees one thousand five hundred.]

[2][(3) The application for grant or renewal of licence to manufacture for sale or for distribution of drugs in [4][Large Volume Parenterals, Sera and Vaccine and Recombinant DNA (r-DNA) derived drugs] shall be made to the licensing authority appointed under this Part in

Form 27D and [1][shall be made up to ten items for each category of drugs categorized in Schedule M and shall be accompanied by a licence fee of rupees six thousand and an inspection fee of rupees one thousand five hundred for every inspection or for the purposes of renewal of licences:]

Provided that if the application for renewal of a licence is made after its expiry but within six months of such expiry, the fee payable for renewal of the licence [1][shall be rupees six thousand plus an additional fee of rupees one thousand per month or a part thereof in addition to the inspection fee of rupees one thousand and five hundred.]

[1][(4) A fee of rupees one thousand shall be paid for duplicate copy of the licence issued under sub-rule (1), sub-rule (2) or sub-rule (3), as the case may be, if the original licence is defaced, damaged or lost.

(5) If the licensee applies for manufacture of more than ten items of each category of drugs, the application shall be accompanied by an additional fee at the rate of rupees three hundred for each additional item of drugs [5][referred to in Schedule M relating to pharmaceuticals products and Schedule M-III relating to medical devices and *in-vitro* diagnostics].]

[3][(6) Where an application under this Rule is for the manufacture of drug formulations falling under the purview of new drugs as defined in Rule 122-E, such application shall also be accompanied with approval, in writing, in favour of the applicant, from the licensing authority as defined in clause (b) of Rule 21.]]

1. Subs. by G.S.R. 601 (E), dt. 24-8-2001.
2. Ins. by G.S.R. 119 (E), dt. 11-3-1996.
3. Ins. by G.S.R. 311 (E), dt. 1-5-2002.
4. Subs. by G.S.R. 26 (E), dt. 19-1-2006.
5. Subs. by G.S.R. 640 (E), dt. 29-6-2016.

[1][**75A**. Loan licences.−(1) Applications for the grant or renewal of loan [2][licences for the manufacture for sale or for distribution] of drugs specified in Schedules C and C(1) [3][excluding those specified in Part X-B and Schedule X] shall be made in

Form 27-A to the licensing authority and [4][shall be made upto ten items for each category of drugs [14][referred to in Schedule M relating to pharmaceuticals products and Schedule M-III relating to medical devices and *in-vitro* diagnostics] and shall be accompanied by a fee of rupees six thousand and an inspection fee of rupees one thousand and five hundred for every inspection or for the purpose of renewal of licences:]

[5][Provided that if the applicant applies for the renewal of a licence after its expiry but within six months of such expiry the fee payable for renewal of the licence shall be [4][rupees six thousand and an inspection of fee of rupees one thousand five hundred plus an additional fee at the rate of rupees one thousand] per month or a part thereof.]

[11][*Explanation*. − For the purpose of this rule a loan licence means a licence which a licensing authority may issue to an applicant who intends to avail the manufacturing facilities owned by a licensee in

Form 28.]

12[(1A) The application for grant or renewal of loan license to manufacture for sale or distribution of drugs in _Large Volume Parenterals', _Sera and Vaccine' and _Recombinant DNA (r-DNA) derived drugs' shall be made to the licensing authority appointed under this Part, in Form 27DA and be made upto ten items for each category of drugs categorized in Schedule M and accompanied by a license fee of six thousand rupees and an inspection fee of one thousand five hundred rupees for every inspection or for the purpose of renewal of licenses:

Provided that if the application for renewal of a license is made after its expiry but within six months of such expiry, the fee payable for renewal of the license shall be six thousand rupees plus an additional fee of one thousand rupees per month or a part thereof in addition to the inspection fee of one thousand and five hundred rupees;]

(2) The licensing authority, shall, before the grant of a loan licence, satisfy himself that the manufacturing unit has adequate equipment, staff, capacity for manufacture and facilities for testing to undertake the manufacture on behalf of the applicant for a loan licence.

13[***]

4[(3) Subject to the provisions of sub-rule (2), the application for manufacture of more than ten items of each category of drugs on a loan license, shall be accompanied by an additional fee at the rate of rupees three hundred for each additional item of drugs.

(4) If the licensing authority is satisfied that a loan licence is defaced, damaged or lost, he may, on payment of a fee of rupees one thousand, issue a duplicate copy of loan licence.]

6[* * * * *]

7[**76**. 8*[Forms of licence to manufacture drugs specified in Schedules C and C(1),* 9[*excluding those specified in Part XB and Schedule X*]*, or drugs specified in Schedules C, C(1) and X and the conditions for the grant or renewal of such licences.*- 10[A licence to manufacture for sale or for distribution of drugs specified in

1. Ins. by F.1-16/57-D, dt. 15-6-1957.
2. Subs. by G.S.R 788 (E), dt. 10-10-1985.
3. Subs. by G.S.R 28 (E), dt. 22-1-1993.
4. Subs. by G.S.R 601 (E), dt. 24-8-2001.
5. Amended by S.O.2139 dt. 13-8-1972.
6. Rule 75B omitted by G.S.R. 944 (E), dt. 21-9-1988.
7. Amended by F- 1- /57-D, dt. 15-6-1969.
8. Subs. by G.S.R. 462 (E), dt. 22-6-1982.
9. Subs. by G.S.R. 28 (E) , dt. 22.1.1993.
10. Subs. by G.S.R. 119 (E), dt. 11-3-1996.
11. Subs. by G.S.R. 724 (E), dt. 7-11-2013.
12. Ins. by G.S.R. 574 (E) , dt. 17.7.2012.
13. Proviso omitted by G.S.R. 574 (E) , dt. 17.7.2012.
14. Subs. by G.S.R. 640 (E), dt. 29-06-2016.

Schedules C and C(1) other than [4][Large Volume Parenterals, Sera and Vaccine and Recombinant DNA (r-DNA) derived drugs] specified in Part X B and Schedule X shall be issued in

Form 28 and a licence to manufacture for sale or distribution of drugs specified under Schedules C and C(1) (other than [4][Large Volume Parenterals, Sera and Vaccine and Recombinant DNA (r-DNA) derived drugs] specified in Part X-B) and Schedule X shall be issued in Form 28B. A licence to manufacture for sale or for distribution of [4][Large Volume Parenterals, Sera and Vaccine and Recombinant DNA (r-DNA) derived drugs] shall be issued in Form 28-D. Before a licence in Form 28 or Form 28B or Form 28D is granted or renewed, the following conditions shall be complied with by the applicant:-

(1) The manufacture will be conducted under the active direction and personal supervision of competent technical staff consisting at least of one person who is a whole time employee and who is

(a) a graduate in Pharmacy or Pharmaceutical Chemistry of [1][a University established in India by law or has an equivalent qualification recognized and notified by the Central Government for such purpose] and has had at least eighteen months' practical experience after the graduation in the manufacture of drugs to which this licence applies; this period of experience may however be reduced by six months if the person has undergone training in manufacture of drugs to which the licence applies for a period of six months during his University course; or

(b) a graduate in Science of [1][a University established in India by law or has an equivalent qualification recognized and notified by the Central Government for such purpose] who for the purpose of his degree has studied Chemistry [3][or Microbiology] as a principal subject and has had at least three years' practical experience in the manufacture of drugs to which this licence applies after his graduation; or

(c) a graduate in Medicine of [1][a University established in India by law or has an equivalent qualification recognized and notified by the Central Government for such purpose] with at least three years' experience in the manufacture and pharmacological testing of biological products after his graduation; or

[2][(d) a graduate in Chemical Engineering of a University recognised by the Central Government with at least three years' practical experience in the manufacture of drugs to which this licence applies after his graduation; or

(e) holding any foreign qualification the quality and content of training of which are comparable with those prescribed in clause (a), clause (b), clause (c) or clause (d) and is permitted to work as competent technical staff under this Rule by the Central Government.]

1. Subs. by G.S.R. 71(E), dt. 30-1-1987.
2. Ins. by F.1-19/59-D, dt. 13-6-1967.
3. Ins. by G.S.R. 245(E), dt. 3-2-1976.
4. Subs. by G.S.R. 26 (E), dt. 19-1-2006.

Provided that any person who was approved by the licensing authority as an expert responsible for the manufacture of drugs for the purpose of rule 76 read with Rule 78 as these Rules were in force immediately before the 29th June, 1957, shall be deemed to be qualified for the purposes of this rule:

[1][Provided that for the drugs specified in Schedules C and C(1) meant for veterinary use, the whole time employee under whose supervision the manufacture is conducted may be a graduate in Veterinary Science or general science or medicine or pharmacy of a University, recognized by the Central Government and who has had at least three years' experience in the manufacture of biological products:

[5][Provided also that for medical devices, the whole time employee under whose supervision the manufacture or testing is conducted shall be—

(i) a graduate in Pharmacy or Engineering (in appropriate branch) from a University recognised by the Central Government for such purposes and has had at least eighteen months practical experience in the manufacturing or testing of

devices to which this licence applies after his graduation; or (ii)a graduate in science, from a University recognised by the Central Government for such purposes, with Physics or Chemistry or Microbiology as one of the subject and has had at least three years practical experience in the manufacturing or testing of devices to which this licence applies after his graduation; or

(iii)a diploma in Pharmacy or Engineering (in appropriate branch) from a Board or Institute recognised by the Central Government or the State Government, as the case may be, for such purposes and has had at least four years practical experience in the manufacturing or testing of devices to which this licence applies after his diploma; or

(iv)having a foreign qualification, the quality and content of training of which are comparable with those specified in clause (i), clause (ii) and clause (iii) and is permitted to work as competent technical staff under this rule by the Central Government.]

6[(2) The applicant proposing to manufacture pharmaceutical products shall comply with the provisions referred to in Schedule M.

(2A) The applicant proposing to manufacture medical devices and in-vitro diagnostics shall comply with the quality management system as referred to in Schedule M-III.

(3) The applicant shall provide adequate space, plant and equipment for pharmaceutical products as referred to in Schedule M and for Medical devices and in-vitro diagnostics as referred to in Schedule M-III.]

3[(4) The applicant shall provide and maintain adequate staff, premises and laboratory equipment for carrying out such tests of the strength, quality and purity of the substances as may be required to be carried out by him under the provisions of Part X of these rules including proper housing for animals used for the purposes of such tests, the testing unit being separate from the manufacturing unit and the head of the testing unit being independent of the head of the manufacturing unit:

Provided that the manufacturing units which before the commencement of the Drugs and Cosmetics (Amendment) Rules, 19774, were making arrangements with institutions approved by the Licensing Authority for such tests to be carried out on their behalf may continue such arrangements upto the 30th June, 1977 :

Provided further that for tests requiring sophisticated instrumentation techniques or biological or microbiological methods other than sterility the Licensing Authority may permit such tests to be conducted by institutions approved by it 2[under Part XV (A) of these rules] for this purpose.

1. Ins. by F.1-6/62-D (SO 2889), dt. 2-7-1969.
2. Ins. by G.S.R 1172 (E), dt. 23-8-1977.
3. Sub. by G.S.R 926 (E), dt. 24-6-1977.
4. These rules came in to force on 28th May, 1977 vide G.S.R 665 (E), dt. 6-5-1977. 5. Sub. by G.S.R 690 (E), dt. 25-9-2014. Earlier Ins. by G.S.R 109 (E), dt. 22-2-1994. 6. Sub. by G.S.R 640 (E), dt. 29-6-2016.

1[(4A) The head of the testing unit referred to in condition (4) shall possess a degree in Medicine or Science or Pharmacy or Pharmaceutical Chemistry of a University recognized for this purpose and shall have experience in the testing of drugs, which in the opinion of the Licensing authority is considered adequate.]

(5) The applicant shall make adequate arrangements for the storage of drugs manufactured by him.

2[(6) The applicant shall furnish to the Licensing Authority, if required to do so, data on the stability of drugs which are likely to deteriorate for fixing the date of expiry which shall be printed on the labels of such drugs on the basis of the data so furnished.]

3[(7) The applicant shall, while applying for licence to manufacture patent or proprietary medicines, furnish to the Licensing Authority evidence and data justifying that the patent or

proprietary medicines−

(i) contain the constituent ingredients in therapeutic/prophylactic quantities as determined in relation to the claims or conditions for which the medicines are recommended for use or claimed to be useful;

(ii) are safe for use in the context of the vehicles, excipients, additives and pharmaceutical aids used in the formulations and under the conditions in which the formulations for administration and use are recommended;

(iii) are stable under the conditions of storage recommended;

(iv) contain such ingredients and in such quantities for which there is therapeutic justification.;] and

[4][(v) have the approval, in writing, in favour of the applicant to manufacture drug formulations falling under the purview of new drug as defined in Rule 122E, from the licensing authority as defined in clause (b) of rule 21.]

[5][(8) The licensee of pharmaceutical products shall comply with the requirements of ‗Good Manufacturing Practices' as laid down in Schedule M and the licensee of Medical Devices and in-vitro diagnostics shall comply with the requirements of ―Quality Management System‖ as laid down in Schedule M-III..]

1. Ins. by G.S.R 681 (E), dt. 5-12-1980.
2. Ins. by G.S.R 444 dt. 31-3-1973.
3. Ins. by G.S.R 515 dt. 24-3-1976.
4. Ins. by G.S.R 311 (E), dt. 1-5-2002.
5. Subs. by G.S.R 640 (E), dt. 29-06-2016. Previously Ins. by G.S.R 735 (E), dt. 24-6-1988.

[1][*Explanation*:- For the purpose of this rule, [6][—Large Volume Parenterals‖ sera and vaccines and recombinant DNA (r-DNA) derived drugs,] shall mean the sterile solutions intended for parenteral administration with a volume of 100 ml. or more (and shall include anti-coagulant solutions) in one container of the finished dosage

form intended for single use.]

[7][(9) The applicant shall make application for grant of licence for a drug formulation containing single active ingredient only in proper name.]

[2][76A. **Forms of loan licenses to manufacture for sale or for distribution drugs specified in Schedule C and C(1) excluding drugs specified in Schedule X or of Large Volume Parenterals, Sera and Vaccine and recombinant DNA (r-DNA) derived drugs, and conditions for the grant or renewal of such license.—**A loan license to manufacture for sale or for distribution of drugs specified in Schedules C and C(1), excluding drugs specified in Schedule X, and Large Volume Parenterals, Sera and Vaccine and Recombinant DNA(r- DNA) derived drugs specified in Part XB shall be issued in

Form 28A and a loan license to manufacture for sale or for distribution of Large Volume Parenterals, Sera and Vaccine and Recombinant DNA (r-DNA) derived drugs shall be issued in Form 28DA, and the applicant shall, while applying for a licence to manufacture patent or proprietary medicines, furnish to the Licensing Authority evidence and data justifying that the patent or proprietary medicines-

(i) contain the constituent ingredients in therapeutic/prophylactic quantities as determined in relation to the claims or conditions for which the medicines are recommended for use or claimed to be useful;

(ii) are safe for use in the context of the vehicles, excipients, additives and pharmaceutical aids used in the formulations, and under the conditions in which the formulations for administration and use are recommended;

(iii) are stable under the conditions of storage recommended; and

(iv) contain such ingredients and in such quantities for which there is therapeutic justification.]

[7][Provided that the application for grant of a licence for a drug formulation containing single active ingredient shall be made only in proper name.]

[3][**77**. *Duration of licence*. An original licence in [4][Form 28, Form 28B and Form 28D or renewed licence in Forms 26, 26F, and Form 26H], unless sooner suspended or cancelled shall be [5][valid for a period of five years on and from the date on which] it is granted or renewed:

1. Ins. by G.S.R. 119 (E), dt. 11-3-1996.
2. Subs. by G.S.R. 574 (E), dt. 17-7-2012.Earlier Subs. by G.S.R. 788 (E), dt. 10-10-1985 and Subs. by G.S.R. 462 (E), dt. 22-6-1982.
3. Amended by No. G.1-10/62-D, dt. 10-4-1964.
4. Subs. by G.S.R. 119 (E), dt. 11-3-1996.
5. Subs. by G.S.R. 601 (E), dt. 24-8-2001.
6. Subs. by G.S.R. 26 (E), dt. 19-1-2006.
7. Ins. by G.S.R. 570 (E) dt. 7-8-2014.

[1][Provided that if the application for the renewal of a licence is made before its expiry, or if the application is made within six months of its expiry after payment of additional fee, the licence shall continue to be in force until orders are passed on the application and the licence shall be deemed to have expired if the application for its renewal is not made within six months of its expiry.]]

[2][**78**. Conditions of licence.−A licence in [3][Form 28, Form 28B or Form 28D] shall be subject to the special conditions, if any, set out in Schedule F or ScheduleF(1), as the case may be, which relate to the substance in respect of which the licence is granted and to the following general conditions:−

(a) (i) The licensee shall provide and maintain an adequate staff and adequate premises and plant for the proper manufacture and storage of the substances in respect of which the licence is issued;

(ii) Without prejudice to the generality of the foregoing requirement, every holder of a licence who for any purpose engaged in the culture or manipulation of pathogenic spore-bearing micro-organisms shall provide to the satisfaction of the Licensing Authority separate laboratories and utensils and apparatus required for the culture or manipulation of such micro-organisms, the laboratories, utensils and apparatus so provided not being used for the manufacture of any other substance;

[4][(b) The licensee shall provide and maintain staff, premises and equipment as specified in Rule 76;]

[5][(c)(i) The licensee shall maintain records of manufacture as per particulars given in Schedule U;

(ii) The licensee shall either in his own laboratory or in any laboratory approved by the Licensing Authority [6][under Part XV (A) of these rules] test each batch or lot of the raw material used by him for the manufacture of his product and also each batch of the final product and shall maintain records or registers showing the particulars in respect of such tests as specified in Schedule U. The records or registers shall be retained in the case of a substance for which a potency date is fixed for a period of two years from the expiry of such date, and in the case of other substances for a period of five years from the date of manufacture;]

(d) The licensee shall allow an [7][Inspector appointed under the Act] to enter, with or without prior notice, any premises where the manufacture is carried on and to inspect the premises, and in the case of substances specified in Schedules C and C(1), to inspect the plant and the process of manufacture and the means employed for standardizing and testing the substance;]

1. Amended by S.O. 2139 dt. 12-8-1972.
2. Amended by F.1-6/62-B, dt. 2-6-1969.
3. Subs. by G.S.R. 119 (E), dt. 11-3-1996.
4. Amended by F.1-16/57-D (SO 2136), dt. 15-6-1957.
5. Amended by F.1-20/64-D (SO 3868), dt. 26-10-1968.
6. Ins. by G.S.R. 1172 (E), dt. 23-8-1977.
7. Subs. by G.S.R. 444 (E), dt. 31-3-1973.

(e) The licensee shall allow an [1][Inspector appointed under the Act] to inspect all registers and records maintained under these Rules and to take samples of the manufactured product and shall supply to such Inspector such information as he may require for the purpose of ascertaining whether the provisions of the Act and Rules thereunder have been observed;]

(f) The licensee shall from time to time report to the Licensing Authority any changes in the expert staff responsible for the manufacture or testing of the substance and any material alterations in the premises or plant used for that purpose which have been made since the date of the last inspection made on behalf of the Licensing Authority before the issue of the licence;

[1][(g) The licensee shall on request furnish to the Licensing Authority, Controlling Authority or to such authorities as the Licensing Authority or the Controlling Authority may direct, from every batch of drug as the Licensing Authority or the Controlling Authority may from time to time specify, a sample of such quantity as may be considered adequate by such Authority for any examination and, if so required, also furnish, full protocols of the tests which have been applied;]

[2][(h) If the Licensing Authority or the Controlling Authority so directs, the licensee shall not sell or offer for sale any batch in respect of which a sample is, or protocols are furnished under the last preceding sub-paragraph until a certificate authorising the sale of the batch has been issued to him by or on behalf of the Licensing Authority or the Controlling Authority;]

[1][(i) The licensee shall on being informed by the Licensing Authority or the Controlling Authority that any part of any batch of the substance has been found by the Licensing Authority or the Controlling Authority not to conform with the standards of strength, quality or purity specified in these rules and on being directed so to do, withdraw the remainder of that batch from sale and so far as may in the particular circumstances of the case be practicable recall all issues already made from that batch;]

(j) No drug manufactured under the licence shall be sold unless the precautions necessary for preserving its properties have been observed throughout the period after manufacture;

[3][(k) The licensee shall comply with the provisions of the Act and of these rules and with such further requirements, if any, as may be specified in any rules subsequently made under Chapter IV of the Act, provided that where such further requirements are specified in the rules, these would come into force four months after publication in the Official Gazette;]

1. Subs. by G.S.R 444, dt. 28-4-1973.

2. Amended by F.1-16/57-D, dt. 15-6-1957.

3. Amended by F.1-14/68-B (SO 3868), dt. 26-10-1968.

[1][(l) The licensee shall maintain an Inspection Book in

Form 35 to enable an Inspector to record his impression and defects noticed.]

[2][(m) The licensee shall maintain reference samples from each batch of the drugs manufactured by him in a quantity which is at least twice the quantity of the drug required to conduct all the tests performed on the batch. In case of drugs bearing an expiry date on the label, the reference samples shall be maintained for a period of three months beyond the date of expiry of potency. In case of drugs where no date of expiry is specified on the label the reference samples shall be maintained for a period of three years from the date of manufacture.]

[3][(n) The licensee, who has been granted a license in

Form 28B shall–

(i) forward to the licensing authority of the concerned States of manufacture and supply of the drug a statement of the sales effected to manufacturers, wholesalers, retailers, hospitals, dispensaries and Nursing Homes and Registered Medical Practitioners every three months;

(ii) maintain accounts of all transactions giving details as indicated below in a register bound and serially page numbered and such records shall be retained for a period of five years or one year after the expiry of potency, whichever is later.

A. Accounts of the drugs specified in Schedule X used for the manufacture:-

1. Date of issue.
2. Name of the drug.
3. Opening balance of stock on the production day.
4. Quantity received, if any, and source from where received.
5. Quantity used in manufacture.
6. Balance quantity on hand at the end of the production day.
7. Signature of the person in charge.

1. Subs. by F.1-14/68-B (SO3868), dt. 26-10-1968.
2. Ins. by G.S.R. 444, dt. 28-4-1973.
3. Ins. by G.S.R. 462 (E), dt. 22-6-1982.

B. Accounts of Production:

1. Date of manufacture.
2. Name of the drug.
3. Batch Number.
4. Quantity of raw material used in manufacture.
5. Anticipated yield.
6. Actual yield.
7 Wastage.
8. Quantity of the manufactured goods transferred.

C. Accounts of the manufactured drugs:

1. Date of manufacture.
2. Name of the drug.
3. Batch Number.
4. Opening Balance.
5. Quantity manufactured.
6. Quantity sold.
7. Name of the purchaser and his address.
8. Balance quantity at the end of the day.

(o) The licensee shall store drugs specified in Schedule X in bulk form and when any of such drug is required for manufacture in a place other than its place of storage it shall be kept in a separate place under the direct custody of a responsible person.]

[1][(p) The licensee shall comply with the requirements of [3][‗Good Manufacturing Practices' as laid down in Schedule L-1 and Good Manufacturing Practices' as laid down in Schedule M.]

[4][(q) No advertisement of the drugs specified in Schedule H, Schedule H1 or Schedule X shall be made except with the previous sanction of the Central Government.]

[2]**[78A. Conditions of license in [5][Form 28A or Form 28DA]-** (1) The license in [5][Form 28A of Form 28DA] shall be deemed to be cancelled or suspended, if the licence owned by the licensee in [6][[5][Form 28 or Form 28D] whose manufacturing facilities have been availed of by the licensee is cancelled or suspended, as the case may be, under these rules.

1. Ins. by G.S.R. 735 (E), dt. 24-6-1998.
2. Amended by F.1-14/68-D (S.O. 3868), dt. 26-10-1968.
3. Ins. by G.S.R. 780 (E), dt. 10-9-2008.
4. Ins. by G.S.R. 289 (E), dt. 15-4-2015.
5. Subs. by G.S.R. 574 (E), dt. 17-7-2012.
6. Subs. by G.S.R. 592 (E), dt. 13-8-2008.

(2) The licensee shall comply with the provisions of the Act, and of these rules and with such further requirements if any, as may be specified in any rules subsequently made under Chapter IV of the Act, provided that where such further requirements are specified in the rules, those would come into force four months after publication in the Official Gazette.

(3) The licensee shall test each batch or lot of the raw material used by him for the manufacture of his products and also each batch of the final product and shall maintain records or registers showing the particulars in respect of such tests as specified in Schedule U. Records or registers shall be retained, in the case of a substance for which a potency date is fixed, for a period of two years from the expiry of such date and in the case of other substances, for a period of five years from the date of manufacture. The licensee shall allow an Inspector to inspect all registers and records maintained under these rules and shall supply to the Inspector such information as he may require for the purpose of ascertaining whether the provisions of the Act and these rules have been observed.

(4) The licensee shall either (i) provide and maintain to the satisfaction of the Licensing Authority adequate staff and adequate laboratory facilities for carrying out tests of the strength, quality and purity of the substances manufactured by him, or (ii) make arrangements with some institution approved by the Licensing Authority for such tests to be regularly carried out on his behalf by the institution.]

[1][(5) The licensee shall furnish to the Licensing Authority, if required to do so, data on the stability of drugs which are likely to deteriorate for fixing the date of expiry which would be printed on the labels of such drugs on the basis of the data so furnished.]

[2][(6) The licensee shall maintain reference samples from each batch of the drug manufactured by him in a quantity which is at least twice the quantity of the drug required to conduct all the tests performed on the batch. In case of drugs bearing an expiry date on the labels, the reference samples shall be maintained for a period of three months beyond the date of expiry of potency. In case of drugs where no date of expiry of potency is specified on the label, the reference samples shall be maintained for a period of three years from the date of manufacture.]

[3][(7) The licensee shall maintain an Inspection Book in

Form 35 to enable an Inspector to record his impressions and the defects noticed.]

4[(8) No advertisement of the drugs specified in Schedule H, Schedule H1 or Schedule X shall be made except with the previous sanction of the Central Government.

5[**79. Inspection before grant or renewal of licence**.–Before a licence under

1. Ins. by G.S.R. 444, dt. 28-4-1973.
2. Subs. by G.S.R. 574 (E), dt. 17-7-2012.
3. Ins. by G.S.R. 331 (E), dt. 8-5-1984.
4. Ins. by G.S.R. 289 (E), dt. 15-4-2015.
5. Subs. by G.S.R. 923 (E), dt. 14-12-1992.

this Part is granted or renewed the Licensing Authority or Central Licence Approving Authority, as the case may be, shall cause the establishment in which the manufacture is proposed to be conducted or being conducted to be inspected by one or more Inspectors appointed under this Act with or without an expert in the concerned field. The Inspector or Inspectors shall examine all portions of the premises, plant and appliances and also inspect the process of manufacture intended to be employed or being employed along with the means to be employed or being employed for standardizing and testing the drugs to be manufactured or being manufactured and enquire into the professional qualifications of the technical staff to be employed. He shall also examine and verify the statements made in the application in regard to their correctness, and the capability of the applicant to comply with the requirements of competent technical staff, manufacturing plants, testing equipments and the ‗Requirements of Good Manufacturing Practices' and the ‗Requirements of Plant and Equipment' as laid down in Schedule M read with the Requirements of Maintenance of Records as laid down in Schedule U.]

1[**80**. ***Report by Inspector.***–The Inspector shall forward a detailed descriptive report giving his findings on each aspect of inspection along with his recommendations after completion of his inspection in accordance with the provisions of Rule 79, to the Licensing Authority or Central Licence Approving Authority, as the case may be.]

81. ***Procedure of Licensing Authority***.–(1) If the Licensing Authority 5[or Central Licence Approving Authority, as the case may be,] after such further enquiry, if any, as he may consider necessary, is satisfied that the requirements of the Rules under the Act have been complied with and that the conditions of the licence and the Rules under the Act will be observed, he 2[shall issue a licence under this Part].

(2) If the Licensing Authority 5[or Central Licence Approving Authority, as the case may be,] is not so satisfied, he shall reject the application and shall inform the applicant of the reasons for such rejection and of the conditions which must be satisfied before a licence can be granted and shall supply the applicant with a copy of the inspection report.

3[**82**. ***Further application after rejection.***–If within a period of six months from the rejection of an application for a licence the applicant informs the Licensing Authority 5[or Central Licence Approving Authority, as the case may be,] that the conditions laid down have been satisfied and deposits an inspection 4[fee of rupees two hundred and fifty] the Licensing Authority 5[or Central Licence Approving Authority, as the case may be,] may, if after causing a further inspection to be made, he is satisfied that the conditions for the grant of a licence have been complied with, 5[in respect of drugs notified under Rule 68-A] issue a licence in Form 28 2[or Form 28-B].

1. Subs. by G.S.R. 923 (E), dt. 14-12-1992.
2. Ins. by G.S.R. 462 (E), dt. 22-6-1982.
3. Ins. by F.1-16/57-D, dt. 15-6-1957.

4. Subs. by G.S.R. 601 (E), dt. 24-8-2001.
5. Ins. by G.S.R. 923 (E), dt. 14-12-1992.

83. Renewal.−On application being made for renewal, the licensing authority may cause an inspection to be made and, if satisfied that the condition of the licence and the Rules under the Act are, and will continue to be observed, [1][he shall prepare a report to that effect in respect of those drugs which have been notified by the Central Government under Rule 68-A and forward it along with the application to the Central Licence Approving Authority], and shall issue a certificate of renewal [3][under this Part].

3[**83-A**. ***Certificate of renewal of a loan licence***.–The certificate of renewal of a loan licence in 8[

Form 28A or Form 28DA] shall be issued in Form 26A or Form 26J respectively.]

4[**83-AA**. ***Duration of loan licence***.−An original loan licence in 8[Form 28A or Form 28DA] or a renewed loan licence in 8[Form 26A or Form J], unless sooner suspended or cancelled, shall be 5[valid for a period of five years on and from the date on which] it is granted or renewed:

6[Provided that if the application for the renewal of a licence is made before its expiry, or if the application is made within six months of its expiry, after payment of the additional fee, the licence shall continue to be in force until orders are passed on the application and the licence shall be deemed to have expired if the application for its renewal is not made within six months of its expiry].]

84. The provisions of this Part shall apply to the manufacture of drugs for sale notwithstanding that such drugs are manufactured for sale outside India.

7[6[**84-A**. ***Provision for appeal to the State Government or Central Government by party whose licence has not been granted or renewed.***−

Any person who is aggrieved by the order passed by the Licensing Authority or the Central Licence Approving Authority, as the case may be, refusing to 2[grant or renew a licence under this Part], may within thirty days from the date of receipt of such order, appeal to the State Government or Central Government, as the case may be, and the State Government or the Central Government may, after such enquiry into the matter,] as is considered necessary and after giving the said person an opportunity for representing his views, may pass such order in relation thereto as it thinks fit.]

1. Ins. by G.S.R. 923 (E), dt. 14-12-1992.
2. Subs. by G.S.R. 119 (E), dt. 11-3-1996..
3. Ins. by F1-16/57-B, dt. 15-6-1957.
4. Ins. by Notfn. No. F. 1-10/62-D, dt. 10-4-1964.
5. Subs. by G.S.R. 601 (E), dt. 24-8-2001.
6. Subs. by S.O. 2139, dt. 12-8-1972.
7. Subs. by G.S.R. 923 (E), dt. 14-12-1992 as corrected by G.S.R. 373 (E), dt. 13-4-1993. 8.
Subs. by G.S.R. 574 (E), dt. 17-5-2012.

6[**84AA.** *Additional information to be furnished by an applicant for licence or a licensee to the licensing authority*.-The applicant for the grant of a licence or any person granted a licence under this Part shall, on demand, furnish to the Licensing Authority, before the grant of the licence or during the period the licence is in force, as the case may be, documentary evidence in respect of the ownership or occupation on rental or other basis of the premises, specified in the application for licence or in the licence granted, constitution of the firm or any other relevant matter which may be required for the purpose of verifying the correctness of the statements made by the applicant or the licensee, while applying for or after obtaining the licence, as the case may be.]

1[**84B.** *Prohibition for the manufacture for sale of cyclamates and preparations containing cyclamates*.–No person shall manufacture for sale cyclamates and preparations containing cyclamates.]

2[**85.** *Cancellation and suspension of licences*.-(1) The Central Licence Approving Authority may, after giving the licensee an opportunity to show cause why such an order should not be passed, by an order in writing stating the reasons therefor, cancel a licence issued under this Part, or suspend it for such period as he thinks fit either wholly or in respect of any of the drugs to which it relates 3[or direct the licensee to stop manufacture, sale or distribution of the said drugs and 4[thereupon order the destruction of drugs and] the stock thereof in the presence of an Inspector], if in his opinion, the licensee has failed to comply with any of the conditions of the licencee or with any provisions of the Act or rules made thereunder.

(2) The Licensing Authority may, for such licences granted or renewed by him, after giving the licensee an opportunity to show cause why such an order should not be passed, by an order in writing stating the reasons therefor, cancel a licence issued under this Part or suspend it for such period as he thinks fit, either wholly or in respect of some of the substances to which it relates, [3][or direct the licensee to stop manufacture, sale or distribution of the said drugs and [4][thereupon order the destruction of drugs and] the stock thereof in the presence of an Inspector] if, in his opinion, the licensee has failed to comply with any of the conditions of the licence or with any provisions of the Act or rules made thereunder.]

[5][(3) A licensee whose licence has been suspended or cancelled by the Central Licence Approving Authority or Licensing Authority under sub-rule (1) or sub-rule (2), as the case may be, may within ninety days of the receipt of a copy of the order by him prefer an appeal to the Central Government or the State Government, as the case may be, and the Central Government or the State Government may after giving the licensee an opportunity of being heard, confirm, reverse or modify such order.]

1. Ins. by S.O.2358, dt. 26-8-1972.

2. Subs. by G.S.R. 923 (E), dt. 14-12-1992 as corrected by G.S.R. 373 (E), dt. 13-4-1993. 3. Ins. by G.S.R. 20 (E), dt. 11-1-1996.

4. Ins. by (Corrigenda) G.S.R. 514 (E), dated 5.11.1996.

5. Ins. by 615 (E), dt. 9-8-1994 as corrected by G.S.R. 55 (E), dt. 7-2-1995.

6. Ins. by S.O. 2139, dt. 5-6-1972.

[1][PART VIIA
[2][MANUFACTURE FOR SALE OR FOR DISTRIBUTION] OF HOMOEOPATHIC MEDICINES

85A .*Manufacture on more than one set of premises*.-If Homoeopathic medicines are manufactured in more than one set of premises a separate application shall be made and a separate licence shall be obtained in respect of each such set of premises.

85B. *Application for licence to manufacture Homoeopathic medicines*. (1) Application for grant or renewal of [2][licence to manufacture for sale or for distribution] of Homoeopathic medicines shall be made to the Licensing Authority appointed by the State Government for the purpose of this Part (hereinafter in this

Part referred to as the Licensing Authority) and shall be made in

Form 24-C.

[3][(2) The application in

Form 24-C shall be accompanied–

(*a*) by a fee of [4][rupees two hundred] for the manufacture of Homoeopathic mother tinctures and potentised preparations and an inspection fee of [4][rupees one hundred] for the first inspection or [4][rupees fifty] in case of inspection for renewal of licence;

(*b*) by a fee of [4][rupees two hundred] for the manufacture of Homoeopathic potentised preparations only, and an inspection fee of [4][rupees one hundred] for

the first inspection or [4][rupees fifty] in case of inspection for renewal of licence;

(*c*) by a fee of [4][rupees two hundred] for the manufacture of potentised preparations from back potencies by pharmacies which are already licensed to sell Homoeopathic medicines by retail and an inspection fee of [4][rupees one hundred] for the first inspection or [4][rupees fifty] in case of inspection for renewal of licence.

1. Ins. under G.S.R. 1185 (E), dt. 18-8-1964.
2. Sub. by G.S.R. 788 (E), dt. 10-10-1985.
3. Sub. by G.S.R. 245, dt. 11-2-1976.
4. Subs. by G.S.R. 601 (E), dt. 24-8-2001.

[1][(3) If a person applies for renewal of a licence after its expiry but within six months of such expiry, the fee payable for the renewal of such a licence shall be_

(*a*) [2][rupees two hundred] plus an additional fee at the rate of [2][rupees one hundred] per month or part thereof and an inspection fee of [2][rupees fifty] for the manufacture of Homoeopathic mother tinctures and potentised preparations;

[4][(*b*)[2][rupees two hundred] plus an additional fee at the rate of [2][rupees one hundred] per month or part thereof and an inspection fee of [2][rupees fifty] for the manufacture of Homoeopathic potentised preparations only;]

(c) [2][rupees two hundred] plus an additional fee at the rate of [2][rupees one hundred] per month or part thereof and an inspection fee of [2][rupees fifty] for the manufacture of Homoeopathic mother tinctures and potentised preparations from back potencies by pharmacies who are already licensed to sell Homoeopathic medicines by retail.]

(4) A fee of [2][rupees fifty] shall be paid for a duplicate copy of the licence for the manufacture of Homoeopathic mother tinctures and potentised preparations issued under sub-rule (1) if the original is defaced, damaged or lost, while the fee to be paid for such a duplicate copy of the licence for the manufacture of Homoeopathic potentised preparations only shall be [2][rupees fifty].

[3][(5) Applications by licensee to manufacture additional items of Homoeopathic medicines shall be made to the Licensing Authority and such applications shall be accompanied by a fee of [2][rupees fifty] for each additional item.]

85C. *Application to manufacture _New Homoeopathic medicines.'* Subject to the other provisions of these Rules

(1) no _New Homoeopathic medicine' shall be manufactured unless it is previously approved by the Licensing Authority mentioned in Rule 21;

(2) the manufacturer of _New Homoeopathic medicine', when applying to the Licensing Authority mentioned in sub-rule (1) shall produce such documentary and other evidence as may be required by the Licensing Authority for assessing the therapeutic efficacy of the medicine including the minimum provings carried out with it.

1. Subs. by G.S.R. 245, dt. 3-2-1976.
2. Subs. by G.S.R. 601 (E), dt. 24-8-2001.
3. Ins. by G.S.R. 13 (E), dt. 7-1-1983.
4. Subs. by G.S.R. 779 (E), dt. 18-7-1980.

(3) While applying for a licence to manufacture a _New Homoeopathic medicine' an applicant shall produce along with his application evidence that the _New

Homoeopathic medicine‘ for the manufacture of which application is made has already been approved.

Explanation.−The term ‗New Homoeopathic medicine‘ in this rule shall have the same meaning as in rule 30AA.

[1][**85D**. *Form of licence to manufacture Homoeopathic medicines*.—Licence for manufacture of Homoeopathic medicines is a licence to manufacture potentised preparations from back potencies by Pharmacies who are already licensed to sell Homoeopathic medicines by retail and shall be granted in Form 25C.]

85E. *Conditions for the grant or renewal of a licence in*

Form 25C–Before a licence in Form 25C is granted or renewed the following conditions shall be complied with by the applicant:—

(1) The manufacture of Homoeopathic medicines shall be conducted under the direction and supervision of competent technical staff consisting at least of one person who is a whole time employee [2][and who is—

(a) a graduate in Science with Chemistry as one of the subjects with three years' experience in manufacture of Homoeopathic Medicines; or

(b) a graduate in Pharmacy with 18 months of experience in the manufacture of Homoeopathic medicines; or

(c) holds qualification as defined under sub-clause (g) of clause (1) of section 2 of Homoeopathy Central Council Act, 1973 (59 of 1973) with 18 months of experience in the manufacture of Homoeopathic medicines:

Provided that the persons who are already in employment with five years' experience in the manufacture of Homoeopathic medicines and whose name was accordingly entered in any licence granted in

Form 25C for manufacture of different classes of Homoeopathic medicines included in them shall be deemed to be qualified for the purpose of this rule.]

3[(2) The factory premises shall comply with the requirements and conditions specified in Schedule M-I:

1. Amended by F.1-59/68-D (SO 4816), dt. 19-11-1969.

2. Subs. by G.S.R. 812 (E), dt. 14-11-1994 as corrected by G.S.R. 517 (E), dt. 26-6-1995. 3. Subs. by G.S.R. 570 (E), dt. 12-6-1987.

Provided that where the Licensing Authority considers it necessary or expedient so to do, it may having regard to the nature and extent of manufacturing operations, relax or suitably alter the said requirements or conditions in any particular case for reasons to be recorded in writing.]

(3) The applicant for manufacture of Homoeopathic mother tinctures shall either (i) provide and maintain adequate staff, premises and laboratory equipment for identifying the raw materials and for testing the mother tinctures wherever possible, or (ii) make arrangements with some institution approved by the Licensing Authority 2[under Part XV(A) of these rules] for such tests, wherever possible, to be regularly carried out on his behalf by that institution.

(4) The premises where Homoeopathic medicines are manufactured shall be distinct and separate from the premises used for residential purposes.

(5) Homoeopathic medicines shall not be manufactured simultaneously with drugs pertaining to other systems of medicine.

(6) The applicant shall make arrangements for proper storage of Homoeopathic medicines manufactured by him:

1[Provided that in case potentised preparations are made in a Pharmacy holding licence in Form 20-C, the conditions (2) and (3) shall not apply. The licensee shall ensure to the satisfaction of the Licensing Authority that the products manufactured by it, conform to the claims made on the label.]

3[**85-EA.** *Inspection before grant or renewal of licence.*-- Before a licence under this Part is granted or renewed in Form 25C or Form 26C, the Licensing Authority shall cause the establishment, in which the manufacture is proposed, to be conducted or being conducted, to be inspected by one or more Inspectors shall examine all portions of the premises, plant and appliances and also inspect the process of manufacture intended to be employed or being employed along with the means to be employed or being employed for standardizing and testing the substances to be manufactured and inquire into the professional qualifications of the technical staff to be employed. He shall also examine and verify the statements made in the application in regard to their correctness, and the capability of the applicant to comply with the requirements of competent technical staff, manufacturing plants, testing equipments and the requirements of plant and equipment as laid down in Part I of Schedule M read with the requirements of maintenance of records as laid down in Schedule U.

1.Amended by F.1-59/68-D (SO 4816), dt. 19-11-1969.
2.Ins. by G.S.R. 1172 (E), dt. 23-8-1977.

3. Ins. by G.S.R. 493 (E), dt. 9-6-1995.

85EB. *Report by Inspector.*—The Inspector or Inspectors shall forward a detailed descriptive report giving his or their findings on each aspect of inspection along with his or their recommendations after completion of his or their inspection to the Licensing Authority.

85EC. *Grant or refusal of licence.*— (1) If the Licensing Authority after such further enquiry, if any, as he may consider necessary is satisfied that the requirements of the rules under the Act have been complied with and that conditions of the licence and the rules under the Act shall be observed, he shall grant or renew a licence in

Form 25C or Form 26C.

(2) If the Licensing Authority is not so satisfied, he shall reject the application and shall inform the applicant of the reasons for such rejection and of the conditions which must be satisfied before a licence can be granted or renewed and shall supply the applicant with a copy of inspection report.]

85ED. *Further application after rejection.* .—If within a period of six months from the rejection of an application for a licence, the applicant informs the Licensing Authority that the conditions laid down have been fulfilled and deposits an inspection fee of [1][rupees two hundred and fifty], the Licensing Authority may, if, after causing further inspection to be made, he is satisfied that the conditions for the grant of licence have been complied with, issue a licence in

Form 25C or Form 26C.

85EE. *Appeal to the State Government.*—Any person who is aggrieved by the order passed by the Licensing Authority refusing to grant or renew a licence under this Part may within ninety days from the date of receipt of such order, appeal to the State Government and the State Government may, after such enquiry into the matter as is considered necessary and after giving the said person an opportunity for representing the case, pass such order as it thinks fit.]

85F. *Duration of licence*.—An original licence or a renewed licence unless it is sooner suspended or cancelled shall be [1][valid for a period of five years on and from the date on which] it is granted or renewed:

[2][Provided that if the application for renewal of a licence in force is made before its expiry or if the application is made within six months of its expiry, after payment of additional fee, the licence shall continue to be in force until orders are passed on the application and the licence shall be deemed to have expired if application for its renewal is not made within six months of its expiry.]

85G. *Certificate of renewal*.—The certificate of renewal of a licence in

Form 25-C shall be issued in Form 26-C.

1. Subs. by G.S.R. 601 (E), dt. 24-8-2001.

2. Subs. by S.O. 2139, dt. 12-8-1972.

85H. *Conditions of licence*.—A licence in Form 25-C shall be subject to the conditions stated therein and to the following further conditions, namely :

(a) the licensee shall provide and maintain staff and premises as specified in Rule 85-E;

(b) the licensee shall allow an [1][Inspector appointed under the Act] to enter, with or without prior notice, any premises where the manufacture of a Homoeopathic medicine in respect of which the licence is issued is carried on, to inspect the premises and to take samples of the manufactured Homoeopathic medicines;

(c) the licensee shall allow an Inspector to inspect all registers and records maintained under these rules and shall supply to the Inspector such information as he may require for the purpose of ascertaining whether the provisions of the Act and the rules made thereunder have been observed;

[2][(d) the licensee shall maintain an Inspection Book in

Form 35 to enable an Inspector to record his impressions and defects noticed;]

(e) the licensee shall comply with the following conditions in respect of mother tinctures manufactured by him_

(i) the crude drug used in the manufacture of the mother tincture shall be identified and records of such identification shall be kept [3][for a period of five years];

(ii) the total solids in the mother tincture shall be determined and records of such tests shall be kept [3][for a period of five years];

(iii) the alcohol content in the mother tincture shall be determined and records of the same shall be maintained [3][for a period of five years];

(iv) the containers of mother tinctures shall preferably be of glass and shall be clean and free from any sort of impurities or adhering matter. The glass shall be neutral as far as possible;

(v) in the process of manufacture of mother tinctures hygienic conditions shall be scrupulously observed by the licensee. Storage and handling conditions shall also be properly observed by the licensee according to Homoeopathic principles;

1. Amended by G. S. R. 444, dt. 28-4-1973.
2. Amended by F-1-14/ 68-D, dt. 26-10-1968.
3. Ins. by G.S.R. 13(E), dt. 7-1-1983.

[1][(ea) no colour shall be added to any Homoeopathic medicines :

Provided that caramel may be added to combination of Homoeopathic preparations with syrup base;]

(f) records shall be maintained of Homoeopathic medicines containing alcohol and the quantities sold together with names and addresses of parties to whom sold.[2] [Such records shall be maintained for a period of five years.]

[3][**85HH.** *Additional information to be furnished by an applicant for the licence or a licensee to the Licensing Authority*.–The applicant for the grant of licence or any other person granted a licence under this Part shall, on demand, furnish to the Licensing Authority, before the grant of the licence or during the period the licence is in force, as the case may be, documentary evidence in respect of the ownership or occupation in rental or other basis of the premises, specified in the application for licence or in the licence granted, constitution of the firm or any other relevant matters which may be required for the purpose of verifying the correctness of the statements made by the applicant or the licensee, while applying for or after obtaining the licence, as the case may be.]

85-I. *Cancellation and suspension of licences*.– (1) The Licensing Autority may, after giving the licensee an opportunity to show cause why such an order should not be passed, by an order in writing stating the reasons therefor, cancel a licence issued under this Part or suspend it for such period as he thinks fit, either wholly or in respect of some of the substances to which it relates if, in his opinion, the licensee has failed to comply with any of the conditions of the licence or with any provisions of the Act or Rules made thereunder.

[4][(2) A licensee whose licence has been suspended or cancelled may, within three months of the date of the order under sub-rule (1), prefer an appeal against that order to the State Government, which shall decide the same.]

PART VIII

MANUFACTURE FOR EXAMINATION, TEST OR ANALYSIS

86. *Conditions relating to manufacture for examination, test or analysis.*–The provisions of Section 18 of the Act shall not apply to the manufacture of any drug in small

quantities for the purpose of examination, test or analysis if the conditions prescribed in this Part are fulfilled.

87. *Labelling*.–Any drug manufactured for the purpose of examination, test or analysis shall be kept in containers bearing labels indicating the purpose for which it has been manufactured.

88. *Labelling of drugs supplied to other persons*.─If any drug manufactured for the purpose of examination, test or analysis is supplied by the manufacturer to any other person, the container shall bear a label on which shall be stated the name and address of the manufacturer, the accepted scientific name of the substance if known, or if not known a reference which will enable the substance to be identified and the purpose for which it has been manufactured.

1. Ins. by G.S.R. 680 (E), dt. 5-12-1980.
2. Ins. by G.S.R. 13 (E), dt. 7-1-1983.
3. Ins. by S. O. 2139, dt. 12-8-1972.
4. Subs. G.S.R. 926, dt. 16-7-1977.

89. *Licence*.—If the person proposing to manufacture a drug for the purpose of examination, test or analysis does not hold a licence in

Form 25 or Form 28 in respect of such drugs he shall, before commencing such manufacture, obtain a licence in Form 29:

[1][Provided that in the case of a drug the composition of which is such that the drug is not generally recognized among experts qualified by scientific training and experience to evaluate the safety of drugs as safe for use, no licence in Form 29 shall be granted unless the applicant produces a certificate from the ―Licensing Authority‖ mentioned in Rule 21, to the effect that there would be no objection to such licence being granted.

90. *Form of application*.―[2][(1)] An application for a licence in Form 29 shall be made to the Licensing Authority appointed by the State Government for the purpose of this Part (hereafter in this Part referred to as the Licensing Authority) in Form 30 and shall be made by or countersigned by the head of the institution in which, or a director of the firm or company by which, the substance will be manufactured.

[4][(2) Every application in Form 29 shall be accompanied by a fee of [3][rupees two hundred fifty].

91. *Duration of licence*.―A licence in Form 29 shall, unless sooner cancelled, be in force for a period of one year from the date of issue, and may thereafter be renewed for periods of one year at a time.

92.*Conditions of licence*. −A licence in Form 29 shall be subject to the following conditions

(a) the licensee shall use the drugs manufactured under the licence exclusively for purpose of examination, test or analysis, and shall carry on the manufacture and examination, test or analysis at the place specified in the licence;

(b) the licensee shall allow any [3][inspector appointed under the Act] to enter, with or without notice, the premises where the drugs are manufactured and to satisfy himself that only examination, test or analysis work is being conducted;

(c) the licensee shall keep a record of the quantity of drugs manufactured for examination, test or analysis and of any person or persons to whom the drugs have been supplied;

(d) the licensee shall comply with such further requirements, if any, applicable to the holders of licences in

Form 29 as may be specified in any rules subsequently made under the Act and of which the Licensing Authority has given him not less than one month's notice;

(e) the licensee shall maintain an Inspection Book to enable an Inspector to record his impressions and defects noticed.

93. *Cancellation of licences.*-

(1) The Licensing Authority may after giving the licensee an opportunity to show cause why such an order should not be passed, by an order in writing stating the reasons therefor, cancel a licence issued under this Part, either wholly or in respect of some of the substances to which it relates, if, in his opinion, the licensee has failed to comply with any of the conditions of the licence or with any provision of the Act or Rules thereunder

1. Ins. under F. 1-19/59-D (SO 1449), dt. 13-6-1961.

2. Re-numbered by S.O. 903, dt. 28-2-1976.

3. Subs. by G.S.R. by 444, dt. 31.3.1973.

4. Ins. by S.O 903, dt. 28-2-1976.

[1][(2) A licensee whose licence has been suspended or cancelled may appeal to the State Government within three months of the date of the order.]

PART IX
LABELLING AND PACKING OF DRUGS OTHER THAN HOMOEOPATHIC MEDICINES

94. *Exemption of certain drugs from certain provisions of this Part.*— (1) Labels on packages or containers of drugs for export shall be adapted to meet the specific requirements of the law of the country to which the drug is to be exported but the following particulars shall appear in a conspicuous position on the innermost container in which the drug is packed and every other covering in which that container is packed:

(a) name of the drug;

(b) the name, address of the manufacturer and the number of the licence under which the drug has been manufactured;

(c) batch or lot number;

(d) date of expiry, if any:

[2][Provided that where a drug, not classified under Schedule F, Schedule F(1) and Schedule X, [5][or blood products defined under rule 122EA] is required by the consignee to be not labelled with the name and address of the manufacturer, the labels on packages or containers shall bear a code number as approved by the Licensing Authority mentioned in Rule 21.]

[4][Provided further that where a drug classified as Narcotic Drug or Psychotropic Substance is to be exported under a code number, the same may be permitted by the said licensing authority on the following conditions, namely:-

(i)Each consignment of export shall be accompanied with requisite import license from the importing country;

(ii)The applicant shall obtain a no objection certificate from the Drugs Controller, India for manufacture of such formulations to be exported with code number against each export order along with certificate from the regulatory authority of the importing country controlling Narotic Drugs and Psychotropic Substances that they do not have any objection for the import of the drug with code number;

(iii)The State Licensing Authority shall issue the manufacturing license for these formulations on each export order on the basis of a No Objection Certificate from Drugs Controller, India;

(iv)A no objection certificate shall be obtained from the drugs Controller, India for export of each consignment; and

(v)A no objection certificate shall be obtained from the Narcotic Commissioner of India,

Gwalior for export of each consignment of the drug.]

3[(2) The provisions of Rules 96 to 101 inclusive, shall not apply to a medicine made up ready for treatment, whether after or without dilution, which is supplied on the prescription of a registered practitioner provided that:

(*i*) the medicine is labelled with the following particulars : ―

(*a*) the name and address of the supplier;

(*b*) the name of the patient and the quantity of the medicine;

(*c*) the number representing serial number of the entry in the prescription register;

1. Subs. by F.1-10/68-D (S.O 2482), dt. 17-6-1969.
2. Ins. by G.S.R. 676 (E), dt. 2-6-1988.
3. Subs. by F.1-19/59-D, dt. 13-6-1961.
4. Ins. by G.S.R. 592 (E), dt. 13-8-2008.
5. Subs. by 592 (E), dt. 13-8-2008.

(*d*) the dose, if the medicine is for internal use;

1[(*e*) the words ―FOR EXTERNEL USE ONLY‖ shall be printed on the label if the medicine is for external application].

(*ii*) Condition (3) of the conditions in Rule 65 is satisfied.]

95. *Prohibition of sale or distribution unless labelled.*—Subject to the other provisions of these Rules, no person shall sell or distribute any drug (including a patent or proprietary medicine) unless it is labelled in accordance with these Rules.

2[**96**. *Manner of Labelling .— (1)* Subject to the other provisions of these Rules, the following particulars shall be either printed or written in indelible ink and shall appear in a conspicuous manner on the label of the innermost container of any drug and on every other covering in which the container is packed, namely :—

(*i*) the name of the drug−

3[(*A*) for this purpose, the proper name of the drug shall be printed or written in a more conspicuous manner than the trade name, if any, which shall be shown immediately after or under the proper name and shall be]—

(*a*) for drugs included in the Schedule F or Schedule F (1), the name given therein;

(*b*) for drugs included in the Indian Pharmacopoeia or the official pharmacopoeias and official compendia of drug standards prescribed in Rule 124, the name or synonym specified in the respective official pharmacopoeias and official compendia of drug standards followed by the letters ‗I.P., or, as the case may be, by the recognized abbreviations of the respective official pharmacopoeias and official compendia of drug standards;

(*c*) for drugs included in the National Formulary of India, the name or synonym specified therein followed by the letters ‗N.F.I.‘;

(*d*) for other drugs, the international non-proprietary name, if any, published by the World Health Organisation or where an international non-proprietary name is not published, the name descriptive of the true nature or origin of the substance;

4[* * * * *]

(*ii*) A correct statement of the net content in terms of weight, measure, volume, number of units of contents, number of units of activity, as the case may be, and the weight, measure and volume shall be expressed in Metric system.

1. Subs. by G.S.R. 462 (E), dt. 22-6-1982.

2 Amended under G.S.R.19, dt. 15-12-1977.

3. Subs. by G.S.R. 27(E), dt. 17-1-1981.

4. Sub-clause (B) omitted by G.S.R. 94 (E), dt. 8-2-2000. Earlier ins. by G.S.R. 27 (F), dt.-1-1981.

(*iii)* The content of active ingredients−

This shall be expressed−

(a) for oral liquid preparations in terms of the content per single dose, being indicated in 5 millilitres [1][** *]:

Provided that where the dose is below 5 millilitres the contents of active ingredients may be expressed in terms of 1 millilitre; [2][or fraction thereof:]

[3][Provided further that where the single dose is more than 5 millilitres, the content of active ingredients shall be expressed in terms of minimum single dose as approved by the licensing authority;]

(*b*) for liquid parenteral preparations ready for administration in terms of 1 millilitre or percentage by volume or per dose in the case of single dose container :

Provided that if the preparation is contained in an ampoule it will be enough if the composition is shown on the label or wrapper affixed to any package in which such ampoule is issued for sale;

(c) for drugs in solid form intended for parenteral administration, in terms of units or weight per milligram or gram;

(d) for tablets, capsules, pills and the like, in terms of the content in each tablet, capsule, pill or other unit, as the case may be;

(e) for other preparations, in terms of percentage by weight or volume or in terms of unitage per gram or millilitre, as the case may be:

Provided that clause (iii) shall not apply to the pharmacopoeial preparations where the composition of such preparation is specified in the respective pharmacopoeia and to a preparation included in the National Formulary of India.

(iv) [4][The name of the manufacturer and the address of the premises of the manufacturer where the drug has been manufactured:]

Provided that if the drug is contained in an ampoule or a similar small container, it shall be enough if only the name of the manufacturer and his principal place of [5][manufacture] is shown.

(v) A distinctive batch number, that is to say, the number by reference to which details of manufacture of the particular batch from which the substance in the container is taken are recorded and are available for inspection, the figure representing the batch number being preceded by the words ‗Batch No.' or ‗B. No.' or ‗Batch' or ‗Lot No.' or ‗Lot'.

NOTES

(1) In the case of drugs manufactured by a continuous process, like manufacture of magnesium sulphate, pharmaceutical chemicals etc., the production resulting in one homogenous mix of the finished products shall be considered as one ―Batch‖.

1. Omitted by G.S.R. 285 (E), dt. 16-7-1996.

2. Ins. by G.S.R. 681(E), dt. 5-12-1980.

3. Ins. by G.S.R. 285 (E), dt. 16-7-1996.

4. Subs. by G.S.R. 491 (E), dt. 25-7-1991.

5. Subs. by G.S.R. 17 (E), dt. 7-1-1986.

(2) In the case of powders, liquid orals, ointments etc., one ―Batch Number‖ shall be assigned to all the containers filled from one homogenous bulk.

(3) In the case of tablets, capsules, lozenges, troches, etc., one ―Batch Number‖ shall be assigned to the products manufactured from one homogenous mix ready for compression or filling.

(4) In the case of parenteral preparations sterilized by steam under pressure, one ―Batch Number‖ shall be assigned to all containers filled from one homogenous bulk solution and sterilized in one sterilizer load.

(5) In the case of containers of parenteral preparations filled from one homogenous bulk solution and sterilized in more than one sterilizer load, the ―Batch Number‖ assigned to the containers in the different sterilizer loads shall be the same ―Batch Number‖ as is assigned to the homogenous bulk solution, provided the samples taken from all the sterilizer loads pass the sterility test, and are kept separate from one another until the report of the sterility test is available.

Explanation.— For the purpose of chemical and other tests, representative samples from all containers filled from the homogenous bulk solution should be taken.

(6) In the case of parenteral and other sterile products filled aseptically, a ―Batch Number‖ shall be assigned to all containers filled from one homogenous mix during one filling operation, the filling operation being completed in a period of not more than a day and during which no schedule change in the filling assembly is made.

When containers are filled from one homogenous mix, in a number of filling operations, the ―Batch Number‖ assigned to the containers filled in individual filling operations shall be the same ―Batch Number‖ as is assigned to the homogenous mix, provided the samples taken from all the different filling operations pass the sterility tests, and are kept separate from one another until the report of the sterility test is available.

Explanation.-For the purpose of chemical and other tests, representative samples from all containers filled from the homogenous mix should be taken.

(7) In the case of medicinal gases produced by a continuous process of operation a week‘s production from one tank load shall be considered as a Batch.

(vi) Every drug manufactured in India shall bear on its label the number of the licence under which the drug is manufactured, the figure representing the manufacturing licence number being preceded by the words ―Manufcaturing Licence Number‖ or ―Mfg. Lic. No.‖ or ―M.L.‖.

(vii) Drugs specified in Schedule P and their preparations including combinations with other drugs shall bear on their labels the date of manufacture, and the date of expiry of potency, and the period between the date of manufacture

and the date of expiry shall not exceed that laid down in the said Schedule [1][under the conditions of storage specified therein. [2][Drugs and their preparations not included in Schedule P], shall bear on their labels the date of their manufacture and also the date of their expiry which shall not exceed sixty months from the date of manufacture:]

Provided that this period may be extended by the Licensing Authority specified in clause (b) of Rule 21 in respect of any specified drug if satisfactory evidence is produced by the manufacturer to justify such an extension.

[7][(viii) Drugs specified in Schedule C(I) and their preparations including combinations in other drugs shall bear on their labels (a) the date of manufacture, and (b) date of expiry of potency fixed by the manufacturer:

3[4[Provided that drugs in bulk form included in Schedule C(I) which are not ready for use and not included in Schedule P need not bear on the label the date of expiry of potency:]

Provided further that no reference shall be made to any other licence number granted by any authority outside India on any label or container or in any covering in which the container is packed or in any other matter or advertisement enclosed therewith].

(ix) Every drug intended for distribution to the medical profession as a free sample shall, while complying with the labelling provisions under clauses (i) to (viii), further bear on the label of the container the words _Physician's Sample—Not to be sold' which shall be overprinted.

5[(x) If any preparation contains not less than 3 per cent by volume of alcohol the quantity of alcohol shall be stated in terms of the average percentage by volume of absolute alcohol in the finished products.]

6[(xi) In addition to the other particulars which are required to be printed or written under these Rules, the label of innermost container of the following categories of drugs and every other covering in which the container is packed shall bear a conspicuous red vertical line on the left side running throughout the body of the label which should not be less than 1mm in width and without disturbing the other conditions printed on the label under these rules, namely: —

1. Subs. by G.S.R. 17 (E), dt. 7-1-1986.
2. Subs. by G.S.R. 285 (E), dt. 16-7-1996.
3. Subs. by G.S.R. 487(E), dt. 2-7-1984.
4. Subs. by G.S.R. 813 (E), dt. 27-7-1988.
5. Ins. by G.S.R. 462 (E), dt. 22-6-1982.
6. Ins. by G.S.R. 597 (E), dt. 17-6-1992.
7. Subs. by G.S.R. 592 (E), dt. 13-8-2008.

Narcotic analgestics, hypnotics, sedatives, tranquillisers, corticosteroids, hormones, hypoglycemics, antimicrobials, antiepileptics, antidepressants, anticoagulants, anti-cancer drugs and all other drugs falling under Schedules _G', _H', and _X' whether covered or not in the above list:

Provided that the provisions of this clause shall not apply to: − (a) preparations intended for animal treatment;

(b) preparations intended for external use;

(c) ophthalmic preparations and ear drops; and

(d) sterile preparations such as sutures, surgical dressings and preparations intended for parenteral use.]

1[(xii) Drugs and their preparations including combinations with other drugs imported into the country shall also bear on the label, the license number under which the drug is imported, preceded by the words ―Import License‖ and the name and address of the importer.]

(2)(i) The particulars to be printed or written on the label of a mechanical contraceptive shall be as specified in Schedule R.

(ii) The following particulars, in addition to those specified under sub-rule (1) shall be either printed or written in indelible ink and shall appear in a conspicuous manner on the label of the innermost container and on every other covering in which the container of a contraceptive, other than a mechanical contraceptive, is packed, namely : −

(a) the date of manufacture;

(b) the date upto which the contraceptive is expected to retain its properties;

(c) the storage conditions necessary for preserving the properties of the contraceptive upto the date indicated in sub-clause (b) :

Provided that for oral contraceptives it shall be sufficient to display on the label of the container the date of manufacture only.

(3)(i) The particulars prescribed in sub-rule (1) shall be printed or written in indelible ink either on the label borne by a container of vaccine lymph or on a label or wrapper affixed to any package in which the container is issued for sale. The said particulars shall be indelibly marked on the sealed container of surgical ligature or suture or printed or written in indelible ink on a label enclosed therein.

(ii) Nothing in these rules shall be deemed to require the labelling of any transparent cover or of any wrapper, case or other covering used solely for the purpose of packing, transport or delivery.

(4) Where by any provision of these rules any particulars are required to be displayed on a label on the container, such particulars may, instead of being displayed on a label, be etched, painted or otherwise indelibly marked on the container:

1. Ins. by G.S.R. 592 (E), dt. 13-08-2008.

Provided that, except where otherwise provided in these rules, the name of the drug or any distinctive letters intended to refer to the drug shall not be etched, painted or otherwise indelibly marked on any glass container other than ampoules.

Explanation.— For the purpose of this rule, the date of expiry shall be in terms of month and year and it shall mean that the drug is recommended till the last day of the month. The date of expiry shall be preceded by the words ‗Expiry date'.]

97. *Labelling of medicines.*— [1][(1) The container of a medicine for internal use shall—

(a) if it contains a substance specified in Schedule G, be labelled with the words ―Caution: it is dangerous to take this preparation except under medical supervision‖ – conspicuously printed and surrounded by a line within which there shall be no other words;

(b) if it contains a substance specified in Schedule H, be labelled with the symbol Rx and conspicuously displayed on the left top corner of the label and be also labelled with the following words:

‗Schedule H drug- Warning: To be sold by retail on the prescription of a Registered Medical Practitioner only',

(c) if it contains a substance specified in Schedule H, and comes within the purview of the [2][Narcotic Drugs and Psychotropic Substances Act, 1985 (61 of 1985)] be labelled with the symbol NRx which shall be in red and conspicuously displayed on the left top corner of the label, and be also labelled with the following words:

‗Schedule H drug -*Warning:* To be sold by retail on the prescription of a Registered Medical Practitioner only';

(d) If it contains a substance specified in Schedule X, be labelled with the symbol XRx which shall be in red conspicuously displayed on the left top corner of the label and be also labelled with the following words : -

‗Schedule X drug -*Warning:* To be sold by retail on the prescription of a Registered Medical Practitioner only'.

[4][(e) if it contains a drug substance specified in Schedule H1, the drug formulation shall be labeled with the symbol Rx which shall be in red conspicuously displsyed on the left top corner of the label, and shall also be labelled with the following words in a box with a red border:

"SCHEDULE H1 DRUG – WARNING.

- It is dangerous to take this preparation except in accordance with the medical advice.
- Not to be sold by retail without the prescription of a Registered Medical

(2) The container of an embrocation, liniment, lotion, [3][ointment, antiseptic cream,] liquid antiseptic or other liquid medicine for external application shall be labelled with the words:

―FOR EXTERNAL USE ONLY‖.

1. Subs. by G.S.R. 462 (E), dt. 22-6-1982.

2. Subs. By G.S.R. 282(E), dt. 16.7.1996. As corrected by G.S.R. 241(E), dt. 15.4.1998.

3. Ins. by G.S.R. 850 (E), dt. 7-12-1994.

4. Subs. by G.S.R. 588 (E), dt. 30-8-2013.

[1][(3) The container of a medicine made up ready only for treatment of an animal shall be labelled conspicuously with the words _Not for human use; for animal treatment only' and shall bear a symbol depicting the head of a domestic animal.] [2][* * * * *]

[10][(3A) The container of a medicine for treatment of food producing animals shall be labeled with the withdrawal period of the drug for the species on which it is intended to be used:

Provided that if the specific withdrawal period has not been validated, the withdrawal period shall not be less than seven days for eggs or milk, twenty eight days for meat from poultry and mammals including fat and offal, five hundred degree days for fish meat.

Explanation:- For the purpose of this Rule, the withdrawal period is the period of interval between the last administration of a veterinary medicine to animals under the normal conditions of use and the production of food stuff from such animals to ensure that food stuffs do not contain residues in quantities in excess of the maximum residue limits laid down.]

[3][(4)] The container of a medicine prepared for treatment of human ailments shall if the medicine contains industrial methylated spirit, indicate this fact on the label and be labelled ~~wi~~th the words :

―For External Use only‖.

[4][(5) Substances specified in Schedule X in bulk form shall bear a label wherein the symbol as specified in sub-Rule (1) shall be given conspicuously in red letters.] [5][* * * * *]

[6][**102**. *Non-Sterile Surgical Ligature and Suture.*- Every container of, and wrapper enclosing surgical ligature or suture other than a ligature or suture offered or intended to be offered for sale as sterile, shall bear a label on which are printed or written in a conspicuous manner in indelible red ink the words ―Non-sterile surgical ligature (suture) – not to be used for operations upon the human body unless efficiently sterilized‖.]

103. [7][* * * * *]

(2) The name and address of the manufacturer shall be printed on the label of the container of a patent or proprietary medicine.

[8][(3) The true formula or list of the ingredients shall be printed or written in indelible ink on the outer label of every package containing patent or proprietary medicine.]

[9][**104 Use of letter I.P. etc.**--The letters _I.P'. and recognized abbreviations of pharmacopoeias and official compendia of drug standards prescribed under these Rules shall be entered on the label of the drug only for the purpose of indicating that the drug is in accordance with standards set out in the Indian Pharmacopoeia or in any such pharmacopoeia or official compendium of drug standards recognized under the Rules.]

1. Subs. by notification No. F.1-6/62-D(S.O.2889),, dt. 2.7.1969.

2. Subs. (4) omitted by G.S.R. 462 (E), dt. 22-1-1982.
3. Sub-rule (5) re-numbered as sub-Rule (4), by G.S.R. 462 (E), dt. 22-6-1982.
4. Ins. by G.S.R. 462 (E), dt. 22-6-1982.
5. Rules 98, 99,100 and 101 omitted, by G.S.R. 462 (E), dt. 22-6-1982.
6. Sub. by F. No. F1-3/51-DS, dt. 15.10.1954.
7. Sub-rule (1) omitted by S.O. 2136, dt. 15.6.1957.
8. Sub. by S.O. 2136, dt. 15.6.1957.
9. Sub. by G.S.R. 19, dt. 15.12.1977.
10. Ins. by G.S.R. 128 (E), dt. 17.1.2012.

1[**104A.** *Prohibition against altering inscriptions on containers, labels or wrappers of drug.* – No person shall alter, obliterate or deface any inscription or mark made or recorded by the manufacturer on the container, label or wrapper of any drug:

Provided that nothing in this rule shall apply to any alteration, any inscription or mark made on the container, label or wrapper of any drug at the instance or direction or with the permission of the Licensing Authority.]

2[**105. Packing of drugs.–**(1) The pack sizes of drugs meant for retail sale shall be as prescribed in Schedule P1 to these rules.

(2) The pack sizes of drugs not covered by Schedule P-1 shall be as given below: –

Unless specified otherwise in Schedule P-1,

(i) The pack sizes for Tablets/Capsules shall be–

Where the number of Tablets (coated or uncoated)/Capsules (hard or soft gelatin) is less than 10, such packing shall be made by the integral number. For numbers above 10, the pack size of Tablets/Capsules shall contain multiples of 5.

(ii) The pack sizes for liquid Oral preparations shall be 30 ml (paediatric only)/60 ml/100 ml/200 ml/450 ml.

(iii) The pack sizes for Paediatric Oral Drops shall be 5 ml/10 ml/15 ml.

(iv) The pack sizes for Eye/Ear/Nasal drops shall be 3 ml/5 ml/10 ml.

(v) The pack size for Eye Ointment shall be 3 gm/5 gm/ 10 gm:

Provided that the provisions of the pack sizes covered under this rule shall not apply to: –

1. Pack sizes or dosage forms not covered by the foregoing provisions of this rule.
2. The imported formulations in finished form.
3. Preparations intended for Veterinary use.
4 Preparations intended for Export.
5. Vitamins/Tonics/Cough Preparations/Antacids/Laxatives in Liquid Oral forms, Unit dose (including applicaps).
6. Pack sizes of dosage forms meant for retail sale to Hospitals, Registered Medical Practitioners, Nursing Homes.
7. Physician‘s Samples.
8. Pack sizes of large volume Intravenous Fluids:

4[Provided further that] pack sizes of any of the new drug as and when approved by the Licensing Authority appointed under Rule 21 and if not covered under this rule, shall be examined for the purpose of approval with specific justification by the said Licensing Authority:

3[4[Provided also that] Oxytocin injection meant for sale shall be in single unit blister pack only:]

5[Provided also that Diclofenac injection for human use shall be in single unit dose pack only.]

1. Ins. by G.S.R. 1242 (E), dt. 17-9-1979.
2. Ins. by G.S.R. 796 (E), dt. 1-10-1992.
3. Sub. by G.S.R. 242 (E), dt. 3-4-2001.
4. Sub. by G.S.R. 558 (E), dt. 17-7-2015.
5. Ins. by G.S.R. 558 (E), dt. 17-7-2015.

[1][**105A**. *Packings of drugs specified in Schedule X.*- The drugs specified in Schedule X shall be marketed in packings not exceeding-

(i) 100 unit doses in the case of tablets/capsules;

(ii) 300 ml in the case of oral liquid preparations; and

(iii) 5 ml in the case of injections:

Provided that nothing in this rule shall apply to packing meant for use of a hospital or a dispensary subject to the conditions that–

(i) such supplies are made by the manufacturers or distributors direct to the hospital/dispensaries; and

(ii) hospital packs shall not be supplied to a retail dealer or to a Registered Medical Practitioner.]

[2][**106**. *Diseases which a drug may not purport to prevent or cure.*—(1) No drug may purport or claim to prevent or cure or may convey to the intending user thereof any idea that it may prevent or cure one or more of the diseases or ailments specified in Schedule J.

(2) No drug may purport or claim to procure or assist to procure, or may convey to the intending user thereof any idea that it may procure or assist to procure, miscarriage in women.

[3][* * * *]

[4][PART IXA

LABELLING AND PACKINGOF HOMOEOPATHIC MEDICINES

106-A. *Manner of labelling of Homoeopathic medicines.*—(A) The following particulars shall be either printed or written in indelible ink and shall appear in a conspicuous manner on the label of the innermost container of any Homoeopathic medicine and on every other covering in which the container is packed—

(i) The words ‗Homoeopathic medicine',

(ii) The name of the medicine—

[5][(a) For drugs specified in the Homoeopathic Pharmacopoeias of India or the United States of America or the United Kingdom, or the German Homoeopathic Pharmacopoeia, the name specified in that Pharmacopoeia.]

(b) For other drugs, the name descriptive of the true nature of the drugs.

1. Ins. by G.S.R. 462 (E), dt. 22-6-1982.

2. Sub. by notification F. 1-16/52-DC (SO 2122), dt. 22-6-1954. 3. Omitted by G.S.R. 462(E), dt. 22.6.1982.

4. Ins. by G.S.R. 1185 (E), dt. 18.8.1964.

5. Subs. by G.S.R. 680 (E), dt. 5-12-1980.

(iii) The potency of the Homoeopathic medicine—For this purpose the potency shall be expressed either in decimal, centesimal or millisimal systems.

[1][(iiiA) In case of Homoeopathic medicine containing two or more ingredients the name of each ingredient together with its potency and proportion expressed in metric system shall be stated on the label.]

[2][(iv) Name and address of the manufacturer when sold in original containers of the manufacturer. In case a Homoeopathic medicine is sold in a container other than that of the manufacturer—the name and address of the seller:]

[5][Provided that where such medicines are imported, the name and address of the importer shall also be mentioned on the label.]

(v) In case the Homoeopathic medicine contains alcohol, the alcohol content in percentage by volume in terms of ethyl alcohol shall be stated on the label:

[3][Provided that in case the total quantity of the pharmacopoeial homoeopathic medicine in the container is 30 millilitres or less, it will not be necessary to state the content of alcohol on the label.]

(B) In addition to the above particulars the label of a Homoeopathic mother tincture shall display the following particulars: −

(i) A distinctive batch number, that is to say, the number by reference to which details of manufacture of the particular batch from which the substance in the container is taken are recorded and are available for inspection, the figures representing the batch number being preceded by the words ―Batch No.‖ or ―Batch‖ or ―Lot Number‖ or ―Lot No.‖ or ―Lot‖ or any distinguishing prefix.

(ii) Manufacturing licence number, the number being preceded by the words ―Manufacturing Licence Number‖ or ―Mfg. Lic. No.‖ or ―M.L.‖.

4[*Explanation*.−This clause shall not apply to a Homoeopathic mother tincture manufactured outside India.

(C) No Homoeopathic medicine containing a single ingredient shall bear a proprietary name on its label.]

1. Subs. by G.S.R. 466 (E), dt. 17-5-1994.
2. Sub. by notification F.1-59/68-D, dt. 19-11-1969.
3. Subs. by G.S.R. 108 (E), dt. 22-2-1994.
4. Ins. by S.O. 2139, dt. 12-8-1972.
5. Ins. by G.S.R. 263 (E), dt. 20-4-2009.

1[**106-B.** *Prohibition of quantity and percentage*.–No Homoeopathic medicine containing more than 12% alcohol v/v (Ethyl alcohol) shall be packed and sold in packing or bottles of more than 30 millilitres, except that it may be sold to hospitals/dispensaries in packings or bottles of not more than 100 millilitres.]

PART X

SPECIAL PROVISIONS RELATING TOBIOLOGICAL AND OTHER SPECIAL PRODUCTS

2[**107**. *Name of substance*.—If any substance specified in Schedule C is advertised or sold as a proprietary medicine or is contained in a medicine so advertised or sold, the proper name of the substance shall appear on the label in the manner prescribed in this Part.

3[*Explanation*.−For the purpose of this rule the expression ―proper name‖ means the proper name stated in Schedule F or if no such name is stated, the name descriptive of the true nature and origin of the substance:

Provided that in the case of veterinary biological product the expression ―proper name‖ means the proper name stated in Schedule F (1) or if no such name is stated, the name or synonym given in the current edition for the time being of the 4[British Pharmacopoea (Veterinary)] , or, if no such name is stated either in Schedule F (1) or the 4[British Pharmacopoea (Veterinary)], the name descriptive of the true nature and origin of the substance approved by the Licensing Authority.

108. *Container*.—5[(1) No substance specified in Schedule C shall be sold or offered for sale unless it has been sealed in a previously sterilized container made of glass or any other suitable material approved for the purpose by the Licensing Authority appointed under rule 21, in such manner as may, in the opinion of the Licensing Authority, suffice to preclude the access of bacteria:

Provided that it shall not be necessary to use a previously sterilized container if the filled and sealed container is to be sterilized after the sealing and such sterilizing procedure would render the product sterile. However, the Licensing Authority may, for any special reasons, direct the licensee to pre-sterile such containers.]

(2) When any such substance is issued in liquid form in containers which are sealed in such a manner that portions of the contents can be withdrawn for use on different occasions, the liquid shall contain a sufficient proportion of some antiseptic to prevent the growth of any organism

which may be accidentally introduced in the process of removing a portion of the contents of the container:

6[Provided that nothing in this sub-rule shall apply to a penicillin suspension in oil and wax.]

1. Ins. by G.S.R. 108 (E), dt. 22-2-1994.
2. Subs. by F. 1-5/47-D (SRO 2889), dt. 25-11-1949.
3. Subs. by F. 1-6/62-D, dt. 2-7-1969.
4. Subs. by G.S.R.647 (E), dt. 28-10-1998.
5. Subs. by G.S.R. 245, dt. 21-2-1976.
6. Ins. by SO 115, dt. 04-1-1961.

1[(3) The container shall comply with such further requirements, if any, as are specified in Schedule F or Schedule F (1) as the case may be, in that behalf.

(4) The Licensing Authority may in the case of any particular preparation of any such substance dispense with any of the requirements of this Rule or Schedule F or Schedule F (1) as the case may be, and may make such additional requirements, as having regard to the nature of the preparation, they may deem necessary.]

2[**109.** *Labelling.*–(1) The following particulars and such further particulars, if any, as are specified in Schedule F or Schedule F (1), as the case may be, shall be printed or written in indelible ink on the label of every phial, ampoule or other container of a substance specified in Schedule C and on every other covering in which such phial, ampoule or container is packed—

(a) where a drug is imported, the number of licence under which it is imported, preceded by the words ‗Import Licence‘:

Provided that no reference shall be made to any other import licence number granted by any authority outside India on any label or container or in any covering in which the container is packed or in any other matter of advertisement enclosed therein;

(b) where a test for potency in units is required by these rules, a statement of the potency in units defined in terms of relation to the standard preparation specified in Schedule F or F (1), as the case may be :

Provided that this clause shall not apply in the case of vaccine lymph;

(c) where a test for potency or maximum toxicity is required the date upto which the substance if kept under suitable conditions may be expected to retain a potency not less than stated on the label of the container or not to acquire a toxicity greater than that permitted by the test, as the case may be. The date of expiry shall be in terms of month and year and it shall mean that the drug is recommended for use till the last day of the month. The date of expiry shall be preceded by the words ‗Expiry date‘ :

Provided that nothing in these rules shall be deemed to require the labelling of any transparent cover or any wrapper, case or other covering used solely for the purpose of packing, transport or delivery.

(2) The particulars prescribed in clause (a) of the preceding sub-rule shall be printed or written in indelible ink either on the label borne by a container of vaccine lymph or on a label or wrapper affixed to any package in which the container is issued for sale. The said particulars shall be indelibly marked on the sealed container of surgical ligature or suture or printed or written in indelible ink on a label enclosed therein.

1. Subs. by F.1-6/62-D (SO 2889), dt. 2-7-1969.
2. Subs. by G.S.R.19, dt. 15-12-1977.

(3) The following particulars, and such further particulars, if any, as are specified in Schedule F or Schedule F (1), as the case may be, shall be printed or written in indelible ink either on the label borne by the container of any substance specified in Schedule C or on a label or wrapper affixed to any package in which any such container is issued for sale, namely:–

(a) the date on which the manufacture of the particular batch from which the substance in the container is taken was completed as defined in Schedule F or Schedule F(1), or if there is no definition in Schedule F or Schedule F(1) as hereafter defined in this rule and in the case of vaccine prepared from concentrates, the date of completion of the final products and the bottling for issue;

(b) where an antiseptic substance has been added, the nature and the percentage proportion introduced;

(c) the precaution necessary for preserving the properties of the contents up to the date indicated in clause (c) of sub-rule (1).

(4) For the purpose of clause (a) of sub-rule (3), the date on which the manufacture of a batch is completed shall be—

(a) in cases where a test for potency or toxicity is required by these rules or not being so required, is accepted by the Licensing Authority as sufficient for the purpose of fixing the date of completion of manufacture, the date on which the substance was removed from cold storage after having been kept at a temperature not exceeding 5° C continuously for a period not exceeding two years from the time when the last test was completed,

(b) in cases where no such test is required or accepted−

(i) if the substance is a serum obtained from a living animal, the earliest date on which any material contributing to the batch was removed from the animal;

(ii) if the substance was obtained by the growth of organisms or artificial media, the earliest date on which growth was terminated in any of the material contributing to the batch:

Provided that if a batch of the substance (including all material contributing to this batch) has for a period of not more than three years been kept in cold storage at a temperature not exceeding 5°C continuously from the earliest practicable date after that on which growth was terminated in the material as the case may be, the date of removal from cold storage shall be treated as the date on which the manufacture of the batch is completed;

(c) in all other cases, the date on which the substance is filled in the container.

[1][**109-A.** *Labelling of Medical Devices.*–Subject to the other provisions of these rules, the following particulars shall be printed in indelible ink on the label or sticker on the shelf pack of the medical device or on the outer cover of such medical device and on every outer covering in which the medical device is packed, namely:—

(a)proper name of the medical device;

(b)the details necessary for the user to identify the device and its use;

(c)the name of the manufacturer and address of the manufacturing premises where the device has been manufactured;

(d)the correct statement of the net quantity in terms of weight, measure, volume, number of units, as the case may be, and the number of the devices contained in the package shall be expressed in metric system; and

(e)the date of manufacture and date of expiry; alternately the label shall bear the shelf life of the product:

1. Sub. by G.S.R. 690 (E), dt. 25-9-2014. Earlier Ins. by G.S.R. 109 (E), dt. 22-2-1994.

Provided that in the case of sterile devices the date of sterilisation may be given as date of the manufacture of the device:

Provided further that the device is made up of stable materials such as stainless steel or

titanium, and supplied non-sterile, date of expiry may not be necessary;

(f)to provide, wherever required, an indication that the device contains medicinal or biological substance;

(g)to provide, a distinctive batch number or lot number preceded by the word ―Lot No.‖ or ―Lot‖ or ―Batch No.‖ or ―B. No.‖;

(h)to indicate, wherever required, any special storage or handling conditions applicable to the device;

(i)to indicate, if the device is supplied as a sterile product, its sterile state and the sterilisation method;

(j)to give, if considered relevant, warnings or precautions for the attention of the user of the medical device;

(k)to label the device, if the device is intended for single use;

(l)to overprint on the label of the container, the words ―FOR CLINICAL INVESTIGATION ONLY‖, if the device is intended for clinical investigation;

(m)to overprint on the label of the device, the words ―Physician‘s Sample—Not to be sold‖, if a medical device is intended for distribution to the medical professional as a free sample;

(n)to provide, except for imported devices, the manufacturing licence number by preceding the words ―Manufacturing Licence Number‖ or ―Mfg. Lic. No.‖ or ―M. L‖;

(o)Devices or In-vitro diagnostics which are not sold to customer or patient directly and are sold for use by hospitals or diagnostic labs shall provide the information affixing additional label or sticker on outer shelf pack;

(p)to provide on the label, in case of imported devices, with the approval of the licensing authority mentioned in rule 21, the import licence number, name and address of the importer and address of the actual manufacturing premises, date of manufacture, (if not already printed at the time of import):

Provided that the label may bear symbols recognised by the Bureau of Indian Standards or International Organisation for Standardisation (ISO) in lieu of text and the device safety is not compromised by a lack of understanding on the part of the user in case the meaning of the symbol is not obvious to the device user.]

[1]**[109B. Exemption of certain labelling requirements for medical devices for export from India.—** The labels on packages or container of devices for export shall be adopted to meet specific requirements of the law of the country to which the device is to be exported, but the following particulars shall appear in conspicuous manner on the label of the shelf pack of the medical device in which the device is packed and every other outer covering in which the container is packed-

(a)name of the Device;

(b)the distinctive batch number or lot number preceded by the word ―Lot No.‖ or ―Lot‖ or ―Batch No.‖ or ―B.No.‖;

(c)the date of expiry, if any;

(d)the name and address of the manufacturer and address of actual premises where the device has been manufactured;

(e)the manufacturing Licence No. preceded by the letters ―M.L. No‖ or ―Manufacturing Licence No‖;

(f)the internationally recognised symbols in lieu of text, wherever required:

1. Ins. by G.S.R. 690 (E), dt. 25-9-2014.

Provided that where a device is required by the consignee not to be labeled with the name and address of the manufacturer, the label on the packages or container shall bear a code number as approved by the licensing authority and the code number shall bear the name of the State or Union territory, in abbreviation, followed by the word ―Device‖ and ―manufacturing licence number:

Provided further that where a device is required by the consignee not to be labeled with the code

number also, the label on the packages or container shall bear a special code number, as requested by the consignee, and approved by the licensing authority under rule 21.]

[1][**109C. Shelf life of the medical devices.**— The shelf life of the medical devices shall not exceed sixty months from the date of manufacture:

Provided that this period may be extended by the licensing authority, in respect of any specified medical device, if satisfactory evidence is produced by the manufacturer to justify such an extension.]

110. *Prohibition of sale of substance after prescribed date.*–No person shall sell, or exhibit for sale any substance specified in Schedule C after the date recorded on the container, label or wrapper as the date upto which the substance may be expected to retain a potency not less than, or not to acquire a toxicity greater than that required or permitted by the prescribed test as the case may be.

[2] [* * * * *]

1. Ins. by G.S.R. 109 (E), dt. 22-2-1994.

2. Rule 110A omitted by G.S.R. 1242(E), dt. 17.9.1979.

[1][**111**. *Standards.*–Every substance specified in Schedules C and C (1) intended for sale shall conform with the standards of strength, quality and purity specified in these Rules and in Schedule F or F(1), as the case may be, and the tests for determining such conformity shall be applied to samples taken from the final product after every manufacturing process has been completed.]

[2][**112**. *Tests for strength and quality.*–The tests, if any, required for determining the strength and quality of each of the substances specified in Schedules C and C (1) shall be those set out in Schedule F or Schedule F (1) [4][or as specified, as the case may be].]

[3][* * * * *]

115. *Application of tests for sterility.*–The tests shall be applied–

(a) to samples taken from each batch of the substance before the operation of filling and sealing the containers in which it is to be issued has commenced except preparations, which after being sealed in the containers are to be sterilized by heat, in a manner satisfactory to the Licensing Authority; and

(b) to the contents of sample containers when ready for issue.

[4][* * * * *]

119.–(1) If at this examination no growth of micro-organisms is found in any tube, the sample may be treated as having passed the test.

(2) If at the examination a growth of micro-organisms is visible, further samples may be taken and the tests may be repeated on the further samples taken; but no container the contents of which form part of the batch shall be issued until such further samples have passed the test. The process of taking samples from the batch for a test may be repeated twice:

Provided that if the same organism is visible in more than one test the batch shall be treated as not sterile and the material contained in the batch shall not be issued or used as part of a further batch unless and until it has been re-sterilized and has passed the tests.

120.–Notwithstanding anything contained in the last preceding rule, in any case where—

(a) a substance is required in an emergency by a registered medical practitioner, but the licensee has no filled containers in stock; or

1. Amended by F.1-6/62-D (SO 2889), dt. 2-7-1969.

2 Subs. by G.S.R. 663(E), dt. 3.7.1992.

3. Rules 113 and 114 omitted by G.S.R. 663(E),dt. 3.7.1992. 4. Rules 116, 117 and 118 omitted by G.S.R. 663 (E), dt. 3-7-1992.

(b) a substance which in the opinion of the Licensing Authority is so unstable in solution that the delay occasioned by the completing of the sterility test on filled containers would render its issue in active

form impossible, the licensee may issue the substance from a batch which has already passed the tests for sterility and freedom from abnormal toxicity, without completing the sterility test on the filled containers, provided that he complies with the following conditions—

(i) the licensee shall before the issue take samples in the required proportion from the containers into which the batch is filled, and after the required inoculation shall examine the tube every day for five days;

(ii) if at any examination any growth is visible in any of the tubes, he shall immediately notify the Licensing Authority;

(iii) he shall keep available for inspection a record of all issues made under this Rule containing such particulars of the circumstances in which the issue is made as the Licensing Authority may require.

[1][**121**. *Test for freedom from abnormal toxicity.* –The test for freedom from abnormal toxicity shall be carried out as per the current edition of Indian Pharmacopoeia in the case of each batch of the serum tested by the licensee or by an institution approved by the Licensing Authority for the purpose of carrying out the test on its behalf.]

[2][**121A**. *Test for pyrogens*–Solution of substances intended for parenteral administration in large volumes (10 ml or more at a time) shall be pyrogen-free and tested for pyrogens. If water or any other aqueous solvent is supplied along with the substances for preparing such solutions, it shall also be pyrogen-free and tested for pyrogens.]

122. *Substances specified in Schedule C(1).* –The following provisions shall apply in the case of a substance specified in Schedule C (1): –

[3][(a) The container shall comply with the requirements, if any, specified in Schedule F or Schedule F (1) [4][or as specified], as the case may be.]

[5] [* * * * *]

(c) The substance shall conform to the standards of strength, quality and purity specified in Schedule F or Schedule F (1) [4][or as specified], as the case may be and the tests for determining the strength, quality and purity of the substance shall be those specified in Schedule F or Schedule F (1) [4][or as specified,] as the case may be.

(d) The tests for determining the strength, quality and purity of a substance specified in Schedule F or Schedule F (1) [3][or as specified] as the case may be shall be applied to samples taken from the final product after each manufacturing process has been completed.

(e) The substance should be stored in a cool place and away from light.

1. Subs. by G.S.R. 834 (E), dt. 29-12-1999.

2. Subs. by SO 1449, dt. 13-06-1961. Earlier Ins. by F.1-27/56-D, dt. 18-12-1956 3.
Subs. by F.1-6/62-D, dt. 2-7-1969

4. Subs. by G.S.R. 663 (E), dt. 3-7-1992

5. Omitted by G.S.R. 19, dt. 15.12.1977.

[1][PART X A.

IMPORT OF MANUFACTURE OFNEW DRUG FOR CLINICAL TRIALS OR MARKETING

122-A. *Application for permission to import new drug.*- [2][(1) (a) No new drug shall be imported, except under, and in accordance with, the permission granted by the Licensing Authority as defined in clause (b) of rule 21.

(b) An application for the grant of permission to import a new drug shall be made in

Form 44 to the Licensing Authority, accompanied by a fee of fifty thousand rupees:

Provided that where a subsequent application by the same applicant for that drug, whether in modified dosage form or with new claims, is made, the fee to accompany such application shall be fifteen thousand rupees.

Provided further that any application received after one year of the grant of approval for the import and sale of new drug, shall be accompanied by a fee of fifteen thousand rupees and such information and data as required by 3[Appendix I or Appendix IA or Appendix IB] of Schedule Y, as the case may be].

(2) The importer of a new drug when applying for permission under sub-rule (1), shall submit data as given in 3[Appendix I or Appendix IA or Appendix IB] to Schedule Y including the results of local clinical trials carried out in accordance with the guidelines specified in that Schedule and submit the report of such clinical trials in the format given in appendix II to the said Schedule:

Provided that the requirement of submitting the results of local clinical trials may not be necessary if the drug is of such a nature that the Licensing Authority may, in public interest, decide to grant such permission on the basis of data available from other countries:

Provided further that the submission of requirements relating to Animal Toxicology, Reproduction studies, Teratogenic studies, Perinatal studies, Mutagenicity and Carcinogenicity may be modified or relaxed in case of new drugs approved and marketed for several years in other countries if he is satisfied that there is adequate published evidence regarding the safety of the drug, subject to the other provisions of these rules.

[2][(3) The Licensing Authority, after being satisfied that the drug if permitted to be imported as raw material (bulk drug substance) or as finished formulation shall be effective and safe for use in the country, may issue an import permission in

Form 45 and/or Form 45- A, subject to the conditions stated therein:

Provided that the Licensing Authority shall, where the data provided or generated on the drug is inadequate, intimate the applicant in writing, and the conditions, which shall be satisfied before permission could be considered.]

122-B. *Application for approval to manufacture new drug* [4]*[***]*.- [2][(1)(a) No new drug shall be manufactured for sale unless it is approved by the Licensing Authority as defined in clause (b) of rule 21.

1. Ins. by G.S.R. 944 (E), dt. 21-9-1988.
2. Subs. by G.S.R. 900 (E), dt. 12.12.2001.
3. Subs. by G.S.R. 918 (E), dt. 30.11.2005.
4. Omitted by G.S.R. 26 (E), dt. 19.01.2006.

(b) An application for the grant of approval to manufacture the new drug and its formulations shall be made in

Form 44 to the Licensing Authority as defined in clause (b) of Rule 21 and shall be accompanied by a fee of fifty thousand rupees:

Provided that where the application is for permission to import a new drug (bulk drug substance) and grant of approval to manufacture its formulation/s, the fee to accompany such application shall be fifty thousand rupees only.

Provided further that where a subsequent application by the same applicant for that drug, whether in modified dosage form or with the new claims, is made, the fee to accompany such subsequent application shall be fifteen thousand rupees:

Provided also that any application received after one year of the grant of approval for the manufacture for sale of the new drug, shall be accompanied by a fee of fifteen thousand rupees and such information and data as required by [4][Appendix 1 or Appendix 1A or Appendix IB] of Schedule Y, as the case may be.]

(2) The manufacturer of a new drug under sub-rule (1) when applying for approval to the Licensing Authority mentioned in the said sub-rule, shall submit data as given in [4][Appendix 1 or Appendix 1A or Appendix IB] to Schedule Y including the results of clinical trials carried out in the country in accordance with the guideline specified in Schedule Y and submit the report of such clinical trials in the same format given in Appendix II to the said Schedule.

[1][(2A) The Licensing authority as defined in clause (b) of rule 21 after being satisfied that the drug if approved to be manufactured as raw material (bulk drug substance) or as finished formulation shall be effective and safe for use in the country, shall issue approval in

Form 46 and/or Form 46A, as the case may be, subject to the conditions stated therein:

Provided that the Licensing Authority shall, where the data provided or generated on the drug is inadequate, intimate the applicant in writing, and the conditions, which shall be satisfied before permission could be considered.]

(3) When applying for approval to manufacture a new drug under sub-rule (1) or its preparations, to the State Licensing Authority, an applicant shall produce along with his application, evidence that the drug for the manufacture of which application is made has already been approved [5][in the name of the applicant] by the Licensing Authority mentioned in Rule 21:

Provided that the requirement of submitting the results of local clinical trials may not be necessary if the drug is of such nature that the [6][Licensing Authority in Rule 21] may, in public interest, decide to grant such permission on the basis of data available from other countries:

Provided further that the submission of requirements relating to Animal Toxicology, Reproduction studies, Teratogenic studies, Perinatal studies, Mutagenicity and Carnicogenicity may be modified or relaxed in case of new drugs approved and marketed for several years in other countries if he is satisfied that there is adequate published evidence regarding the safety of the drug, subject to the other provisions of these rules.

[2] [* * * * *]

[3][**122D.** *Permission to import or manufacture fixed dose combination.*- (1) An application for permission to import or manufacture fixed dose combination of two or more drugs as defined in clause (c) of rule 122-E shall be made to the Licensing Authority as defined in clause (b) of Rule 21 in

Form 44, accompanied by a fee of fifteen thousand rupees and shall be accompanied by such information and data as is required in Appendix VI of Schedule Y.

1. Ins. by G.S.R. 900(E), dt. 12-12-2001.
2. Rules 122-C omitted, by G.S.R. 900(E), dt. 12-12-2001.
3. Subs. by G.S.R. 900(E), dt. 12-12-2001.
4. Subs. by G.S.R. 918(E), dt. 30-11-2015.
5. Ins. by G.S.R. 26 (E), dt. 19-01-2006.
6. Subs. by G.S.R. 26 (E), dt. 19-01-2006.

(2) The Licensing Authority after being satisfied that the fixed dose combination if approved to be imported or manufactured as finished formulation shall be effective and safe for use in the country, shall issue permission in

Form 45 or Form 46, as the case may be, subject to the conditions stated therein:

Provided that the Licensing Authority shall, where the data provided or generated on the fixed dose combination is inadequate, intimate the applicant in writing, and the conditions which shall be satisfied before grant of approval/permission could be considered.

122DA. *Application for permission to conduct clinical trials for New Drug/Investigational New Drug.*− (1) No clinical trial for a new drug, whether for clinical investigation or any clinical experiment by any institution, shall be conducted except under, and in accordance with, the permission, in writing, of the Licensing Authority defined in clause (b) of Rule 21.

(2) An application for grant of permission to conduct−

(a) human clinical trials (Phase-I) on a new drug shall be made to the Licensing Authority in

Form 44 accompanied by a fee of fifty thousand rupees and such information and data as required under Schedule Y.

(b) exploratory clinical trials (Phase-II) on a new drug shall be made on the basis of data emerging from Phase-I trial, accompanied by a fee of twenty-five thousand rupees;

(c) confirmatory clinical trials (Phase-III) on a new drug shall be made on the basis of the data emerging from Phase-II and where necessary, data emerging from Phase-I also, and shall be accompanied by a fee of twenty-five thousand rupees:

Provided that no separate fee shall be required to be paid along with application for import/manufacture of a new drug based on successful completion of phases clinical trials by the applicant:

Provided further that no fee shall be required to be paid along with the application by Central Government or State Government Institutes involved in clinical research for conducting trials for academic or research purposes.

(3) The Licensing Authority after being satisfied with the clinical trials, shall grant permission in

Form 45 or Form 45-A or Form 46 or Form 46-A, as the case may be, subject to the conditions stated therein:

Provided that the Licensing Authority shall, where the data provided on the clinical trials is inadequate, intimate the applicant in writing, within six months from the date of such intimation or such extended period, not exceeding a further period of six months, as the Licensing Authority may, for reasons to be recorded in writing, permit, intimating the conditions which shall be satisfied before permission could be considered.

[1][(4) No permission for conduct of clinical trial intended for academic purposes in respect of approved drug formulation shall be required for any new indication or new route of administration or new dose or new dosage form where,-

(a) the trial is approved by the Ethics Committee; and

(b) subject to the provisions of sub-rule 5, the data generated is not intended for submission to licensing authority.

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Ins. by G.S.R. 313(E), dt. 16-03-2016.

(5) The Ethics Committee shall however inform the licensing authority about the cases approved by it and also about cases where there could be an overlap between the clinical trial for academic and regulatory purposes and where the said authority does not convey its comments to the Ethics Committee within a period of thirty days from the date of receipt of communication from the Ethics Committee, it shall be presumed that no permission from the licensing authority is required.]

[1][*Explanation:*- —For the purposes of these rules,—

(a) ―Clinical Trial‖ means a systematic study of any new drug(s) in human subject(s) to generate data for discovering and/or verifying the clinical, pharmacological (including pharmacodynamic and pharmacokinetic), and/or adverse effects with the objective of determining safety and/or efficacy of the new drug;

(b) ―Global Clinical Trial‖ means any clinical trial which is conducted as part of multi-national clinical development of a drug;

(c) ―Investigational New Drug‖ means a new chemical entity or a product having therapeutic indication but which has never been tested earlier on human being;

(d) ―New Chemical Entity‖ means an active substances in developmental stage which may be specified as a drug under the Act, after undergoing any clinical trial.]

[2][****]

[3]**[122-DAB-** *Compensation in case of injury or death during clinical trial.*-

[4][(1) In case of an injury occurring to the subject during the clinical trial, free medical management shall be given as long as required or till such time it is established that the injury is not related to the clinical trial, whichever is earlier.]

(2) In case, the injury occurring to the trial subject is related to the clinical trial, such subject shall also be entitled for financial compensation as per order of the Licensing Authority defined under clause (b) of Rule 21, and the financial compensation will be over and above any expenses incurred on the medical management of the subject.

[5][(2A) In case, there is no permanent injury, the quantum of compensation shall be commensurate with the nature of the non-permanent injury and loss of wages of the subject.]

(3) In the case of clinical trial related death of the subject, his / her nominee(s) would be entitled for financial compensation, as per the order of the Licensing Authority defined under clause (b) of Rule 21 and the financial compensation will be over and above any expenses incurred on the medical management of such subject.

(4) The expenses on medical management and financial compensation in the case of clinical trial injury or death of the trial subject shall be borne by the sponsor of the clinical trial.

(5) Any injury or death of the subject occurring in clinical trial due to following reasons shall be considered as clinical trial related injury or death and the subject or his/her nominees(s), as the case may be, are entitled for financial compensation for such injury or death:

(a) Adverse effect of investigational product(s);

(b) Violation of the approved protocol, scientific misconduct or negligence by the sponsor or his representative or the investigator;

1. Subs. by G.S.R. 826 (E), dt. 30-10-2015 with following explanation.

―*Explanation.*−For the purpose of these rules Investigational New Drug means a new chemical entity or a product having therapeutic indication but which have never been earlier tested on human beings.‖

2. Omitted rule 122DAA by G.S.R. 826 (E), dt. 30-10-2015, before omission it stood as under:

―*122DAA.Definition of Clinical trial*.--For the purpose of this Part, ―Clinical trial‖ means a systematic study of new drug(s) in human subject(s) to generate data for discovering and/or verifying the clinical, pharmacological (including pharmacodynamic and pharmacokinetic) and/or adverse effects with the objective of determining safety and / or efficacy of the new drug.‖

3. Ins. by G.S.R. 53 (E), dt. 30-01-2013.

4. Subs. by G.S.R. 889 (E), dt. 12-12-2014.

5. Ins. by G.S.R. 889 (E), dt. 12-12-2014.

(c) Failure of investigational product to provide intended therapeutic effect, where, the standard care, though available, was not provided to the subject as per the clinical trial protocol;

(d) Use of placebo in a placebo-controlled trial where, the standard care, though available, was not provided to the subject as per the clinical trial protocol;

(e) Adverse effects due to concomitant medication excluding standard care, necessitated as part of approved protocol;

(f) For injury to a child in-utero because of the participation of parent in clinical trail; (g) Any clinical trial procedures involved in the study.

(6) The sponsor, whether a pharmaceutical company or an institution shall give an undertaking along with the application for clinical trail permission to the Licensing Authority defined in clause (b) of Rule 21, to provide compensation in the case of clinical trial related injury or death for which subjects are entitled to compensation.

(7) In case, the sponsor fails to provide medical management for the injury to the subject and / or financial compensation to the trial subject for clinical trial related injury or financial compensation to the subject‘s nominee(s) in case of clinical trial related death of the subject, the Licensing Authority may after giving an opportunity to show cause why such an order should not be passed, by an order in writing, stating the reasons thereof, suspend or cancel the clinical trial and / or restrict Sponsor including his representative(s) to conduct any further clinical trials in the country or take any other action deemed fit under the rules.]

1**[122 DAC.** *Permission to conduct clinical trial:-* (1)The Licensing Authority as defined in clause (b) of Rule 21, on being satisfied that the data submitted along with the application in support of the proposed clinical trial is adequate in all respects, issue permission for conduct of clinical trial, subject to the following conditions, namely:-

(a) Clinical trial shall be conducted in compliance with the approved protocols, requirements of Schedule Y annexed to these rules, Good Clinical Practice Guidelines for conduct of clinical trials in India and other applicable regulations;

(b) Approval of the Ethics Committee shall be obtained before initiation of the study; (c) Clinical trial shall be registered at Clinical Trials Registry of India before enrolling the first patient for the study;

(d) Annual status report of each clinical trial, as to whether it is ongoing, completed or terminated, shall be submitted to the Licensing Authority and in case of termination of any clinical trial the detailed reasons for the same shall be communicated to the said Licensing Authority;

(e) Any report of serious adverse event occurring during clinical trial to the subject, after due analysis, shall be forwarded within ten days of its occurrence as per Appendix XI and in compliance with the procedures prescribed in Schedule Y;

(f) In case of an injury or death during the clinical trial to the subject of the clinical trial the applicant shall provide complete medical management and compensation in the case of trial related injury or death in accordance with Rule 122 DAB and the procedures prescribed under Schedule Y, and the details of compensation provided in such cases shall be intimated to the Licensing Authority within thirty days of the receipt of the order of the said authority; (g)

The premises of Sponsor including their employees, subsidiaries and branches, their agents, contractors and sub-contractors and clinical trial sites shall be open to inspection by the officers authorized by the Central Drugs Standard Control Organization, who may be accompanied by an officer of the State Drug Control Authority concerned, to verify compliance to the requirements of Schedule Y, Good Clinical Practices guidelines for conduct of clinical trials in India and other applicable regulations;

1. Ins. by G.S.R. 63 (E), dt. 01-02-2013.

(h) The Sponsor including their employees, subsidiaries and branches, their agents, contractors and sub-contractors and clinical trial sites and the investigator shall allow officers authorized by the Central Drug Standard Control Organization, who may be accompanied by an officer of the State Drug Control Authority concerned, to enter with or without prior notice, any premises of sponsor including their employees, subsidiaries and branches, their agents, contractors and sub-contractors and clinical trial sites to inspect, search and seize any record, data, document, books, investigational drugs etc. related to clinical trials and provide adequate replies to any queries raised by the inspecting authority in relation to the conduct of clinical trial;

(2) Notwithstanding the conditions specified in sub-Rule (1), the Licensing Authority, on being satisfied that the data submitted along with the application in support of the proposed clinical trial is adequate in all respect, may also impose such additional conditions for issuance of permission in respect of specific clinical trials, if considered necessary, regarding the objective, design, subject population, subject eligibility, assessments, conduct and treatment of such clinical trial.

(3) If any Sponsor including their employees, subsidiaries and branches, their agents, contractors and sub-contractors, Investigators conducting clinical trial and clinical trial sites fail to comply with any of the above conditions, the Licensing Authority, may, after giving an opportunity to show cause why such an order should not be passed, by an order in writing stating the reasons thereof,-

(a) Issue warning letter giving details of deficiency found during the inspection, which might affect the right or well-being of the clinical trial subject or the validity of the study conducted at that site;

(b) Recommend that study may be rejected or discontinued;

(c) Suspend or cancel the clinical trial permission;

(d) Debar the Investigator(s), Sponsor including their employees, subsidiaries and branches, their agents, contractors and sub-contractors to conduct any clinical trial in future.

(4) The Sponsor including their employees, subsidiaries and branches, their agents, contractors and sub-contractors and clinical trial Investigators, against whom action as mentioned in sub- Rule (3) has been taken by the Licensing Authority, may, within ninety days of the receipt of the copy of the order of the Licensing Authority prefer an appeal to the Central Government, and the Central Government may, after giving such appellant an opportunity of being heard, confirm, reverse or modify such order.]

122DB. *Suspension or cancellation of Permission/Approval*.- If the importer or manufacturer under this Part fails to comply with any of the conditions of the permission or approval, the Licensing Authority may, after giving an opportunity to show cause why such an order should not be passed, by an order in writing stating the reasons therefor, suspend or cancel it.

122DC. *Appeal.*- Any person aggrieved by an order passed by the Licensing Authority under this Part, may within sixty days from the date of such order, appeal to the Central Government, and the Central Government may, after such enquiry into the matter as is considered necessary, pass such order in relation thereto as it thinks fit.

[1][**122 DD.** *Registration of Ethics Committee:*- (1) No Ethics Committee shall review and accord its approval to a clinical trial protocol without prior registration with the Licensing Authority as defined in clause (b) of Rule21:

Provided that any Ethics Committee, existing on the date of commencement of the Drugs and Cosmetics (Third Amendment) Rules, 2013, who has already reviewed and accorded approval to clinical trial protocol, shall obtain registration within a period of forty-five days from the date of commencement of Drugs and Cosmetics (Third Amendment) Rules, 2013.

1. Ins. by G.S.R. 72 (E), dt. 08-02-2013.

(2) An application for registration of Ethics Committee shall be made to the Licensing Authority in accordance with the requirements as specified in the Appendix VIII of Schedule Y.

(3) The Licensing Authority after being satisfied that the requirements have been complied with, may grant registration to the Ethics Committee subject to such conditions as may be stated therein.

(4) The Ethics Committee shall review and accord its approval to a clinical trial and also carry ongoing review of the trial at appropriate intervals, as specified in Schedule Y, and the Good Clinical Practice Guidelines for Clinical Trials in India and other applicable regulatory requirements for safeguarding the rights, safety and well-being of the trial subjects.

(5) In the case of any serious adverse event occurring to the clinical trial subjects during the clinical trial, the Ethics Committee shall analyze and forward its opinion as per procedure specified under APPENDIX XII of Schedule Y.

(6) The Ethics Committee shall allow inspectors or officials authorized by the Central Drugs Standard Control Organization to enter its premises to inspect any record, data or any document related to clinical trial and provide adequate replies to any query raised by such inspectors or officials, as the case may be in relation to the conduct of clinical trial.

(7) The registration, unless it is suspended or cancelled, shall be valid for a period of three years from the date of issue:

Provided that if the application for re-registration is received by the Licensing Authority within three months before the expiry, the registration shall continue to be in force until orders are passed by the said authority:

Provided further that the Licensing Authority shall be informed in writing in case of any change in the membership or the constitution of the Ethics Committee takes place.

(8) If the Licensing Authority is not satisfied, he shall reject the application and shall inform the applicant of the reasons for such rejection and the conditions which must be satisfied before the registration can be granted.

(9) If the Ethics Committee fails to comply with any of the conditions of registration, the Licensing Authority may, after giving an opportunity to show cause why such an order should not be passed, by an order in writing stating the reasons therefor, suspend or cancel the registration of the Ethics Committee for such period as considered necessary.

(10) The Ethics Committee whose registration has been suspended or cancelled by the Licensing Authority, may, within ninety days of the receipt of the copy of the order, prefer an appeal to the Central Government and the Central Government may after giving an opportunity of being heard, confirm, reverse or modify such order.

Explanation:- For the purpose of this Rule an Ethics Committee is a committee comprising of medical, scientific, non-medical and nonscientific members, whose responsibility is to ensure the protection of the rights, safety and will-being of human subjects involved in a clinical trial and it shall be responsible for reviewing and approving the protocol, the suitability of the

investigators, facilities, methods and adequacy of information to be used for obtaining and documenting informed consent of the study subjects and adequacy of confidentiality safeguards.]

122E. ***Definition of new drug.***- For the purpose of this Part, new drug shall mean and include-

[1][(a) A drug, as defined in the Act including bulk drug substance [2][or phytopharmaceutical drug] which has not been used in the country to any significant extent under the conditions prescribed, recommended or suggested in the labelling thereof and has not been recognized as effective and safe by the licensing authority mentioned under rule 21 for the proposed claims:

1. Ins. by G.S.R. 591 (E), dt. 17-8-1999.

2. Ins. by G.S.R. 918 (E), dt. 30-11-2015.

Provided that the limited use, if any, has been with the permission of the licensing authority.]

(b) A drug already approved by the Licensing Authority mentioned in Rule 21 for certain claims, which is now proposed to be marketed with modified or new claims, namely, indications, dosage, dosage form (including sustained release dosage form) and route of administration.

(c) A fixed dose combination of two or more drugs, individually approved earlier for certain claims, which are now proposed to be combined for the first time in a fixed ratio, or if the ratio of ingredients in an already marketed combination is proposed to be changed, with certain claims, viz. indications, dosage, dosage form (including sustained release dosage form) and route of administration. (*See* items (b) and (c) of Appendix VI to Schedule Y.)

Explanation.- For the purpose of this rule−

[1][(i) all vaccines and Recombinant DNA (r-DNA) derived drugs shall be new drugs unless certified otherwise by the Licensing Authority under Rule 21;]

(ii) a new drug shall continue to be considered as new drug for a period of four years from the date of its first approval [2][***].]

1. Ins. by G.S.R. 45(E), dt. 24.01.2011.

2. Omitted by G.S.R. 724(E), dt. 7.11.2013, the following words,-

―or its inclusion in the Indian Pharmacopoeia Whichever is earlier‖.

[1][PART XB

REQUIREMENTS FOR THE COLLECTION, STORAGE, PROCESSING AND DISTRIBUTION OF WHOLE HUMAN BLOOD, HUMAN BLOOD COMPONENTS BY BLOOD BANKS ANDMANUFACTURE OF BLOOD PRODUCTS

[2][**122EA**. ***Definitions.***- (1) In this Part and in the Forms contained in Schedule A and in Part XII-B, [3][Part XII-C and Part XIID] of Schedule F, unless there is anything repugnant in the subject or context−

(a) ―apheresis‖ means the process by which blood drawn from a donor, after separating plasma or platelets, or leucocytes, is re-transfused simultaneously into the said donor;

(b) ―autologous blood‖ means the blood drawn from the patient for re-transfusion unto himself later on;

(c) ―blood‖ means and includes whole human blood, drawn from a donor and mixed with an anti-coagulant;

(d) ―blood bank‖ means a place or organization or unit or institution or other arrangements made by such organization, unit or institution for carrying out all or any of the operations for collection, apheresis, storage, processing and distribution of blood drawn from donors and/or for preparation, storage and distribution of blood components;

(e) ―blood component‖ means a drug prepared, obtained, derived or separated from a unit of blood drawn from a donor;

(f) ―blood product‖ means a drug manufactured or obtained from pooled plasma of blood by fractionation, drawn from donors;

[4][(fa) ―cord blood bank‖ means a place or organization or unit for carrying out and responsible for operations of collection, processing, testing, banking, selection and release of cord blood units;]

(g) ―donor‖ means a person who voluntarily donates blood after he has been declared fit after a medical examination, for donating blood, on fulfilling the criteria given hereinafter, without accepting in return any consideration in cash or in kind from any source but does not include a professional or a paid donor.

Explanation.- For the purposes of this clause, benefits or incentives like pins, plaques, badges, medals, commendation certificates, time-off from work, membership of blood assurance programme, gifts of little or intrinsic monetary value shall not be construed as consideration;

(h) ―leucapheresis‖ means the process by which the blood drawn from a donor, after leucocyte concentrates have been separarated is re-transfused simultaneously into the said donor;

(i) ―plasmapheresis‖ means the process by which the blood drawn from a donor, after plasma has been separated, is re-transfused during the same sitting into the said donor;

(j) ―plateletpheresis‖ means the process by which the blood drawn from a donor, after platelet concentrates have been separated, is re-transfused simultaneously into the said donor;

(k) ―professional donor‖ means a person who donates blood for a valuable consideration, in cash or kind, from any source, on behalf of the recipient-patient and includes a paid donor or a commercial donor;

(l) ―replacement donor‖ means a donor who is a family friend or a relative of the patient-recipient.]

1. Ins. by G.S.R. 28(E), dt. 22-1-1993.
2. Ins. by G.S.R. 245 (E), dt. 5-04-1999.
3. Subs. by G.S.R. 899 (E), dt. 27-12-2011.
4. Ins. by G.S.R. 899 (E), dt. 27-12-2011.

[4][(m) ―umbilical cord blood‖ is the whole blood including Hematopoietic Progenitor Cells collected from placental and or Umbilical cord blood vessels after the umbilical cord have been clamped.]

122-F. ***Form of application for licence for operation of Blood Bank/processing of whole human blood for components/manufacture of blood products for sale or distribution*** [4]***, collection, processing, testing, storage, banking and release of umbilical cord blood stem cells.]-***

(1) Application for the grant and/or renewal of licence for the operation of a Blood Bank/processing of human blood for components/manufacture of blood products [4][collection, processing, testing, storage, banking and release of umbilical cord blood stem cells]shall be made to the Licensing Authority appointed under Part VII in [1][

Form 27-C or [5][Form 27-E or Form 27-F], as the case may be], and shall be accompanied by [3][licence fee of rupees six thousand and an inspection fee of rupees one thousand and five hundred for every inspection thereof or for the purpose of renewal of licence]:

Provided that if the applicant applies for renewal of licence after its expiry but within six months of such expiry the fee payable for the renewal of the licence [3][shall be rupees six thousand and inspection fee of rupees one thousand and five hundred plus an additional fee at the rate of rupees one thousand per month or a part thereof in addition to the inspection fee]:

[5][Provided further that a licensee holding a license in Form 28-C, Form 28-E or Form 28-F as the case may be, for operation of Blood Bank/ processing of whole human blood for components / manufacture of blood products / collection, processing testing storage, banking and release of umbilical cord blood stem cells shall apply for grant of license under sub Rule (1) before the expiry of the said license in Form 27-C, Form 27-E or Form 27-F as the case may be and he shall continue to operate the same till the orders on his application are communicated to him.]

[2][***]

(2) A fee of [3][rupees one thousand] shall be paid for a duplicate copy of a licence issued under this rule, if the original is defaced, damaged or lost.

(3) Application by a licensee to manufacture additional drugs listed in the application shall be accompanied by a fee of [3][rupees three hundred] for each drug listed in the application.

(4) On receipt of the application for the grant or renewal of such licence, the Licensing Authority shall,–

(i) verify the statements made in the application form;

(ii) cause the manufacturing and testing establishment to be inspected in accordance with the provision of rule 122-I; and

(iii) in case the application is for renewal of licence, call for information of past performance of the licensee.

(5) If the Licensing Authority is satisfied that the applicant is in a position to fulfil the requirements laid down in the rules, he shall prepare a report to that effect and forward it [6][along with the application and the licence (in triplicate) to be granted or renewed, duly completed] to the Central Licence Approving Authority:

Provided that if the Licensing Authority is of the opinion that the applicant is not in a position to fulfil the requirements laid down in these rules, he may, by order, for reasons to be recorded in writing, refuse to grant or renew the licence, as the case may be.

(6) If, on receipt of the application and report of the Licensing Authority referred to in sub-rule [7][(5)] and after taking such measures including inspection of the premises by the Inspector, appointed by the Central Government under section 21 of the Act, and/or along

1. Subs. by G.S.R. 245(E), dt. 5.4.1999. 4. Ins. by G.S.R. 899 (E), dt. 27-12-2011.

2. Explanation omitted by G.S.R. 733 (E), dt. 21.12.2005 earlier Ins. by G.S.R. 89(E), dt. 14-2-1996. 3. Subs. by G.S.R. 601(E), dt. 24-8-2001. 5. Subs. by G.S.R. 899 (E), dt. 27-12-2011. 6. Ins. by G.S.R. 89 (E), dt. 14.2.1996.

7. Corrected by corrigendum G.S.R. 447 (E), dt. 10-06-1993.

with the Expert in the field concerned if deemed necessary, the Central Licence Approving Authority is satisfied that the applicant is in a position to fulfil the requirements laid down in these rules, he may grant or renew the licence, as the case may be:

Provided that if the Central Licence Approving Authority is of the opinion that the applicant is not in a position to fulfil the requirements laid down in these rules he may, notwithstanding the report of the Licensing Authority, by order, for reasons to be recorded in writing, reject the application for grant or renewal of licence, as the case may be, and shall supply the applicant with a copy of the inspection report.

122G. ***Form of Licence for the operation of a Blood Bank/processing of whole human blood for components and manufacture of blood products*** [3]***[/manufacture of blood products/collection, processing, testing, storage, banking and release of umbilical cord blood stem cells] and the conditions for the grant or renewal of such licence.***— [2][(1)] A licence for the operation of a Blood Bank or for processing whole human blood for components and [3][/manufacture of blood products/collection, processing, testing, storage, banking and release of umbilical cord blood stem cells] shall be issued in [1][

Form 28C or Form 28E or [3][Form 28F or Form 26G or Form26-I or Form 26J, as the case may be, before a license in Form 28C or Form 28E or Form28-F or Form 26G or Form 26-I or Form 26-J], as the case may be,] is granted or renewed the following conditions shall be complied with by the applicant:-

[1][(i) The operation of Blood Bank and/or processing of whole human blood for components shall be conducted under the active direction and personal supervision of competent technical staff consisting of at least one person who is whole time employee and who is Medical Officer, and possessing-

(a) Postgraduate degree in Medicine - M.D (Pathology/Transfusion Medicines); or

(b) Degree in Medicine (M.B.B.S.) with Diploma in Pathology or Transfusion Medicines having adequate knowledge in blood group serology, blood group methodology and medical principles involved in the procurement of blood and/or preparation of its components; or

(c) Degree in Medicine (M.B.B.S.) having experience in Blood Bank for one year during regular service and also has adequate knowledge and experience in blood group serology, blood group methodology and medical principles involved in the procurement of blood and/or preparation of its components,

the degree or diploma being from a University recognized by the Central Government.

Explanation.- For the purposes of this condition, the experience in Blood Bank for one year shall not apply in the case of persons who are approved by the Licensing Authority and/or Central Licence Approving Authority prior to the commencement of the Drugs and Cosmetics (Second Amendment) Rules, 1999].

(ii) The applicant shall provide adequate space, plant and equipment for any or all the operations of blood collection or blood processing. The space, plant and equipment required for various operation is given in Schedule ‗F', Part XIIB and/or XIIC [4][or XIID].

(iii) The applicant shall provide and maintain adequate technical staff as specified in Schedule F, Part XIIB and/or XIIC [4][or XIID].

(iv) The applicant shall provide adequate arrangements for storage of whole human blood, human blood components and blood products.

(v) The applicant shall furnish to the Licensing Authority, if required to do so, data on the stability of whole human blood, its components or blood products which are likely to deteriorate, for fixing the date of expiry which shall be printed on the labels of such products on the basis of the data so furnished.

1. Ins. by GSR 245(E), dt. 5-4-1999.

2. Renumbered as sub-rule (1) by GSR 733(E), dt. 21-12-2005.

3. Subs. by GSR 899(E), dt. 27-12-2011. 4. Ins. by GSR 899(E), dt. 27-12-2011.

[3][(2) Application for grant or renewal of a licence for operation of Blood Bank or processing of human blood components shall be made by the Blood Bank run by the Government, Indian Red Cross Society, hospital, charitable trust or voluntary organization approved by a State/ Union Territory Blood Transfusion Council only.

Explanation.– For the purpose of this sub-rule, ―renewal‖ shall include renewal of any licenceissued prior to the commencement of the Drugs and Cosmetics (……..Amendment) Rules,2005.]

122H. ***Duration of licence.-*** An original licence in [1][Form 28C or Form 28E [4][or Form 28F] or a renewed licence in Form 26G or Form 26-I] [4][or Form 26J] unless sooner suspended or cancelled shall be [2][valid for a period of five years on and from the date on which] it is granted or renewed.

122-I. ***Inspection before grant or renewal of licence for operation of Blood Bank, processing of whole human blood for components and manufacture of blood products.-*** Before a licence in [1][Form 28C or Form 28E [4][or Form 28F] is granted or a renewal of licence in form 26G or Form 26-I [4][or Form 26J] is made, as the case may be,] the Licensing Authority or the Central Licence Approving Authority, as the case may be, shall cause the establishment in which Blood Bank is proposed to be operated/whole human blood for components is processed/ blood products are manufactured to be inspected by one or more Inspectors, appointed under the Act and/or along with the Expert in the field concerned. The Inspector or Inspectors shall examine all portions of the premises and appliances/equipments and inspect the process of manufacture intended to be employed or being employed along with the means to be employed or being employed for operation of blood bank/processing of whole human blood for components/manufacture of blood products together with their testing facilities and also enquire into the professional qualification of the expert staff and other technical staff to be employed.

122J. ***Report by Inspector.-***The Inspector or Inspectors shall forward a detailed descriptive report giving his findings on each aspect of inspection along with his recommendation in accordance with the provisions of rule 122-I to the Licensing Authority or to the Central Licence Approving Authority.

122K. ***Further application after rejection***.- If within a period of six months from the rejection of application of a licence the applicant informs the Licensing Authority that the conditions laid down have been satisfied and deposits an inspection 2[fee of rupees two hundred and fifty] the Licensing Authority may, if after causing further inspection to be made is satisfied that the conditions for the 1[grant or renewal of a licence have been complied with, shall grant or renew the licence in

Form 28C or Form 28E [4][or Form 28F]:

Provided that in the case of a drug notified by the Central Government under rule 68-A, the application, together with the inspection report and the Form of licence (in triplicate to be granted or renewed), duly completed shall be sent, to the Central Licence Approving Authority, who may approve the same and return it to the Licensing Authority for issue of the licence.]

122L. ***Delegation of powers by the Central Licence Approving Authority.-*** The Central Licence Approving Authority may, with the approval of the Central Government, by notification delegate his powers of signing licences and any other power under rules to persons under his control having same qualifications as prescribed for Controlling Authority under rule 50-A, for such areas and for such periods as may be specified.

122M. ***Provision for appeal to the State Government by a party whose licence has not been granted or renewed.-*** Any person who is aggrieved by the order passed by the Licensing Authority or Central Licence Approving Authority, as the case may be, may within thirty days from the date of receipt of such order, appeal to the State Government or Central Government, as the case may be, after such enquiry into the matter as it considers necessary and after giving the said person an opportunity for representing his view in the matter may pass such order in relation thereto as it thinks fit.

1. Ins. by G.S.R 245(E), dt. 5-4-1999. 3. Ins. by G.S.R 733(E), dt. 21-12-2005. 2. Subs. by G.S.R 601(E), dt. 24-8-2001. 4. Ins. by GSR 899(E), dt. 27-12-2011.

122-N. ***Additional information to be furnished by an applicant for licence or by a licensee to the Licensing Authority.-***The applicant for the grant of licence or any person granted a licence under the Part shall, on demand furnish to the Licensing Authority, before the grant of the licence or during the period the licence is in force, as the case may be, documentary evidence in respect of the ownership or occupation, rental or other basis of the premises, specified in the application for licence or in the licence granted, constitution of the firm or any other relevant matter, which may be required for the purpose of verifying the correctness of the statement made by the applicant or the licensee, while applying for or after obtaining the licence, as the case may be.

122-O. ***Cancellation and suspension of licences.***− (1) The Licensing Authority or Central Licence Approving Authority may for such licences granted or renewed by him after giving the licensee an opportunity to show cause why such an order should not be passed by an order in writing stating the reason thereof, cancel a licence issued under this part or suspend it for such period as he thinks fit, either wholly or in respect of some of the substances to which it relates [1][or direct the licensee to stop collection, storage, processing, manufacture and distribution of the said substances and [2][thereupon order the destruction of substances and] stocks thereof in the presence of an Inspector], if in his opinion, the licensee has failed to comply with any of the conditions of the licence or with any provisions of the Act or Rules thereunder.

(2) A licensee whose licence has been suspended or cancelled may, within three months of the date of the order under sub-rule (1) prefer an appeal against the order to the State Government or Central Government, which shall decide the same.

122-P. ***Conditions of licence.-*** [3][A licence in Form 28C, Form 28E, [4][Form 28F, Form 26G, Form 26-I or Form 28J shall be subject to the special conditions set out in Schedule F, Part XII-B and Part XII C, Part XIID,] as the case may be, which relate to the substance in respect of which the licence is granted or renewed and to the following general conditions, namely:-]

(i) (a) The licensee shall provide and maintain adequate staff, plant and premises for the proper operation of a Blood Bank for processing whole human blood, its components and/or manufacture of blood products.

(b) The licensee shall maintain staff, premises and equipment as specified in Rule 122-G. The licensee shall maintain necessary records and registers as specified in Schedule F, Parts XII-B and XII-C.

(c) The licensee shall test in his own laboratory whole human blood, its components and blood products and maintain records and registers in respect of such tests as specified in Schedule F, Parts XIIB and XIIC [5][or XIID]. The records and register shall be maintained for a period of five years from the date of manufacture.

(d) The licensee shall maintain/preserve reference sample and supply to the Inspector the reference sample of the whole human blood collected by him in an adequate quantity to conduct all the prescribed tests. The licensee shall supply to the Inspector the reference sample for the purpose of testing.

1. Subs. by G.S.R. 20(E), dt. 11-1-1996.
2. Ins. by (Corrigenda) G.S.R. 514 (E), dt. 6-11-1996.
3. Subs. by G.S.R. 245(E), dt. 5-4-1999.
4. Subs. by GSR 899(E), dt. 27-12-2011.
5. Ins. by GSR 899(E), dt. 27-12-2011.

(ii) The licensee shall allow an Inspector appointed under the Act to enter, with or without prior notice, any premises where the activities of the Blood Bank are being carried out for the processing of Whole Human Blood and/or Blood Products, to inspect the premises and plant and the process of manufacture and the means employed for standardizing and testing the substance.

(iii) The licensee shall allow an Inspector appointed under the Act to inspect all registers and records maintained under these rules and to take samples of the manufactured product and shall supply to the Inspector such information as he may require for the purpose of ascertaining whether the provisions of the Act and rules thereunder have been observed.

(iv) The licensee shall from time to time report to the Licensing Authority any changes in the expert staff responsible for the operation of a Blood Bank/processing of whole human blood for components and/or manufacture of blood products and any material alterations in the premises or plant used for that purpose which have been made since the date of last inspection made on behalf of the Licensing Authority before the grant of the licence.

(v) The licensee shall on request furnish to the Licensing Authority, or Central Licence Approving Authority or to such Authority as the Licensing Authority, or the Central Licence Approving Authority may direct, from any batch unit of drugs as the Licensing Authority or Central Licence Approving Authority may from time to time specify, sample of such quantity as may be considered adequate by such Authority for any examination and, if so required, also furnish full protocols of the test which have been applied.

(vi) If the Licensing Authority or the Central Licence Approving Authority so directs, the licensee shall not sell or offer for sale any batch/unit in respect of which a sample is, or protocols are furnished under the last preceding sub-paragraph until a certificate authorizing the sales of batch/unit has been issued to him by or on behalf of the Licensing Authority or the Central Licence Approving Authority.

(vii) The licensee shall on being informed by the Licensing Authority or the Controlling Authority that any part of any batch/unit of the substance has been found by the Licensing Authority or the Central Licence Approving Authority not to conform with the standards of strength, quality or purity specified in these Rules and on being directed so to do, withdraw, from sales and so far as may in the particular circumstances of the case be practicable recall all issues already made from that batch/unit.

(viii) No drug manufactured under the licence shall be sold unless the precautions necessary for preserving its properties have been observed throughout the period after manufacture. Further no batch/unit manufactured under this licence shall be supplied/distributed to any person without prescription of a Registered Medical Practitioner.

(ix) The licensee shall comply with the provisions of the Act and of these Rules and with such further requirements, if any, as may be specified in any Rules subsequently made under

Chapter IV of the Act, provided that where such further requirements are specified in the Rules, these would come in force four months after publication in the Official Gazette.

(x) The licensee shall maintain an Inspection Book in

Form 35 to enable an Inspector to record his impression and defects noticed.

(xi) The licensee shall destroy the stock of batch/unit which does not comply with standard tests in such a way that it would not spread any disease/infection by way of proper disinfection method.

[1][(xii) All bio-medical waste shall be treated, disposed of or destroyed as per the provisions of the Bio-Medical Wastes (Management and Handling) Rules, 1996.

(xiii) The licensee shall neither collect blood from any professional donor or paid donor nor shall he prepare blood components and/or manufacture blood products from the blood drawn from such a donor.]

PART XI

EXEMPTIONS

123. The drugs specified in Schedule K shall be exempted from the provisions of Chapter IV of the Act and the Rules made thereunder to the extent and subject to the conditions specified in that Schedule.

PART XII
STANDARDS

[2][**124.** ***Standards of drugs***: –

(1) For drugs included in the Indian Pharmacopoeia—

(a) The standards for identity, purity and strength shall be those as may be specified in the edition of the Indian Pharmacopoeia for the time being in force.

(b) In case the standards for identity, purity and strength for drugs are not specified in the edition of the Indian Pharmacopoeia for the time being in force but are specified in the edition of the Indian Pharmacopoeia immediately preceding, the standards for identity, purity and strength shall be those occurring in such immediately preceding edition of the Indian Pharmacopoeia.

(2) For other drugs–

(a) The standards for identity, purity and strength shall be those as may be specified in the edition of the official pharmacopoeia, for the time being in force, of any country to which the drug claims to comply with,

(b) In case the standards for identity, purity and strength for drugs are not specified in the edition of such official pharmacopoeia for the time being in force, but are specified in the edition immediately preceding, the standards for identity, purity and strength shall be those occurring in such immediately preceding edition of such official pharmacopoeia to which the drug claims to comply with.

(c) For drugs for which standards are not included in the edition of the official pharmacopoeia, for the time being in force, of any country or in edition immediately preceding, but included in the official compendia of drug standards, namely, the British Pharmaceutical Codex or the National Formulary of the United States, for the time being in force, to which the drug claims to comply with.]

[3][**124A**. ***Standards for veterinary drugs.*** –For drugs intended for veterinary use, the standards shall be those given in the current edition for the time being in force of the [4][British Pharmacopoeia (Veterinary)].

1. Subs. by G.S.R. 245(E), dt. 5-4-1999.

2. Subs. by G.S.R. 19, dt. 15-12-1977.
3. Ins. by notification F. 1-6/62-D (SO 2889), dt. 2-7-1969.
4. Subs. by G.S.R. 647 (E), dt. 28-10-1998.

1[**124B.** ***Standards for patent or proprietary medicines.***— The standards for patent or proprietary medicines shall be those laid down in Schedule V and such medicines shall also comply with the standards laid down in the Second Schedule to the Act.

2[**124C**. ***Standards for Surgical Dressings*.**-The standards for Surgical Dressings shall be such as are laid down in Schedule F (II).]

3[**124D**. ***Standards for Sterilised Umbilical tapes.***- The standards for Sterilised Umbilical tapes shall be as laid down in Schedule F(III).]

4[**125**. ***Standards for substances (other than food) intended to affect the structure or any function of human body—contraceptives.***—(1) The standards for mechanical contraceptives shall be such as are laid down in Schedule R.

(2) The standards which other contraceptives will have to comply with shall be in conformity with the formulae approved as safe and efficacious by the Central Government. Such formula shall be displayed on the label of every container of such contraceptive.

5[**125A**. ***Standards for Medical Devices.***—The standards for the Medical Devices shall be such as are laid down in Schedule R-1.]

6[**126**. ***Standards for substances intended to be used for the destruction of vermin or insects which cause*** 9[***] ***disease in human beings or animals.- Disinfectants.***

The standards of disinfectants shall be such as are laid down in Schedule O.]

7[**126A** ***Standards for ophthalmic preparations*** 8[***including Homoeopathic ophthalmic preparations***].—The standards for ophthalmic preparations 8[including Homoeopathic ophthalmic preparations] shall be those laid down in Schedule FF, and such preparations shall also comply with the standards set out in the Second Schedule to the Act.]

1. Ins. by G.S.R. 665, dt. 28-5-1977.
2. Ins. by G.S.R. 318 (E), dt. 1-5-1984.
3. Ins. by G.S.R. 1115 (E), dt. 30-9-1986.
4. Amended by F-1-28/65D (SO 886), dt. 8-3-1966.
5. Ins. by G.S.R. 109 (E), dt. 22-2-1994.
6. Amended by F.1-20/60-D, dt. 24-1-1964.
7. Ins. by F 1-113/60-D (SO 23), dt. 23-12-1969.
8. Subs. by G.S.R. 245 (E), dt. 17-6-1996.
9. Subs heading ―Insecticides‖ and the entry relating thereto omitted by GSR 139, dt. 8-1-1976.

1[**127**. ***List of colours permitted to be used in drugs.***−(1) No drug shall contain a colour other than specified below :-

(1) ***Natural Colours***

Annatto

Carotene

Chlorophyll

Cochineal

Curcumin

Red Oxide of iron

Yellow Oxide of iron

[2] [Titanium Oxide]

[3][Black Oxide of iron]

[6][Titanium dioxide coated mica pearlescent pigments]

(2) *Artificial Colours*

Caramel

[4][Riboflavin]

(3) *Coal Tar Colours*

Common name of the colour	Colour Index Number	Chemical Name
1	2	3
GREEN		
Quinazarine Green S.S.	61565	1, 4-bis (p-Toluino) anthraquinone.
Alizarin Cyanine Green F.	61570	Disodium salt of 1, 4-bis (O-sulfo-p-Toluino) anthra-quinone.
[2][Fast Green F.C.F.	42053	Disodium salt of 4-{[4-(N-ethyl-p Sulfobenzylamino)-phenyl-]-(4-hydroxy-2- sulfoniumphenyl)-methylene} [1-(N-ethyl-N-p-sulfobenzyl]Δ 2, 5-cyclohexadienimine].
[5][** * * *]		
YELLOW		
Tartrazine	19140	Trisodium salt of 3-carboxy-5- hydroxy-l-p-sulfophenyl-4-p- Sulfophenyl azopyrazole.
Sunset Yellow FCF	15985	Disodium salt of 1-p-sulfophenyl azo-2-naphthol-6-sulfonic acid.

1. Amended by S.O. 289, dt. 20-12-1972.
2. Ins. by X.11013/3/76-DM.S (SO 1074), dt. 19-8-1978.
3. Ins. by G.S.R. 370 (E), dt. 7-4-1994.
4. Ins. by G.S.R. 681 (E), dt. 6-6-1988.
5. —Green Sl omitted by G.S.R. 753 (E), dt. 4-11-1999.
6. Ins. by G.S.R. 76 (E), dt. 8-2-2012.

(1)	(2)	(3)
[1][Quinoline Yellow WS	47005	Disodium salt of disulfonic acid of 2(2-quinolyl)-1, 3-indandione.]
RED		
[2][** ** *]		
Erythrosine	45430	Disodium salt of 9-0-carboxyphenyl 6-hydroxy 2,4-5,7-tetriodo-3-isoxanthone
Eosin YS or Eosine G	45380	Disodium of salt of 2,4,5, 7-Tetrabromo- 9-p-carboxyphenyl-6-hydroxy 3-isoxanthone.
Toney Red or Sudan III	26100	1-p-phenylazophenylaze-2-naphthol.

Ponceau 4 R	16255	Trisodium salt of 1-(4-sulpho-1-1- Napthylazo)-2 napthol-6 : 8-disulphonic acid.
Carmoisine	14720	Disodium salt of 2-(4-sulpho-1-napthylazo)-1 napthol-4 sulphonic acid.

[3][*** * *]

BLUE

Indigo Carmine	73015	Disodium salt of indigotin-5 : 5 Disu lphonic Acid
[4][Brilliant Blue FCF	42090	Disodium salt of 4-[{4-(N-ethyl-p-sulfobenzylamino)-phenyl }-](2- sulfonium phenyl)-methylene)-1-(N- ethyl-N-p-sulfobenzyl)- Δ 2, 5-cyclohexadienimine.

ORANGE

Orange G disulfonic acid.	16230	Disodium salt of 1-phenylazo-2- naphthol-6, 8-

BROWN

Resorcin Brown xylylazo-1, 3 resorcinol.	20170	Monosodium salt of 4-p-sulfophenylazo-2-(2, 4-

BLACK

Naphthol Blue Balck 2-phenylazo-1-naphthol-3, 6-disulfonic acid.	20470	Disodium salt of 8-amino-7-p-nitro- phenylazo-

1. Subs. by G.S.R. 11(E), dt. 7-1-1991.
2. _Amaranth' omitted by G.S.R. 753(E) dt. 4.11.1999.
3. Fast Red omitted by G.S.R. 753, dt. 4-11-1999.
4. Ins. by X.11013/3/76-DM.S, dt. 19-8-1978.

(4) *LAKES*

The aluminum or calcium salts (lakes) of any of the water-soluble colours listed above:

[5][Provided that disinfectants may also contain colours specified under Schedule Q, which are non-staining.]

(2) The label on the container of a drug containing a permitted colour shall indicate the common name of the colour.]

128. The following rules are hereby repealed except as respects things done or omitted to be done under these rules, namely :---

Andhra Pradesh Drugs Rules, 1945.

Assam Drugs Rules, 1945.

Bihar Drugs Rules, 1945.

Bombay Drugs Rules, 1946.

East Punjab Drugs Rules, 1945.

C.P. & Berar Drugs Rules, 1945.

Madras Drugs Rules, 1945.

Orissa Drugs Rules, 1945.

Rajasthan Drugs Rules, 1953.

Saurashtra Drugs Rules, 1953.

Travancore-Cohin Drugs Rules, 1953.

United Provinces Drugs Rules, 1945.

West Bengal Drugs Rules, 1946.

[2][Mysore Drugs Rules, 1954].

[1][PART XIII
[3][IMPORT AND REGISTRATION OF COSMETICS]

[4]**[129**. ***Registration of cosmetic products imported into the country***.- No cosmetic shall be imported into India unless the product is registered under the rules by the licensing authority appointed by the Central Government under rule 21 or by any person to whom such powers may be delegated under rule 22.

129A. ***Form and manner of application for Registration Certificate***.- (1) An application for issue of a Registration Certificate for cosmetics intended to be imported into India shall be made in Form 42 either by the manufacturer himself or by his authorised agent or importer in India or by the subsidiary in India authorised by the manufacturer and shall be accompanied by a fee of two hundred and fifty US dollars or its equivalent to Indian rupees for each brand of cosmetic. The application shall be accompanied by a treasury challan as specified in sub-rule (3) along with the information and undertaking as specified in Schedule D (III) duly signed by or on behalf of the manufacturer or by his authorised agent or importer in India or by the subsidiary in India authorised by the manufacturer.

1. Ins. by G.S.R. 1183 dt. 17-8-1964.
2. Added by notification F. 1-37/58-D, dt. 21-7-1958.
3. Subs. by G.S.R. 426 (E), dt. 19-5-2010.
4. Rules 129 to 129H subs. by G.S.R. 426 (E), dt. 19-5-2010.
5. Ins. by G.S.R. 76 (E), dt. 8-2-2012.

(2) An authorisation by the manufacturer to his agent in India shall be duly authenticated either in India before a First Class Magistrate or in the country of origin before such an equivalent authority.

(3) The fees shall be paid through a challan in the designated branches of Bank of Baroda either in US dollars or in equivalent Indian rupees under Head of Account ―0210-MEDICAL AND PUBLIC HEALTH, 04 PUBLIC HEALTH, 104-FEES AND FINES‖ and the original copy of the treasury challan shall be submitted along with the application for product registration.

Provided that in the case of any direct payment of fees by a manufacturer in the country of origin, the fees shall be paid through Electronic Clearance System (ECS) from any bank in the country of origin to the Bank of Baroda, Kasturba Gandhi Marg, New Delhi, through the Electronic Code of the bank in the Head of Account ―0210-MEDICALAND PUBLIC HEALTH, 04 PUBLIC HEALTH, 104-FEES AND FINES‖ and the original receipt of the said transfer shall be treated as an equivalent to the bank challan subject to the approval by the Bank of Baroda that they have received the payment.

(4) The applicant shall be liable for the payment of testing fees directly to a testing laboratory approved by the Central Government, as may be, required for examination, tests and analysis of cosmetics.

(5) A fee of one hundred US dollars or its equivalent shall be paid for a duplicate copy of the Registration Certificate, if the original is defaced, damaged or lost.

129B. ***Registration Certificate for the import of cosmetics manufactured by one manufacturer*****.-**A single application may be made and a single Registration Certificate in

Form 43 may be issued in respect of import of one or more than one cosmetics manufactured by the same manufacturer: Provided that the cosmetics are manufactured at one factory or more than one factory functioning conjointly as a single manufacturing unit.

129C. ***Grant of Registration Certificate*****.-** (1) On receipt of an application for Registration Certificate in the form and manner specified in rule 129A, the licensing authority shall, if satisfied, issue a Registration Certificate in

form 43 subject to the conditions of the registration certificates in form 43:
Provided that if the application is complete in all respects and information specified in Schedule D III is in order, the licensing authority shall, within six months from the date of receipt of an application, issue such Registration Certificate, and in exceptional circumstances and for reasons to be recorded in writing, the Registration Certificate may be issued within such extended period, not exceeding three months, as the licensing authority may deem fit.

(2) If the applicant does not receive the Registration Certificate within the period as specified above, he may appeal to the Central Government and the Central Government may after such enquiry into the matter, as it considers necessary, may pass such orders in relation thereto as it thinks fit.

129D. ***Duration of Registration Certificate*****.-** A Registration Certificate, unless it is sooner suspended or cancelled, shall be valid for a period of three years from the date of its issue: Provided that if application for a fresh Registration Certificate is made within six months before the expiry of the said certificate, the existing Registration Certificate shall be deemed to continue to remain in force until orders are passed on the application.

129E. ***Suspension and cancellation of Registration Certificate*****.-** If the manufacturer fails to comply with any of the conditions of the Registration Certificate, the licensing authority may after giving him an opportunity to show cause why such an order should not be passed, by an order in writing, stating the reasons therefor, suspend or cancel the Registration Certificate for such period as it thinks fit either wholly or in respect of some of the cosmetics to which it relates: Provided that a person who is aggrieved by the order passed by the licensing authority under this rule may, within thirty days of the receipt of the order, appeal to the Central Government and the Central Government may after such enquiry into the matter as it considers necessary and after giving the said appellant an opportunity of being heard pass orders as it thinks fit.

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129F. ***Prohibition of import of certain cosmetic*****.-** No cosmetic, the manufacture, sale or distribution of which is prohibited in the county of origin, shall be imported under the same name or under any other name except for the purpose of examination, test or analysis.

129G. ***Standard for imported cosmetics*****.-** No cosmetic shall be imported unless it complies with the specifications prescribed under Schedule S and Schedule Q or any other standards of quality and safety, applicable to it, and other provisions under the rules. In case the cosmetic is not included under Schedule S, it shall meet with specifications under the rules and standards applicable to it in the country of origin.

129H. ***Labeling and Packing of Cosmetics*****.-** No cosmetic shall be imported unless it is packed and labeled in conformity with the rules in Parts XV. Further the label of imported cosmetics shall bear registration certificate number of the product and the name and address of the registration certificate holder for marketing the said product in India.]

130. ***Documents to be supplied to the Collector of Customs.***− Before any cosmetics are imported, a declaration signed by or on behalf of the manufacturer or by on behalf of the importer that the cosmetics comply with the provisions of Chapter III of the Act, and the Rules made there under, shall be supplied to the Collector of Customs.

131. ***Procedure for the import of cosmetics.***− (1) If the officer appointed at the post of entry by the Central Government has reason to believe that any cosmetic contravenes any of the provisions of the Act or the rules made thereunder he may take sample of the cosmetic from the consignment for inspection. If on examination of the sample defects are noticed the officer shall advise the Collector of Customs for further action to be taken.

If the suspected contravention of the provisions of the Act or the Rules is such as may have to be determined by test, the officer shall send the sample to the laboratory established for the purpose for performing such tests. The consignment of the said cosmetic shall be detained till such time that the test report on such sample is received from the Director of the said laboratory or

any other officer of the laboratory empowered by him in this behalf with the approval of the Central Government:

Provided that if the importer gives an undertaking in writing not to dispose of the cosmetic without the consent of the Collector of Customs and to return the consignment or such portion thereof as may be required, the Collector of Customs shall make over the consignment to the importer.

(2) If the importer who has given an undertaking under the proviso to sub-rule (1) is required by the Collector of Customs to return the consignment or portion thereof, he shall return the consignment or portion thereof within ten days of receipt of the notice.

Further procedure on receipt of the report of analysis

(3) If the Director of the Laboratory established for the purpose by the Central Government or any other officer of the laboratory empowered by him in this behalf with the approval of the Central Government, reports to the Collector of Customs or to the officer mentioned in sub-rule (1) above that the sample of any cosmetic in a consignment contravenes the provisions of Chapter III of the Act or the Rules made thereunder and that the contravention is such that it cannot be remedied by the importer, the Collector of Customs shall communicate the report forthwith to the importer who shall within two months of receiving such a communication either send back all the cosmetic of that description to the country in which it was manufactured or to the country from which it was imported or hand it over to the Central Government which shall cause it to be destroyed:

Provided that the importer may within thirty days of receipt of the report make a representation against the report to the Collector of Customs who shall forward the representation with a fresh sample of the cosmetic to the Drugs Controller, India, who after

obtaining, if necessary, the report of the Director of the Central Drugs Laboratory shall pass orders thereon which shall be final.

(4) If the Drugs Controller or any other officer empowered by him in this behalf with the approval of Central Government reports to the Collector of Customs after the inspection of the sample of cosmetic and if necessary, after obtaining a test report thereon that the sample of the said cosmetic contravenes in any respect the provisions of Chapter III of the Act or the Rules made thereunder but that the contravention is such that it can be remedied by the importer, the Collector of Customs shall communicate the report forthwith to the importer and permit him to import the cosmetic on his giving an undertaking in writing not to dispose of the cosmetic without the permission of the officer authorised in this behalf by the Central Government.

132. ***Exemption of cosmetics***—Cosmetics as may be specified in Schedule D shall be exempted from the provisions of Chapter III of the Act and the Rules made thereunder to the extent and subject to the conditions specified in that Schedule.

133. ***Import through points of entry***—No cosmetic shall be imported into India except through the points of entry specified in rule 43A.

[1][**134.** ***Cosmetic to contain Dyes, Colours and Pigments***.- No Cosmetic shall contain Dyes, Colours and Pigments other than those specified by the Bureau of Indian Standards (IS:4707 Part 1 as amended) and Schedule Q.

The permitted Synthetic Organic Colours and Natural Organic Colours used in the Cosmetic shall not contain more than:-

(i) 2 parts per million of arsenic calculated as arsenic trioxide.

(ii) 20 parts per million of lead calculated as lead.

(iii) 100 parts per million of heavy metals other than lead calculated as the total of the respective metals.]

[2][**134-A** ***Prohibition of import of cosmetic containing Hexachlorophene***.— No cosmetic containing hexachlorophene shall be imported.

135. ***Import of cosmetic containing Lead or Arsenic compound prohibited***.—No cosmetic shall be imported in which a Lead or Arsenic compound has been used for purposes of colouring.

[3][**135-A**. ***Import of cosmetics containing mercury compounds prohibited***.–No cosmetic shall be imported which contains mercury compounds.]

[5][**135-B**. ***Prohibition of import of cosmetics tested on animals***.–No cosmetic that has been tested on animals after the commencement of the Drugs and Cosmetics (Fifth Amendment) Rules, 2014 shall be imported into the country.]

136. ***Import of cosmetic for personal use***—Small quantities of cosmetics the import of which is otherwise prohibited under section 10 of the Act, may be imported for personal use subject to the following conditions: —

(i) The cosmetics shall form part of a passenger's baggage and shall be the property of and intended for, the *bona fide* use of the passenger; and

(ii) The cosmetics shall be declared to the Customs authorities, if they so direct.

[4][PART XIV
MANUFACTURE OF COSMETIC FOR SALE OR FOR DISTRIBUTION]

137. ***Manufacture on more than one set of premises***. — If cosmetics are manufactured on more than one premises, a separate application for each such premises shall be made and a separate licence obtained for each such premises.

1. Subs. by G.S.R. 811 (E), dt. 14-11-1994.
2. Added by G.S.R. 116, dt. 25-1-1975.
3. Ins. by X.11013/76-D & MS, dt. 19-8-1978.
4. Subs. by G.S.R. 788 (E), dt. 10-10-1985.
5. Ins. by G.S.R. 718 (E), dt. 13-10-2014.

138. ***Application for 5[licence to manufacture cosmetics for sale and distribution]***—3[(1) Application for grant or renewal of 5[licence to manufacture any cosmetic for sale or for distribution] 1[shall be made up to ten items of each category of cosmetics categorized in Schedule MII to the Licensing Authority appointed by the State Government for the purpose of this Part (hereinafter in this Part referred to as the Licensing Authority) in

Form 31 and shall be accompanied by a licence fee of rupees two thousand and five hundred and an inspection fee of rupees one thousand for every inspection thereof or for the purpose of renewal of licence].

[2][* * * **]

[3][(2) If a person applies for the renewal of licence after expiry but within six months of such expiry, the fee payable for the renewal of such licence shall be [1][rupees two thousand five hundred plus an additional fee at the rate of rupees four hundred per month or part thereof in addition to an inspection fee of rupees one thousand.]

[2][* * * * *]

(3) Application by a licensee to manufacture additional items of cosmetics shall be accompanied by a fee of [1][rupees one hundred for each item subject to a maximum of rupees three thousand for each application.]

[2][* * * * *]

[6][(4) A fee of [1][rupees two hundred and fifty] shall be paid for a duplicate copy of a licence under sub-rule (1), if the original is defaced, damaged or lost.]

[4] [**138A.** ***Application for loan licence to manufacture cosmetics***.−(1) Application for grant or renewal of a loan licence for the manufacture for sale of cosmetics [1][shall be made up to ten items of each category of cosmetics categorized in Schedule M-II in

Form 31-A to the Licensing Authority and shall be accompanied by a licence fee of rupees two thousand and five hundred and an inspection fee of rupees one thousand for every inspection thereof].

Explanation.--For the purpose of this rule a ‗loan licence' means a licence, which a Licensing Authority may issue to an applicant who does not have his own arrangements to manufacture but who intends to avail himself of the manufacturing facilities owned by a licensee in

Form 32.

(2) If a person applies for the renewal of a loan licence after the expiry but within six months of such expiry, the fee payable for the renewal of such a licence shall be

1. Subs. by G.S.R. 601(E), dt. 24-8-2001.
2. Omitted by G.S.R. 331(E),dt. 8.5.1984.
3. Amended by G.S.R. 245, dt. 21.2.1976.
4. Ins. by G.S.R. 444, dt. 28-4-1973.
5. Subs. by G.S.R. 788 (E), dt. 10-10-1985.
6. Subs. by G.S.R. 331(E),dt. 8.5.1984.

[1][rupees two thousand and five hundred plus an additional fee at the rate of rupees four hundred for each month or part thereof.]

(3) The Licensing Authority shall before the grant of a loan licence satisfy himself that the manufacturing unit has adequate equipment, staff, capacity for manufacture and facilities to undertake the manufacture on behalf of the applicant for a loan licence.

(4) The loan licence shall be granted by the Licensing Authority to only such applicants who propose to avail of the facilities of manufacture of cosmetics in the premises of a manufacturer located in the same State where the applicant is located. In case the manufacture of cosmetic involves any special process of manufacture or use of equipment which are not available in the State where the applicant is located, the Licensing Authority after consulting the Licensing Authority where the manufacturing unit is located, may grant the loan licence.

(5) Subject to the provisions of sub-rule (2), application for manufacture of additional items on a loan licence shall be accompanied by a fee of [1][rupees one hundred for each item subject to a maximum of rupees three thousand per application.] (6) A fee of [1][rupees two hundred and fifty] shall be paid for a duplicate copy of a licence issued under sub-rule (1) if the original is defaced, damaged or lost.

139. ***Conditions for the grant or renewal of a licence in***

Form 32—Before a licence in Form 32 is granted or renewed, the following conditions shall be complied with by applicant:-

(1) The manufacture shall be conducted under the direction and personal supervision of a competent technical staff consisting of at least one person who is a whole time employee and who possesses any one of the following qualifications:

(a) holds a Diploma in Pharmacy approved by the Pharmacy Council of India under the Pharmacy Act, 1948 (8 of 1948), or

(b) is registered under the Pharmacy Act, 1948 (8 of 1948), or

(c) has passed the Intermediate Examination with Chemistry as one of the subjects or an examination recognized by the Licensing Authority as equivalent to it.

2[* * * * *]

1. Subs. by G.S.R. 601(E), dt. 24-8-2001.
2. Omitted by. G.S.R. 331(E), dt. 8.5.1984

1[(2) The factory premises shall comply with the requirements and conditions specified in Schedule M-II.]

2 [* * * * *]

(5) The applicant shall either--

(i) provide and maintain adequate staff, premises and laboratory equipment for testing the cosmetic manufactured, and the raw materials used in the manufacture; or

(ii) make arrangements with some institution approved by the Licensing Authority 3[under Part XV (A) of these rules] for such tests to be regularly carried out in this behalf by the institution.

4[**139A.** ***Form of 5[licence to manufacture cosmetics for sale or for distribution]***.—A 5[licence to manufacture cosmetics for sale or for distribution] against application in Form 31, shall be granted in Form 32.]

6[**139AA.** ***Inspection before grant or renewal of licence***.- Before a licence under this Part is granted or renewed in Form 32, Form 32A or Form 33, the Licensing Authority shall cause the establishment, in which the manufacture is proposed to be conducted or being conducted, to be inspected by one or more Inspectors appointed under the Act. The Inspector or Inspectors shall examine all portions of the premises, plant and appliances and also inspect the process of manufacture intended to be employed or being employed along with the means to be employed or being employed for standardizing and testing the substances to be manufactured and enquire into the professional qualifications of the technical staff to be employed. He shall also examine and verify the statements made in the application in regard to their correctness, and the capability of the applicant to comply with the requirements of competent technical staff, manufacturing plant, testing equipments and the requirements of plant and equipments as laid down in Schedule M-II read with requirements of maintenance of records as laid down in Schedule U-1.]

6[**139AB**. ***Report by Inspector***.- The Inspector or Inspectors shall forward a detailed descriptive report giving his or their findings on each aspect of inspection along with his or their recommendations after completion of his or their inspection to the Licensing Authority.]

[6][**139AC.** ***Grant or refusal of licence***.- (1) If the Licensing Authority after such further enquiry, if any, as he may consider necessary is satisfied that the requirements of the rules under the Act have been complied with and that the conditions of the licence and the rules under the Act shall be observed, he shall grant or renew a licence in

form 32, Form 32-A or Form 33.

1. Subs. by G.S.R. 723 (E), dt. 11-8-1992.
2. Omitted condition (3) and (4) by G.S.R. 723 (E), dt. 11-8-1992.
3. Ins. by G.S.R. 1172 (E), dt. 23-8-1977.
4. Ins. by G.S.R. 444, dt. 28-4-1973.
5. Subs. by G.S.R. 788 (E), dt. 10-10-1985.
6. Ins. by G.S.R. 493 (E), dt. 9-6-1995.

(2) If the Licensing Authority is not so satisfied, he shall reject the application and shall inform the applicant of the reasons for such rejection and of the conditions which must be satisfied before a licence can be granted or renewed and shall supply the applicant with a copy of inspection report.]

[1][**139AD.** ***Further application after rejection***.–If within a period of six months from the rejection of an application for a licence, the applicant informs the Licensing Authority that the conditions laid down have been fulfilled and deposits an inspection [2][fee of rupees two hundred and fifty], the Licensing Authority may, if, after causing further inspection to be made, he is satisfied that the conditions for the grant of licence have been complied with, issue a licence in

Form 32, Form 32-A or Form 33.]

[1][**139AE.** ***Appeal to the State Government***.- Any person who is aggrieved by the order passed by the Licensing Authority refusing to grant or renew a licence under this Part may, within ninety days from the date of receipt of such order, appeal to the State Government and the State Government may, after such enquiry into the matter as is considered necessary and after giving the said person an opportunity for representing the case, pass such order as it thinks fit.]

[3][**139B.** ***Form of loan*** [4]***[licence to manufacture cosmetics for sale or for distribution]***.−A loan [4][licence to manufacture cosmetics for sale or for distribution] against application in Form 31-A shall be granted in Form 32-A.

140. ***Duration of licence***.- An original licence or a renewed licence shall unless sooner suspended or cancelled be [2][valid for a period of five years on and from the date on which] it is granted or renewed:

[5][Provided that if the application for renewal of a licence in force is made before its expiry or if the application is made within six months of its expiry, after payment of additional fee, the licence shall continue to be in force until orders are passed on the application and the licence shall be deemed to have expired, if application for its renewal is not made within six months of its expiry.]

141. ***Certificate of renewal***.−The certificate of renewal of a licence in

Form 32 shall be issued in Form 33.

1. Ins. by G.S.R. 493 (E), dt. 9-6-1995.
2. Subs. by G.S.R. 601 (E), dt. 24-8-2001.
3. Ins. by G.S.R. 444, dt. 28-4-1973.
4. Subs. by G.S.R. 493 (E), dt. 9-6-1995.
5. Amended by S.O. 2139, dt. 12.8.1972.

[1][**141A**. ***Certificate of renewal of a loan licence***—The certificate of renewal of a licence in

Form 32-A shall be issued in Form 33-A.]

[1][**141AA.** ***Duration of a loan licence***.–An original loan licence in Form 32A or a renewed loan licence in Form 33-A, unless sooner suspended or cancelled, shall be [2][valid for a period of five years on and from the date on which] it is granted or renewed:

Provided that if the application for the renewal of a licence is made before its expiry, or if the application is made within six months of its expiry, after payment of the additional fee, the licence shall continue to be in force until orders are passed on the application. The licence shall be deemed to have expired if the application for its renewal is not made within six months of its expiry.]

142. ***Conditions of licence***—A licence in Form 32 shall be subject to the conditions stated therein and to the following other conditions, namely: –

(a) the licensee shall provide and maintain staff, premises and equipment as specified in rule 139;

(b) the licensee shall comply with the provisions of the Act and the Rules made thereunder and with such further requirements, if any, as may be specified in any rules to be made hereafter under Chapter IV of the Act;

[3] [(b1) the licensee shall keep records of the details of each batch of cosmetic manufactured by him and of raw materials used therein as per particulars specified in Schedule U(1) and such records shall be retained for a period of three years;]

(c) the licensee shall test each batch or lot of the raw materials used by him for the cosmetics and also each batch of the final product and shall maintain records or registers showing the particulars in respect of such tests. The records or registers shall be retained for a period of three years from the date of manufacture;

(d) the licensee shall allow any [1][Inspector appointed under the Act] to enter with or without prior notice any premises where the manufacture of a substance in respect of which the licence is issued is carried on, to inspect the premises and to take samples of the manufactured products under a receipt;

1. Ins. by G.S.R. 444, dt. 28-4-1973.
2. Subs. by G.S.R. 601 (E), dt. 24-8-2001.
3. Ins. by G.S.R. 1594, dt. 28-10-1976.

(e) the licensee shall allow an Inspector to inspect all registers and records maintained under these rules and shall supply to the Inspector such information as he may require for the purpose of ascertaining whether the provisions of the Act and the Rules made thereunder have been complied;

[1][(f) the licensee shall maintain an Inspection Book in

Form 35 to enable an Inspector to record his impression and the defects noticed:

[2][Provided that clauses (b-1) and (c) shall not apply to the manufacture of soap and the procedure for testing of raw materials and the records to be maintained by the manufacturer of soap shall be such as are approved by the Licensing Authority.]

[4][**142A.** ***Additional information to be furnished by an applicant for licence or a licensee to the Licensing Authority***.—The applicant for the grant of a licence or any person granted a licence under this Part shall, on demand, furnish to the Licensing Authority, before the grant of the licence or during the period the licence is in force, as the case may be, documentary evidence in respect of the ownership or occupation on rental or other basis of the premises, specified in the application for licence or in the licence granted, constitution of the firm, or any other relevant matter, which may be required for the purpose of verifying the correctness of the statements made by the applicant or the licensee, while applying for or after obtaining the licence as the case may be.]

[1][**142B.** ***Conditions of licence in Form 32-A***.–

(a) A licence in Form 32-A shall be deemed to be cancelled or suspended, if the licence owned by the licensee, in Form 32, whose manufacturing facilities are cancelled or suspended, as the case may be under these rules.

(b) The licensee shall comply with the provisions of the Act and these rules and with each further requirements, if any, as may be specified from time to time in Chapter IV of the Act, provided that where such further requirements are specified in the rules, these would come into force four months after publication in the Official Gazette.

[3][(b1) The licensee shall keep records of the details of each batch of cosmetic manufactured by him and of raw materials used therein as per particulars specified in Schedule U(1) and such records shall be retained for a period of three years.]

(c) The licensee shall test each batch or lot of the raw materials used by him for the manufacture of the cosmetics and also each batch of the final product and shall maintain records of registration showing the particulars in respect of such tests. The records or registers shall be retained for a period of three years from the date of manufacture.

1. Ins. by G.S.R. 444, dt. 28-4-1973.
2. Ins. by G.S.R. 681 (E), dt. 6-6-1988.
3. Ins. by G.S.R. 1594, dt. 28-10-1976.
4. Ins. by S.O.2139, dt. 12-8-1972.

(d) The licensee shall allow an Inspector appointed under the Act to enter with or without prior notice any premises where the manufacture of a substance in respect of which licence is issued is carried on, to inspect the premises and to take samples of the manufactured products under a receipt.

(e) The licensee shall allow an Inspector to inspect all registers and records maintained under these rules and shall supply to the Inspector such information as he may require for the purpose of ascertaining whether the provisions of the Act, and the rules made thereunder have been complied.

(f) The licensee shall maintain an Inspection Book in

Form 35 to enable an Inspector to record his impressions and the defects noticed.]

143. ***Cancellation and suspension of licence***.−(1) The Licensing Authority may, after giving the licensee an opportunity to show cause why such an order should not be passed, by an order in writing stating the reasons therefor, cancel a licence issued under this Part or suspend it for such period as he thinks fit, either wholly or in respect of some of the substances to which it relates, if in his opinion, the licensee has failed to comply with any of the conditions of the licence or with any provisions of the Act or the rules made thereunder.

(2) A licensee whose license has been suspended or cancelled may appeal within a period of three months from the date of the order to the State Government which shall after considering the appeal, pass orders, and such orders shall be final.

[1][**144**. ***Prohibition of manufacture of cosmetics containing colours other than those prescribed***.- No Cosmetic shall be manufactured which contains Dyes, Colours and Pigments other than the one specified by the Bureau of Indian Standards (IS: 4707 Part I as amended) and Schedule Q.

The permitted Synthetic Organic colours and Natural Organic colours used in the Cosmetic shall not contain more than−

(i) 2 parts per million of arsenic calculated as arsenic trioxide.

(ii) 20 parts per million of lead calculated as lead.

(iii) 100 parts per million of heavy metals other than lead calculated as the total of the respective metals.]

[2][**144A**. ***Prohibition of manufacture of cosmetics containing Hexachlorophene***.—No cosmetic containing Hexachlorophene shall be manufactured:]

1. Subs. by G.S.R. 811(E), dt. 14-11-1994.
2. Ins. by G.S.R. 116, dt. 15.1.1975.

[1][Provided that in the case of soaps Hexachlorophene may be used in concentrations not exceeding one per cent weight by weight:

Provided further that the following cautionary note shall be printed and shall appear in a conspicuous manner on the wrapper of package of each soap, namely:-

―Contains Hexachlorophene – not to be used on babies‖.]

145. ***Use of Lead and Arsenic compounds for the purpose of colouring cosmetics prohibited.***—The use of Lead and Arsenic compounds for the purpose of colouring cosmetics is prohibited.

[2][**145A**. ***Form of intimation for purpose of taking samples of cosmetics.***—Where an Inspector takes a sample of a cosmetic for the purpose of test or analysis, he shall intimate such purpose in writing in

Form 17 to the person from whom he takes it.]

[3][**145AA**. ***Form of receipt of samples of cosmetics where fair price tendered is refused***.- Where the fair price, for the samples of Cosmetics taken for the purpose of test or analysis, tendered under sub-section (1) of section 23 has been refused, the Inspector shall tender a receipt therefor to the person from whom the said samples have been taken as specified in

Form 17A.]

[2][**145B**. ***Form of receipt for seized cosmetics***.−A receipt by an Inspector for the stock of any cosmetic seized under clause (c) of sub-section (1) of section 22 of the Act shall be in

Form 15.]

4[**145BA.** ***Manner of certifying copies of seized documents***.-The Drugs Inspector shall return the documents, seized by him under clause (cc), or produced before him under clause (cca), of sub-section (1) of section 22 of the Act, within a period of twenty days of the date of such seizure or production, to the person from whom they were seized or, as the case may be, the person who produced them, after copies thereof or extracts therefrom have been signed by the Drugs Inspector concerned and the person from whom they were seized, or, as the case may be, who produced such records.]

[5][**145C.** ***Form of order not to dispose of stocks of cosmetics***—An order in writing by an Inspector under clause (c) of sub-section (1) of section 22 of the Act requiring a person not to dispose of any stock of cosmetics in his possession shall be in

Form 15.]

6[**145D.** ***Prohibition of manufacture of cosmetics containing mercury compounds***.–No cosmetics containing mercury compounds shall be manufactured.]

1. Ins. by G.S.R. 1049 (E), dt. 29-8-1986.
2. Ins. by S.O. 2139, dt. 5.6.1972.
3. Ins. by G.S.R. 292 (E), dt. 29-5-1997.
4. Ins. by G.S.R. 89(E), dt. 16-2-1985.
5. Ins. by G.S.R. 1594, dt. 28-10-1976.
6. Ins. by G.S.R. 1074, dt. 19.8.1978 (w.e.f. 2.9.1978).

PART XV

1[LABELLING, PACKING AND STANDARDS OF COSMETICS]

146. ***Prohibition of sale or distribution***.–Subject to other provisions of these rules, no person shall sell or distribute any cosmetic unless the cosmetic, if of Indian origin is manufactured by a licensed manufacturer and labelled and packed in accordance with these rules.

2[**147**. ***Exemption of cosmetics not manufactured for consumption or sale in India from the provisions of this Part***.– Labels on packages or containers of cosmetics not manufactured for consumption or sale in India shall be adopted to meet the specific requirements, if any, of the consignee:

Provided that where a cosmetic is required by the consignee to be not labelled with the name and address of the manufacturer, the labels on packages or containers shall bear a code number as approved by the Licensing Authority mentioned in rule 21.]

148. ***Manner of labelling***.–Subject to other provisions of the rules, a cosmetic shall carry.–

(1) on both the inner and outer labels;

(a) the name of the cosmetic,

3[(b) the name of the manufacturer and complete address of the premises of the manufacturer where the cosmetic has been manufactured.

Provided that if the cosmetic is contained in a very small size container where the address of the manufacturer cannot be given, the name of the manufacturer and his principal place of manufacture shall be given along with pin code.]

(2) On the outer label.–

A declaration of the net contents expressed in terms of weight for solids, fluid measure for liquids, weight for semi-solids, combined with numerical count if the content is sub-divided:

Provided that this statement need not appear in case of a package of perfume, toilet water or the like the net content of which does not exceed 60 ml or any package of solid or semi- solid cosmetic the net content of which does not exceed 30 grams.

(3) On the inner label, where a hazard exists–

(a) adequate direction for safe use,

(b) any warning, caution or special direction required to be observed by the consumer,

(c) a statement of the names and quantities of the ingredients that are hazardous or poisonous.

1. Subs. by S.O. 3408, dt. 1.11.1996.
2. Subs. by G.S.R. 682 (E), dt. 5-12-1980.
3. Subs. by G.S.R. 352 (E), dt. 26-4-2000.

1[(4) A distinctive batch number, that is to say, the number by reference to which details of manufacture of the particular batch from which the substance in the container is taken are

recorded and are available for inspection, the figures representing the batch number being preceded by the letter ―B‖:

Provided that this clause shall not apply to any cosmetic containing 10 grams or less if the cosmetic is in solid or semi-solid state, and 25 millilitres or less if the cosmetic is in a liquid state:

[2][Provided further that in the case of soaps, instead of the batch number, the month and year of manufacture of soap shall be given on the label.]

[1][(5) manufacturing licence number, the number being preceded by the letter ‗M‘.]

(6) Where a package of a cosmetic has only one label, such label shall contain all the information required to be shown on both the inner and the outer labels, under these Rules.

[5][(7) The list of ingredients, present in concentration of more than one percent shall be listed in the descending order of weight or volume at the time they are added, followed by those inconcentration of less than or equal to one percent, in any order, and preceded by the words ‗INGREDIENTS‘.

Provided that this statement need not appear for packs of less than 60 ml of liquid and30 gm of solid and semi-solids.

(8) Labeling requirement, if any, specified in the relevant Indian standard as laid down by the ‗Bureau of Indian Standards‘ for the cosmetics covered under Schedule S.]

[3][**148A**. ***Prohibition against altering inscriptions on containers, labels or wrappers of cosmetics***.- No person shall alter, obliterate or deface any inscription or mark made or recorded by the manufacturer on the container, label or wrapper of any cosmetic:

Provided that nothing in this rule shall apply to any alteration, inscription or mark made on the container, label or wrapper of any cosmetic at the instance or direction or with the permission of the licensing authority.]

[5]**[148B - *Prohibition against false or misleading claims* :-** No cosmetic may purport or claimto purport or convey any idea which is false or misleading to the intending user.]

149. [4][***Labelling of Hair dyes containing Dyes, Colours and Pigments***.—Hair dyes containing Para-Phenylenediamine or other Dyes, Colours and Pigments] shall be labelled with the following legend in English and local languages and these shall appear on both the inner and the outer labels.

―*Caution*—This product contains ingredients which may cause skin irritation in certain cases and so a preliminary test according to the accompanying direction should first be made. This product should not be used for dyeing the eye-lashes or eye-brows; as such a use may cause blindness‖.

Each package shall also contain instructions in English and local languages on the following lines for carrying out the test:

―This preparation may cause serious inflammation of the skin in some cases and so a preliminary test should always be carried out to determine whether or not special sensitivity exists. To make the test, cleanse a small area of skin behind the ear or upon the inner surface of the forearm, using either soap and water or alcohol. Apply a small quantity of the hair dye as prepared for use to the area and allow it to dry.

After twenty-four hours, wash the area gently with soap and water. If no irritation or inflammation is apparent, it may be assumed that

1. Subs. by G.S.R. 245, dt. 3-2-1976.
2. Ins. by. 681(E), dt. 6-8-1988.
3. Ins. by G.S.R. 351 (E), dt. 26-4-2000.
4. Subs. by G.S.R. 811 (E), dt. 14-11-1994.
5. Ins. by. 46 (E), dt. 22-1-2009.

no hypersensitivity to the dye exists. The test should, however, be carried out before each and every application. This preparation should on no account be used for dyeing eye- brows or eye-lashes as severe inflammation of the eye or even blindness may result.]

[1][**149A**. **Special provisions relating to toothpaste containing fluoride**.-

(i) Fluoride content in tooth paste shall not be more than 1000 ppm and the content of fluoride in terms of ppm shall be mentioned on the tube and carton.

(ii) Date of expiry should be mentioned on tube and carton.]

150. ***Report of result of test or analysis of cosmetics***.—Test reports on samples of cosmetics taken for test or analysis under these rules shall be supplied in Form 34.

[2][**150-A**. ***Standard for cosmetics***.- Subject to the provisions of these rules, the standards for cosmetics shall be such as may be prescribed in Schedule S.]

[3] [**PART XV (A)**
APPROVAL OF INSTITUTIONS FOR CARRYING OUT TESTS ON DRUGS, COSMETICS AND RAW MATERIALS USED IN THEIR MANUFACTURE ON BEHALF OF LICENSEES FOR MANUFACTURE FOR SALE OF DRUGS / COSMETICS

150-B. ***Application for grant of testing drugs/cosmetics***— (1) Application for grant or renewal of approval for carrying out tests for identity, purity, quality and strength on drugs or cosmetics or the raw materials used in the manufacture thereof on behalf of licensees for manufacture for sale of drugs or cosmetics, shall be made in

Form 36 to the Licensing Authority appointed by the State Government for the purposes of Part VII, VII (A) or XIV of these Rules, as the case may be and referred to as the ―approving authority‖ under this Part and shall be accompanied by an inspection fee of [2][rupees six thousand] in the case of testing of drugs specified in Schedules C and C (1) and [2][rupees one thousand five hundred] in the case of testing of drugs other than those specified in Schedules C and C (1), homoeopathic drugs and cosmetics:

Provided that the applicant shall furnish to the approving authority such additional information as may be required by him in connection with the application in

Form 36:

4[Provided further that if the applicant applies for renewal of approval after its expiry but within six months of such expiry, the inspection fee payable shall be rupees six thousand in the case of testing of drugs specified in Schedules C and C (1) and rupees one thousand five hundred in the case of testing of drugs other than those specified in Schedules C and C (1), Homoeopathic medicines and cosmetics plus an additional fee at the rate of rupees one thousand per month.]

4[(2) A separate application shall be made for grant of approval for carrying out tests on additional categories of drugs or items of cosmetics and shall be accompanied by an inspection fee of rupees one thousand five hundred in the case of drugs specified in Schedule C and Schedule C(1) and rupees one thousand each in case of drugs other than those specified in Schedule C and Schedule C(1), homeopathic medicines and cosmetics.

1. Ins. by G.S.R. 223 (E), dt. 19-4-1991.

2. Ins. by G.S.R. 510 (E), dt. 26-7-1982.

3. Ins. rule 150B to 150K by X.1104/7/76-D&M, dt. 23-8-1977. 4.
Subs. by G.S.R. 601(E), dt. 24-8-2001.

Explanation—For the purpose of this Part, the words ‗drugs' and ‗cosmetics' shall also mean and include the raw materials used in the manufacture of drugs including Homoeopathic drugs or cosmetics, as the case may be.]

150-C. ***Form in which approval to be granted for carrying out tests on drugs / cosmetics on behalf of licensees for manufacture of drugs/cosmetics and conditions for grant or renewal of such approval***.– *(1)* Approval for carrying out such tests of identity, purity, quality and strength of drugs or cosmetics as may be required under the provisions of these rules, on behalf of licensee for manufacture of drugs or cosmetics shall be granted in Form 37.

(2) Before approval in Form 37 is granted or renewed, the following conditions shall be complied with by the applicant–

(1) The premises where the tests are being carried out shall be well lighted and properly ventilated except where the nature of tests of any drug or cosmetic warrants otherwise. Wherever necessary, the premises shall be air conditioned so as to maintain the accuracy and functioning of laboratory instruments or to enable the performance of special tests such as sterility tests, microbiological tests, etc.

(2) The applicant shall provide adequate space having regard to the nature and number of samples of drugs or cosmetics proposed to be tested.

Provided that the approving authority shall determine from time to time whether the space provided continues to be adequate.

(3) If it is intended to carry out tests requiring the use of animals, the applicant shall provide for an animal house and comply with the following requirements–

(a) The animal house shall be adequate in area, well lighted and properly ventilated and the animals undergoing tests shall be kept in air conditioned area.

(b) The animals shall be suitably housed in hygienic surroundings and necessary provisions made for removal of excreta and foul smell.

(c) The applicant shall provide for suitable arrangements for preparation of animal feed.

(d) The applicant shall provide for suitable arrangements for quarantining of all animals immediately on their receipt in the institution.

(e) The animals shall be periodically examined for their physical fitness.

(f) The applicant shall provide for isolation of sick animals as well as animals under test.

(g) The applicant shall ensure compliance with the requirements of the Prevention of Cruelty to Animals Act, 1960 (59 of 1960).

(h) The applicant shall make proper arrangements for the disposal of the carcasses of animals in a manner as not to cause hazard to public health.

(4) The applicant shall provide and maintain suitable equipment having regard to the nature and number of samples of drugs or cosmetics intended to be tested which shall be adequate in the opinion of the approving authority.

(5) The testing of drugs or cosmetics, as the case may be, shall be under the active direction of a person whose qualifications and experience are considered adequate in the opinion of the approving authority and who shall be held responsible for the reports of test or analysis issued by the applicant.

(6) The testing of drugs or cosmetics, as the case may be, for identity, purity, quality and strength shall be carried out by persons whose qualifications and experience of testing are adequate in the opinion of the approving authority.

(7) The applicant shall provide books of standards recognized under the provisions of the Act and the Rules made thereunder and such books of reference as may be required in connection with the testing or analysis of the products for the testing of which approval is applied for.

150D. ***Duration of approval***. –An approval granted in Form 37 or renewed in Form 38, unless sooner suspended or withdrawn, shall be [1][valid for a period of five years on and from the date on which] it is granted or renewed:

Provided that if an application for the renewal of an approval in

Form 37 is made before its expiry or if the application is made within six months of its expiry after the payment of the additional fee, the approval shall continue to be in force until orders are passed on the applications and the approval shall be deemed to have expired if the application for its renewal is not made within six months of its expiry.

150E. ***Conditions of approval*** –An approval in Form 37 shall be subject to the following general conditions: —

(a) The institution granted approval under this Part (hereinafter referred to as the approved institution) shall provide and maintain an adequate staff and adequate premises and equipment as specified in rule 150-C [2][and Schedule L-1].

(b) The approved institution shall provide proper facilities for storage so as to preserve the properties of the samples to be tested by it.

(c) The approved institution shall maintain records of tests for identity, purity, quality and strength carried out on all samples of drugs or cosmetics and the results thereof together with the protocols of tests showing the readings and calculation in such form as to be available for inspection and such records shall be retained in the case of substances for which an expiry date is assigned for a period of two years from the expiry of such date and in the case of other substances for a period of six years.

(d) The approved institution shall allow the Inspector appointed under this Act to enter with or without prior notice the premises where the testing is carried on and to inspect the premises and the equipment used for test and the testing procedures employed. The institution shall allow the Inspectors to inspect the registers and records maintained under these Rules and shall supply to such Inspectors such information as they may require for the purpose of ascertaining whether the provisions of the Act and Rules made thereunder have been observed.

(e) The approved institution shall from time to time report to the approving authority any changes in the person-in-charge of testing of drugs or cosmetics or in the expert staff responsible for testing as the case may be and any material alteration in the premises or changes in the equipment used for the purposes of testing which have been made since the date of last inspection made on behalf of the approving authority before the grant or renewal of approval.

1. Subs. by G.S.R. 601 (E), dt. 24-8-2001.

2. Ins. by G.S.R. 780 (E), dt. 10-11-2008.

(f) The approved institution shall furnish reports of the results of test or analysis in

Form 39.

(g) In case any sample of a drug or a cosmetic is found on test to be not of standard quality, the approved institution shall furnish the approving authority [1][and the licensing authority of the State where the manufacturer and/or sender of the drug or cosmetic is located] with copy of the test report on the sample with the protocols of tests applied.

(h) The approved institution shall comply with the provisions of the Act and Rules made thereunder and with each further requirements, if any, may be specified in the rules subsequently made under Chapter IV of the Act of which the approving authority has given the approved institution not less than four months notice.

(i) The approved institution shall maintain an Inspection Book to enable the Inspectors to record his impression or defects noticed.

150F. ***Inspection before grant of approval***.— Before an approval in Form 37 is granted, the approving authority shall cause the institution at which the testing of drugs or cosmetics, as the case may be, is proposed to be carried out to be inspected jointly by the Drugs Inspectors of the Central Drugs Standard Control Organisation and the State Drugs Control Organisation who shall examine the premises and the equipment intended to be used for testing of drugs or cosmetics and inquire into the professional qualifications of the expert staff to be employed.

150G. ***Report of Inspection***.— The Drug Inspector mentioned in rule 150-F shall forward to the approving authority a detailed report of the result of the inspection.

150H. ***Procedure of approving authority***.— (1) If the approving authority after such further enquiry, if any, as he may consider necessary, is satisfied that the requirements of the rules made under the Act have been complied with and that the conditions of the approval and the rules made under the Act will be observed, he shall grant an approval in

Form 37.

(2)If the approving authority is not so satisfied, he shall reject the application and shall inform the applicant of the reasons for such rejection and of the conditions which must be satisfied before an approval could be granted.

150-I. ***Further application after rejection***.— If within a period of six months from the rejection of an application for approval, the applicant informs the approving authority that the conditions laid down have been satisfied and deposits inspection fee of [2][rupees two hundred and fifty], the approving authority may, if, after causing a further inspection to be made, he is satisfied that the conditions for grant of approval have been complied with, grant the approval in

Form 37.

1. Ins. by G.S.R 93 (E), dt. 24-2-1995.

2. Subs.by G.S.R 601 (E), dt. 24-8-2001.

Drugs and Cosmetics Rules 1945

150J. ***Renewal***. – On an application being made for renewal the approving authority may cause an inspection to be made and if satisfied that the conditions of the approval and the rules made under the Act are and shall continue to be observed shall issue a certificate of renewal in

Form 38.

150K. ***Withdrawal and suspension of approvals*** – (1) The approving authority may, after giving the approved institution an opportunity to show cause why such an order should not be passed, by an order in writing stating the reasons therefor, withdraw an approval granted under this Part or suspend it for such period as he thinks fit either wholly or in respect of some of the categories of drugs or items of cosmetics to which it relates, if in his opinion the approved institution has failed to comply with any of the conditions of the approval or with any provisions of the Act or the Rules made thereunder.

(2) Any approved institution whose approval has been suspended or withdrawn may within three months of the date of the order, appeal to the State Government which shall dispose of the appeal in consultation with a panel of competent persons appointed by it in this behalf and notified in the Official Gazette.]

[1][PART XVI

MANUFACTURE FOR SALE OF AYURVEDIC (INCLUDING SIDDHA) OR UNANI DRUGS

151. ***Manufacture on more than one set of premises***.—If Ayurvedic (including Siddha) or Unani drugs are manufactured on more than one set of premises, a separate application shall be made and a separate licence shall be obtained in respect of each such set of premises.

152. ***Licensing Authorities***.—For the purpose of this Part the State Government shall appoint such Licensing Authorities and for such areas as may be specified in this behalf by notification in the Official Gazette.

153. ***Application for licence to manufacture Ayurvedic (including Siddha) or Unani drugs***.— (1) An application for the grant or renewal of a licence to manufacture for sale any Ayurvedic (including Siddha) or Unani drugs shall be made in

Form 24-D to the Licensing Authority along with [2][a fee of rupees one thousand]:

Provided that in the case of renewal the applicant may apply for the renewal of the licence before its expiry or within one month of such expiry:

Provided further that the applicant may apply for renewal after the expiry of one month but within three months of such expiry in which case the [2][fee payable for renewal of such licence shall be rupees one thousand and two hundred plus an additional fee of rupees six hundred].

(ii) [2][A fee of rupees three hundred] shall be payable for a duplicate copy of a licence issued under this rule, if the original licence is defaced, damaged or lost.

1. Parts XVI, XVII and XVII added by S.O. 642, dt. the 2-2-1970 (w.e.f. 21.2.1970)

2. Subs. by G.S.R 79 (E), dt. 14-2-2005.

[1] [**153A**. ***Loan Licence***.—(i) An application for the grant of renewal of a loan licence to manufacture for sale of any Ayurvedic (including Siddha) or Unani drugs shall be made in

Form 25-E to the Licensing Authority along with [2][a fee of rupees six hundred.]

Explanation—For the purpose of this rule, a loan licence means a licence which a Licensing Authority may issue to an applicant who does not have his own arrangements for manufacture but intends to avail himself of the manufacturing facilities owned by a licence in

Form 25-D:

Provided that in the case of renewal the applicant may apply for the renewal of the licence before its expiry or within one month of such expiry:

Provided further that the applicant may apply for renewal after the expiry of one month, but within three months of such expiry in which case [2][the fee payable for renewal of such licences shall be rupees six hundred plus an additional fee of rupees three hundred.]]

(ii) [2][A fee of rupees one hundred and fifty] shall be payable for a duplicate copy of a licence issued under this rule, if the original licence is defaced, damaged or lost.]

154. ***Form of licence to manufacture Ayurvedic (including Siddha) or Unani drugs.***— (1) Subject to the conditions of rule 157 being fulfilled, a licence to manufacture for sale any Ayurvedic (including Siddha) or Unani drugs shall be issued in

Form 25-D. The licence shall be issued within a period of three months from the date of receipt of the application.

(2) A licence under this rule shall be granted by the licensing authority after consulting such expert in Ayurvedic (including Siddha) or Unani Systems of medicine as the case may be, which the State Government may approve in this behalf.

[1][**154A.** ***Form of loan licence to manufacture for sale of Ayurvedic (including Siddha) or Unani drugs***.—

(1) A loan licence to manufacture for sale of any Ayurvedic (including Siddha) or Unani drugs shall be issued in Form 25E.

(2) A licence under this rule shall be granted by the Licensing Authority after consulting such expert in Ayurvedic (including Siddha) or Unani systems of medicine, as the case may be, which the State Government may approve in this behalf.

(3) The Licensing Authority shall, before the grant of a loan licence, satisfy himself that the manufacturing unit has adequate equipment, staff, capacity for manufacture and facilities for testing, to undertake the manufacture on behalf of the applicant for a loan licence.]

155. ***Certificate of renewal***—The certificate of renewal of a licence in

Form 25-D shall be issued in Form 26-D.

1. Ins. by G.S.R. 376(E), dt. 20-7-1978.
2. Subs. by G.S.R 79 (E), dt. 14-2-2005.

[1] [**155A.** ***Certificate of renewal of a loan licence***.—The certificate of renewal of a loan licence in

Form 25-E shall be issued in Form 26-E.]

[2][**155B.** ***Certificate of award of G.M.P. of Ayurveda, Siddha and Unani Drugs***.— [3][(1)]The certificate of Good Manufacturing Practices to manufacturers of Ayurveda, Siddha or Unani drugs shall be issued to licensees who comply with the requirements of Good Manufacturing Practice of Ayurveda, Siddha and Unani drugs as laid down in Schedule T.] [4][(2) The certificate referred to in sub-rule (1) shall be issued for a period of five years from the date of issuance of the license.]

156. ***Duration of licence***—An original licence in Form 25-D or a renewed licence in Form 26-D, unless sooner suspended or cancelled shall be [5][valid for a period of [6][five years] from the date of its issue]:

Provided that if the application for the renewal of a licence is made before its expiry or within one month of its expiry after payment of the additional fee of rupees thirty, the licence shall continue to be in force until orders are passed on the application. The licence shall be deemed to have expired, if the application for its renewal is not made within three months of its expiry.]

[1] [**156A**. ***Duration of loan licence***.—An original loan licence in Form 25-E or a renewed loan licence in Form 26-E, unless sooner suspended or cancelled, shall be valid up to the 31st December of the year following the year in which it is granted or renewed:

Provided that if the application for the renewal of a loan licence is made in accordance with rule 153-A, the loan licence shall continue to be in force until orders are passed on the application. The licence shall be deemed to have expired, if the application for its renewal is not made within three months of its expiry.]

157. ***Conditions for the grant or renewal of a licence in***

Form 25-D.—Before a licence in Form 25-D is granted or renewed in Form 26-D the following conditions shall be complied with by the applicant, namely: —

(1) The manufacture of Ayurvedic (including Siddha) or Unani drugs shall be carried out in such premises and under such hygienic conditions as are specified in Schedule T.

[2][(IA) For issuing of the certificate of Good Manufacturing Practices, the Licensing Authority shall verify the requirements as per schedule T and issue the Good Manufacturing Practices certificate in

form 26 E-I, simultaneously along with grant or renewal of licence in form 25D].

[7][(IB) No manufacturer shall use any prefix or suffix with the name of any Ayurvedic, Siddha or UnaniTibb drug falling under clause (a) of section 3 of the Act, except as described in the authoritative books specified in the First Schedule to the Act:

Provided that a formulation without any specific name, described in the authoritative books may be named on the basis of the ingredients of the formulation.

(IC) The name of any Ayurvedic, Siddha or UnaniTibb drug falling under clause (a) of section 3 of the Act shall not be used for naming any patent or proprietary medicine relating to Ayurvedic, Siddha or UnaniTibb systems of medicine referred to in sub-clause (i) of clause (h) of the said section:

Provided that this rule shall not be applicable for single plant-ingredient based Ayurvedic, Siddha or UnaniTibb formulation licensed or to be licensed as patent or proprietary medicine under sub-clause (i) of clause (h) of section 3 of the Act.]

1. Ins. by G.S.R. 376 (E),dt. 20-7-1978.
2. Subs. by G.S.R. 376 (E),dt. 3-5-2010. Earlier Ins. by G.S.R. 198 (E), dt. 7-3-2003.
3. Rule 155B renumbered as sub-rule (1) by G.S.R. 376 (E),dt. 3-5-2010.
4. Ins. by G.S.R. 376 (E),dt. 3-5-2010.
5. Subs. by G.S.R 79 (E), dt. 14-2-2005.
6. Subs. by G.S.R. 376 (E),dt. 3-5-2010.
7. Ins. by G.S.R. 390 (E),dt. 18.5.2015.

(ID) Notwithstanding the period for renewal of licence provided in rules 156 and 156 A, the licensee of the Ayurvedic, Siddha or UnaniTibb drug, which is not in conformity with sub-rules (1B) and (1C), shall seek renewal of the licence with appropriate name of the drug within a period of one year from the date of commencement of Drugs and Cosmetics (4th Amendment) Rules, 2015:

Provided that this rule shall not be applicable to any batch of Ayurvedic, Siddha or UnaniTibb drugs manufactured prior to the date of commencement of the Drugs and Cosmetics (4th Amendment) Rules, 2015.

(IE) Whoever contravenes the provisions of rules (IB) to (ID) shall be punishable under section 33-I of the Act.]

(2) The manufacture of Ayurvedic (including Siddha) or Unani drugs shall be conducted under the direction and supervision of competent technical staff consisting at least of one person, who is a whole time employee and who possesses the following qualifications, namely:–

(a) A degree in Ayurveda or Ayurvedic Pharmacy, Siddha or Unani system of medicine, as the case may be, conferred by a University, a State Government or Statutory Faculties, Councils and Boards of Indian Systems of Medicines recognized by the Central Government or a State Government for this purpose, or

(b) a diploma in Ayurveda, Siddha or Unani system of medicine granted by a State Government for this purpose, or

(c) a graduate in Pharmacy or Pharmaceutical Chemistry or Chemistry or Botany of a University recognized by the Central Government with experience of at least two years in the manufacture of drugs pertaining to the Ayurvedic or Siddha or Unani systems of medicines, or

(d) a Vaid or Hakim registered in a State Register of Practitioners of indigenous systems of medicines having experience of at least four years in the manufacture of Ayurvedic or Siddha or Unani drugs, or

(e) a qualification as Pharmacist in Ayurvedic (including Siddha) or Unani systems of medicines, possessing experience of not less than eight years in the manufacture of Ayurvedic or Siddha or Unani drugs as may be recognized by the Central Government.

(3) The competent technical staff to direct and supervise the manufacture of Ayurvedic drugs shall have qualifications in Ayurveda and the competent technical staff to

direct and supervise the manufacture of Siddha drugs and Unani drugs shall have qualification in Siddha or Unani, as the case may be.

[3]**[157A. Maintaining of records of raw material used by licensed manufacturing unit of Ayurveda, Siddha and Unani drugs in the preceding financial year.-** Each licensed manufacturing unit of Ayurveda or Siddha or Unani drugs shall keep a record of raw material used by each licensed manufacturing unit of Ayurveda, Siddha or Unani drugs as the case may be in the proforma given in Schedule TA in respect of all raw materials utilized by that unit in the manufacture of Ayurveda or Siddha or Unani drugs in the preceding financial year, and shall submit the same by the 30th day of June of the succeeding financial year to the State Drug Licensing Authority of Ayurveda, Siddha and Unani drugs and to the National Medicinal Plants Board or any agency nominated by the National Medicinal Plant Board for this purpose.]

158. ***Conditions of licence***.—A licence in Form 25D shall be subject to the conditions stated therein and to the following further conditions, namely:–

(a) The licensee shall maintain proper records of the details of manufacture and of the tests, if any, carried out by him, or by any other person on his behalf, of the raw materials and finished products.

(b) The licensee shall allow an Inspector appointed under the Act to enter any premises where the manufacture of a substance in respect of which the licence is issued is carried on, to inspect the premises, to take samples of the raw material as well as finished the products, and to inspect the records maintained under these rules.

[1][(c) The licensee shall maintain an Inspection Book in

Form 35 to enable an Inspector to record his impressions and the defects noticed.]

[2][**158-A.** *Condition of loan licence.*—A licence in Form 25E shall be subject to the conditions stated therein and to the following conditions, namely:—

(a) The licence in

Form 25E shall be deemed to be cancelled or suspended, if the licence owned by the licensee in Form 25D whose manufacturing facilities have been availed of by the licensee is cancelled or suspended, as the case may be, under these rules.

(b) The licensee shall comply with the provisions of the Act and of the rules and with such further requirements, if any, as may be specified in any rules subsequently made under Chapter IV-A of the Act, provided that where such further requirements are specified in the rules; these would come into force four months after publication in the Official Gazette.

(c) The licensee shall maintain proper records of the details of manufacture and of the tests, if any, carried out by him, or any other person on his behalf, of the raw materials and finished products.

(d) The licensee shall allow an Inspector appointed under the Act to inspect all registers and records maintained under these rules and shall supply to the Inspector such information as he may require for the purpose of ascertaining whether the provisions of the Act and the rules have been observed.

[1][(e) The licensee shall maintain an Inspection Book in

form 35 to enable an Inspector to record his impressions and the defects noticed.]

1. Ins. by G.S.R. 331 (E),dt. 8.5.1984.
2. Ins. by G.S.R. 376 (E), dt. 20.7.1978.
3. Ins. by G.S.R. 512 (E),dt. 9.7.2008.

[1][158(B) Guidelines for issue of license with respect to Ayurveda, Siddha or Unani drugs.-

I. (A). Ayurveda, Siddha Unani Medicines under section 3(a):- Ayurveda, Siddha or Unani drugs includes all medicines intended for internal or external use for or in the diagnosis, treatment, mitigation or prevention of disease or disorder in human beings or animals, and manufactured exclusively in accordance with the formulae described in the authoritative books of Ayurvedic, Siddha and Unani Tibb system of medicine, as specified in the First Schedule;

(B). Patent or Proprietary medicine under section 3(h);

(i)In relation to Ayurvedic, Siddha and Unani Tibb system of medicine of all formulations containing only such ingredients mentioned in the formulae described in the authoritative books of Ayurveda, Siddha or Unani Tibb system of medicines specified in the First Schedule, but does not include a medicine which is administered by parenteral route and also a formulation included in the authoritative books as specified in clause (a);

(ii)Balya/Poshak/Muqawi/Unavuporutkal/positive health Promoter formulations having ingredients mentioned in books of First Schedule of the Drugs and Cosmetics Act and recommended for promotional and preventive health.

(iii)Saundarya Prasadak (Husane afza)/Azhagh-sadhan formulation having ingredients mentionedin Books of First Schedule of the Drugs and Cosmetics Act and recommended for oral, skin, hair and body care.

(iv)Aushadh Ghana (Medicinal plant extracts - dry/wet) extract obtained from plant mentioned in books of First Schedule of the Act including Aqueous or hydro-alcohol.

II.(A) For issue of licence to the medicine with respect to Ayurvedic, Siddha and Unani, the conditions relating to safety study and the experience or evidence of effectiveness shall be such as specified in columns (5) and (6) of The Table given below:-

Serial number	Category	Ingredient (S)	Indication (s)	Safety study	Experience/Evidence of Effectiveness	
1	2	3	4	5	6	
					Published Literature	Proof of Effectiveness
1	(A) Ayurveda, siddha and Unani drugs, given in 158 B as referred in	As per text	As per text	Not Required	Required	Not Required

2	(B) Any change in dosage form of Ayurveda, siddha and Unani drugs, as described in section 3 (a) of the Drugs and	As per text	As per text	Not Required	Required	Not Required

	Act, 1940					
3	(C) Ayurveda, siddha and Unani drugs, referred in 3(a) to be used for new	As per text	New	Not Required	If Required	Required

II.B For issue of license with respect to Patent or Proprietary medicine. The condition relating to Safety studies and experience or evidence of effectiveness shall be specified as follows:-

Serial number	Category	Ingredient (S)	Indication (s)	Safety study	Experience/Evidence of Effectiveness	
1	2	3	4	5	6	
					Published Literature	Proof of Effectiveness
1	Patent orProprietary medicine	As per text	Textual Rationale	Not Required	Of Ingredients	Pilot study as per relevant protocol for Ayurveda, siddha and
2	Ayurveda, siddha and Unani drugswith any of the ingredients of Schedule E(1) of the Drugs and Cosmetics	As per text	Existing	Required	Required	Required

III. For issue of license with respect to Balya and Poshak medicines the person who applied for license is required to submit the following:

(i) Photo-copy of the textual reference of ingredients used in the formulation as mentioned in the book of 1st schedule;

(ii) Conduct safety studies in case the product contains of any of the ingredients as specified in the Schedule E (1), as per the guidelines for evaluation of Ayurveda Siddha and Unani Drugs formulations;

(iii) For textual indications the safety and effectiveness study is not required.

IV. For issue of license with respect to Saundarya Prasadak (Husane afza/Azhagu Sodhan) the person who applied for license is required to:-

(i) Submit photo-copy of the textual reference of ingredients used in the formulation as mentioned in the book of 1st schedule;

1. Ins. by G.S.R. 663 (E),dt. 10.10.2010.

(ii) Conduct safety studies, in case the formulation contains of any of the ingredients as specified in the Schedule E (1), as per the guidelines for evaluation of Ayurveda, Siddha and Unani formulation;

(iii) For textual indications the safety and effectiveness study is not required.

V. For issue of license with respect to medicine Aushadh Ghana extract of medicinal plant (dry or wet).

Serial number	Category	Ingredien t (S)	Indication (s)	Safety study	Experience/Evidence of Effectiveness	
1	2	3	4	5	6	
					Published Literature	Proof of Effectiveness
1	(A) Aqueous	As per text	As per text	Not Required	Not Required	Not Required
2	(Al). Aqueous	As per text	New Indication**	Not Required	Not Required	Required
3	(B) Hydro-Alcohol	As per text	As per text	Not Required	If Required	Not Required
4	(B1) Hydro-Alcohol	As specified	New Indication**	Required	If Required	Required
5	Other than Hydro/ HydroAl c ohol	As specified	As specified	Required Acute, Chronic, mutagenicity and teratogenicit y	If Required	Required

* The standard protocol will also include concept of Anupan, Prakriti & Tridosh etc. published by Central

Research Councils Ayurveda, Siddha, Unani and other Government/Research Bodies.

** New indication means which is other than mentioned in 1st schedule books of Drugs & Cosmetics Act 1940.]

[1][158C. **Form of Free Sale Certificate and Non-Conviction Certificate. –** The State Drug Controller or Licensing Authority shall, on request by the Ayurveda, Siddha and Unani Drugs manufacturer, issue, within 15 days; from the date of application, Free Sale Certificate in

Form 26 E2-I for original License holder or in Form 26 E2-II for loan license and Non Conviction Certifacate for both original and loan license holder in Form 26 E3 or in the format as specified by the importing country or tenderer respectively, after fulfilment of all requisite formalities as required in the respective formats.]

1. Ins. by G.S.R. 153 (E),dt. 5.3.2014.

159. ***Cancellation and suspension of licences***— (1) The Licensing Authority may, after giving an opportunity to show cause within a period which shall not be less than fifteen days from the date of receipt of such notice, why such an order should not be passed, by an order in writing stating the reasons therefor, cancel a licence issued under this Part or suspend it for such period as he thinks fit, either wholly or in respect of some of the drugs to which it relates, if in his opinion, the licensee has failed to comply with any of the conditions of the licence or with any provisions of the Act and the rules made thereunder.

(2) A licensee whose licence has been suspended or cancelled may appeal to the State Government within a period of three months from the date of receipt of the order which shall, after considering the appeal, decide the same.

160. ***Identification of raw materials***.— Raw materials used in the preparation of Ayurvedic (including Siddha) or Unani drugs shall be identified and tested, wherever tests are available for their genuineness, and records of such tests as are carried out for the purpose and the methods thereof shall be maintained.

[1][PART XVI (A)

APPROVAL OF INSTITUTIONS FOR CARRYING OUT TESTS ON AYURVEDIC, SIDDHA AND UNANI DRUGS AND RAW MATERIALS USED IN THEIR MANUFACTURE ON BEHALF OF LICENSEES FOR MANUFACTURE FOR SALE OF AYURVEDIC, SIDDHA AND UNANI DRUGS

160-A. ***Application for grant of approval for testing Ayurvedic, Siddha and Unani drugs***.- Application for grant or renewal of approval for carrying out tests for identity, purity, quality and strength of Ayurvedic, Siddha and Unani drugs or the raw materials used in the manufacture thereof on behalf of licensees for manufacture for sale of the said Ayurvedic, Siddha and Unani drugs, shall be made in

Form 47 to the Licensing Authority appointed by the State Government for the purposes of Part XVI, XVII or XVIII of these rules, as the case may be, and referred to as the _approving authority‘ under this Part and shall be accompanied by an inspection fee of six thousand rupees in respect of the drugs specified in the books prescribed in First Schedule to the Act.

1. Subs. by G.S.R.73 (E), dt. 31-01-2003 and earlier Ins. by G.S.R. 701(E), dt. 27-9-2001.

Provided that the applicant shall furnish to the approving authority such additional information as may be required by it in connection with the application in

Form 47:

Provided further that if the applicant applies for renewal of approval after its expiry but within six months of such expiry, the inspection fee payable shall be six thousand rupees plus an additional inspection fee at the rate of one thousand rupees per month in the case of testing of Ayurvedic, Siddha and Unani drugs specified in First Schedule to the Act.

Explanation. - For the purpose of this Part, the words ―Ayurvedic, Siddha and Unani drugs‖ shall also mean and include the raw materials used in the manufacture of Ayurvedic, Siddha and Unani drugs, as the case may be.

160B. ***Form in which approval to be granted for carrying out tests on Ayurvedic, Siddha and Unani drugs on behalf of licensees for manufacture of Ayurvedic, Siddha and Unani drugs and conditions for grant or renewal of such approval.--***(1) Approval for carrying out such tests of identity, purity, quality and strength of Ayurvedic, Siddha and Unani drugs as may be required under the provisions of these rules, on behalf of licensee for manufacture of Ayurvedic, Siddha and Unani drugs shall be granted in Form 48.

(2) Before approval in Form 48 is granted or renewed, the following conditions shall be complied with by the applicants, namely: -

(i) The premises where the tests are carried out shall be well lighted and properly ventilated except where the nature of tests of any Ayurvedic, Siddha and Unani drug warrants otherwise. Wherever necessary, the premises shall be air-conditioned so as to maintain the accuracy and functioning of laboratory instruments or to enable the performance of special tests such as sterility tests and microbiological tests.

(ii) (a) The applicant shall provide adequate space having regard to the nature and number of samples of drugs proposed to be tested:

Provided that the approving authority shall determine from time to time whether the space provided continues to be adequate:

Provided further that separate section shall be provided for (i) Chemistry, (ii) Pharmacognosy, (iii) Ayurveda, Siddha and Unani, (iv) Microbiology, (v) Sample Room, (vi) Office-cum-Record Room, with proper partitions and minimum required area is 800 sq. ft.

1[(b) The applicant shall provide a list of persons who may be employed with him as experts, such as Chemist, Botanist and expert in Ayurveda/Siddha/Unani or Pharmacist who shall possess a degree in Chemistry, Botany, Ayurveda/Siddha/Unani/Bachelor in Pharmacy from a recognized University or equivalent, with experience for 2 years for carrying out tests or analysis as per the Ayurvedic, Siddha and Unani Pharmacopoeias].

The applicant shall provide adequate equipment essential for carrying out tests for identity, purity, quality and strength of Ayurvedic, Siddha and Unani drugs as per pharmacopoeial standards or other available standards.

1. Subs. by G.S.R. 674 (E), dt. 10-11-2005.

List of equipment recommended is given below:

Chemistry Section

1. Alcohol determination apparatus complete set.
2. volatile oil determination apparatus.
3. Boiling point determination apparatus.
4. Melting point determination apparatus.
5. Refractometer.
6. Polarimeter.
7. Viscometer (Ostwalds, Redwood Viscometer).
8. Tablet disintegration apparatus.

9. Moisture determination apparatus (IC filtrator).
10. U.V.Spectro-photometer.
11. Muffle furnace.
12. Electronic Balance.
13. Hot air oven(s) different range of temperature/vacuum oven.
14. Refrigerator.
15. Glass distillation apparatus/plant.
16. Water supply demineralised exchange equipment/distillation equipment. 17. Air conditioner.
18. LPG Gas cylinder with burners.
19. Water bath (temperature controlled).
20. Heating mantle(4) or as required.
21. TLC apparatus with all accessories.
22. Sieves 10 to 120 with sieve shaker.
23. Centrifuge machine.
24. Dehumidifier.
25. pH meter.
26. G.L.C. with F.I. detector.
27. Silica crucible.
28. Tablet friability tester.
29. Tablet dissolution tester.
30. Other related equipment, reagents, glasswares etc.

Pharmacognosy Section

1. Microscope binocular.
2. Dissecting Microscope.
3. Microtome.
4. Chemical balance.
5. Microslide cabinet.
6. Aluminium slide trays.
7. Hot air oven.
8. Occular Micrometer.
9. Stage Micrometer.
10. Camera Lucida Prism type and mirror type.
11. Hot plates.
12. Refrigerator.
13. LPG Cylinder with burners.
14. Other related equipments, reagents, glasswares etc.

Note: Instuments like HPLC, HPTLC, Atomic Absorption spectrophotometer could be arranged by tie up with other laboratories.

Microbiology section

1. Laminar air flow bench (L.A.F.)
2. B.O.D. Incubator.
3. Plain Incubator.
4. Serological water bath.
5. Oven.
6. Autoclave/sterilizer.
7. Microscope (high power).
8. Colony counter.
9. Other related equipment and reagents.

(3). The applicant shall provide and maintain suitable equipment having regard to the nature and number of samples of Ayurvedic, Siddha and Unani drugs intended to be tested which shall be adequate in the opinion of the approving authority.

(4) The testing of Ayurvedic, Siddha and Unani drugs, as the case may be, for identity, purity, quality and strength shall be carried out under the active direction of one of the experts stated in clause (b) of sub-rule (2) who shall be the person-in-charge of testing and shall be held responsible for the reports of test issued by the applicant.

(5) The testing of Ayurvedic, Siddha and Unani drugs, as the case may be, for identity, purity, quality and strength shall be carried out by persons whose qualifications and experience of testing are adequate as stated in clause (b) of sub-rule (2).

(6) The applicant shall provide books of standards recognized under the provisions of the Act and the rules made thereunder and such books of reference as may be required in connection with the testing or analysis of the products for the testing of which approval is applied for.

(7) The applicant shall provide list of standard Ayurvedic, Siddha and Unani drugs (Reference samples) recognized under the provisions of the Act and rules made thereunder and such reference samples kept in the laboratory may be required in connection with the testing or analysis of the products of which approval is applied for.

160C. ***Duration of approval***. **-** An approval granted in Form 48 or renewed in Form 49 unless sooner suspended or withdrawn, shall be valid for a period of three years from the date on which it is granted or renewed:

Provided that if an application for the renewal of an approval in

Form 40 is made before its expiry or if the application is made within six months of its expiry after the payment of the additional inspection fee, the approval shall continue to be in force until orders to the contrary are passed on the application and approval shall be deemed to have expired if the application for renewal is not made within six months of expiry.

160D. ***Conditions of approval***.–An approval in Form 48 shall be subject to the following conditions, namely: -

I. The Institution granted approval under this Part (hereinafter referred to as the approved laboratory) shall provide and maintain adequate staff and adequate premises and equipment as specified in rule 160-B.

II. The approved laboratory shall provide proper facilities for storage so as to preserve the properties of the samples to be tested by it.

III. The approved laboratory shall maintain records of tests for identity, purity, quality and strength carried out on all samples of Ayurvedic, Siddha and Unani drugs and the results thereof together with the protocols of tests showing the readings and calculation in such form as to be available for inspection and such records shall be retained in the case of substances for which date of expiry is assigned; for a period of two years from such date of expiry and in the case of other substances, for a period of three years.

IV. The approved laboratory shall allow the Inspector appointed under this Act to enter with or without prior notice the premises where testing is carried out and to inspect the premises and the equipment used for test and the testing procedures employed. The laboratory shall allow the Inspectors to inspect the registers and records maintained under these rules and shall supply to such Inspectors such information as they may require for the purpose of ascertaining whether the provisions of the Act and rules made thereunder have been observed.

V. The approved laboratory shall from time to time report to the approving authority any changes in the person-in-charge of testing of Ayurvedic, Siddha and Unani drugs or the expert staff responsible for testing, as the case may be, and any material alterations in the premises or changes in the equipment used for the purposes of testing which have been made since the date of last inspection made on behalf of the approving authority before the grant or renewal of approval.

VI. The approved laboratory shall furnish reports of the results of tests or analysis in

Form 50.

VII. In case any sample of Ayurvedic, Siddha and Unani drug is found on test to be not of standard quality, the approved laboratory shall furnish to the approving authority and the licensing authority of the State where the manufacturer and/or sender of the Ayurvedic, Siddha and Unani drugs is located, a copy of the test report of the sample with the protocols of tests applied.

VIII. The approved laboratory shall comply with the provisions of the Act and rules made thereunder and with such further requirements, if any, as may be specified in the rules made from time to time under Chapter IV-A of the Act of which the approving authority has given the approved laboratory not less than four months' notice.

IX. The approved laboratory shall maintain an inspection book to enable the Inspector to record his impression or defects noticed.

160-E. ***Inspection before grant of approval***.— Before an approval in Form 48 is granted, the approving authority shall cause the laboratory at which the testing of Ayurvedic, Siddha and Unani drugs, as the case may be, is proposed to be carried out to be inspected jointly by the Inspectors appointed or designated by the Central Government and State Government for this purpose, who shall examine the premises and the equipment intended to be used for testing of drugs and verify into the professional qualifications of the expert staff who are or may be employed by the laboratory.

160F. ***Report of inspection***.— The Inspectors appointed by the Central Government as stated in Rule 160-E shall forward to the approving authority a detailed report of the results of the inspection.

160G. ***Procedure of approving authority***. - (1) If the approving authority after such further enquiry, if any, as it may consider necessary, is satisfied that the requirements of the rules made under the Act have been complied with and that the conditions of the approval and the rules made under the Act have been observed, it shall grant approval in

Form 48.

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(2) If the approving authority is not satisfied, it shall reject the application and shall inform the applicant of the reasons for such rejection and of the conditions which shall be satisfied before approval could be granted.

160H. ***Application after rejection***. - If within a period of six months from the rejection of an application for approval, the applicant informs the approving authority that the conditions laid down have been satisfied and deposits inspection fee of two thousand rupees, the approving authority may, if, after causing a further inspection to be made and after being satisfied that the conditions for grant of approval have been complied with, grant the approval in

Form 48.

160-I. ***Renewal***. - On an application being made for renewal, the approving authority shall, after causing an inspection to be made and if satisfied that the conditions of the approval and the rules made under the Act have been complied with, shall issue a certificate of renewal in

Form 49.

160J. ***Withdrawal and suspension of approvals***. - (1) The approving authority may, after giving the approved laboratory an opportunity to show cause why such an order should not be passed, by an order in writing stating the reasons therefor, withdraw an approval granted under this Part or suspend it for such period as it thinks fit either wholly or in respect of testing of some of the categories of Ayurvedic, Siddha and Unani drugs to which it relates, if in his opinion the approved laboratory had failed to comply with any of the conditions of the approval or with any provision of the Act or the rules made thereunder.

(2) Any approved laboratory, whose approval has been suspended or withdrawn, may, within three months of the date of the order of suspension or withdrawal, appeal to the State Government which shall dispose of the appeal in consultation with a panel of competent persons appointed by the Department of Indian Systems of Medicine & Homoeopathy, Government of India in this behalf and notified in the Official Gazette.]

[1][PART XVII

[2][LABELLING, PACKING AND LIMIT OF ALCOHOL IN] AYURVEDIC (INCLUDING SIDDHA) OR UNANI DRUGS

161. [2][***Labelling, packing and limit of alcohol***.]—(1) There shall be conspicuously displayed on the label of the container or package of an Ayurvedic (including Siddha) or Unani drug, the true list of all the ingredients [3][with the botanical names of plant based ingredients along with plant part(s) and form of ingredients, in which, these are] used in the manufacture of the preparation together with quantity of each of the ingredients incorporated therein and a reference to the method of preparation thereof as detailed in the standard text and Adikarana, as are prescribed in the authoritative books specified in the First Schedule to the Act [3][and in respect of Patent or Proprietary Ayurveda, Siddha or Unani drugs, the true list of all ingredients with the botanical names of plant based ingredients along with part(s) and form of ingredients, in which, these are used in the formulation, with their quantity]:

Provided that if the list of ingredients contained in the medicine is large and cannot be accommodated on the label, the same may be printed separately and enclosed with packing and reference be made to this effect on the label.

(2) The container of a medicine for internal use made up ready for the treatment of human ailments shall, if it is made up from a substance specified in Schedule E (1), be labelled conspicuously with the words _Caution: To be taken under medical supervision‘ both in English and Hindi language.

1. Ins. by notification F.1-23/6, dt. 2.2.1970.
2. Subs. by G.S.R. 904(E), dt. 2.11.1992.
3. Ins. by G.S.R. 844(E), dt. 26.11.2012

(3) Subject to the other provisions of these rules, the following particulars shall be either printed or written in indelible ink and shall appear in a conspicuous manner on the label of the innermost container of any Ayurvedic (including Siddha) or Unani drug [2][Patent or Proprietary Ayurveda, Siddha or Unani drugs] and on any other covering in which the container is packed', namely−

(i) The name of the drug. [3][For Ayurveda, Siddha or Unani drugs] this purpose the name shall be the same as mentioned in the authoritative books included in the First Schedule of the Act.

(ii) A correct statement of the net content in terms of weight, measure or number as the case may be. The weight and volume shall be expressed in metric system.

(iii) The name and address of the manufacturer.

(iv) The number of the licence under which the drug is manufactured, the figure representing the manufacturing licence number being preceded by the words _Manufacturing Licence Number‘ or _Mfg. Lic. No.‘ or _M.L.‘.

(v) A distinctive batch number, that is to say, the number by reference to which details of manufacture of the particular batch from which the substance in the container is taken are recorded and are available for inspection, the figure representing the batch number being preceded by the words ―Batch No.‖ or ―Batch‖ or ―Lot Number‖ or ―Lot No.‖ or ―Lot‖ or any distinguishing prefix.

(vi) The date of manufacture. For this purpose the date of manufacture shall be the date of completion of the final products, or the date of bottling or packing for issue.

(vii) The words ―Ayurvedic medicine‖ or ―Siddha medicine‖ or ―Unani medicine‖ as the case may be.

(viii) The words ―FOR EXTERNAL USE ONLY‖ if the medicine is for external application.

(ix) Every drug intended for distribution to the medical profession, as a free sample shall, while complying with the labelling provisions under clauses (i) to (viii), further bear on the label of the container the words ―Physicians sample. Not to be sold‖ which shall be over-printed.

[1][(x)(a) Preparation (Asavas) with high content of alcohol as base

Name of the drug	Maximum size of packing
(i) Karpur Asava	15 ml
(ii) Ahiphenasava	15 ml
(iii) Margamadasava	15 ml

(ix)(b) Preparations containing self-generated alcohol

Name of the drug	Maximum content of alcohol (Ethyl alcohol v/v)	Maximum size of packing
(i) Mritsanjivani Sura	16 per cent	30 ml.
(ii) Mahadrakshasava	16 per cent	120 ml.]

1. Subs. by G.S.R. 904 (E), dt. 2-11-1992.

2. Ins. by G.S.R. 844(E), dt. 26.11.2012.

3. Subs. by G.S.R. 844(E), dt. 26.11.2012.

(4) Nothing in these rules shall be deemed to require the labelling of any transparent cover or of any wrapper case or other covering used solely for the purpose of packing, transport or delivery.

[1][**161A.** ***Exemption in labeling and packing, provisions for export of Ayurvedic (including Siddha) and Unani drugs***.- (1) Labels and packages or containers of Ayurvedic, Siddha and Unani drugs for export may be adopted to meet the specific requirements of the law of the country to which the said drug is to be exported, but the following particulars shall appear in conspicuous position on the container in which drug is packed and on every other covering in which that container is packed, namely :

(a) Name of the Ayurvedic, Siddha and Unani drug (Single or compound formulations;

(b) the name, address of the manufacturer and the number of licence under which the drug has been manufactured;

(c) batch or lot number;

(d) date of manufacture, along with the date for ―Best for use before‖;

(e) main ingredients, if required by the importing country;

(f) for export:

Provided that where Ayurvedic, Siddha and Unani Single or compound drug not classified under the First Schedule or Schedule E-(I), is required by the consignee to be not labeled

with the name and address of the manufacturer, the labels on packages or containers shall bear a code number as approved by the Licensing Authority mentioned in rule 152.

(2) the provisions of Rule 161 shall not apply to a medicine made up ―ready for treatment‖, whether after, or without, alteration, which is supplied on the prescription of a registered medical practitioner if the medicine is labeled with the following particulars, namely:–

(a) the name and address of the suppliers;

(b) the words ―For External Use Only‖, if the medicine is for external application.]

2[**161B**. 1. The date of expiry of Ayurveda, Siddha and Unani medicines shall be conspicuously displayed on the label of container or package of an Ayurvedic, Siddhas and Unani medicines, and after the said date of expiry, these medicines shall not be in circulation.

2. The Shelf-life i.e. for Ayurveda, Siddha and Unani medicines shall be as follows:-

(i) Shelf life or date of expiry for Ayurvedic medicines.

Sl. No.	Name of the Group of Ayurvedic Medicine	Shelf life and date ofexpiry with effect fromthe date of manufacture
1.	Churna, Kwatha Churna	2 years
2.	Gutika (Vati-Gutti, Pills, Tablets except Gutika with Rasa)	3 years
3.	(i) Gutika Tablet containing Kasth aushadhi (ii) Gutika,Tablet containing Kasth aushadi and Rasa, Uprasa, Metallic Bhasmas, and Guggulu.	3 years 5 years
4.	Rasaushadhies	No expiry date1
5.	Asava Arista	No expiry date1
6.	Avaleha	3 years
7.	Guggulu	5 years
8.	Mandura - Lauha	10 years

1. Ins. by G.S.R. 787 (E), dt. 17-10-2000.

2. Ins. by G.S.R. 764 (E), dt. 15-10-2009.

9.	Ghrita	2 years
10.	Taila	3 years
11.	Arka	1 year
12.	Dravaka, Lavana, Ksara	5 years
13.	Lepa Churna	3 years
14.	Dant Manjan Powder	2 years
15.	Dant Manjan Paste	2 years
16.	Lepa Guti	3 years
17.	Lepa Malahar (Ointment)/Liniment/Gels/ lotions /creams	3 years
18.	Varti	2 years (one time use)
19.	Ghana Vati	3 years
20.	Kupipakva Rasayan	No expiry date1
21.	Parpati	No expiry date1
22.	Sveta parpati	2 years
23.	Pisti and Bhasma	No expiry date1
24.	Svarna, Rajata, Lauha, Mandura, Abhraka bhasma,Godanti, ShankhaBhasma, etc.	No expiry date1
25.	Naga Bhasma, Vanga Bhasma, Tamra Bhasma2	5 years2
26.	Capsules made of soft gelatin (depending upon thecontent material) for Kashtha aushadhi	3 years
27.	Capsules of hard gelatin (depending upon the content material) -containing Kasth aushdhi with Rasa, Bhasma Parad-Gandhak	5 years2

28.	Syrup/liquid oral	3 years
29.	(Kama/Nasa Bindu) Ear/Nasal drops Eye drops	2 years 1 year
30.	Khand/Granule/Pak	3 years
31.	Dhoopans-Inhalers	2 years
32.	Pravahi Kwatha (with preservatives)	3 years

Note 1. Item at Sr. No.4, 5, 19, 20, 22, 23 have very long shelf life and they became more efficacious with the passage of time and period of ten years shall be mandatory for keeping the records of such items.

Note 2. Bhasmas at Sr. No. 23, start solidifying after five years and they need one or two _Puta'again before using in the dosage form.

(ii) Shelf life or date of expiry for Siddha Medicines

Sl. No.	Name of the Group of Medicine	Shelf life and date ofexpiry with effect from the date of manufacture
1.	Karpam	No expiry date*
2.	Cunnam	5 years
3.	Kalanku	No expiry date*
4.	Kattu	No expiry date*
5.	Parpam	No expiry date*
6.	Centuram	No expiry date*
7.	Karuppu	No expiry date*
8.	Patankam	5 years
9.	Kulampu	5 years
10.	Meluku	5 years
11.	Tinir	2 years
12.	Tiravakam	2 years
13.	Mattirai	3 years

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14.	Tailam	3 years
15.	Ilakam	3 years
16.	Iracayanaam	3 years
17.	Ney	2 years
18.	Manappaku	3 years
19.	Venney	3 years
20.	Vatakam	3 years
21.	Curanam	2 years
22.	Pura Maruntukal	5 years

Note. * Items at Sr. No.1, 3, 4, 5, 6, 22 have very long shelf life and they became more efficacious with the passage of time and period of ten years shall be mandatory for keeping the records of such items.

(iii) Shelf life or date of expiry for Unani System of Medicines

Sl. No.	Name of the Group of Medicine	Shelf life and date ofexpiry with effect from the date of manufacture
1.	Habb (Pills)	3 years
2.	Qurs (Tablets)	3 years
3.	Majoon/Dawa	3 years
4.	Khamira	3 years
5.	Itrifal	3 years
6.	Tiryaq	3 years
7.	Laooq	2 years
8.	Laboob	2 years
9.	Halwa	2 years
10.	Mufarreh/Yaqooti	2 years
11.	Burood/Surma/Kohal	3 years

12.	Kushta	5 years
13.	Raughaniyat	3 years
14.	Marham/Zimad/Qairooti	3 years
15.	Ayarij/Sufoof	2 years
16.	Safoof (Namak wala/containing salt)	1 year
17.	Sharbat/Sikanjabeen	3 years
18.	Jawarish	3 years
19.	Capsule	3 years
20.	Arq	1 year
21	Qutoor	1 year
22.	Nabeez	5 years
23.	Murabba	1 year
24.	Tila	2 years]

[1][PART XVIII

GOVERNMENT ANALYSTS AND INSPECTORS FOR AYURVEDIC (INCLUDING SIDDHA) OR UNANI DRUGS

162. ***Duties of Inspectors specially authorised to inspect the manufacture of Ayurvedic (including Siddha) or Unani drugs***—Subject to the instructions of the controlling authority, it shall be the duty of an Inspector authorised to inspect the manufacture of Ayurvedic (including Siddha) or Unani drugs–

1. Ins. by notification F.1-23/6, dt. 2-2-1970.

(i) to inspect not less than twice a year, all premises licensed for manufacture of Ayurvedic (including Siddha) or Unani drugs within the area allotted to him and to satisfy himself that the conditions of the licence and the provisions of the Act and the rules made thereunder are being observed;

(ii) to send forthwith to the controlling authority after each inspection a detailed report indicating whether or not the conditions of the licence and the provisions of the Act and the rules made thereunder are being observed;

(iii) to take samples of the drugs manufactured on the premises and send them for test or analysis in accordance with these rules;

(iv) to institute prosecutions in respect of violation of the Act and the Rules made thereunder.

[1][**162A.** ***Qualifications of the State Drug Licensing Authority for Licensing of Ayurvdeda , Siddha and Unani drugs***– *(a)* The Ayurvedic/ Siddha/ Unani qualifications as per Schedule II of the Indian Medicine Central Council Act, 1970 (84 of 1970)/ B Pharma (Ayurveda) of a recognized University.

(b) At least 5 years experience in the Ayurveda/ Siddha/ Unani drug manufacturing or testing of Ayurvedic, Siddha and Unani drugs or enforcement of provisions of Chapter IVA of the Drugs and Cosmetics Act,1940 and Rules made thereunder or teaching/ research on clinical practice of Ayurveda/ Siddha/ Unani System.]

163. ***Procedure for despatch of sample to Government Analyst and its receipt by the Government Analyst***—(1) Sample for test or analysis shall be sent to the Government Analyst by registered post or by hand in a sealed package, enclosed together with a memorandum in

Form 18-A in an outer cover addressed to the Government Analyst.

(2) The package as well as the outer cover shall be marked with a distinguishing number.

(3) A copy of the memorandum and a specimen impression of the seal used to seal the package shall be sent by registered post or by hand to the Government Analyst.

(4) On receipt of the package from an Inspector, the Government Analyst or an Officer authorised by him in writing in this behalf shall open the package and shall also record the conditions of the seals on the package.

(5) After the test or analysis has been completed, one copy of the results of the test or analysis shall be supplied forthwith to the sender in

Form 13-A. A copy of the result in Form 13A shall also be sent simultaneously to the Controlling Authority and to the Drugs Controller, India.

[2][PHARMACOPOEIAL LABORATORY FOR INDIAN MEDICINES TO FUNCTION AS CENTRAL DRUGS LABORATORY FOR THE PURPOSE OF TESTING OR ANALYSIS OF AYURVEDA, SIDDHA AND UNANI DRUGS

163.A ***Functions*** - The Pharmacopoeial Laboratory for Indian Medicine at Ghaziabad shall function as a Central Drugs Laboratory for the purpose of testing or analysis of Ayurveda, Siddha and Unani Drugs.

Its functions shall be:-

(1)to develop Pharmacopoeial standards and draft monographs and amendments alongwith standardized methods for the Ayurvedic, Siddha, Unani drugs;

(2)to act as Central Appellate Drug Laboratory for testing of Ayurveda, Siddha and Unani drugs,

(3)to analyse or test such samples of Ayurvedic, Siddha, Unani drugs as may be sent to it under sub-section (2) of section 11, or under sub-section (4) or section 25, of the Act; (4)to maintain reference museum and herbarium for the drugs used in Ayurveda, Siddha and Unani (ASU) system.

(5)to run a training centre for quality control methods in the Ayurveda, Siddha or Unani systems of medicines;

(6)to carry out such other duties as may be entrusted to it by the Government of India.

1. Ins. by G.S.R. 76 (E), dt. 3.2.2003.
2. Ins. by G.S.R. 352 (E), dt. 1.6.2006.

163B. The functions of the Central Drug Laboratory in respect of Ayurvedic, Siddha and Unani drugs shall be carried out at the Pharmacopoeial Laboratory for Ayurvedic, Siddha and Unani medicine, Ghaziabad, (Uttar Pradesh) and the functions of the Director in respect of the said drugs shall be exercised by the Director of the said laboratory.

163C. ***Despatch of samples for test or analysis*** - (1) Samples for testing or analysis of Ayurveda, Siddha and Unani drugs under Sub-section (2) of Section 11 or sub-section (1) of section 25 and section 33-H of the Act shall be sent by registered post in a sealed packet, enclosed with a memorandum in

Form 1 A, specified in Schedule A, in an outer cover addressed to the Director, Pharmacopoeial Laboratory for Indian Medicine.

(2) The packet as well as the outer cover, shall be marked with a distinguished number.

(3) A copy of the memorandum in

Form 1A and a specimen impression of the seal used to seal the packet shall be sent separately by registered post to the Director, Pharmacopoeial Laboratory for Indian Medicine.

163D. ***Recording of condition of seals*** - On receipt of the packet, it shall be opened by an officer authorized in writing on that behalf by the Director, Pharmacopoeial laboratory for Indian Medicine, who shall record the condition of the seal on the packet.

163E. ***Report of result of test or analysis*** - After test or analysis, the result of the test or analysis, together with full protocols of the tests applied, shall be supplied forthwith to the sender in

Form 2A of as specified in the said schedule.

163F. ***Fees*** - The fees for test and analysis shall be as specified in Schedule B-1

163G. ***Signature on certificates*** - Certificates issued under these rules by the Pharmacopoeial Laboratory for Indian Medicine, shall be signed by the Director or by an officer authorized by the Central Government to sign such certificates.

164. ***Method of test or analysis to be employed in relation to Ayurvedic (including Siddha) or Unani drugs***.—The method of test or analysis to be employed in relation to an Ayurvedic (including Siddha) or Unani drug shall be such as may be specified in the Ayurvedic (including Siddha) or Unani Pharmacopoeia, or if no such pharmacopoeias are available or if no tests are specified in such pharmacopoeias, such tests as the Government Analyst may employ, such tests being scientifically established to determine whether the drug contains the ingredients as stated on the label.

165. ***Qualifications of Government Analyst***. —A person who is appointed a Government Analyst under section 33 F of the Act shall be a person possessing the qualifications prescribed in rule 44 or a degree in Ayurveda, Siddha or Unani System, as the case may be, conferred by a University, a State Government or Statutory Faculties, Councils and Boards of Indian Systems of Medicine recognized by the Central or State Government, as the case may be, for this purpose and has had not less than three years' post graduate experience in the analysis of drugs in a laboratory under the control of (i) a Government Analyst appointed under the Act, or (ii) a Chemical Examiner to Government, or (iii) the Head of an institution specially approved for the purpose by the appointing authority.

166. ***Duties of Government Analyst***– (1) The Government Analyst shall analyze or test or cause to be analyzed or tested such samples of Ayurvedic (including Siddha) or Unani drugs as may be sent to him by Inspectors or any other persons or authority authorised by the Central Government or State Government under the provisions of Chapter IV A of the Act and shall furnish reports of the results of test or analysis in accordance with these rules.

(2) A Government Analyst appointed under section 33F shall from time to time forward to the Government reports giving the result of analytical work and research with a view to their publications at the discretion of the Government.]

[1][**167.** ***Qualifications of Inspector***.–A person who is appointed an Inspector under section 33G shall be a person who—

(a) has the qualifications laid down under rule 49 and shall have undergone practical training in the manufacture of Ayurvedic (including Siddha) or Unani drug, as the case may be; or

(b) has a degree in Ayurvedic or Siddha or Unani System or a degree in Ayurveda Pharmacy, as the case may be, conferred by a University or State Government or a Statutory Faculty, Council or Board of Indian Systems of Medicine recognized by the Central Government or the State Government for this purpose; or

(c) has a diploma in Ayurveda, Siddha or Unani Systems, as the case may be, granted by a State Government or an Institution recognized by the Central Government or a State Government for this purpose.

[2][**PART XIX**
STANDARDS OF AYURVEDIC, SIDDHA AND UNANI DRUGS

168. *Standards to be complied with in manufacture for sale or for distribution of Ayurvedic, Siddha and Unani Drugs.-*

Class of Drugs	Standards to be complied with

1. [3][* * *] drugs included in Ayurvedic Pharmacopoeia. 2. Asavas and Arishtas	The standards for identity, purity and strength as given in the editions of Ayurvedic Pharmacopoeia of India for the time being in force. The upper limit of alcohol as self generated alcohol should not exceed 12% v/v excepting those that are otherwise notified by the Central Government from time to time.]

1. Amended by G.S.R. 376 (E), dt. 20.7.1978.

2. Ins. by G.S.R. 519(E), dt. 26.6.1995.

3.The word ―Singlel omitted by G.S.R. 422(E), dt. 11.6.2002.

Drugs and Cosmetics Rules 1945

[1]**[169. Permitted Excipients.-** Permitted Excipients along with their standards i.e. additives, preservatives, antioxidants, flavouring agents, chelating agents etc. permitted in the Indian Pharmacopoeia (IP), Prevention of Food Adulteration Act, 1954 and Bureau of Indian Standard Act, 1986 are permitted for use in Ayurveda, Siddha and Unani drugs with the following conditions, namely:-

1.The above excipients shall be used in the permissible limits as prescribed in the Indian Pharmacopoeia/ Prevention of Food Adulteration Act, 1954/ Food Product Order/ Bureau of Indian Standard Act, 1986 and they shall comply with the respective quality specifications, not exceeding any specified limits of usage therein, and except Hydrogenated vegetable oil.

2.Only Natural coloring agents as permitted under rule 26 of Prevention of Food Adulteration Rules, 1955 will be used for Ayurveda, Siddha and Unani drugs and additionally, colors permitted under Rule 127 of the Drugs and Cosmetics Rules, 1945 shall be used for Proprietary Ayurveda, Siddha and Unani drugs as defined in subclause (i) of clause (h) of section 3 of Drugs and Cosmetics Act, 1940, not exceeding any specified limits of usage therein.

3.Preservatives and Coloring agents shall be mentioned on the label for the information of the consumer as required under rule 161 of the Drugs and Cosmetics Rules, 1945.

4.Additives used in various processes and in formulating dosage forms shall be mentioned clearly with quantities used, in the application for licenses and the record for the same shall be maintained by the manufacturers.

5.Manufacturers shall be responsible to ensure rationality, safety and quantity used of various excipients in the formulation.

6.If any excipients or additive or preservative etc. referred in Indian Pharmacopoeia/ Prevention of Food Adulteration Act, 1954/ Food Product Order/ Bureau of Indian Standard Act, 1986 is deleted at a particular point of time, this will also be deleted simultaneously for the use in Ayurveda, Siddha and Unani drugs.

7.Following artificial sweeteners as per maximum limit indicated below may be used in various dosage forms of Ayurveda, Siddha, Unani Proprietary Medicines:-

Artificial sweeteners may be used only in proprietary ASU products and the label of such products should carry a statutory warning stating the name and quantity of the artificial sweetener used.

The recommended Acceptable Daily Intake (ADI) of these sweeteners as laid down by US FDA is as follows:

Sr. No.	Sucralose	Aspartame	Saccharin	Acesulfame K
1	5 mg/kg body weight	40 mg/kg body weight	5 mg/kg body	15 mg/kg body weight

One third of the above ADI would be permissible for use in Ayurveda, Siddha, Unani Patent and Proprietary Drugs.

8.Any previous notification issued by the Department of AYUSH regarding use of excipients / additives or preservatives in Ayurveda, Siddha and Unani medicines stands superseded.]

1. Subs. by G.S.R. 755 (E), dt. 23.10.2008. Earlier ins. by G.S.R. 285 (E), dt. 11.5.2005.

SCHEDULE A

FORM 1

(*See* rule 4)

Memorandum to the Central Drugs Laboratory

Serial Number .....

To the Director, Central Drugs Laboratory .....

From.....

I send herewith, under the provisions of section 25 (4) of the Drugs and Cosmetics Act, 1940, sample(s) of a drug purporting to be .....for test or analysis and request that a report of the result of the test or analysis may be supplied to this Court.

(2) The distinguishing number on the packet is .....

(3) Particulars of offence alleged .....

(4) Matter on which opinion is required .....

(5) A fee of Rs ..... has been deposited in Court.

Date ..... ……..

Magistrate

[1][**FORM 1**

(*See* rule 163C)

Memorandum to the Pharmacopoeial Laboratory for Indian Medicine (PLIM) From .....

(Full name, Designation and Postal address of the sender)

Serial No.....

To the Director,

Pharmacopoeial Laboratory for Indian Medicine,

I send herewith, under the provisions of section 11(2)/section 25(4) and section 33H of the Drugs and Cosmetics Act, 1940, sample(s) of a drug purporting to be .....for test or analysis and request that a report of the result of the test or analysis may be supplied to this Court.

(2) The distinguishing number on the packet is .....

(3) Particulars of offence alleged .....

(4) Matter on which opinion is required .....

(5) A fee of Rs ..... has been deposited in Court.

Date ..... ……..

Magistrate/Authorized Signatory]

1. Ins. by G.S.R. 352(E) , dt. 1.6.2006.

FORM 2

(*See* rule 6)

Certificate of test or analysis by the Central Drugs Laboratory

Certified that the sample bearing number.....
……..

purporting to be a sample of. ..... received on ..... with memorandum No ..... dated..... from .....has been tested / analysed and that t he result of such t e s t / analysis is as stated below.

2. The condition of the seals on the packet on receipt was as follows: —

*3. In the opinion of the undersigned the sample is of standard quality is not of standard quality as defined in the Drugs and Cosmetics Act, 1940 and Rules thereunder for the reasons given below:–

Director

Date…… Central Drugs Laboratory or other authorised officer

Details of results of test or analysis with protocols of test applied

Director

Date.....Central Drugs Laboratory or other authorised officer

* *If opinion is required on any other matter, the paragraph should be suitably amended.*

[1]**[FORM 2A**

(*See* rule 163E)

Certificate of test or analysis from the Pharmacopoeial Laboratory for Indian Medicine or Governmen Analyst

Certified that the sample bearing number.....
……..

purporting to be a sample of. ..... received on ..... with memorandum No ..... dated..... from .....has been tested / analysed and that t he result of such t e s t / analysis is as stated below.

2. The condition of the seals on the packet on receipt was as follows: —

*3. In the opinion of the undersigned the sample is of standard quality as defined in the Drugs and Cosmetics Act, 1940 and Rules thereunder for the reasons given below.

Or

In the opinion of the undersigned the sample is not of standard quality as defined in the Drugs and Cosmetics Act, 1940 and Rules thereunder for the reasons given below.

—**Note**: *delete whichever is not applicable.‖

(Signature of the Analyst Person-in-Charge of testing) Date…….

Place…….

Name & Designation and Seal…….

Name and Address of the laboratory ……]

1. Ins. by G.S.R. 352(E) , dt. 1.6.2006.

Drugs and Cosmetics Rules 1945

[1]**FORMS 3-7 (*Omitted*)**

[2]**[FORM 8**

(*See* rule 24)

***Application for licence to import drugs (excluding those specified in Schedule X) to the Drugs and Cosmetics Rules*, 1945**

I/We* ..... (full address with telephone number, fax number and e-mail address) hereby apply for a licence to import drugs specified below manufactured by M/s ..... (full address with telephone no, fax and e-mail no.).

2. Names of the drugs to be imported:

(1)

(2)

(3)

3. I/We* ..... enclose herewith an undertaking in

Form 9 dated ……signed by the manufacturer as required by rule 24 of the Drugs and Cosmetics Rules, 1945.

4. I/We* ..... enclose herewith a copy of Registration Certificate concerning the drugs to be imported in India, issued under

Form 41 of the rules, vide Registration Certificate No .....dated ..... issued through M/s.

..... (name and full address) .....valid up to .....

5 I/We* ..... hold a valid wholesale licence for sale or distribution of drugs or valid licence to manufacture drugs, under the provisions of the Act and rules made thereunder. A copy of the said licence is enclosed.

6. A fee of .....has been credited to Government under the Head of Account "0210-Medical and Public Health, 04-Public Health, 104-Fees and Fines" under the Drugs and Cosmetics Rules, 1945 - Central vide Challan No ..... dated .....(attached in original)

Signature .....

Name.....

Designation .....

Seal/Stamp of Manufacturer's agent in India. Place: .....

Date: .....

**Delete whichever is not applicable*.]

1. Forms 3 to 7 omitted by Notfn. No. F. 1-16/57-D, dt. 15-6-1957.
2. Subs. by G.S.R. 604(E) , dt. 24.8.2001.

1[FORM 8A

(*See* rule 24)

***Application for licence to import drugs specified in Schedule X to the Drugs and Cosmetics Rules,* 1945**

I/We* ..... (full address with telephone number, fax number and e-mail address) hereby apply for a licence to import drugs specified below manufactured by M/s ..... (full address with telephone no, fax and e-mail no.).

2. Name of the drugs to be imported:

(1)
(2)
(3)

3. I/We* ..... enclose herewith an undertaking in Form 9 dated……signed by t h e manufacturer a s required by rule 24 of the Drugs a nd Cosmetics Rules, 1945.

4. I/We* ..... enclose herewith a copy of Registration Certificate concerning the drugs to be imported in India, issued under

Form 41 of the rules, vide Registration Certificate No dated issued through M/s.

..... (name and full address) ..... …… valid upto……

5. I/We* ..... hold a valid wholesale licence for sale or distribution of drug or licence to manufacture drugs, under the provisions of the Act and rules made thereunder. A copy of the said licence is enclosed.

6. A fee of ..... has been credited to Government under the Head of Account "0210 - Medical and Public Health, 04- Public Health, 104- Fees and Fines" under the Drugs and Cosmetics Rules 1945 - Central vide Challan No ..... dated ..... (attached in original).

Signature .....

Name .....

Designation .....

Seal/Stamp of Manufacturer's agent in India.]

Place: .....

Date: .....

**Delete whichever is not applicable.*

1. Subs. by G.S.R. 604(E), dt.24.8.2001.

FORM 9

(*See* rule 24)

Form of undertaking to accompany an application for an import licence

Whereas ..... of..... intends to apply for a licence under the Drugs and Cosmetics Rules, 1945, for the import into India, of the drugs specified below manufactured by us, we……of……..hereby give this undertaking that for the duration of the said licence—

(1) the said applicant shall be our agent for the import of drugs into India;

(2) we shall comply with the conditions imposed on a licence by [1][rules 74 and 78] of the Drugs and Cosmetics Rules, 1945;

(3)we declare that we are carrying on the manufacture of the drugs mentioned in this undertaking at the premises specified below, and we shall from time to time report any change of premises on which manufacture will be carried on and in cases where manufacture is carried on in more than one factory any change in the distribution of functions between the factories;

(4) we shall comply with the provisions of Part IX of the Drugs and Cosmetics Rules, 1945;

(5) every drug manufactured by us for import under licence into India shall as regards strength, quality and purity conform with the provisions of Chapter III of the Drugs and Cosmetics Act, 1940, and the Drugs and Cosmetics Rules, 1945;

(6) we shall comply with such further requirements, if any, as may be specified by Rules, by the Central Government under the Act and of which the licensing authority has given to the licensee not less than four months' notice.

Names of drugs and classes of drugs

Particulars of premises where manufacture is carried on.

Date.....

[2][*Signature, Name, Designation Seal/Stamp of manufacturer or on behalf of the manufacturer*.]

1. Subs. by. G.S.R. 462(E), dt. 22.6.1982.
2. Subs. by G.S.R. 604(E), dt. 24.8.2001

.

[1][FORM 10

(*See* rules 23 and 27)

Licence to import drugs (excluding those specified in Schedule X) to the Drugs and Cosmetic Rules, 1945

Licence Number ..... Date...……..

1. ..... (Name and full address of the importer) is hereby licensed to import into India during the period for which the licence is in force, the drugs specified below, manufactured by M/s ..... (name and full address) and any other drugs manufactured by the said manufacturer as may from time to time be endorsed on this licence.

2. This licence shall be in force from ..... to ..... unless it is sooner suspended or cancelled under the said rules.

3. Names of drugs to be imported.

Place : ……..

Date : ……. *Licensing Authority*

Seal/Stamp

Conditions of Licence.

1. A photocopy of licence shall be displayed in a prominent place in a part of the premises, and the original licence shall be produced, whenever required.
2. Each batch of drug imported into India shall be accompanied with a detailed batch test report and a batch release certificate, duly signed and authenticated by the manufacturer with date of testing, date of release and the date of forwarding such reports. The imported batch of each drug shall be subjected to examination and testing as the licensing authority deems fit prior to its marketing.
3. The licensee shall be responsible for the business activities of the manufacturer in India along with the registration holder and his authorised agent.
4. The licensee shall inform the licensing authority forthwith in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the licensing authority in the name of the firm with the changed constitution.]

1. Subs. by G.S.R. 604(E) ,dt. 24.8.2001.

Drugs and Cosmetics Rules 1945

[1][FORM 10A

(*See* rules 23 and 27)

Licence to import drugs specified in Schedule X to the Drugs and Cosmetics Rules, 1945

Licence Number ..... Date…….

.....(Name and full address of the importer) is hereby licensed to import into India during the period for which the licence is in force, the drugs specified below, manufactured by M/s ..... (name and full address) and any other drugs manufactured by the said manufacturer as may from time to time be endorsed on this licence.

2. This licence shall be in force from ..... to ..... unless it is sooner suspended or cancelled under the said rules.

3. Names of drugs to be imported.

Place:.....

Date: .....

Licensing Authority

Seal/Stamp.

**Delete whichever is not applicable.*

Conditions of Licence

1. A photocopy of licence shall be displayed in a prominent place in a part of the premises, and the original licence shall be produced, whenever required.
2. Each batch of drug imported into India shall be accompanied with a detailed batch test report and a batch release certificate, duly signed and authenticated by the manufacturer with date of testing, date of release and the date of forwarding such reports. The imported batch of each drug shall be subjected to examination and testing as the licensing authority deems fit prior to its marketing.

3. The licensee shall be responsible for the business activities of the manufacturer in India along with the registration holder and his authorised agent.

4. The licensee shall inform the licensing authority forthwith in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the licensing authority in the name of the firm with the changed constitution.]

1. Subs. by G.S.R. 604(E), dt. 24.8.2001.

FORM 11

(*See* rule 33)

Licence to import drugs for the purposes of examination, test or analysis

1 ……of ..... is hereby licensed to import from..... the drugs specified below for the purposes of examination, test or analysis at .....or in such other places as the licensing authority may from time to time authorise.

2. This licence is subject to the conditions prescribed in the Rules under the Drugs and Cosmetics Act, 1940.

3. This licence shall, unless previously suspended or revoked, be in force for a period of one year from the date specified below:–

Name of drugs	*Quantities which may be imported*

Date..... *Licensing Authority*
Seal/Stamp

[1] **[FORM 11A**

(*See* rule 33A)

Licence to import drugs by a Government Hospital or Autonomous Medical Institution for the treatment of patients

Licence No ……. Date……. Dr. ..... ……Designation ……..of ……

(Name of College/Hospital/Autonomous Institution)

is hereby licenced to import from M/s .....(name and full address) the drugs specified below for the purpose of treatment of patients for the disease (name of the disease) ..... at ..... or in such other places as the licensing authority may from time to time authorise.

2. This licence shall, unless previously suspended or revoked, be in force for a period of one year from the date of issue specified above.

3. Names of drugs to be imported:

Name of drugs Quantities which may be imported

Place : .....

Date :.....

Licensing Authority Seal / Stamp

Conditions of Licence

1. The licence shall be displayed in the Office of the Medical Superintendent of Government Hospital / Head of Institution of Autonomous Medical Institution.

2. The licensee shall store the drugs imported under this licence under proper storage conditions.

3. The drugs imported under this licence shall be exclusively used for the treatment of patients, and a record shall be maintained in this regard, by a registered pharmacist giving the full name(s) and address(es) of the patients, diagnosis, dosage schedule, total quantity of drugs imported and issued, and shall be countersigned by the Medical Superintendent of the Government Hospital or Head of the Autonomous Medical Institution which shall be produced, on demand by an Inspector appointed under the Act.]

1. Subs. by G.S.R.. 604(E), dt. 24.8.2001.

Drugs and Cosmetics Rules 1945

FORM 12

(*See* rule 34)

Application for licence to import drugs for purpose of examination, test or analysis

I,… ……resident of ……. by occupation……. hereby apply for a licence to import the drugs specified below for

the purposes of examination, test or analysis at ..... from .....and I undertake to comply with the conditions applicable to the licence.

[1][A fee of rupees ..... has been credited to Government under the head of Account ―0210-Medical and Public Health, 04-Public Health, 104-Fees and Fines‖ under the Drugs and Cosmetics Rules, 1945—Central vide Challan No…….dated……(attached in original).]

Name of drugs	*Quantities which may be imported*

Place……..

Date…… *Licensing Authority*

1. Subs. by G.S.R. .604(E), dt. 24.8.2001.

[1]**[FORM 12A**

(*See* rule 36, Second Proviso)

Application for the issue of a permit to import small quantities of drugs for personal use

I, ... resident of .....by occupation..... hereby apply for a permit to import the drugs specified below for personal use from .....

I attach a prescription from a registered medical practitioner in regard to the need for the said drugs.

Name of drugs	*Quantities which may be imported*

Date..... *Signature*.....

1. Added by Notifn No. F.1-36/54-DS, dt: 3.3.1955.

Drugs and Cosmetics Rules 1945

[1]**[FORM 12AA**

(*See* rule 34A)

Application for licence to import small quantities of new drugs by a Government Hospital or Autonomous Medical Institution for the treatment of patients.

I, ... …… (name and designation) ..... …….. of …… (name of the Hospital/Autonomous Medical Institution) hereby apply for a licence to import small quantities of new drugs specified below for the purpose of treatment of patients for the disease ..... (name of the disease)…… … …… at…….(name and place of the hospital) and I undertake to comply with the conditions applicable to the licence and other provisions of the Drugs and Cosmetics Act, 1940 and the rules made thereunder, from time to time.

1. A fee of rupees ..... has been credited to Government under the Head of Account "0210-Medical and Public Health, 04- Medical and Public Health, 104- Fees and

Fines" under the Drugs and Cosmetics Rules, 1945 - Central vide Challan No……..dated ..... (attached in original).

2. Name of new drugs to be imported:

Name of drugs	Quantities which may be imported

Place: …….. *Signature……..*

Date: …….. *Name……*

Seal/Stamp……

Certificate

Certified that the drugs specified above for import are urgently required for the treatment of patients suffering from and that the said drug(s) is/are not available in India.

Place…….. *Signature ..... ……..*

Date ..... *Medical Superintendent of the Government Hospital / Head of Autonomous Medical Institution* *Seal / Stamp*.]

1. Subs. by G.S.R. 604(E), dt. 24.8.2001.

Drugs and Cosmetics Rules 1945

[1][FORM 12B

(*See* rule 36, Second Proviso)

Permit for the import of small quantities of drugs for personal use

……of ..... is hereby permitted to import from..... the drugs specified below for personal use.

2. This permit is subject to the conditions prescribed in the Rules under the Drugs and Cosmetics Act, 1940.

3. This permit shall, unless previously suspended or revoked, be in force for a period of six months from date specified below.

Name of drugs	Quantities which may be imported

Date…….. *Licensing Authority]*

FORM 13

(*See* rule 46)

***Certificate of test or analysis by Government Analyst under section 25 (1) of the Drugs and Cosmetics Act,* 1940**

1. Name of Inspector from whom received .....
2. Serial No. and date of Inspector's memorandum.....
3. Number of sample .....
4. Date of receipt .....
5. Name of drugs purporting to be contained in the sample .....
6. Condition of seals on the [2][packet or on portion of sample or container] .....
7. Result of test or analysis with protocols of test or analysis applied .....

In the opinion of the undersigned the sample referred to above (is of standard/is not of standard) quality as defined in the Drugs and Cosmetics Act, 1940 and Rules thereunder for the reasons given below.

for the reasons given below:-

Date..... *Government Analyst.*

1. Subs. by. G.S.R. 753(E), dt. 4.11.1999.
2. Subs. by G.S.R. 59(E), dt. 7.2.1995.

Drugs and Cosmetics Rules 1945

[1]**[FORM 13A**

[*See* rule 163

(5)]

Certificates of tests or analysis by Government Analyst under section 33H of the Drugs and Cosmetics Act, 1940

1. Names of Inspector from whom received .....
2. Serial No. and date of Inspector's memorandum .....
3. Number of sample.....
4. Date of receipt .....
5. Names of ingredients purporting to have been used in the preparation of the sample…..
6. Condition of seals on the package .....
7. Results of test or analysis ……..

[2][In the opinion of the undersigned the sample referred to above is of standard/is not of standard quality as defined in the Drugs and Cosmetics Act, 1940 and the rules made thereunder for the reasons given below]

Date..... *Government Analyst..]*

FORM 14A

(*See* rule 47)

Application from a purchaser for test or analysis of a drug under Section 26 of the Drugs and Cosmetics Act, 1940

1. Full name and address of the applicant .....

2. Occupation.....

3. Name of drug purporting to be contained in the sample .....

4. Name and full address of the pharmacy or concern where the drug was purchased…….

5. Date on which purchased.....

6. Reasons why the drug is being submitted for test or analysis…….

[3] [7. A fee of rupees ..... *vide* Schedule B of the Drugs and Cosmetics Rules, 1945, has been credited to Government under the head of account "080—Medical—Miscellaneous—Fees under the Drugs and Cosmetics Rules, 1945—Central/State"—*vide* treasury receipt attached.]

I hereby declare that the drug being submitted for test was purchased by or for me. I further declare that the sample of the drug being sent for test or analysis is exactly as it was purchased and has not been tampered with in any way to reduce its potency.

Date..... *Signed*.... …..

1. Added by Notfn. No. F 1-23/67-D (S.O. 642), dt. 2.2.1970.

2. Ins. By G.S.R. 376(E), dt: 3..5.2010.

3. Added by Notfn. No. F. 1-3/51-D.S., dt. 15-10-1954

FORM 14-B

(*See* rule 47)

Certificate of test or analysis by Government Analyst under Section 26 of the Drugs and Cosmetics Act, 1940

1. Name of person from whom sample received .....

2. Date of receipt .....

3. Name of drug purporting to be contained in the sample .....

4. *Opinion of the Government Analyst*—The sample referred to above is/is not of standard quality as defined in the Drugs and Cosmetics Act, 1940 and Rules thereunder.

Date..... *Government Analyst……..*

[1]**[FORM15**

(*See* rules 54 and 145C)

Order under section 22 (1)(c) of the Drugs and Cosmetics Act, 1940 requiring a person not to dispose of stock in his possession

Whereas, I have reasons to believe that the stocks of drugs/cosmetics in your possession, detailed below contravene the provisions of section 18 of the Drugs and Cosmetics Act, 1940;

Now, therefore, I hereby require you under clause (c) of sub-section (1) of section 22 of the said Act not to dispose of the said stock for a period of..... days from the date of this order.

Date..... *Inspector……..*

Details of stock of drugs/ cosmetics

Date..... *Inspector.....*]

[2]**[FORM 16**

(*See* rules 55 and 145-B)

Receipt for stock of drugs or cosmetics for record, register, document or material object seized under section 22 (1) (c) or (cc) of the Drugs and Cosmetics Act, 1940.

The stock of drugs or cosmetics for records, registers, documents or material objects detailed below has / have this day been seized by me under the provisions of clause (c) or clause (cc) of sub-section (1) of section 22 of the Drugs and Cosmetics Act. 1940 (23 of 1940) from the premises of ..... situated at.....

Date..... *Inspector. .....*

Details of drugs, cosmetics, records, registers, documents or material objects seized.

Date..... *Inspector. .....*]

1. Subs. by G.S.R. 1594, dt. 28.10.1976.
2. Subs. by. G.S.R. 926 , dt. 24-6-1977.

Drugs and Cosmetics Rules 1945

[1] **[FORM 17**

(*See* rules 56 and 145A)

Intimation to person from whom sample is taken

I have this day taken from the premises of ……..situated at..... samples of the drugs / cosmetics specified below for the purpose of test or analysis.

Date..... *Inspector. .....*

Details of samples taken

Date..... *Inspector. .....*]

[2]**[FORM 17A**

(See rules 56A and 145AA)

Receipt for samples of drugs or cosmetics taken where fair price tendered thereof under sub- section (I) of Section 23 of the Drugs and Cosmetics Act, 1940 is refused

To .....

Whereas I, this..... day of ..... [3][20] ....., have taken from the premises of…….. situated at..... samples of drugs/cosmetics as specified below:-

Details of Samples……

And whereas I had offered to pay you rupees ..... as the fair price of the samples of drugs/cosmetics taken:

And whereas, you have refused to accept the fair price tendered thereof.

Now, therefore, I give you the receipt as the fair price tendered for the samples of the drugs/cosmetics taken by me.

Date: ..... *Inspector* ….. …..]

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1. Subs. by S.O. 2139, dt. 5.6.1972.
2. Ins. by G.S.R. 292(E) , dt. 29.5.1997.
3. Subs. by G.S.R. 592(E) , dt. 13.8.2008.

FORM 18

(*See* Rule 57)

Memorandum to Government Analyst

Serial No. of Memorandum .....

From:

To

The Government Analyst

……

……

The portion of sample / container described below is sent herewith for test or analysis under the provisions of clause (i) of sub-section (4) of Section 23 of the Drugs and Cosmetics Act, 1940.

The portion of sample/container has been marked by me with the following mark.

Details of portion of sample or container with [1][name of drug/cosmetic] which it purports to contain—

Date..... *Inspector*. .....

[2][FORM 18A

(*See* Rule 163 (1))

Memorandum to Government Analyst Serial No……..

From

To

The Government Analyst

……

……

The portion of sample / container described below is sent herewith for test or analysis under the provisions of Section 33H of the Drugs and Cosmetics Act, 1940.

The portion of sample / container has been marked by me with the following mark.

Details of portion of sample or container with name of ingredients from which it is claimed to be made.

Date..... *Inspector*. .....

1. Subs. by G.S.R. 370(E), dt. 7.4.1994.

2. Added by Notfn. No. F 1-23/67-D, dt. 2-2-1970.

[1][FORM 19

[*See* rule 59 (2)]

Application for grant or renewal of a [2][licence to sell, stock or exhibit or offer for sale, or distribute] of drugs other than those specified in Schedule

1 . I / We* .....hereby apply for licence to sell by wholsesale/retail drugs specified in Schedules C and C(1) excluding those specified in Schedule X *and/or drugs other than those specified in Schedules C, C(1) and X to the Drugs and Cosmetics Rules, 1945 *and also to operate a pharmacy on the premises situated at.....

2. ** The sale and dispensing of drugs will be made under the personal supervision of the registered pharmacists namely:-

(Name) ..... (Qualification)……

(Name) .....(Qualification)…… 3. Categories of drugs to be sold .....

4.*** Particulars of special storage accommodation ..... 5. A fee of rupees..... has been credited to the Government account under the head of account .....

Date..... *Signature .....*]

** Delete whichever is not applicable.*

*** To be deleted if drugs will be sold only by wholesale.*

****Required only if products requiring special storage are to be sold.*

1. Subs. by G.S.R. 462(E), dt. 22.6.1982.
2. Subs. by G.S.R. 788(E), dt. 10.10.1985.

FORM 19A

[*See* rule 59 (2)]

Application for the grant or renewal of a restricted [1]***[licence to sell, stock or exhibit or offer for sale, or distribute] drugs by retail by*** [2]***[***] dealers who do not engage the services of a registered pharmacist***

1. I/We .....of. .....hereby apply for a licence to sell by retail

(i) [3][Drugs other than those specified in Schedule C, C1 and X] on the premises situated at……/[2][***]

or (ii) [4] [Drugs specified in Schedule C(1)] on the premises situated at ……/

[4][Drugs specified in Schedule C(1)] as vendor in the area……

2. Sales shall be restricted to such drugs as can be sold without the supervision of a registered pharmacist under the Drugs and Cosmetics Rules.

3. Names or classes of drugs proposed to be sold .....

*4. Particulars of the storage accommodation for the storage of [5][Schedule C(1)] on the premises referred to above.

**5. The drugs for sale will be purchased from the following dealers and such other dealers as may be endorsed on the licence by the Licensing Authority from time to time. Name of the dealers.....Licence No.....

Drugs and Cosmetics Rules 1945

6. A fee of rupees [2][***]/#twenty has been credited to Government under the head of account.....

Date..... *Signature* .....

**Delete whichever is not required.*

**Applies only to an itinerant vendor.

Rupees five for itinerant vendors and applicant from a village or town having a population of 5000 or less, and rupees twenty for other restricted licence.

1. Subs. by G.S.R. 788(E) ,dt. 10.10.1985.
2. Omitted by. G. S. R. 231(E) , dt. 4.6.1996.
3. Subs. by G.S.R. 462(E), dt. 22.6.1982.
4. Subs. by.G.S.R. 487(E) , dt. 2.7.1984.

[1]**[FORM 19AA**

(*See* rule 62C)

Application for grant or renewal of a [2]**[*licence to sell, stock or exhibit or offer for sale by wholesale, or distribute*] *drugs from a motor vehicle***

I / W e * _____ of _____ hereby apply for [2][licence to sell, stock or exhibit or offer for sale by wholesale, or distribute] drugs specified in Schedules C and C (1) and /or drugs other than those specified in Schedules C and C (1) from the vehicle bearing registration no._____ assigned under the Motor Vehicles Act, 1939.

2.Categoriesofdrugstobesold / distributed

3. A fee of rupees _____has been credited to Government under the headof account

*4.Particulars of the storage accommodation for the storage of drugs specified in Schedules C and C (1) on the vehicle referred to above.

Date *Signature*

**Delete* if not required.

1. Ins. by. G.S.R. 42 (E), dt. 25.1.1979.
2. Subs. by.G.S.R. 788(E), dt. 10.10.1985.

FORM 19B

(*See* rule 67A)

Application for* [1]*[licence to sell, stock or exhibit or offer for sale, or distribute] Homoeopathic medicines

1 . I / We* .....of..... hereby apply for a licence to sell by

*wholesale/*retail Homoeopathic medicines on the premises situated at .....

**2. The sale and dispensing of Homoeopathic medicines shall be made under the personal supervision of the following competent person in -charge.

Name .....

3 . A f ee o f rup e e s .....has been credited to Government under the head of account.....

Date..... *Signature* .....

**Delete whichever is not required.*

** To be deleted if Homoeopathic medicines will be sold by wholesale.

1. Subs. By G.S.R. 788(E), dt.10.10.1985.

[1]**[FORM 19C**

[*See* rule 59(2)]

Application for grant or renewal of a* [2]*[licence to sell, stock, exhibit or offer for sale, or distribute] of drugs specified in Schedule .

1. I/We* ..... of.....hereby apply for a licence to sell by *wholesale/*retail drugs specified in Schedule X to the Drugs and Cosmetics Rules, 1945. We operate a pharmacy on the premises, situated at .....

2. ** The sale and dispensing of drugs will be made under the personal supervision of the registered pharmacists mentioned below:-

(Name) ..... (Qualification)

(Name) .....(Qualification)

3. Name of drugs to be sold.

4. *** Particulars of storage accommodation.

5. A fee of rupees ..... has been credited to Government account under the head of account .....

Date ..... *Signature* .....

** Delete whichever is not applicable.*

** To be deleted if drugs will be sold only by wholesale.

***Required only if products requiring special storage are to be sold.]

1. Subs. by G.S.R. 462(E), dt. 22.6.1982.

2. Subs. by G.S.R. 788(E), dt. 10.10.1985.

FORM 20

[*See* rule 61(1)]

[1][*Licence to sell, stock or exhibit or offer for sale, or distribute*] *drugs by retail other than those specified in* [2][*Schedules C, C(1) and X*]

1. ..... is hereby [1][licensed to sell, stock or exhibit or offer for sale, or distribute] by retail drugs other than those specified in [2][Schedules C, C (1) and X] of the Drugs and Cosmetics Rules 1945, *and to operate a pharmacy on the premises situated at..... subject to the conditions specified below and to provisions of the Drugs and Cosmetics Act, 1940 and the Rules thereunder.

2 The licence shall be in force from..... to .....

3. Name (s) of qualified person (s) in charge .....

4. Categories of drugs.....

Name of the dealer……..Licence No……

Date..... *Licensing Authority ..... ……*

** Delete whichever is applicable*

Conditions of Licence

1. This licence shall be displayed in a prominent place in a part of the premises open to the public.
2. The licensee shall comply with the provisions of the Drugs and Cosmetics Act, 1940 and the Rules thereunder for the time being in force.
3. The licensee shall report to the Licensing Authority any change in the qualified staff in charge within one month of such change.

4. No drug shall be sold unless such drug is purchased under cash or credit memo from a duly licensed dealer or a duly licensed manufacturer.
5. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.

1. Subs. by G.S.R. 788(E), dt. 10.10.1985
2. Subs. by.G.S.R. 462(E), dt. 22.6.1982

FORM 20A

[*See* rule 61 (1)]

Restricted [1]**[*Licence to sell, stock or exhibit or offer for sale, or distribute*] *drugs by retail other than those specified in*** [2] **[*Schedules C, C (1) and X*] *for*** [3]***[***] dealers who do not engage the services of a registered pharmacist***

1. .....is hereby [1][licensed to sell, stock or exhibit or offer for sale, or Distribute] on the premises situated at [3][***] .....the following drugs being drugs other than those specified in [2][Schedules C, C (1) and X] of the Drugs and Cosmetics Rules, 1945, subject to the conditions specified below and to the provisions of the Drugs and Cosmetics Act, 1940 and the Rules made thereunder.

2. The licence shall be in force from..... to .....

3 The licensee can deal only in such drugs as can be sold without the supervision of qualified person under the Drugs and Cosmetics Rules, 1945.

[4] [***]

Name of the dealer ..... *Licence No* .....

Date..... *Licensing Authority*

Conditions of Licence

1. This licence shall be displayed in a prominent place in a part of the premises open to the public. [3][***].
2. The licensee shall comply with the provisions of the Drugs and Cosmetics Act, 1940 and the Rules thereunder for the time being in force.
3. No drug shall be sold unless such drug is purchased under a cash or credit memo from a duly licensed dealer or a duly licensed manufacturer.
4. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence h as been taken from the Licensing Authority in the name of the firm with the changed constitution.

1. Subs. by.G.S.R. 788(E), dt. 10.10.1985

2. Subs. by G.S.R. 462(E), dt. 22.6.1982.

3. Omitted by G.S.R. 231 (E) , dt. 4.6.1996

4 Sl. No. 4 omitted by G.S.R. 504(E) dt. 18.7.2002.

FORM 20B

[*See* rule 61 (1)]

[1]*[Licence to sell, stock or exhibit or offer for sale, or distribute] by wholesale, drugs other than those specified in* [2][*Schedules C, C(I) and X*]

1 ..... is hereby [1][licensed to sell, stock or exhibit or offer for sale, or distribute] by wholesale drugs other than those specified in [2][Schedules C, C(1) and X] on the premises situated at ..... subject to the conditions specified below and to the

provisions of the Drugs and Cosmetics Act, 1940, and the Rules thereunder.

2. The licence shall be in force from.....to .....

Date..... *Licence No……*

Licensing Authority.

Conditions of Licence

1. This licence shall be displayed in a prominent place in part of the premises open to the public.

2. The licensee shall comply with the provisions of the Drugs and Cosmetics Act, 1940 and the Rules thereunder for the time being in force.

[3] [3 (i) No drug shall be sold unless such drug is purchased under a cash or credit memo from a duly licensed dealer or a duly licensed manufacturer.

(ii) No sale of any drug shall be made to a person not holding the requisite [1][licence to sell, stock or exhibit for sale, or distribute] the drug. Provided that this condition shall not apply to the sale of any drug to—

(a) an officer or authority purchasing on behalf of Government, or

(b) a hospital, medical, educational or research institution or a registered medical practitioner for the purpose of supply to his patients, or

[4][(c) a manufacturer of beverages, confectionery biscuits and other non-medicinal products, where such drugs are required for processing these products.]

[5][***]

5. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.

1. Subs. by.G.S.R. 788(E), dt. 10.10.1985.

2. Subs. by G.S.R. 462(E) , dt. 22.6.1982.

3. Subs. by Notfn. No. F. 1/63/61-D, dt. 17.7.1963.

4.Ins. by S.O.23, dt:23.12.1969.

5.Clause 4 ommited by S.O. 289, dt:20.12.1992. Earlier clause 4 added by Notfn. F. No. 1-113/69-D, dt. 23.12.1969.

[1][FORM 20BB

(*See* rule 62-D)

[2]*[Licence to sell, stock or exhibit or offer for sale by wholesale, or distribute] drugs other than those specified in Schedule C and Schedule C (1) to the Drugs and Cosmetics Rules, 1945 from a motor vehicle*

1. ..... is hereby [2][licensed to sell, stock or exhibit or offer for sale by wholesale, or distribute] drugs other than those specified in Schedule C and Schedule C(1) from the vehicle bearing registration no._____ assigned under under Motor Vehicles Act, 1939, subject to the conditions specified below and to the

provisions of the Drugs and Cosmetics Act, 1940 and the Rules made thereunder.

2.The licence shall be inforce from_____ to 3.

Categories of drugs .....

Date:…….. *Licence No……..*

Licensing Authority.

Conditions of Licence

1. This licence shall be displayed in a prominent place on the vehicle.

2. The licensee shall comply with the provisions of the Drugs and Cosmetics Act, 1940 and the Rules made thereunder for the time being in force.

3 (i) No drugs shall be sold by wholesale or distributed unless such drug is purchased under a cash or credit memo from a duly licensed dealer or a duly licensed manufacturer.

(ii) No sale by wholesale or distribution of any drug shall be made to a person not holding the requisite [2][licensed to sell, stock or exhibit or offer for sale by wholesale, or distribute] the drug:

Provided that this condition shall not apply to the sale of any drug to—

(a) an officer or authority purchasing on behalf of the Government, or

(b) a hospital, medical, educational or research institution or a registered medical practitioner for the purpose of supply to his patients, or

(c) a manufacturer of beverages, confectionery, biscuits and other non-medical products, where such drugs are required for processing these products.

4. The licensee shall inform the Licensing Authority in writing in the event of change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.

5. The licensee shall inform the Licensing Authority in writing in the event of any change in ownership of the vehicle specified in this licence within seven days of such change.

_

1. Added by Notfn. No. X. 11013/7/76-D&MS (G.S.R. 42(E)), dt. 25.1.1979.

2. Subs. by G.S.R .788(E), dt.10.10.1985

[1] **[FORM 20-C**

(*See* rule 67-C)

[2][*Licence to sell, stock or exhibit or offer for sale, or distribute*] *Homoeopathic medicines by retail*

1. ……is hereby [2][l i c e n s e d to sell, stock or exhibit or offer for sale by wholesale, or distribute]by retail Homoeopathic medicines on the premises situated at .....subject to the conditions specified below and to the provisions of the Drugs and Cosmetics Act, 1940 and the Rules made thereunder.

2. The licence shall be in force from..... to .....

3. Name of the competent person in-charge.

Date..... *Licensing Authority*

Conditions of Licence

1. The licence shall be displayed in a prominent place in a part of the premises open to the public.

2. The licensee shall comply with the provisions applicable to homoeopathic

medicines under the Drugs and Cosmetics Act, 1940 and the Rules made thereunder for the time being in force.

3. The licensee shall report to the Licensing Authority any change in the competent staff within one month of such change.

[3][4. This licence authorises the sale of Homoeopathic medicines made from one earlier potency up to a quantity of 30 ml at a time.]

[4][5. Where any change in the constitution of the firm takes place, a licensee shall inform the Licensing Authority in writing about the same and the current licence shall be valid only for a period of three months from the date on which the change takes place unless, in the meantime, name of the firm with the changed constitution.]

1. Added by Notfn. No. F. 1-35/64-D (G.S.R. 1185), dt. 18.8.1964.
2. Subs. by.G.S.R. 788(E), dt. 10.10.1985.
3. Added by.Notfn. No. F. 1-59/68-D (S.O. 4816), dt. 19.11.1969.
4. Added. G.S.R. 665, dt. 28-5-1977.

[1][FORM 20D

(*See* rule 67C)

[2][Licence to sell, stock or exhibit or offer for sale, or distribute] Homoeopathic medicines by wholesale

1. ..... is hereby [2][licensed to sell, stock or exhibit or offer for sale, or distribute] by wholesale Homoeopathic medicines on the premises situated at.....subject to the conditions specified below and to the provisions of the Drugs and Cosmetics Act,. 1940 and the Rules made thereunder.

2. The licence shall be in force from.....to……..

Date..... *Licensing Authority.*

Conditions of Licence

1. This licence shall be displayed in a prominent place on the premises.
2. The licensee shall comply with the provisions as applicable to Homoeopathic medicines under the Drugs and Cosmetics Act, 1940 and the Rules made thereunder for the time being in force.
3. No sale of any drug shall be made to a person not holding the requisite [2][l i c e n s e d to sell, stock or exhibit or offer for sale, or distribute] the drug. Provided that this conditions hall not apply to the sale of any drug to (a) an authority purchasing on behalf of Government, or (b) a hospital, medical, educational or research institute or a Homoeopathic medical practitioner for the purpose of supply to his patients.

[3][4 The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence and the current licence shall be valid only for a period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.]

1. Added by Notfn. No. F.1-35/64-D, dt. 18.8.1964.
2. Subs. by.G.S.R. 788(E), dt. 10.10.1985.
3. Added by G.S.R. 665, date 28.5.1977.

Drugs and Cosmetics Rules 1945

[1] [FORM 20E

(*See* rule 67 EE)

Certificate of renewal of [2][Licence to sell, stock or exhibit or offer for sale, or distribute] Homoeopathic medicines

1. Number of licence and date of issue .....……

Certified that licence no ..... in Form 20C / 20D granted on the ..... to.....

for sale of Homoeopathic medicines at the premises situated at .....has been renewed

for a period from..... to .....

2. Name of competent persons in-charge.

Date..... *Licensing Authority.*

1. Added by Notfn. No. F. 1-14/67-D, dt. 3.2.1969.
2. Subs. by G.S.R. 788 (E), dt. 10.10.1985

[1][FORM 20F

[*See* rule 61(3)]

Licence to sell, stock or exhibit for sale or distribute by retail drugs specified in Schedule X

1. ……..is hereby licensed to sell, stock or exhibit for sale or distribute by retail drugs specified in Schedule X to the Drugs and Cosmetics Rules, 1945 on the premises situated at……..

2. Names of drugs.

3. This licence shall be in force from..... …….to.....……

4. Name(s) of registered pharmacist in-charge.

5. The licence is subject to the conditions stated below and the provisions of the Drugs and Cosmetics Act, 1940 and the Rules made thereunder.

Date:.....

Licence No……..

Licensing Authority……..

Conditions of Licence

1. This licence shall be displayed in a prominent place in a part of the premises open to the public.

2. The licensee shall report to the licensing authority any change in the qualified staff in charge within one month of such change.

3. No drug shall be stocked or sold unless such drug has been purchased under cash/credit memo from a duly licensed dealer or a duly licensed manufacturer.

4. The licensee shall inform the licensing authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless in the meantime, a fresh licence has been taken from the licensing authority in the name of the firm with the changed constitution.

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1. Ins. by G.S. R. 462(E) , dt. 22.6.1982 corrected vide corrigendum G.S.R. 373(E) , dt. 2.5.1983.

Drugs and Cosmetics Rules 1945

[1] [FORM 20G

[*See* rule 61(3)]

[2][*Licence to sell, stock or exhibit or offer for sale, or distribute*] *by wholesale drugs specified in Schedule X*

1. ……is hereby [2][licensed to sell, stock or exhibit or offer for sale, or distribute] by wholesale drugs specified in Schedule X to the Drugs and Cosmetics Rules, 1945 on the premises situated at……..

2. Names of drugs……

3. This licence shall be in force from..... to .....

4. The licence is subject to the conditions stated below and the provisions of the Drugs and Cosmetics Act, 1940 and the Rules made thereunder.

Date:.....

Licence No……..

Licensing Authority……..

Conditions of license

1. This licence shall be displayed in a prominent place in a part of the premises open to the public.

2. The licensee shall comply with the provisions of the Drugs and Cosmetics Act, 1940 and the rules made thereunder.

3. No drug shall be stocked or sold unless such drug has been purchased under a cash or credit memo from a duly licensed dealer or a duly licensed manufacturer.

4. The licensee shall forward to the licensing authority copies of the invoices of sales made to the retail dealers.

5. No sale of any drug by wholesale shall be made to a person not possessing the requisite [2] [licence to sell, stock or exhibit or offer for sale, or distribute] drugs specified in Schedule X :

Provided that this condition shall not apply to the sale of any drug to -

(a) an officer or authority purchasing on behalf of Government;

(b) a hospital, medical, educational or research institution, nursing home, Registered Medical Practitioner for the purpose of supply to its/his patients or manufacturer holding a licence in

Form 25-E or 28-B to manufacture the drugs containing drugs included in Schedule X.

[3] [The licensee shall inform the licensing authority in writing in the event of any change in the constitution of the firm operating under the licence, where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless in the meantime, a fresh licence has been taken from the licensing authority in the name of the firm with the changed constitution.]]

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1. Ins. by. G..S. R. 462(E) , dt. 22.6.1982.
2. Ins. by. G.S..R. 788(E) , dt. 10.10.1985.
3. Ins. by 370(E), dt. 7.4.1994.

FORM 21

[*See* rule 61 (2)]

[1][*Licence to sell, stock or exhibit or offer for sale,or distribute*] *by retail drugs specified in Schedules C and C (1)* [2][*excluding those specified in Schedule X*]

[3][1..... is hereby [1][licensed to sell, stock or exhibit or offer for sale, or distribute] by retail the following categories of drugs specified in Schedules C and C (1) [2][excluding those specified in Schedule X] to the Drugs and Cosmetics Rules, 19454 and to operate a pharmacy on the premises situated at ..... subject to the conditions specified below and to the provisions of the Drugs and Cosmetics Act, 1940 and the Rules thereunder.]

2. The licence shall be in force from .....to .....

3. Name(s) of registered pharmacists in charge .....

[3][4. Categories of drugs .....]

Date.....

Licence No .....

**Delete if not applicable.*

Conditions of License

1. This licence shall be displayed in a prominent place in a part of the premises open to the public.

2. The licensee shall report to the Licensing Authority any change in the qualified staff in charge within one month of such change.

[4] [***]

4. If the licensee wants to sell, stock or exhibit for sale, or distribute, during the currency of the licence, additional categories of drugs listed in Schedules C and C(I) [2][excluding those specified in Schedule X] but not included in this licence, he should apply to the Licensing Authority for the necessary permission. This licence will be deemed to extend to the categories of drugs in respect of which such permission is given. This permission shall be endorsed on the licence by the Licensing Authority.

[5] [5. No drug shall be sold unless such drug is purchased under a cash or credit memo from a duly licensed dealer or a duly licensed manufacturer.]

6. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place, unless in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.

_____ 1.

Subs. by G.S.R.788(E), dt. 10.10.1985.

2. Subs. by G.S.R. 462(E), dt. 22.6.1982

3. Amended by. S.O. 2139 ,dt. 12-8-1972.

4. Omitted by. G.S.R. 17(E) , dt. 7.1.1986.

5. Inerted. by Notfn. No. F. 1-63/61, dt. 17.7.1963

FORM 21A

[*See* rule 61 (2)]

[1][*Licence to sell, stock or exhibit or offer for sale, or distribute] by retail drugs specified in [2][Schedule C (1)] [3][excluding those specified in Schedule X] [4][***] for dealers who do not engage the services of a registered pharmacist*

1. ……is hereby [1][licensed to sell, stock or exhibit or offer for sale, or distribute] by retail on the premises situated at [4][***] the following drugs being drugs specified in [2][Schedule C (1)] [3][excluding those specified in Schedule X] to the Drugs and Cosmetics Rules, 1945, subject to the conditions specified below and to the provisions of the Drugs and Cosmetics Act, 1940 and the Rules thereunder.

2. The licence will be in force from…….. .

3. Particulars of [2][Schedule C (1)] [3][excluding those specified in Schedule X] drugs to be sold.

[5] [***]

Name of dealer(s)…… Date.....

Conditions of Licence.

1.This licence shall be displayed in a prominent and conspicuous place in a part of the premises open to the public [6][***]

[7][***]

3. The licensee shall deal only in such drugs as can be sold without the supervision of a "qualified person" as defined in the Explanation to sub-rule (15) of rule 65 of the Drugs and Cosmetics Rules, 1945.

4. No drug shall be sold unless such drug is purchased under cash or credit memo from duly licensed manufacturer.

5. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.

1 Subs. by G.S.R.788(E), dt. 10.10.1985.

2 Ins. By S.O. 1458, dt:27.4.1965.

3. Ins. by G.S.R. 462(E), dt. 22.6.1982.

4. Amended. by G.S.R 487(E), dt. 2.7.1984.

5. Item 4 omitted G.S.R. 504(E), dt. 18.7.2002

6. Certain words omitted by G.S.R. 231 (E), dt. 4.6.1996

7. Condition No. 2 omitted by G.S.R. 17 (E), dt:7.1.1986.

FORM 21B

[*See* rule 61(2)]

[1][*Licence to sell, stock or exhibit or offer for sale, or distribute] by wholesale drugs specified in Schedules C and C (1) [2][excluding those specified in Schedule X*

1. ……is hereby [1][licensed to sell, stock or exhibit or offer for sale, or distribute] by wholesale on the premises situated at the following categories of drugs specified in Schedule. C and C (1) [2] [excluding those specified in Schedule X] to the Drugs and Cosmetics Rules, 1945.

Categories of drugs

2. This licence shall be in force from..... to…….

[3][2A. The sale shall be made under the personal supervision of a competent person. (Name of the competent person)].

3. This licence is subject to the conditions stated below and to the provisions of the Drugs and Cosmetics Act, 1940 and the rules thereunder.

Licence No ……..

Date..... *Licensing Authority.*

Conditions of Licence

1. This licence shall be displayed in a prominent place in a part of the premises open to the public.

[4][2.***]

3. If the licensee wants to sell, stock or exhibit for sale or distribute during the currency of the licence additional categories of drugs listed in Schedules C and C (1) [2][excluding those specified in Schedule X] but not included in this licence, he should apply to the Licensing Authority for the necessary permission. This licence will be deemed to extend to the categories of drugs in respect of which such permission is given. This permission shall be endorsed on the licence by the Licensing Authority.

[5] [4. (i) No drug shall be sold unless such drug is purchased under a cash or credit memo from a duly licensed dealer or a duly licensed manufacturer.

(ii) No sale of any drug shall be made for purposes of resale to a person not holding the requisite licence to sell, stock or exhibit for sale or distribute the drug:

Provided that this condition shall not apply to the sale of any drug to —

(a) an officer or authority purchasing on behalf of Government, or

(b) a hospital, medical, educational or research institute or a registered medical practitioner for the purpose of supply to his patients, or

[6][(c) a manufacturer of hydrogenated vegetable oils, beverages, confectionary and other non-medicinal products, where such drugs are required for processing these products.] [7][5.***]

[8][6. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from Licensing Authority in the name of the firm with the changed constitution.

_____ 1.

Subs. by. G.S.R.788(E), dt. 10.10.1985.

2. Subs. by.G.S.R.462(E), dt. 22.6.1982

3. Ins. by.G.S.R. 681(E), dt. 6.6.1988.

4. Condition no. 2 omitted by.G.S.R. 17(E), dt. 7.1.1986

5 Added by. Notfn. No. F. 1-63/61 -D, dt. 17.7.1963.

6.Added by Notfn. No. F. 1-113/69-D, dt. 23.12.1969.

7. Condition 5 omitted by S.O. 289, dt 20.12.1973 (w.e.f. 3.2.1973) 8. Ins. By S.O. 1458, dt:27.4.1965.

Drugs and Cosmetics Rules 1945

[1][FORM 21BB

[*See* Rule 62D]

Licence to sell by wholesale or to distribute drugs specified in Schedule C and Schedule C (1) to the Drugs and Cosmetics Rules, 1945 from a motor vehicle.

1. ..... is hereby licensed to sell by wholesale, or to distribute drugs specified in Schedule C and Schedule C(1) from the vehicle bearing registration no. ..... assigned under Motor Vehicles Act, 1939, subject to the conditions specified below and to the provisions of the Drugs and Cosmetics Act, 1940 and the Rules made thereunder.

2. The licence shall be in force from..... to .....

3. Categories of drugs .....

Date ..... *Licence No……*

Licensing Authority……..

Conditions of licence

1. This licence shall be displayed in a prominent place on the vehicle.
2. No drugs to which this licence applies shall be sold by wholesale or distributed unless the precautions as are published by the Licensing Authority from time to time in the Official Gazette have been observed throughout the period during which it has been in the possession of the licensee.
3. If the licensee wants to sell by wholesale or distribute during the currency of the licence, additional categories of drugs listed in Schedules C and C (1) not included in this licence, he shall apply to the Licensing Authority for necessary permission. This licence shall be deemed to extend to the categories of drugs in respect of which such permission is given. This shall be endorsed on the licence by the Licensing Authority.
4. (i) No drugs shall be sold by wholesale or distributed unless such drug is purchased under a cash or credit memo from a duly licensed manufacturer.

(ii) No sale for wholesale or distribution of any drug shall be made for the purpose of resale to a person, not holding the requisite licence to sell, stock or exhibit for sale or distribute the drug:

Provided that this condition shall not apply to the sale of any drug to—

(a) an officer or authority purchasing on behalf of the Government, or

(b) a hospital, medical, educational or research institution or a registered medical practitioner for the purpose of supply to his patients, or

(c) a manufactures of hydrogenated vegetable oils, beverages, confectionery and other non-medical products, where such drugs are required for processing their products.

5. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.
6. The licensee shall inform the Licensing Authority in writing in the event of any change in the ownership of the vehicle specified in this licence within seven days of such change.]

1. Added by Notfn. No. 11013/7/76DSMS (G.S.R. 42(E), dt. 25.1.1979.

FORM 21C

(*See* rule 63A)

Certificate of renewal of [1]***[licence to sell, stock or exhibit or offer for sale, or distribute] drugs***

Number of licence and date of issue……

1. Certified that licence No ..... in [2][Form 20, 20A, 20B, 20F, 20G, 21, 21A or 21B], granted on the.....to ..... for sale of the following drugs at the premises situated at..... has been renewed for a period from .....to ..... 2. Categories or particulars of drugs .....

3. Name (s) of registered pharmacist(s) in-charge.....

Date..... *Licensing Authority.*

1. Subs. by G.S.R. 788(E),dt. 10.10.1985.
2. Subs. by .S.R. 462(E),dt. 22.6.1982.

[1]**[FORM 21CC**

(*See* rule 63B)

Certificate of renewal of [2]***[licence to sell, stock or exhibit or offer for sale by wholesale, or distribute] drugs from a motor vehicle***

Number of licence and date of issue……..

1. Certified that licence no……in Form 20-BB or Form 21-BB granted on the…….to……..for sale by wholesale or distribution of the following drugs from the vehicle bearing registration No……. assigned under the Motor Vehicles Act, 1939 has been renewed for a period from……..to ……

2. Categories of the drugs:

…….

…….

Date…….. *Licensing Authority.*

1. Subs. by G.S.R. 788(E), dt.10.10.1985.

2. Added by Notfn. No. 11013/7/76DSMS (G.S.R. 42(E), dt. 25.1.1979.

FORM 22

(*See* rule 67)

(Omitted by S.O. 289, dt. 20.12.1972)

FORM 23

(*See* rule 67)

(Omitted by S.O. 289, dt. 20.12.1972)

FORM 24

(*See* rule 69)

Application for the grant of or renewal of a [1][*licence to manufacture for sale or for distribution] of drugs other than those specified in* [2][*Schedules C and C (1) and X*]

Drugs and Cosmetics Rules 1945

1 . I / We .....of. ..... hereby apply for the grant / renewal of a licence to manufacture on the premises situated at ..... the following drugs being drugs other than those specified in [2][Schedules C and C (1) and X] of the Drugs and Cosmetics Rules, 1945.

2. Names of drugs categorized according to Schedule M.

3. Names, qualifications and experience of technical staff employed for manufacture and testing.

4. A fee of rupees ..... has been credited to Government under the head of account .....

Date..... *Signature* .....

Note: The application should be accompanied by a plan of the premises.

1.

1. Subs. by. G.S.R. 788(E), dt. 10.10.1985.
2. Subs. by G.S.R. 462(E), dt. 22.6.1982.

FORM 24A

(*See* rule 69A)

Application for grant or renewal of a loan [1]***[licence to manufacture for sale or for distribution] of drugs other than those specified in*** [2]***[Schedules C and C (I) and X]***

1 . I /We*.....of# .....hereby apply for the grant/renewal of a loan licence to manufacture on the premises situated at..... C/o§ ..... the under- mentioned drugs, other than those specified in [2] [Schedules C and C(1) and X] to the Drugs and Cosmetics Rules, 1945.

Names of drugs (each substance to be separately specified).

2. The names, qualifications and experience of the expert staff actually connected with the manufacture and testing of the specified products in manufacturing premises.

3. I/We enclose–

(a) A true copy of a letter from me/us to the manufacturing concern whose manufacturing capacity is intended to be utilized by me/us.

(b) A true copy of a letter from the manufacturing concern that they agree to lend the services of their expert staff, equipment and premises for the manufacture of each item required by me/us and that they will analyse every batch of finished product and maintain the registers of raw materials, finished products and reports of analysis separately in this behalf.

(c) Specimens of labels, cartons of the products proposed to be manufactured.

4. A fee of rupees.....has been credited to Government under the head of account .....

Date..... *Signature* .....

* *Enter here the name of the proprietor, partners of Managing Director as the case may be.*

#*Enter here the name of the applicant firm and the address of the principal place of business.*§ *Enter here the name and address of the manufacturing concern where the manufacture will be actually carried out and also the Licence number under which the latter operates.*

1. Subs. by G.S.R. 788(E), dt. 10.10.1985.

2. Subs. by G.S.R. 462(E), dt. 22.6.1982.

Drugs and Cosmetics Rules 1945

[1][FORM 24B

(*See* rule 69A)

Application for grant or renewal of licence to repack for sale or distribution of drugs, being drugs other than those specified in Schedules C and C (1) [2]***[excluding those specified in Schedule X]***

1.1 / We ……of…….hereby apply for grant/renewal of a licence to repack the following drugs at the premises situated at……...

2. Names of the drugs to be repacked..... ….

3. Name, qualification and experience of competent staff .....

4. A fee of rupees …… …… has been credited to Government under the head of account ..... ……

Date..... *Signature of applicant.*

NOTE :—The application shall be accompanied by a plan of the premises.

1. Ins. By S.O. 1196, dt:6.5.1960.

2. Subs. by G.S.R. 462(E), dt. 22.6.1982.

[1] [FORM 24C

(*See* rule 85B)

Application for the grant or renewal of a [2][licence to manufacture for sale or for distribution of] Homoeopathic medicines or a licence to manufacture potentised preparations from back potencies by licensees holding licence in

Form 20C

[3][1 . I / W e * ..... of ..... holder of licence no ..... in Form 20-C hereby apply for the grant/renewal of licence to manufacture the undermentioned Homoeopathic mother tinctures/potentised preparations on the premises situated at…… …….

Name of the Homoeopathic preparations ..... …… …. (*Ea c h i t e m t o b e separately specified*)].

2. Names, qualifications and experience of technical staff employed for manufacture and testing of Homoeopathic medicines.

3. A fee of rupees ..... has been credited to Government under head of account .....

Date..... *Signature*.....

Note 1. Delete whichever portion is not applicable.

2. The application should be accompanied by a plan of the premises.

_____ 1. Amended by Notfn. No. F. 1-598-D, dt. 19.11.1969
2. Subs. by. G.S.R.788(E) dt. 10.10.1985.
3. Subs. by. G.S.R. 13(E) dt. 7.1.1983.

[1] **[FORM 24D**

(*See* rule 153)

Application for the grant / renewal of a licence to manufacture for sale of Ayurvedic/ Siddha or Unani drugs

1 . I / W e .....of.....hereby apply for the grant / renewal of a licence to manufacture Ayurvedic (including Siddha) or Unani drugs on the premises situated at..... …….

2. Names of drugs to be manufactured (with details)

3. Names, qualifications and experience of technical staff employed for manufacture and testing of Ayurvedic (including Siddha) or Unani drugs .....

4. A fee of rupees ..... has been credited to the Government under the head of account ..... and the relevant Treasury Challan is enclosed herewith.

Date..... *Signature* .....

(applicant)

Note—The application should be accompanied by a Plan of the premises.]

1. Added by Notfn. No. 1-23/67-D,dt. 2.2.1970.

[1]**[FORM 24E**

(*See* rule 154A)

Application for grant or renewal of a loan licence to manufacture for sale Ayurvedic (including Siddha) or Unani Drugs

1. I / We* .....of**..... hereby apply for the grant / renewal of a loan licence to manufacture Ayurvedic (including Siddha) or Unani Drugs on the premises situated at.....…….. C/o*** .....……

2. Names of drugs to be manufactured (with details).

3. The names, qualifications and experience of technical staff actually connected with the manufacture and testing of Ayurvedic (including Siddha) or Unani drugs in the manufacturing premises.

4. I / We* enclose,

(a) A true copy of a letter from me/us to the manufacturing concern whose manufacturing capacity is intended to be utilized by me / us.

(b) A true copy of a letter from the manufacturing concern that they agree to lend the services of their competent technical staff, equipment and premises for the manufacture of each item required by me/us and that they shall maintain the registers of raw materials and finished products separately in this behalf.

(c) Specimen of labels, cartons of the drugs proposed to be manufactured.

5. A fee of Rs ..... has been credited to Government under the head of account ..... and the relevant Treasury Challan is enclosed herewith.

Date ..... *Signature* .....

……] *(applicant)*

* *Enter here the name of the proprietor, partners or Managing Director as the case may be.*

***Enter here the name of the applicant firm and the address of the principal place of business.*

*** *Enter here the name and address of the manufacturing concern where the manufacture will be actually carried out and also the licence number under which the letter operates.*

_____ 1. Added by G.S.R. 376 (E), dt. 20.7.1978.

[1] **[FORM 24F**

(*See* rule 69)

Application for the grant or renewal of a [2][licence to manufacture for sale or for distribution of] drugs specified in Schedule X and not specified in Schedules C and C(1)

1. I/We ..... of .....hereby apply for the grant/renewal of licence to manufacture on premises situated at ..... the undermentioned drugs, specified in Schedule X to the Drugs and Cosmetics Rules, 1945.

2. Names of drugs.

3. Names, qualifications and experience of technical staff employed for manufacture and testing.

4. A fee of rupees..... has been credited to Government account under the head of account.....

Signature ..... …….

Date:..... *Designation* ..... …….*]*

1. Subs. by .G.S.R. 462(E) ,dt. 22.6.1982.
2. Subs. by G.S.R. 788(E) dt. 10.10.1985.

FORM 25

(*See* rule 70)

[1][Licence to manufacture for sale or for distribution of] drugs other than those specified in [2][Schedules C and C(1) and X]

Number of Licence and date of issue .....

1 ..... is hereby licensed to manufacture the following categories of drugs being drugs other than those specified in [2][Schedules C and C (1) and X] to the Drugs and Cosmetics Rules, 1945, on the premises situated at..... under the direction and supervision of the following [3][competent technical staff]:

(a) [3][Competent technical staff]. (Names)……

(b) Names of Drugs (each item to be separately specified).....….

2. The licence authorises the sale by way of wholesale dealing and storage for sale by the licensee of the drugs manufactured under the licence, subject to the conditions applicable to licence for sale.

3. The licence shall be in force from..... to .....

4. The licence is subject to the conditions stated below and to such other conditions as may be specified in the Rules for the time being in force under the Drugs and Cosmetics Act, 1940.

Date .....

Signature .....

Designation.....

[4][*Licensing Authority/
*Central Licence Appoving Authority.]

**Delete whichever is not applicable.*

Conditions of Licence

1. This licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.

2. Any change in the expert staff named in the licence shall be forthwith reported to the Licensing Authority.

3. If the licensee wants to manufacture for sale additional items of drugs not included above he should apply to the Licensing Authority for the necessary endorsement as provided in Rule 69(5). This licence will be deemed to extend to the categories so endorsed.

4. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.

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1. Subs. by. G.S.R. 788(E) ,dt. 10.10.1985
2. Subs. by G.S.R. 462(E), dt. 22.6.1982.
3. Subs. by G.S.R. 231(E), dt. 4.6..1996.
4 Subs. by G.S.R. 923(E), dt. 14.12.1992.

FORM 25A

(*See* rule 70A)

***Loan* [1][*licence to manufacture for sale or for distribution of*] *drugs other than those specified In* [2][*Schedules C and C (1) and X*]**

1. Number of licence and date of issue .....

2..... of ..... is hereby granted a loan licence to manufacture the following drugs other than those specified in [2][Schedules C and C(1) and X] to the Drugs and Cosmetics Rules, 1945, on the premises situated at C/o under the direction and supervision of the following [3][competent technical staff]:

(a) [3][competent technical staff] (Names):…….

(c) Names of drugs .....

3. The licence authorises the sale by way of wholesale dealing and storage for sale by the licensee of the drugs manufactured under the licence subject to the conditions applicable to licences for sale.

4. The licence is subject to the conditions stated below and to such other conditions as may be specified in the Rules for the time being in force under the Drugs and Cosmetics Act, 1940.

Date..... *Signature* ……..

Designation .. ..

Conditions of Licence

1. This licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.

2. Any change in the [3][competent technical staff] named in the licence shall be forthwith reported to the Licensing Authority.

3. If the licensee wants to undertake during the currency of the licence the manufacture for of sale additional drugs he should apply to the Licensing Authority for the necessary endorsement to the licence as provided in Rule 69-A. This licence will be deemed to extend to the drugs so endorsed.

4. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.

1. Subs. by G.S.R. 788(E) , dt.10.10.1985.
2. Subs. by G.S.R. 462(E), dt. 22.6.1982.
3. Subs. by. G.S.R. 231(E) ,dt. 4.6.1996.

[1][FORM 25B

(*See* rule 70)

Licence to repack for sale or distribution of drugs being drugs other than those specified in Schedules C and C (1) [2][excluding those specified in Schedule X]

Number of licence and date of issue.

1. …….. ..... of .....is hereby granted a licence to repack the following drugs for sale or distribution on the premises situated at..... under the supervision of the following competent staff.

(a) Names of drugs to be repacked.

(b) Names of competent staff.

2. The licence shall be in force from..... to .....

3. The licence authorises the sale by way of wholesale dealing by the licensee and storage for sale by the licensee of the drugs repacked under the licence subject to conditions applicable to licences for sale.

4. The licence is subject to the conditions stated below and to such other conditions as may be specified in the Rules for the time being in force under the Drugs and Cosmetics Act, 1940.

Date..... *Signature*... ……..

Conditions of Licence

1. This licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.

2. Any change in the expert staff named in the licence shall be forthwith reported to the Licensing Authority.

3. If the licensee wants to repack for sale or distribution additional items he should apply to the Licensing Authority for the necessary endorsement to this licence. This licence will be deemed to extend to only those items so endorsed.

4. The drugs repacked under this licence shall bear on their label, apart from other particulars required by these Rules, the name and address of the licensee and the number of the licence under which the drug is repacked preceded by the words "Rpg. Lic. No.".

5. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.

1. Added by Notfn. No. F. 1-22/59-D, dt. 9-4-1960.

2. Subs. by G.S.R. 462(E), dt. 22.6.1992.

[1][FORM 25C

(*See* rule 85D)

[2][*Licence to manufacture for sale or for distribution of*] *Homoeopathic medicines*

Number of Licence and date of issue .....

[3] [*1. ……. of..... who holds a licence in Form 20-C is hereby licensed to manufacture undermentioned Homoeopathic Mother Tinctures/ potentised and other preparations on the premises situated at .... under the direction and supervision of the following technical staff:

Names of the Homoeopathic
preparations.
(*Each item to be separately specified*).

Names of the Technical Staff.....]

2. The licence shall be in force from ..... to .....

3. The licence is subject to the conditions stated below and to such other conditions as may be specified in the Rules for the time being in force under the Drugs and Cosmetics Act, 1940.

Date..... *Signature……*

Designation….

Conditions of Licence

1. This licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.
2. Any change in the expert staff named in the licence shall be forthwith reported to the Licensing Authority.

[4][3. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.]

**Delete* the words ―who holds a licence in

Form 20C‖ in case this is not applicable.

1. Added by Notfn No. F.1-36/64-D, dt:18.8.1964

2. Subs. by.. G.S.R.788(E) , dt. 10.10.1985.

3. Subs. by. G.S.R. 13(E) , dt. 7.1.1983.

4. Added by S.O. 903, dt. 28.2.1976.

1[FORM 25D

(*See* rule 154)

Licence to manufacture for sale of Ayurvedic (including Siddha) or Unani drugs

No. of Licence……

1. …. ..... is / are hereby licensed to manufacture the following Ayurvedic (including Siddha) or Unani drugs on the premises situated at..... under the direction and supervision of the following technical staff: —

(a) Technical staff (Names).

(b) Names of drugs (each item to be separately specified).

2. The licence shall be in force from ..... to .....

3. The licence is subject to the conditions stated below and to such other conditions as may be specified in the Rules for the time being in force under the Drugs and Cosmetics Act, 1940.

Date of issue: …….. *Signature .....*

Designation .....

Conditions of Licence

1. This licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.

2. Any change in the Technical staff named in the licence shall be forthwith reported to the Licensing Authority.

3. This licence shall be deemed to extend to such additional items as the licensee may intimate to the Licensing Authority from time to time, and as may be endorsed by the Licensing Authority.

4. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be

deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.]

1. Added by Notfn. No. 1-23/67 –D (S.O. 642), dt. 2-2-1970.

1 [FORM 25E

(*See* rule 154A)

Loan Licence to manufacture for sale Ayurvedic (including Siddha) or Unani Drugs

1. Number of Licence…….

2 .....of..... is hereby granted a loan licence to manufacture for sale Ayurvedic (including Siddha) or Unani drugs, on the premises situated at ..... C/o.....under the direction and supervision of the following expert technical staff:

(a) Technical staff (Names)…….

(b) Names of drugs (each item to be separately specified)

3. The licence shall be in force from ..... to……

4. The licence is subject to the conditions stated below and to such other conditions as may be specified in the Rules for the time being in force under the Drugs and Cosmetics Act, 1940.

Date of Issue.....

Signature .....

Designation .....

Conditions of Licence

1. This licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced on the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.

2. Any change in the technical staff named in the licence shall be forthwith reported to the Licensing Authority.

3. This licence shall be deemed to extend to such additional items as the licensee may intimate to the Licensing Authority from time to time, and as may be endorsed by the Licensing Authority.

4. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.

---

1. Added by G.S.R. 376 (E), dt. 20.7.1978

[1] **[FORM 25F**

(*See* rule 70)

[2][*Licence to manufacture for sale or for distribution of*] *drugs specified in Schedule X and not specified in Schedules C and C(I)*

1. .....of .....is hereby licensed to manufacture at the premises situated at……the following drugs specified in Schedule X to the Drugs and Cosmetics Rules, 1945.

Drugs and Cosmetics Rules 1945

2. Names of drugs.

3. Names of approved [3][competent technical staff]

4. The licence authorises the sale by way of wholesale dealing and storage for sale by the licensee of the drugs manufactured under the licence subject to the conditions applicable to licence for sale.

5. The licence shall be in force ..... to.....

6. The licence is subject to conditions stated below and to other conditions as may be specified in the rules for the time being in force under the Drugs and Cosmetics Act, 1940.

Date of issue..... *Signature* .....

Licence No ..... *Designation* .....

[4][*Licensing Authority/Central Licence Approving Authority.]

**Delete* whichever portion is not required.

Conditions of Licence

1. The licence and any certificate of renewal in force shall be kept on the licensed premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.

2. If the licensee wishes to undertake during the currency of the licence the manufacture of any drug specified in Schedule X not included above, he should apply to the Licensing Authority for the necessary endorsement of this licence. This licence shall be deemed to extend to only those items so endorsed.

3. Any change in the [3][competent technical staff] shall be forthwith reported to the Licensing Authority.

4. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.

5. The licensee shall furnish to the Licensing Authority copies of the invoices of sales made to dealers.

6. The licensee shall not manufacture drugs covered by this licence for use as 'Physician's Samples'.]

_____ 1. Subs. by G.S.R. 462(E) dt. 22.6.1982.
2. Subs. by G.S.R.788(E) dt. 10.10.1985.
3. Subs. by G.S.R.231(E) dt. 4.6.1996.
4. Subs. by G.S.R. 923(E) dt. 14.2.1992.

[1] [FORM 26

(*See* rules 73 and 83)

Certificate of renewal of licence to manufacture for sale of drugs other than those specified in Schedule X

1. Certified that licence No ..... granted on the..... to ..... for the manufacture of the following categories of drugs being *drugs other than those specified in Schedules C, C (1) and X/*drugs specified by Schedules C and C (1) excluding those specified in Schedule X to the Drugs and Cosmetics Rules, 1945, at the premises situated at ..... has been renewed from..... to.....

2. Name(s) of approved [2][competent technical staff] .....

Drugs and Cosmetics Rules 1945

[3][3 Names of the drugs (each item to be separately specified) .....

Signature .....

Date..... *Designation* .....

[4][Licensing Authority/ *Central Licence Approving Authority.] **Delete* whichever portion is not required.]

1. Subs. by G.S.R. 462(E) dt. 22.6.1982.
2. Subs. by G.S.R.231(E) dt. 4.6.1996
3. Ins. By G.S.R. 370(E) dt. 7.4.1994.
4. Subs. by G.S.R. 923(E), dt. 14.12.1992.

[1][FORM 26A

(*See* rules 73A and 83A)

Certificate of renewal of loan licence to manufacture for sale of drugs other than those specified in Schedule X

1. Certified that a loan licence No .....granted on the..... to..... for the manufacture of the *drugs other than those specified in Schedules C, C (1) and X the undermentioned drugs being drugs specified in Schedules C and C (1) excluding those specified in Schedule X, to the Drugs and Cosmetics Rules, 1945, at the premises situated at..... C/o .....has been renewed from ..... to.....

2. Names of the drugs (each substance to be separately specified).

3. Names of the approved [2][competent technical staff]

Date .....

Signature……..

Designation……

*] * Delete whichever is not applicable.*

1.Ins. by G.S.R. 462(E), dt. 22.6.1982.

2. Subs. by G.S.R.231(E) dt. 4.6.1996.

[1]**[FORM 26B**

(*See* rule 73B)

Certificate of renewal of licence to repack for sale or distribution of drugs being drugs other than those specified in Schedules C and C (1) [2]***[excluding those specified in Schedule X*]**

1. Certified that licence No ..... granted on the..... to.....for the repacking of the following drugs at the premises situated at .....has been renewed from ..... to.....Names of drugs to be repacked .....

2. Names of competent staff. .....

Date : .....

Signature……

Designation……

.

Drugs and Cosmetics Rules 1945

[3][*Licensing Authority.

*Central licence Approving Authority.]

* *Delete* whichever is not applicable.]

1 Added by Notfn. No. F.1-22/5 9-D, dt. 9.4.1964.

2 Subs. by G.S.R. 462(E) dt. 22.6.1982.

3. Ins. by G.S.R. 923(E) dt. 14.12.1992

FORM 26C

(*See* rule 85G)

Certificate of renewal of licence to manufacture for sale of Homoeopathic medicines

1. Certified that licence No ..... granted on the……. to…… for the manufacture for sale of the Homoeopathic mother tinctures/potentised preparation at the premises situated at ..... has been renewed for a period from the .....to ..... ……

2. Name of the technical staff ..... ……

[1][3. Names of the drugs (*each item to be separately specified*).....]

Date……..

Signature .....……..
Designation .. ……..

1. Ins. by G.S.R. 370(E) dt. 7.4.1994.

[1]**[FORM 26D**

(*See* rule 155)

Certificate of renewal of licence to manufacture for sale of Ayurvedic / Siddha or Unani drugs

1. Certified that licence No ..... granted on the……to Shri/ Messers ..... for the manufacture of Ayurvedic/Siddha/Unani drugs at the premises situated at…….has been renewed from……to .....

2. Names of technical staff .....

[2][3. Names of drugs (each item to be separately specified).]]

Date …….. *Signature……..*
Designation……..

1. Ins. by F. No.1 -23/67-D, dt. 2-2-1970.
2. Ins. by G.S.R 376 (E), dt. 20.7.1978

[1]**[FORM 26E**

(*See* rule 155A)

Certificate of renewal of loan licence to manufacture for sale of Ayurvedic / Siddha or Unani Drugs

1. Certified that loan Licence No .....granted on the……to……..…… for the man ufacture ofAyurvedic/ Siddha or Unani drugs at the premises situated at..... C/o ..... has been renewed from.....to ..... ……

Drugs and Cosmetics Rules 1945

2 Names of technical staff.

Date: ……Signature.....

Designation……..

1. Added by G.S.R. 376(E), dt. 20.7.1978.

[1]**[FORM 26E-I**

(*See* rule 157B)

Certificate of Good Manufacturing Practices (GMP) to manufacture of Ayurveda, Siddha or Unani drugs

Certified that manufacturing unit licensee, namely ..... situated at .....

State ..... Licence No ..... comply with the requirements of Good Manufacturing Practices of Ayurveda-Siddha-Unani drugs as laid down in Schedule T of the Drugs and Cosmetics Rules, 1945.

This certificate is valid for a [2][period of five years and the Good Manufactruing Practices (GMP) is valid for the various dosage forms or Rasaushadhis, as follows:]

Date :..... *Signature……..*

Place : .... *Designation……*

Licensing Authority for Ayurveda/ Siddha/ Unani Drugs.]

1.subs. by G.S.R.198(E), dt. 7.3.2003. Earlier Ins. by G.S.R. 561(E), dt. 23.6.2000.
2.Subs. by G.S.R. 376(E), dt. 3.5.2010

[1]**[FORM 26E2-I**

(*See* rule 158C)

State Drug Controller or Licensing Authority for Ayurveda, Siddha and Unani Medicines

Name of the State or Union territory……..

Free Sale Certificate

It is certified that M/s. …….(Name of the company)……..situated at ……. (Address) ..... is holding valid Ayurvedic/Siddha/Unani Drug Manufacturing License Number..... valid till ……and certificate of Good Manufacturing Practices for the State or Union territory of ……The manufacturer has applied for renewal of license on .....(to be mentioned, if application for renewal of license has not been rejected).

It is also certified that the manufacturing plant siuated at ……..(Address)……..in which the Ayurvedic or Unani or Sidhha products are manufactured, conforms to the requirement of Good Manufacturing Practices and is subjected to inspection as per rules.

The firm has been permitted under License Number……..to manufacture and market the following products (attach list of products, if multiple) freely for sale in India under the provisions of the Drugs and Cosemtics Atc, 1940 and the rules thereunder.

(i)……
(ii)……
(iii)……..

Date :..... *(Seal of issuing Officer)* … … … … … … … … …

Drugs and Cosmetics Rules 1945

(Signature and Name)

State Drug Controller/Licensing Authority

Address……

Name of State or Union territory……..]

1.Ins. by G.S.R. 153 (E), dt. 5.3.2014.

[1]**[FORM 26E2-II**

(*See* rule 158C)

State Drug Controller or Licensing Authority for Ayurveda, Siddha and Unani Medicines

Name of the State or Union territory……..

Free Sale Certificate

It is certified that M/s. …….(Name of the company)……..situated at ……. (Address) ..... is holding valid Ayurvedic/Siddha/Unani Drug Manufacturing Loan License Number..... valid till ……and the valid certificate of Good Manufacturing

Practices for the State or Union territory of ……The manufacturer has applied for renewal of loan license on .....(to be mentioned, if application for renewal of license has not been rejected).

It is also certified that the manufacturing plant siuated at ……..(Address)……..in which the Ayurvedic or Unani or Sidhha products are manufactured, conforms to the requirement of Good Manufacturing Practices and is subjected toinspection as per rules.

The firm has been permitted under Loan License Number……..to manufacture and market the following products (attach list of products, if multiple) freely for sale in India under the provisions of the Drugs and Cosemtics Atc, 1940 (23 of 1940) and the rules thereunder.

(i)……

(ii)……

(iii)……..

Date :..... *(Seal of issuing Officer) … … … … … … .*

(Signature and Name)

State Drug Controller/Licensing Authority

Address……

Name of State or Union territory……]

1.Ins. by G.S.R. 153 (E), dt. 5.3.2014.

[1][**FORM 26 E3**

(*See* rule 158C)

State Drug Controller or Licensing Authority for Ayurveda, Siddha and Unani Medicines

Name of the State or Union territory……..

Non-Conviction Certificate

It is certified that M/s. …….(Name of the company)……..situated at ……. (Registered Address) ..... is holding valid Ayurvedic/Siddha/Unani Drug Manufacturing License Number..... in Form 25D/25E valid till ……and certificate of Good

Manufacturing Practices/valid Good Manufacturing Practices certificate of principal or original manufacturer for the State or Union territory of ……The manufacturer has applied for renewal of license on .....(date to be mentioned, if application for renewal of license has not been rejected).

As per the records of the State Drug Controller or Licensing Authority, as it may be, and affidavit (Annexure I) given by the company, the firm has not been conicted under the Drugs and Cosmetics Act, 1940 (23 of 1940) and the rules thereunder in the State or Union territory of …….., during the last three years of the issuing of this certificate.

This certificate shall be valid only for six months from the date of issue.

Date :..... *(Seal of issuing Officer) … … … … … … … … … … … … … .*

(Signature and Name)
State Drug Controller/Licensing Authority for
Ayurveda, Siddha and Unani Medicines.
Address……
Name of State or Union territory……..]

[1][ANNEXURE-1

(Proforma of Affidavit to be submitted on stamp paper of Rs. 50 attested by Magistrate not below the rank of first class)

I, ……S/O…….age…….working as …….of……..(Name and address of the company)……from ……to……do hereby solemnly affirm and declare as under:

1.That I, in the capacity of Authorized Signnatory of ……(name and address of the company)….,am duly competent to depose and verify the present affidavit.

2.That I apply for Non-conviction Certificate on behalf of M/s. ……..

3.Thar I declare that I am aware of the details of my organization asnd day to day activities from….to….

4.That I hereby undertake that the Non-Conviction Certificate, if issued, will be utilized for the bona fide purpose only.

5.I declare that the aforesaid firm is not convicted under the Drugs and Cosmetics Act, 1940 and rules thereunder during the last three years.

6.That it is my true statement.

…….
Signatature of Deponent

Verification

Verified at…….(Palce and State)…….….today on this……..…..day of…..(month)….(Year)…..that the contents of the above affidavit are true to my knowledge and belief and no part of it is false and nothing has been concealed therefrom.

…….
Signature of Deponent]

Witness with Address
1.
2.

1.Ins. by G.S.R. 153 (E), dt. 5.3.2014.

Drugs and Cosmetics Rules 1945

[1]**[FORM 26F**

(*See* rules 73 and 83)

Certificate of renewal of licence to manufacture for sale of drugs specified in Schedule X

1. Certified that licence No ..... granted on the ..... to ..... for the manufacture of drugs specified in Schedule X to the Drugs and Cosmetics Rules, 1945, at the premises situated at…….. has been renewed from……. to……

2. Names of drugs (each substance to be separately specified).

3. Names of the approved [2][competent technical staff].

Date:……

Date of issue……

Signature……..

Designation……..

*[3][*Licensing Authority/Central Licence Approving Authority]*

**Delete whichever is not applicable.*

1. Ins. by. G.S.R. 462(E) ,dt. 22.6.1982.
2. Subs. by G.S.R. 231(E), dt. 4.6.1996.
3. Subs. by G.S.R. 923(E), dt. 14.12.1992.

[1]**[FORM 26G**

(*See* rules 122F)

Certificate of renewal of licence to operate a Blood Bank for processing of whole human blood and/or* for preparation for sale or distribution of its components

1. Certified that Licence No ..... . granted on …….. to M/s……. ..... for the operation of a Blood Bank for processing of whole human blood and*/or for preparation of its components at the premises situated at.....is hereby renewed with effect from…….. to .....

2. Name(s) of items :

   1.

   2.

   3.

3. Name(s) of competent Technical Staff:

   1.

   2.

   3.

Dated……..

Signature……..

Designation……..

*[*Licensing Authority/Central Licence Approving Authority]*

** Delete whichever is not applicable.*

1. Subs. by G.S.R 245(E) dt. 5.4.1999.

Drugs and Cosmetics Rules 1945

[1]**[FORM 26H**

(*See* rules 68A, 76, 77, 78)

Certificate of renewal of licence to manufacture for sale of [2][Large Volume Parenterals/Sera and Vaccines/recombinant DNA (r-DNA)derived drugs] specified in

Schedules C and C(I) excluding those specified in Schedule X

1. Certified that licence No..... granted on the ..... to ..... for the manufacture of following [2][Large Volume Parenterals/Sera and Vaccines/recombinant DNA (r-DNA) derived drugs] at the premises situated at..... has been renewed from.....to……

2. Name(s) of drug(s) ..... …….

(each item to be separately specified).

3. Name(s) of competent technical staff:

(a) responsible for manufacturing	(b) responsible for testing
1.	1.
2.	2.
3. 3.	
4. 4.	

Date:……

Signature……..

Designation……..

*[*Licensing Authority/Central Licence Approving Authority]*

** Delete whichever is not applicable.*

1. Ins. by G.S.R. 119(E), dt. 11.3.1996.
2. Subs. By G.S.R. 26 (E), dt: 19.1.2006.

[1]**[FORM 26-I**

(*See* rules 122-I)

Certificate of renewal of licence for manufacture of blood product.

1. Certified that licence no ..... granted on the ..... to M/s. ..... for

the manufacture of blood products at the premises situated at .....is hereby renewed with effect from.....…… to……

2. Name(s) of item (s):

1.
2.
3.

3. Name(s) of competent technical staff:

(a) responsible for manufacturing	(b) responsible for testing
1.	1.
2.	2.
3. 3.	
4.	4.

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Date:……

Signature……..

Designation……..

*[*Licensing Authority/Central Licence Approving Authority]*

** Delete whichever is not applicable.*

1. Ins. by G.S.R 245(E), dt. 5.4.1999.

[1]**[FORM 26-J**

(*See* rules 122G, 122H, 122I, 122P)

Certificate of renewal of licence for collection, processing, testing, storage, banking and release of umblical cord blood stem cells.

Certified that licence no ..... granted on the ..... to M/s. ..... for collection, processing, testing, storage, banking and release of umblical cord blood stem cells at the premises situated at .....is hereby renewed with effect from.....……..… to……

1.Name(s) of competent technical staff:

1……..

2……..

3……..

Date:……

Signature……

….

Designation……

*[*Licensing Authority/Central Licence Approving Authority]*

* *Delete whichever is not applicable.*

1. Ins. by G.S.R 899(E), dt. 27.12.2011.

[1]**[FORM 26J**

(*See* rules 83A and 83AA)

Certificate of renewal of loan licence to manufacture for sale of Large Volume Parenterals/Sera and Vaccines/recombinant DNA (r-DNA) derived drugs specified in Schedules C and C(I) excluding those specified in Schedule X

Certified that licence no ..... granted on the ..... to M/s. ..... for the manufacture of following Large Volume Parenterals/Sera and Vaccines/recombinant DNA (r-DNA) derived drugs at the premises situated at .....has been renewed from .....……..… to……

2.Name(s) of drug (s)……(Each item to be separately specified)

3.Name(s) of competent technical staff:

(a) responsible for manufacturing	(b) responsible for testing
1.	1.
2.	2.
3.	3.
4.	4.

Date:……

Signature……

….

Designation……

*[*Licensing Authority/Central Licence Approving Authority]*

* *Delete whichever is not applicable.*

1. Ins. by G.S.R 574(E), dt.17.6.2012.

FORM 27

Application for grant or renewal of a [1][licence to manufacture for sale or for distribution] of drugs specified in Schedules C and C (1) [2][excluding those specified in [3][Part XB and] Schedule X]

1.I / We ..... hereby apply for the grant / renewal of a licence to manufacture on the premises situated at the undermentioned drugs, being drugs specified in Schedules C and C (1) [2][excluding those specified in [3][Part XB and] Schedule X] to the Drugs and Cosmetics Rules, 1945.

Names of drugs……..……(each item to be separately specified).

2. The names, qualifications and experience of the expert staff responsible for the manufacture and testing of the above mentioned drugs.

(a) Name (s) of staff responsible for test .....

(b) Name (s) of staff responsible for manufacture.....

3. The premises and plan are ready for inspection/ will be ready for inspection on…..

4. A fee of rupees ..... and an inspection fee of rupees ……has been credited to Government under the head of account…….

Date ..... *Signature……*

Designation.....

Note-The application shall be accompanied by a plan of premises.

_

1. Ins. by. G.S.R. 788(E), dt. 10.10.1985. 3. Ins. by G.S.R. 28(E), dt. 22.1.1993. 2. Subs. by G.S.R. 462(E), dt. 22.6.1982.

FORM 27A

(*See* rule 75A)

Application for grant or renewal of a loan [1][licence to manufacture for sale or for distribution of] drugs specified in Schedules C and C(1) [2][excluding those specified in Part XB and Schedule X]

1. I / We*.....of# ..... …..hereby apply for the grant/ renewal of Loan Licence to manufacture on the premises situated at C/o$……. the undermentioned drugs, being drugs specified in Schedules C and C (1) [2][excluding those specified in Part XB and Schedule X] to the Drugs and Cosmetics Rules.

Names of drugs (each substance to be separately specified).

2. The names, qualifications and experience of the expert staff actually connected with the manufacture and testing of the specified products in the manufacturing premises.

(a) Name (s) of expert staff responsible for manufacture .....

(b) Name (s) of the expert staff responsible for testing .....

3. I /We enclose:

(a) A true copy of a letter from me / us to manufacturing concern whose manufacturing capacity is intended to be utilized by me / us.

(b) A true copy of a letter from the manufacturing concern that they agree to lend the services of their competent technical staff, equipment and premises for the manufacture of each item required by me / us and that they shall

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will analyse every batch of finished product and maintain the registers of raw materials, finished products and reports of analysis separately on this behalf.

(c) Specimens of labels, cartons of the drugs proposed to be manufactured.

4. A fee of Rs ..... has been credited to Government under the head of account..... …….

Date ..... *Signature* ..... ……

Designation……..

** Enter here name of the proprietor, partners or Managing Director, as the case may be.*

Enter here name of the applicant firm and the address of the principal place of business.

$ *Enter here the name and address of the manufacturing concern where the manufacture will be actually carried out and also the licence number under which the latter operates.*

1. Subs. by G.S.R. 788(E) ,dt. 10.10.1985.
2. Ins. By G.S.R. 462(E), dt: 22.6.1982.

[1][FORM 27B

Application for grant or renewal of a [2][licence to manufacture for sale or for distribution of] drugs specified in Schedules C, C(I) and X

1. I/We..... of ..... hereby apply for the grant/renewal of a licence to manufacture on the premises situated at…… the undermentioned drugs, specified in Schedules C, C(I) and X to the Drugs and Cosmetics Rules, 1945.

2. Names of drugs.

3. The names, qualifications and experience of the expert staff responsible for the manufacture and testing of the abovementioned drugs.

(a) Name(s) of staff responsible for testing:

(b) Name(s) of staff responsible for manufacture:

4. The premises and plant* are ready for inspection/will be ready for inspection on .....

5. A fee of rupees ..... and an inspection fee of rupees..... has been credited to the Government under the head of account .....

Date..... *Signature*……

Note: The application shall be accompanied by a plan of the premises.]

** Delete whichever is not applicable.*

1. Subs. by G.S.R. 462(E) dt. 22.6.1982.
2. Subs. by G.S.R. 788(E) ,dt. 10.10.1985.

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[1][FORM 27C

(*See* rule 122-F)

Application for grant/renewal* of licence for the operation of a Blood Bank for processing of whole blood and/or* preparation of Blood Components

1. I/We, ... of M/s ..... hereby apply for the grant of licence/renewal of licence number ..... dated…….to operate a Blood Bank, for processing of whole blood and/or* for preparation of its components on the premises situated at ……..

2. Name(s) of the item(s)

   1.

   2.

   3.

3. The name(s), qualification and experience of competent Technical Staff are as under:

   (a) Name(s) of Medical Officer.

   (b) Name(s) of Technical Supervisor

   (c) Name(s) of Registered Nurse.

   (d) Name(s) of Blood Bank Technician.

4. The premises and plant are ready for inspection/will be ready for inspection on..... ….

5. A licence fee of rupees ..... and an inspection fee of rupees..... has been credited to the Government under the Head of Account..... (receipt enclosed)

Signature .... ……

Dated. ..... *Name and Designation*……

** Delete whichever is not applicable.*

Notes:

1. The application shall be accompanied by a plan of the premises, list of machinery and equipment for collection, processing, storage and testing of whole blood and its components, memorandum of association/constitution of the firm, copies of certificate relating to educational qualifications and experience of the competent technical staff and documents relating to ownership or tenancy of the premises.

2. A copy of the application together with the relevant enclosures shall also be sent to the Central Licence Approving Authority and to the Zonal/Sub-Zonal Officers concerned of the Central Drugs Standard Control Organization].

1. Subs. by G.S.R. 245(E), dt. 5.4.1999.

[1][FORM 27D

(See rule 75)

Application for grant or renewal of a licence to manufacture for sale or for distribution of [2][Large Volume Parenterals/Sera and Vaccines/recombinant DNA (r-DNA) derived drugs] excluding those specified in Schedule X

1. I/We ..... of .....hereby apply for grant/renewal of a licence to manufacture for sale or distribution on the premises situated at……..…the undermentioned [2][Large Volume Parenterals/Sera and Vaccines/recombinant DNA (r-DNA) derived drugs], specified in Schedules C and C(1) to the Drugs and Cosmetics Rules, 1945.

2. Name(s) of drug(s) ..... (*each item to be separately specified*).

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3. The name(s), qualifications and experience of the competent technical staff responsible for the manufacture of the above mentioned drugs.

(a) Name(s) of staff responsible for testing .....

(b) Name(s) of staff responsible for manufacturing .....

4. The premises and plant are ready for inspection/will be ready for inspection on……

5. A fee of rupees ..... and an inspection fee of rupees .....has been credited to the Government under the Head of Account.....

Date: ..... *Signature .....*

Designation.....

Notes:

1. The application is to be accompanied by a plan of the premises, list of machinery and equipment to be employed for manufacture and testing, memorandum of association/constitution of the firm, copies of qualification and experience of competent technical staff and documents relating to ownership or tenancy of the premises.
2. A copy of the application together with the relevant enclosures shall also be sent each to the Central Licence Approving Authority and concerned Zonal/Sub-Zonal Officers of Central Drugs Standard Control Organization].

_
1. Ins. by. G.S.R.119(E), dt. 11-3-1996.
2. Subs. By G.S.R.26 (E) dt: 19.1.2006.

[1][FORM 27DA

(See rule 75A)

Application for grant or renewal of a loan licence to manufacture for sale or for distribution of Large Volume Parenterals/Sera and Vaccines/recombinant DNA (r-DNA) derived drugs excluding those specified in Schedule X

1. I/We* ..... of #.....hereby apply for grant/renewal of a loan licence to manufacture on the premises situated at c/o @……..…the undermentioned drugs being Large Volume Parenterals/Sera and Vaccines/recombinant DNA (r-DNA) derived drugs specified in Schedules C,C(1) excluding those specified in Schedule X to the Drugs and Cosmetics Rules, 1945.

2. Name(s) of drug(s) ..... (*each item to be separately specified*).

3. The name(s), qualifications and experience of the competent technical staff responsible for the manufacture of the above mentioned drugs.

(a) Name(s) of competent technical staff responsible for testing .....

(b) Name(s) of competent technical staff responsible for manufacturing .....

4. I /We enclose:

(a) A true copy of a letter from me / us to manufacturing concern whose manufacturing capacity is intended to be utilized by me / us.

(b) A true copy of a letter from the manufacturing concern that they agree to lend the services of their competent technical staff, equipment and premises for the manufacture of each item required by me / us and that they shall will analyse every batch of finished product and maintain the registers of raw materials, finished products and reports of analysis separately on this behalf.

(c) Specimens of labels, cartons of the drugs proposed to be manufactured.

5. A fee of rupees .....has been credited to the Government under the Head of Account.....]

Drugs and Cosmetics Rules 1945

Date: ..... *Signature*

..... *Designation*.....

* Enter here name of the proprietor, prtners or managing director, as may be.

Enter here nam of the applicant firm and the address of the principal place of business. @ Enter here the name and address of the manufacturing concern where the manufacture will be actually carried out and also the license number under which the latter operates.

1. Ins. by. G.S.R. 574 (E), dt.07-7-2012.

[1]**[FORM 27E**

(See rule 122F)

Application for grant/renewal* of licence to manufacture blood products for sale or distribution

1. I/We ..... of M/s ..... hereby apply for the grant of licence/renewal of licence number ..... dated…….. to manufacture Blood products on the premises situated at ..... …….

2. Name(s) of the item(s)

1.

2.

3.

4.

3. The name(s), qualification and experience of competent Technical Staff are as under:

(a) responsible for manufacturing	(b) responsible for testing
1.	1.
2.	2.
3.	3.

4. The premises and plant are ready for inspection/will be ready for inspection on.....

5. A licence fee of rupees …… ..... …….and an inspection fee of rupees ..... has been credited to the Government under the Head of Account..... (receipt enclosed)

Signature .... ……..

Dated. ..... *Name and Designation..... ....*

** Delete whichever is not applicable.*

Notes:

1. The application shall be accompanied by a plan of the premises, list of machinery and equipment for manufacture of blood products, memorandum of association/constitution of the firm, copies of certificate relating to educational qualifications and experience of the competent technical staff and documents relating to ownership or tenancy of the said premises.

2. A copy of the application together with the relevant enclosures shall also be sent to the Central Licence Approving Authority and to the Zonal/Sub-Zonal Officers concerned of the Central Drugs Standard Control Organization].

1. Ins. by G.S.R. 245(E), dt. 5-4-1999.

Drugs and Cosmetics Rules 1945

[1][FORM 27F

(See rule 122F)

Application for grant/renewal* of licence for collection, processing, testing, storage, banking and release of umblical cord blood stem cells

1. I/We ..... of M/s ..... hereby apply for the grant of licence/renewal* of licence number ..... dated…….. for collection, processing, testing, storage, banking and release of umblical cord blood stem cells on the premises situated at ..... …….

2. Name(s), qualification and experinec of competent technical staff are as under:
   1. Medical Director
   2.Laboratory In-charge
   3.Technical Supervisor
   4.Cord Blood Bank Technician (s)

3. The premises and plant are ready for inspection/will be ready for inspection on.....

4. A licence fee of rupees …… ..... ……and an inspection fee of rupees .....has been credited to the Government under the Head of Account..... (receipt enclosed)

Signature .... ……..

Dated. ..... *Name and Designation..... ....*

* *Delete whichever is not applicable.*

Notes:

1. The application shall be accompanied by a plan of the premises, list of machinery and equipment for manufacture of blood products, memorandum of association/constitution of the firm, copies of certificate relating to educational qualifications and experience of the competent technical staff and documents relating to ownership or tenancy of the said premises.

2. A copy of the application together with the relevant enclosures shall also be sent to the Central Licence Approving Authority and to the Zonal/Sub-Zonal Officers concerned of the Central Drugs Standard Control Organization].

1. Ins. by G.S.R. 899(E), dt. 27-12-2011.

FORM 28

(*See* rule 76)

[1]***[Licence to manufacture for sale or for distribution of] drugs specified in***

Schedules C and C (1) [2]***[excluding those specified in Schedule X]***

Number of Licence and date of issue .....

1. ……. is hereby licensed to manufacture at the premises situated at the following drugs, being drugs specified in Schedules C and C (1) [2][excluding those specified in Schedule X] to the Drugs and Cosmetics Rules, 1945.

Names of drugs .....

2. Names of approved [3][competent technical staff].

3. The licence authorises the sale by way of wholesale dealing and storage for sale by the licensee of the drugs manufactured under the licence subject to the conditions applicable to licences for sale.

4. The licence will be in force from .....to .....

Drugs and Cosmetics Rules 1945

5. The licence is subject to the conditions stated below and to such other conditions as may be specified in the Rules for the time being in force under the Drugs and Cosmetics Act,1940.

Date:……

Signature……..

Designation……..

[4]*[*Licensing Authority/Central Licence Approving Authority]*

**Delete whichever is not applicable*

Conditions of Licence

1 This licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.

2 If the licensee wants to undertake during the currency of the licence the manufacture any drug specified in Schedules C and C (1) [2][excluding those specified in Schedule X] not included above, he should apply to the Licensing Authority for the necessary endorsement as provided in rule 75(3). This licence will be deemed to extend to the items so endorsed.

3 Any change in the [3][competent technical staff] shall be forthwith reported to the Licensing Authority.

4 The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.

1. Subs. by G.S.R. 788(E), dt. 10.10.1985.
2. Ins. by G.S.R. 462(E), dt. 22.6.1982.
3. Subs. by G.S.R. 231(E), dt. 4.6.1996
4. Subs. by G.S.R. 923(E), dt. 14.12.1992.

FORM 28A

(*See* rule 76-A)

Loan [1][Licence to manufacture for sale or for distribution of] drugs specified in Schedules C and C (1) [2][excluding those specified in Schedule X]

1. Number of licence and date of issue .....

2. ……. of.....……..is hereby granted a loan licence to manufacture on the premises situated at ……... C/o ..... the following drugs being drugs specified in Schedules C and C (1) [2][excluding those specified in Schedule X] to the Drugs and Cosmetics Rules, 1945.

Names of Drugs .....

3. Names of [3][competent technical staff] .....

[4][3A. The licence shall be in force from ..... to.....

4. The licence authorises the sale by way of wholesale dealing by the licensee and storage for sale by the licensee of the drugs manufactured under the licence subject to the conditions applicable to licence for sale.

5 The licence is subject to the conditions stated below and to such other conditions as may be specified in the Rules for the time being in force under the Drugs and Cosmetics Act, 1940.

Drugs and Cosmetics Rules 1945

Date of issue: ……..

Signature……..

Designation .....

Conditions of Licence

1. This licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.
2. If the licensee wishes to undertake during the currency of the licence to manufacture any drugs specified in Schedules C and C (1) [2][excluding those specified in Schedule X] not included above, he should apply to the Licensing Authority for the necessary endorsement to the licence as provided in rule 75A. This licence will be deemed to extend to the items so endorsed.
3. Any change in the [3][competenet technical staff] shall be forthwith reported to the Licensing Authority.
4. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.

1. Subs. by G.S.R 788(E), dt. 10-10-1985.
2. Ins. by G.S.R. 462(E), dt. 22.6.1982.
3. Subs. by G.S.R.231(E) dt. 4.6.1996.
4. Added by Notfn. F. No. 1-10/62-D, dated 10.4.1964.

[1] [FORM 28B

(*See* rule 76)

[2][Licence to manufacture for sale or for distribution of] drugs specified in Schedules C, C(I) and X

No of Licence……

1. ..... is hereby licensed to manufacture at the premises situated at ..... the following drugs specified in Schedules C, C(I) and X to the Drugs and Cosmetics Rules, 1945.

Name of drugs……

2. Names of [3][competent technical staff]

3. The licence authorises the sale by way of wholesale dealing and storage for sale by the licensee of the drugs manufactured under the licence subject to the conditions applicable to licence for sale.

4. The licence will be in force.....to .....

5. The licence is subject to conditions stated below and to other conditions as may be specified in the rules for the time being in force under the Drugs and Cosmetics Act, 1940.

Date:……

Signature……..

Designation……..

[4]*[*Licensing Authority/Central Licence Approving Authority]*

**Delete whichever is not applicable*

Drugs and Cosmetics Rules 1945

Conditions of Licence

1. The licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.

2. If the licensee wishes to undertake during the currency of the licence the manufacture of any drug specified in Schedule X not included above, he should apply to the Licensing Authority for the necessary endorsement as provided in Rule 75(4). This licence will be deemed to be applicable to the items so endorsed.

3. Any change in the [1][competent technical staff] shall be forthwith reported to the Licensing Authority.

4. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.

5. The licensee shall furnish to the Licensing Authority copies of the invoices of sales made to dealers.

6. The licensee shall not manufacture drugs specified in Schedule X covered by this licence for use as ―Physicians Samples‖.]

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1. Subs. by G.S.R. 462(E) dt. 22.6.1982.
2. Subs. by G.S.R.788(E) dt. 10.10.1985.
3. Subs. by G.S.R.231(E) dt. 4.6.1996.
4. Subs. by G.S.R. 923(E) dt. 14.12.1992.

[1]**[FORM 28C**

(*See* rule 122-G)

Licence to operate a Blood Bank for collection, storage and processing of whole human blood and/or* its components for sale or distribution

1. Number of licence..... date of issue ..... at the premises situated at

……

2. M/s..... is hereby licensed to collect, store, process and distribute whole blood and/or its components.

3. Name(s) of the item(s) :

1.

2.

4. Name(s) of the Competent Technical Staff:

1.

2.

3.

5. The licence authorises licensee to collect, store, distribute and processing of whole blood and/or blood components subject to the conditions applicable to this licence.

6. The licence shall be in force from ..... …….to..……..

7. The licence shall be subject to the conditions stated below and to such other conditions as may be specified from time to time in the Rules made under Drugs and Cosmetics Act, 1940.

Dated: ……

Drugs and Cosmetics Rules 1945

Signature……

Name and Designation .....

*Licensing Authority/

*Central Licence Approving Authority

** Delete whichever is not applicable*

Conditions of Licence

1. The licensee shall neither collect blood from any professional donor or paid donor nor shall he prepare blood components from the blood collected from such a donor.

2. The licence and any certificate of renewal in force shall be displayed on the approved premises and the original shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.

3. Any change in the technical staff shall be forthwith reported to the Licensing Authority and/or Central Licence Approving Authority.

4. The licensee shall inform the Licensing Authority and/or Central Licence approving Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes places, the current licence shall be deemed to be valid for maximum period of three months from the date on which the change has taken place unless, in the meantime, a fresh licence has been taken from the Licensing Authority and/or Central Licence Approving Authority in the name of the firm with the changed constitution.]

1.Ins. by G.S.R. 245(E), dt. 5.4.1999.

[1]**[FORM 28D**

(See Rules 76)

Licence to manufacture for saleor for distribution of [2][Large Volume Parenterals/Sera and Vaccines/recombinant DNA (r-DNA) derived drugs] specified in Schedules C and C(I) excluding those specified in Schedule X

Number of licence ..... and date of issue…….

1. ..... is hereby licensed to manufacture at the premises situated at..... the following [2][Large Volume Parenterals/Sera and Vaccines/recombinant DNA (r-DNA) derived drugs] specified in Schedules C and C(1) excluding those specified in Schedule X to the Drugs and Cosmetics Rules, 1945.

2. Name(s) of drug(s).....(each item to be separately specified).

3. Name(s) of competent technical staff:

(a) responsible for manufacturing	(b) responsible for testing
1.	1.
2.	2.

4. The licence authorises the sale by way of wholesale dealing and storage for sale

Drugs and Cosmetics Rules 1945

by the licensee of the drugs manufactured under the licence, subject to the conditions applicable to licence for sale.

5. The licence shall be in force from..... to .....

6. The licence shall be subject to the conditions stated below and to such other conditions as shall be specified in the rules for the time being in force under the Drugs and Cosmetics
Act, 1940.

Date: …….

Signature……

Designation……

*Licensing Authority/*Central Licence Approving Authority *

Delete whichever is not applicable

Conditions of Licence

1. The licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.

2. If the licensee wishes to undertake during the currency of the licence to manufacture of any drug specified in Schedule C and/or C(I) excluding those specified in Schedule X not included above, he should apply to the Licensing Authority and or Central Licence Approving Authority for the necessary endorsement as provided in the rules. This licence shall be deemed to extend to the items so endorsed.

3. Any change in the competent technical staff named in the licence shall be forthwith reported to the Licensing Authority and/or Central Licence Approving Authority.

4. The licensee shall inform the licensing authority and/or Central Licence Approving Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licnece shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been applied along with prescribed fee and necessary documents to the Licensing Authority and/or Central Licence Approving

Authority in the name of the firm with the changed constitution.]

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1. Ins. by G.S.R. 119(E), dt: 11.3.1996.

2.Subs. By G.S.R. 26(E), dt: 19.1.2006.

[1][FORM 28DA

(See Rules 76A, 78A, 83AA)

Loan licence to manufacture for sale or for distribution of Large Volume Parenterals/Sera and Vaccines/recombinant DNA (r-DNA) derived drugs excluding those specified in Schedule X

Number of licence ..... and date of issue…….

1. ..... of ……..is hereby granted a loan license to manufacture o n the premises situated at.....c/o..... the following drugs being [2][Large Volume Parenterals/Sera and Vaccines/recombinant

DNA (r-DNA) derived drugs] specified in Schedules C and C(1) excluding those specified in Schedule X to the Drugs and Cosmetics Rules, 1945.

2. Name(s) of drug(s).....(each item to be separately specified).

3. Name(s) of competent technical staff:

(a) responsible for manufacturing	(b) responsible for testing
1.	1.
2.	2.

4. The licence authorises the sale by way of wholesale dealing and storage for sale by the licensee of the drugs manufactured under the licence, subject to the conditions applicable to licence for sale.

5. The licence shall be in force from..... to .....

6. The licence shall be subject to the conditions stated below and to such other conditions as shall be specified in the rules for the time being in force under the Drugs and Cosmetics Act, 1940.

Date: ……..

Signature…….

Designation……

*Licensing Authority/*Central Licence Approving Authority *

Delete whichever is not applicable

Conditions of Licence

1. The licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.

2. If the licensee wishes to undertake during the currency of the licence to manufacture of any drug specified in Schedule C and/or C(I) excluding those specified in Schedule X not included above, he should apply to the Licensing Authority and or Central Licence Approving Authority for the necessary endorsement as provided in the rules. This licence shall be deemed to extend to the items so endorsed.

3. Any change in the competent technical staff named in the licence shall be forthwith reported to the Licensing Authority and/or Central Licence Approving Authority.

4. The licensee shall inform the licensing authority and/or Central Licence Approving Authority in writing in the event of any change in the constitution of the firm operating under the

licence. Where any change in the constitution of the firm takes place, the current licnece shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been applied along with prescribed fee and necessary documents to the Licensing Authority and/or Central Licence Approving Authority in the name of the firm with the changed constitution.]

_____ 1. Ins. by G.S.R. 574(E), dt: 17.7.2012.

[1] **[FORM 28E**

(*See* rule 122 G)

Licence to manufacture and store blood products for sale or distribution.

l. Number of licence ..... date of issue ..... at the premises situated at…….....

Drugs and Cosmetics Rules 1945

2. M/s..... is hereby licensed to manufacture, store, sell or distribute the following blood products:-

3. Name(s) of the item(s) :

1.

2.

3.

4. Name(s) of the competent technical staff:

(a) responsible for manufacturing	(b) responsible for testing
1.	1.
2.	2.
3.	3.

5. The licence authorises licensee to manufacture, store, sell or distribute the blood products, subject to the conditions applicable to this licence.

6. The licence shall be in force from ..... to.....

7. The licence shall be subject to the conditions stated below and to such other conditions as may be specified from time to time in the rules made under Drugs and Cosmetics Act, 1940.

Dated.: .....
Signature.....……..

Name and Designation..
……..
*Licensing Authority/ *Central Licence Approving Authority *

Delete whichever is not applicable

Conditions of License

1. The licensee shall not manufacture blood products from the blood drawn from any professional donor or paid donor.

2. The licence and any certificate of renewal in force shall be displayed on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.

3. Any change in the technical staff shall be forthwith reported to the Licensing Authority and/or Central Licence Approving Authority.

4. The licensee shall inform the Licensing Authority and/or Central Licence Approving Authority in writing any change in the constitution of the firm

operating under the licence. In the event of any change in the constitution of the firm, the licence shall be deemed to be valid for a period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority and/or Central Licence Approvin g Auth ority in the name of the firm with the ch anged constitution.]

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1. Ins. by G.S.R. 245(E), dt. 5.4.1999.

[1] [FORM 28F

(*See* rules 122 F to 122-I, 122K, 122P)

Licence To Collect, Process, Test, Store, Banking And Release Of Umbilical Cord Blood Stem Cells.

Drugs and Cosmetics Rules 1945

l. Number of licence ..... date of issue ..... at the premises situated at…….....

2. M/s..... is hereby licensed to collect, process, test, store, banking and release of umbilical cord blood stem cells.

3. Name(s) of competent technical staff :

1.

2.

3.

4. The licence authorises licensee to collect, process, test, store, banking and release of umbilical cord blood stem cells.

5. The licence shall be in force from ..... to.....

6. The licence shall be subject to the conditions stated below and to such other conditions as may be specified from time to time in the rules made under Drugs and Cosmetics Act, 1940.

Dated.: .....
Signature.....……..

Name and Designation..
……..

*Licensing Authority/ *Central Licence Approving Authority *

Delete whichever is not applicable

Conditions of License

1. Umbilical cord blood specific for an individual will be collected after signing an agreement with the parent(s), whose child‘s umbilical cord blood is to be collected, and the cord blood bank.

2. Umbilical cord blood shall be collected from hospitals, nursing homes, birthing centres and from any other place where a consenting mother delivers, under the supervision of the qualified Registered Medical Practitioner responsible for the delivery.

3. The licence and any certificate of renewal in force shall be displayed on the approved premises and the original shall be produced at the request of an inspector appointed under the Drugs and Cosmetics Act, 1940.

4.Any change in the technical staff shall be forthwith reported to the Licensing Authority and/or Central Licence Approving Authority.

5. The licensee shall inform the Licensing Authority and/or Central Licence Approving Authority in writing any change in the constitution of the firm operating under the licence. In the event of any change in the constitution of the firm, the licence shall be deemed to be valid for a period of three months from the

date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority and/or Central Licence Approving Authority in the name of the firm with the changed constitution.]

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1. Ins. by G.S.R. 889(E), dt. 27.12.2011.

FORM 29

(*See* rule 89)

Licence to manufacture drugs for purposes of examination, test or analysis

Drugs and Cosmetics Rules 1945

1. ….....of…… is hereby licensed to manufacture the drugs specified below for purposes of examination, test or analysis at……

2. This licence is subject to the conditions prescribed in Part VIII of the Drugs and Cosmetics Rules, 1945.

3. This licence shall be in force for one year from date specified below.

Names of drugs

Date : …… *Licensing Authority……*

FORM 30

(*See* rule 90)

Application for licence to manufacture drugs for purposes of examination, test or analysis

1. …….of..... ……by occupation ..... hereby apply for licence to manufacture the drugs specified below for purposes of examination, test or analysis at and I undertake to comply with the conditions applicable to the licence.

Names of Drugs

Date.....
Signature……..

[1][FORM 31

(*See* rule 139)

Application for grant or renewal of a [2][*licence to manufacture cosmetics for sale or for Distribution*]

1.1 / We.....of. ..... hereby apply for grant /renewal of a licence to manufacture on the premises situated at..... the following cosmetics :-

2. Names of Cosmetics .....

3. Names, qualifications and experience of technical staff employed for manufacture and testing..... ……

4. A fee of rupees .....has been credited to Government under the head of account.....

Date..... *Signature*……..

Note: The application should be accompanied by a plan of the premises.

1. Added by Notfn No.F.1-36/64-D (G.S.R.1183), dt:17.8.1964.
2. Subs. by G..S.R .788 (E), dt. 10.10.1985.

[1][FORM 31A

(*See* rule138A)

***Application for grant or renewal of loan* [2][*licence to manufacture cosmetics for sale or for distribution*]**

Drugs and Cosmetics Rules 1945

1. I / W e .....of. .....hereby apply for grant/r enewal of a loan licence to ma nufacture co smetics for sale on the premises s i t u at e d at……C/o .....……the following cosmetics :—

2. Names of Cosmetics.....

3. The names, qualifications and experience of the expert shall actually connected with the manufacture and testing of the specified products in the manufacturing premises.

4. I /We enclose−

(a) A true copy of a letter from me / us to the manufacturing concern whose manufacturing capacity is intended to be utilized by me / us.

(b) A true copy of a letter from the *manufacturing concern that they agree to lend the services of their competent technical staff, equipment and premises for the manufacture of each item required by me / us and that they will analyse every batch of and maintain the registers of raw materials , finished products and reports of analysis separately in this behalf.

(c) specimen of labels, cartons of the products proposed to be manufactured.

5. A fee of rupees..... has been credited to Government under the head of account.....

Date…….. *Signature……..*

**Enter here the name and address of the manufacturing concern where the manufacture will be actually carried out and also their licence number.*

1. Ins. by G.S.R. 444, dt. 28-4-1973.

2. Subs. by G.S.R. 788(E), dt. 10.10.1985.

[1][FORM 32

(*See* rule140)

[2][Licence to manufacture cosmetics for sale or for distribution]

Number of Licence and date of issue

1 ...……is hereby licensed to manufacture on the premises situated at ..... the following cosmetics under the supervision of the following technical staff:-

(a) Names of cosmetics.

(b) Names of technical staff

2. The licence shall remain in force from……..to……(both days inclusives)

3. The licence is subject to the conditions stated below and to such other conditions as may be specified in the Drugs and Cosmetics Rules, 1945.

Date..... *Signature .....*

Designation .....

Conditions of Licence

1. This licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.

2. Any change in the technical staff shall be forthwith reported to the Licensing Authority.

3. If the licensee wants to manufacture for sale of additional items he should apply to the Licensing Authority for the necessary endorsement to the licence as provided in rule 138 (3). This licence shall be deemed to extend to the cosmetics so endorsed.

[3][4. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.]

1. Added by Notfn No.F.1-36/64-D, dt:17.8.1964.

2. Subs. by G.S.R. 788 (E), dt. 10.10.1985.

3. Added by S.O. 903, dt. 10-2-1976.

[1][FORM 32A

(*See* rule 139B)

***Loan* [2][*licence to manufacture cosmetics for sale or for distribution*]**

1. Number of Licence and date of issue……

2 . .....of. ..... is hereby granted a loan licence to manufacture the following cosmetics on the premises situated

at.....C/o..... under the direction and personal supervision of the following technical staff:

(a) Names of technical staff.

(b) Names of cosmetics.

3. The licence shall remain in force from ..... to .....

4. The licence is subject to the conditions stated below and to such other conditions as are specified in the rules for the time being in force under the Drugs and Cosmetics Act, 1940.

Date..... *Signature* .....

Designation .....

Conditions of Licence

1. This licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.

2. Any change in the technical staff shall be forthwith reported to the Licensing Authority.

3. If the licensee wants to manufacture for sale additional items he should apply to the Licensing Authority for the necessary endorsement to the licence as provided in rule 138A(5).This licence shall be deemed to extend to the cosmetics so endorsed.]

_____ 1. Ins. by G.S.R. 444, dt. 28-4-1973.

2. Ins. by G.S.R. 788 (E), dt. 10.10.1985.

[1][FORM 33

(*See* rule 141)

Certificate of renewal of licence to manufacture cosmetics for sale

Drugs and Cosmetics Rules 1945

1. Certified that licence No…….granted on the……. to……f or th e ma nufactu re fo r sale o f the fo llowin g cosmetics at the premises situated at……has been renewed from……and shall expire on……

2. Names of cosmetics.

3. Names of technical staff

Date…….. *Signature*……..

Designation……..]

_____ 1. Ins. by G.S.R. 1183, dt. 17.8.1964.

[1][FORM 33A

(*See* rule 141-A)

Certificate of renewal of loan licence to manufacture cosmetic for sale

1. Certified that loan licence No…….granted on the …….. . to……for the manufacture for sale of the following cosmetics at the premises situated at C/o……has been renewed from……to .....

2. Names of cosmetics.

3. Names of technical staff.

Date…… *Signature*……..

Designation……]

1. Added by G.S.R. 444, dt. 28-4-1973.

[1][FORM 34

(See rules 131 and 150)

Certificate of test or analysis of cosmetic by the Central Drugs Laboratory or the Government Analyst

1. Name of the officer or Inspector from whom received ..... 2. Serial number and date of the Officer's / Inspector's memorandum ..... 3. Number of sample .....
4. Date of receipt .....
5. Name of the Cosmetic purporting to be contained in the sample…….
6. Condition of seals on the [2][packet or on portion of sample or container]
7. *Results of test or analysis* :— The sample of cosmetics—

(a) contains a prescribed colour only/does not contain a prescribed colour.

(b) does not contain harmful ingredients/ contains harmful ingredients

(c) conforms/does not conform to claims m,ade on the label as to the nature and quality of the cosmetics.

[3][(d) contains not more than …….parts per million of Lead and ……..parts per million of Arsenic……../contains more than ……parts per million of Lead and ……parts per million of Arsenic.]

Date……

Director……..

Central Drugs Laboratoy/Government Analyst]

Drugs and Cosmetics Rules 1945

1. Added by Notfn No.F.1-36/64-D (G.S.R 1183), dt:17.8.1964.
2. Subs. by G.S.R. 59(E), dt. 7.2.1995.
3. Subs. by G.S.R. 510(E), dt. 26.7.1982.

[1][FORM 35

[2][*See* Rules 65, 67-G, 74, 74A, 74B, 78, 78A, 85H, 122P, 142, 142-B, 150E, 158 and 158A]

Form in which the Inspection Book shall be maintained

(A) The cover of the Inspection Book shall contain the following particulars, namely :—

1. The name and address of the licensee.....
2. Licence number and the date upto which the licence is valid .....

(B) (i) The pages of the Inspection Book shall be serially numbered and duly stamped by the Licensing Authority. The pages, other than the first and the last pages, shall have the following particulars:--

Name and designation of the Inspector who inspects the premises of the licensee:−

Date of Inspection.....

Observations of the Inspector .....

Signature of the Inspector (ii) The first and last pages of the Inspection Book shall be endorsed by the Licensing Authority with the following words, namely:—

Inspection Book maintained by M/s……

situated at …… for licence number …… in Form …….. under the Drugs and Cosmetics Rules, 1945.

Seal and Signature of the Licensing Authority.

Notes:-

(i) Printed copy of the Inspection Book may be obtained by the licensee from the Licensing Authority on payment.

(ii) The Inspection Book shall be maintained at the premises of the licensee.

(iii) The observations made by the Drug Inspector shall be in triplicate. The original copy shall be retained in the Inspection Book to be maintained in the premises of the licensee. The duplicate copy shall be sent to the Licensing Authority. The triplicate copy shall be taken as record by the Inspector.

1. Added by Notfn. No.F.1-14/68-D (G.S.R. 3869), dt. 26.10.1968.
2. Subs. by G.S.R. 592(E), dt: 13.8.2008.

[1][FORM 36

(*See* rule 150B)

Application for grant or renewal of approval for carrying out tests on drugs/ cosmetics or raw materials used in the manufacture thereof on behalf of licensees for manufacture for sale of drugs /cosmetics

(1) *I/We…….of…….hereby apply for the grant or renewal of approval for carrying out tests of identity, purity, quality and strength on the following categories of drugs / items of cosmetics or

raw materials used in the manufacture thereof on behalf of licensees for manufacture for sale of drugs / cosmetics.

(2) *Categories of drugs, items of cosmetics:

(a) Drugs other than those specified in Schedules C and C (1) and also excluding Homoeopathic Drugs:-

1. Crude vegetable drugs.
2. Mechanical contraceptives.
3. Surgical dressings.

4. Drugs requiring the use of ultravoilet / Infra Red. or Chromatography.

5. Disinfectants.

6. Other drugs.

(b) Drugs specified in Schedules C and C (1):— 1. Sera, Vaccines, Antigens, Toxins, Antitoxins, Toxoids, Bacteriophages and similar Immunological Products.

2. Antibiotics.

3. Vitamins

4. Parenteral preparations.

5. Sterilized surgical ligature / suture.

6. Drugs requiring the use of animals for their test.

7. Drugs requiring microbiological tests.

8. Drugs requiring the use of Ultravoilet/ Infra Red/ Spectrophotomete or Chromatography.

9. Other drugs.

(c) Homoeopathic drugs.

(d) Cosmetics.

(3) Name, qualifications and experience of expert staff employed for testing and the person-in-charge of testing.

(4) List of testing equipments provided.

(5) *I/We enclose a plan of the testing premises showing the location and area of the different sections thereof.

(6) An inspection fee of rupees .....has been credited to Government under the Head of Account.....

Date..... *Signature……]*

** Delete whichever is not applicable*

1. Ins. by Notfn. No .X. 11014/7/76-D&MS (G.S.R 1172), dt. 23-8-1977.

[1][FORM 37

(*See* rule 150C)

Approval for carrying out tests on drugs / cosmetics and raw materials used in their manufacture on behalf of licensees for manufacture for sale of drugs /cosmetics

Number of approval and date of issue:……

Drugs and Cosmetics Rules 1945

(1) Approval is hereby granted to..... …….for carrying out tests for identity, purity, quality and strength on the following categories of drugs/items of cosm etic s a n d the ra w m a terials use d in the m a nufac ture thereof on the premise s situated .....

Categories of drugs / items of cosmetics

……..

……..

……..

(2) Names of [2][competent technical staff] employed for testing and the person-in- charge of testing.

(3) The approval shall be in force from..... to.....

(4) The approval is subject to the conditions stated below and such other conditions as may be specified in the rules for the time being in force under the Act.

Date..... *Signature* .....

Designation .....

Conditions of Approval

(1) This approval and any certificate of renewal in Form 38 shall be kept in the approved premises and shall be produced at the request of the Inspectors appointed under the Act.

(2) If the approved institution wishes to undertake during the currency of the approval the testing of any other category of drugs or items of cosmetics it should apply to the approving authority for necessary endorsement as provided in rule 150-B.This approval will be deemed to extend to the item so endorsed.

(3) Any change in the analytical staff or in the person-in-charge of the testing shall be forthwith reported to the approving authority.

[3][(4) The approved institution shall inform the approving authority in writing in the event of any change of the constitution of the institution operating under this Form. Where any change in the constitution of the institution takes place, the current approval shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless in the meantime, a fresh approval has been taken from the approving authority in the name of the institution with the changed constitution.]

1.Ins. by G.S.R.1172, dt:23.8.1977.

2. Subs. by. G.S.R. 231(E), dt. 4.6.1996.

3. Ins. by G.S.R. 681 (E), dt. 5-12-1980.

[1][FORM 38

(*See* rule 150J)

Certificate of renewal of approval for carrying out tests on drugs / cosmetics and raw materials used in the manufacture thereof on behalf of licensees for manufacture for sale of drugs / cosmetics

(1) Certified that approval number ..... granted on the ..... for carrying out tests of identity, purity, quality and strength on the following categories of drugs/ items of cosmetics and the raw materials used in the manufacture thereof at the premises situated at……has been renewed from……to .....

Categories of drugs/items of cosmetics

……..

……

Drugs and Cosmetics Rules 1945

(2) Names of [2][competent technical staff] and person-in-charge of testing.

Date .....

Signature.....……

….

Designation……

.....

1. Ins. By G.S.R. 1172, dt:23.8.1977.

2.Subs. by. G.S.R.231(E) ,dt. 4.6.1996.

[1][FORM 39

[*See* rule150E(f)]

Report of test or analysis by approved institution

(1) Name of manufacturer from whom sample received together with his manufacturing licence number under the Act and under the rules made thereunder.

(2) Reference number and date of the letter from the manufacturer under which the sample was forwarded.

(3) Date of receipt of the sample.

(4) Name of drug / cosmetics / raw material purporting to be contained in the sample.

(5) Details of raw material/final product in bulk/final product (in finished pack)* as obtained from the manufacturer:

(a) Original manufacturer's name in the case of raw materials and drugs repacked.

(b) Batch number.

[2][(c) Batch size as represented by sample.]

(d) Date of manufacture, if any.

(e) Date of expiry, if any.

(6) Results of test or analysis with protocols of test or analysis applied.

In the opinion of the undersigned, the sample referred to above is **of standard quality/is not of standard quality* as defined in the Act and the rules made thereunder for the reasons given below.

Date..... .....

Signature of Person-in-charge of testing

Note:- Final product includes repacked material.

**Delete whichever is not applicable*

1. Ins. By G.S.R. 1172, dt:23.8.1977.
2. Subs. by. G.S.R. 681(E), dt. 6.6.1988.

[1][Forms 40 to 43

(Pertaining to Ayurveda, Siddha and Unani drugs replaced by Forms Nos .47 to 50.)

[1. Ins. by G.S.R. 701(E), dt. 27.9.2001]

[1][FORM 40

(See rule 24-A)

Application for issue of Registration Certificate for import of drugs into India under the Drugs and Cosmetics Rules 1945

Drugs and Cosmetics Rules 1945

I/We* …… (Name and full address) hereby apply for the grant of Registration Certificate for the manufacturer, M/s……..……. (full address with telephone, fax and E-mail address of the foreign manufacturer) for his premises, and manufactured drugs meant for import into India.

1. Names of drugs for registration.

[2][***]

2. I/We enclose herewith the information and undertakings specified in Schedule D (1) and Schedule D(II) duly signed by the manufacturer for grant of Registration Certificate for the premises stated below.

3. A fee of_____for registration of premises, the particulars of w hich are g iv en belo w, o f the manufactu rer h as b een cred ited to th e Government under the Head of Account "0210-Medical and Public Health, 04-Public Health, 104-Fees and Fines‖ under the Drugs and Cosmetics Rules, 1945-Central *vide* Challan No._____ dated_____(attached in original).

4. A fee of_____for registration of the drugs for import as specified at Serial No. 2 above has been credited to the Government under the Head of Account "0210-Medical and Public Health, 04-Public Health, 104-Fees and Fines" under the Drugs and Cosmetics Rules, 1945-Central vide Challan No._____, dated_____. (attached in original).

5. Particulars of premises to be registered where manufacture is

carried on: Address (es)……..

Telephone No……..

Fax……

E-mail……

I/We* undertake to comply with all terms and conditions required to obtain Registration Certificate and to keep it valid during its validity period.

Place:

Date:

Signature
Name
Designation

_____ *Seal/Stamp of manufacturer or his authorised Agent in India.*

(**Note**: In case the applicant is an authorised agent of the manufacturer in India, the Power of Attorney is to be enclosed).

**Delete whichever is not applicable.*

---

1. Ins. by G.S.R. 604(E) dt. 24-8-2001 (w.e.f. 1-1-2003).
2. Figures 1,2,3 omitted by G.S.R. 35(E), dt. 20.1.2005.

[1][FORM 41

(*See* rule27 A)

Registration

Certificate

Registration Certificate to be issued for import of drugs into India under Drugs and Cosmetics Rules, 1945

Registration Certificate No……. Date……

Drugs and Cosmetics Rules 1945

M/s _____ (Name and full address of registered office) having factory premises at……..(full address) has been registered under rule 27-A as a manufacturer and is hereby issued this Registration Certificate.

2. Name (s) of drugs which may be imported under this Registration Certificate:

[2][***]

3. This Registration Certificate shall be in force from _____ to_unless it is sooner suspended or cancelled under the rules.

4. This Registration Certificate is issued through the office of the manufacturer

or his authorised agent in India M/s (name and full address)_____ who will be responsib le for th e business activities of th e manufacturer, in India in all respects.

5. This Registration Certificate is subject to the conditions, stated below and to such other conditions as may be specified in the Act and the rules, from time to time.

Place…….

Date…….

Licensing Authority
Seal/Stamp

Conditions of the Registration Certificate.

1. The Registration Certificate shall be displayed at a prominent place by the authorised agent.

2. No drug shall be registered unless it has a free sale approval in the country of origin, and/or in other major countries.

3. The manufacturer or his authorised agent in India shall comply with the conditions of the import licence issued under the Drugs and Cosmetics Rules, 1945.

4. The manufacturer or his authorised agent in India shall inform the licensing authority forthwith in the event of any administrative action taken due to adverse reaction, viz. market withdrawal, regulatory restrictions, or cancellation of authorization, and/or not of standard quality report of any drug pertaining to this Registration Certificate declared by the Regulatory Authority of the country of origin or by any Regulatory Authority of any other country, where the drug is marketed/sold or distributed.

The dispatch and marketing of the drug in such cases shall be stopped immediately, and the licensing authority shall be informed immediately. Further action in respect of such stopped marketing of drug shall be followed as per the direction of the licensing authority. In such cases, action equivalent to that taken with reference to the concerned drug in the country of origin or in the country of marketing shall be followed in India also, in consultation with the licensing authority. The licensing authority may, however, direct any further modification to this course of action, including the withdrawal of the drug from Indian market within 48 hours time period.

5. The manufacturer or his authorised agent in India shall inform the licensing authority within 30 days in writing in the event of any change in manufacturing process, or in packaging, or in labelling or in testing, or in documentation of any of the drugs pertaining to this Registration Certificate.

In such cases, where there shall be any major change/modification in manufacturing, or in processing or in testing, or in documentation as the case may be, at the discretion of the licensing authority, the manufacturer or his authorised agent in 269

Drugs and Cosmetics Rules 1945

India shall obtain necessary approval within 30 days by submitting a separate application along with the registration fee, as specified in clause (ii) of sub-rule (3) of rule 24-A.

6. The manufacturer or his authorised agent in India shall inform the licensing authority immediately in writing in the event of any change in the constitution of the firm and / or address of the registered office / factory premises operating under this Registration Certificate. Where any such change in the constitution of the firm and/or address takes place, the current Registration Certificate shall be deemed to be valid for a maximum period of three months from the date on which the change has taken place unless, in the meantime, a fresh Registration Certificate has been taken from the licensing authority in the name of the firm with the changed constitution of the firm and/or changed address of the registered office or factory premises.]

1. Ins. by G.S.R. No.604(E), dt. 24-8-2001 (w.e.f. 1-1-2003)

2. Figures 1,2,3 omitted by G.S.R. 32, dt. 20.1.2005.

[1][FORM 42

(See rule 129A)

Application for issue of Registration Certificate for import of cosmetics into India under the Drugs and Cosmetics Rules, 1945

I/We* …… (Name and full address) hereby apply for the grant of Registration Certificate for the manufacturer, M/s……. (full address with telephone, fax and E-mail address of the foreign manufacturer) for his premises, and manufactured cosmetics meant for import into India.

1. Name of cosmetics along with their brand name and pack size(s) and variants for registration.

(1) …… (4)……..
(2)……. (5)……..
(3)……. (6)……...

2. I/We* enclose herewith the information and undertakings specified in Schedule D (III) duly signed by the manufacturer for grant of Registration Certificate for the premises stated below.

3. A fee of_____for registration of cosmetics for import as specified at serial no. 2 above has b een cred ited to th e C e n t r a l Government under the Head of Account "0210-Medical and Public Health, 04-Public Health, 104-Fees and Fines‖ under the Drugs and Cosmetics Rules, 1945-Central *vide* Challan No._____ dated_____(attached in original).

4. Particulars of premises to be registered where manufacture is carried on:

Address (es)……..

Telephone No……..

Fax……..

E-mail…….

I/We* undertake to comply with all terms and conditions required to obtain Registration Certificate and to keep it valid during its validity period.

Place:…...

Date:……

Signature……..
Name……
Designation……
Seal/Stamp of manufacturer or his authorised Agent in India.

Drugs and Cosmetics Rules 1945

(**Note**: In case the applicant is an authorised agent of the manufacturer in India, the Power of Attorney is to be enclosed).

**Delete whichever is not applicable.*

_____ 1. Ins. by G.S.R. 4 2 6 (E) dt. 19-5-2010, read with corrigendum G.S.R263(E) dt:30.3.2011, corrigendum G.S.R. 733(E) dt:29.9.2011, corrigendum G.S.R.270(E) dt:30.3.2012 and corrigendum G.S.R. 733(E) dt:29.9.2012.

1[FORM 43

(*See* rule 129C)

Registration Certificate

Registration Certificate to be issued for import of cosmetics into India under Drugs and Cosmetics Rules, 1945

Registration Certificate No……. Date……..…

M/s _____ (Name and full address of registered office)…….having factory premises at … … … … . . (full address) has been registered under rule 1 2 9 A as a manufacturer and is hereby issued this Registration Certificate.

2. Name (s) of cosmetics, along with thrir brand names and pack size(s) and variants which may be imported under this Registration Certificate:

(1)……
(2)……
(3)……

3. This Registration Certificate shall be in force from …… to……..unless it is sooner suspended or cancelled under the rules.

4. This Registration Certificate is issued through the office of the manufacturer or his authorised agent or importer in India or by the subsidiary in India authorized by the manufacturer, namely.-M/s (name and full address)_____ who shall be responsib le for th e business activities of th e manufacturer, in India in all respects.

5. This Registration Certificate is subject to the conditions, stated below and to such other conditions as may be specified in the Drugs and Cosmetics Act, 1940 and the rules made thereunder, from time to time in this regard..

Place…….

Date…….

Licensing Authority
Seal/Stamp

Conditions of the Registration Certificate.

1. The Registration Certificate shall be produced by the authorised importer/distributor/agent as and when required by the licensing authority/regulatory authority.

2. The manufacturer or his authorised importer/distributor/agent in India shall inform the licensing authority forthwith in the event of any administrative action taken namely, market withdrawal, regulatory restrictions, or cancellation of authorization, and/or not of standard quality report of any cosmetic pertaining to this Registration Certificate declared by the Regulatory Authority of the country of origin or by any Regulatory Authority of any other country, where the cosmetic is marketed/sold or distributed.

The dispatch and marketing of the cosmetic in such cases shall be stopped immediately, and the licensing authority shall be informed immediately. Further action in respect of such stopped marketing of drug shall be followed as per the

direction of the licensing authority. In such cases, action equivalent to that taken with reference to the concerned cosmetic in the country of origin or in the country of marketing shall be followed in India also, in consultation with the licensing authority. The licensing authority may, however, direct any further modification to this course of action, including the withdrawal of the c o s m e t i c from Indian market within 48 hours time period.

3. The manufacturer or his authorised agent/importer/distributor or subsidiary in India shall inform the licensing authority within 30 days in writing in the event of additional variants/additional cosmetic category/additional manufacturing location or any change in labeling or in testing, or in documentation of any of the c o s m e t i c pertaining to this Registration Certificate.

In such cases, where there shall be additional variants/additional cosmetic category/additional manufacturing location, as the case may be, at the discretion of the licensing authority, the manufacturer or his authorised agent/importer/distributor/subsidary in India shall apply for necessary approval within 30 days by submitting a separate application along with the registration fee.

4. The manufacturer or his authorised agent in India shall inform the licensing authority immediately in writing in the event of any change in the constitution of the firm and / or address of the registered office / factory premises operating under this Registration

Certificate. Where any such change in the constitution of the firm and/or address takes place, the current Registration Certificate shall be deemed to be valid for a maximum period of three months from the date on which the change has taken place unless, in the meantime, a fresh Registration Certificate has been taken from the licensing authority in the name of the firm with the changed constitution of the firm and/or changed address of the registered office or factory premises.]

1. Ins. by G.S.R. 4 2 6 (E) dt. 19-5-2010, read with corrigendum G.S.R263(E) dt:30.3.2011, corrigendum G.S.R. 733(E) dt:29.9.2011, corrigendum G.S.R.270(E) dt:30.3.2012 and corrigendum G.S.R. 733(E) dt:29..2012.

[1][FORM 44

(*See* rules 122A, 122B, 122D and 122 DA)

Application for grant of permission to import or manufacture a New Drug or to undertake clinical trial.

I/We*…… of M/s..... ……..

(address) hereby apply for grant of permission for import of and/or clinical trial or for approval to manufacture a new drug or fixed dose combination or subsequent permission for already approved new drug. The necessary information / data is given below :

1. *Particulars of new drug :*
   (1) Name of the drug.
   (2) Dosage form.
   (3) Composition of the formulation :
   (4) Test specification.
      (i) active ingredients.
      (ii) inactive ingredients.
   (5) Pharmacological classification of the drug.
   (6) Indications for which proposed to be used.
   (7) Manufacturer of the raw material (bulk drug substances).
   (8) Patent status of the drug.

2. Data submitted along with the application (as per Schedule Y with indexing and page numbers:)

A. Permission to market a new drug :

Chemical and Pharmaceutical information.
(2) Animal Pharmacology.
(3) Animal Toxicology.
(4) Human / Clinical Pharmacology (Phase I).
(5) Exploratory Clinical Trials (Phase II).
(6) Confirmatory Clinical Trials (Phase III) (including published review articles)
(7) Bio-availability, dissolution and stability study data.
(8) Regulatory status in other countries.
(9) Marketing information :
(a) Proposed product monograph.
(b) Drafts of labels and cartons.
(10) Application for test licence.
[2][(11) New Chemical Entity and Global Clinical Trial-
(a) Assessment of risk versus benefit to the patients (b) Innovation vis-à-vis existing therapeutic option (c) Unmet medical need in the country.]

B. Subsequent approval / permission for manufacture of already approved new drug :
(a) Formulation:
(1) Bio-availability / bio-equivalence protocol.

(2) Name of the investigator/center.

(3) Source of raw material (bulk drug substances) and stability study data.

(b) Raw material (bulk drug substances):

(1) Manufacturing method.

(2) Quality control parameters and/or analytical specification, stability report. (3) Animal toxicity data.

C. Approval / Permission for fixed dose combination:

(1) Therapeutic Justification.

(authentic literature in [3][pre-reviewed journals]/text books) (2) Data on pharmacokinetics/pharmacodynamics combination.

(3) Any other data generated by the applicant on the safety and efficacy of the combination.

D. Subsequent Approval or approval for new indication - new dosage form: (1) Number and date of Approval / permission already granted. (2) Therapeutic justification for new claim / modified dosage form (3) Data generated on safety, efficacy and quality parameters.

A total fee of rupees ..... (in words) ..... has been credited to the Government under the Head of Account..... (Photocopy of receipt is enclosed).

Dated : .....

Signature……..

Designation……….

Note: **Delete whichever is not applicable.*

_

1. Forms 44 to 46 A ins. by No.G.S.R. 900 (E), dt. 12.12.2001. 2. Ins. By G.S.R. 826 (E), dt. 30.10.2015.

3. Subs by G.S.R. 26(E), dt. 19.1.2006.

Drugs and Cosmetics Rules 1945

[1][FORM 45

(*See* rules 122 A, 122 D and 122 DA)

Permission to import Finished Formulation of a New Drug

Number of the permission and date of issue…….. M/s ..... of……. (address) is hereby permitted to import the following new drug formulation under rule 122 A /122 D/122 DA of the Drugs and Cosmetics Rules, 1945.

(1) Name of the New Drug :

(2) Dosage form :

(3) Composition :

(4) Indications :

Dated:.....

Signature.....

Name and designation of Licensing Authority

Conditions for Grant of Approval / Permission.

(1) The formulation shall conform to the specifications approved by the Licensing Authority.

(2) The proper name of the drug shall be printed or written in indelible ink and shall appear in a more conspicuous manner than the trade name, if any, which shall be shown immediately after or under the proper name on the label of the innermost container of the drug or every other covering in which the container is packed.

(3) The label of the innermost container of the drug and every other covering in which the container is packed shall bear a conspicuous red vertical line on the left side running

throughout the body of the label which shall not be less than 1 mm in width and without disturbing the other conditions printed on the label to depict it as prescription drug.

(4) The label on the immediate container of the drug as well as the packing in which the container is enclosed should contain the following warning:

"WARNING : To be sold by retail on the prescription of a ..... Only."

[2][(5) Post marketing surveillance study shall be conducted during initial period of two years of marketing of the new drug formulation, after getting the protocol and the names of the investigator duly approved by the Licensing Authority.] (6) All reported adverse reactions related to the drug shall be intimated to the Drugs Controller, India and Licensing Authority and regulatory action resulting from their review should be complied with.

(7) No claims except those mentioned above shall be made for the drug without the prior approval of the Licensing Authority.

(8) Specimen of the carton, labels, package insert that will be adopted for marketing the drug in the country shall be got approved from the Licensing Authority before the drugs is marketed.

(9) Each consignment of imported drug shall be accompanied by a test/analysis report.

1. Ins. by No.G.S.R. 900 (E), dt. 12.12.2001.
2. Subs by G.S.R. 101(E), dt. 18.2.2011.

[1][FORM 45A

(*See* rules 122A and 122DA)

Permission to import raw material (new bulk drug substance)

Number of the permission and date of issue…….

M/s .....of……(address) is hereby permitted to import the following raw material (new bulk drug substances) under rule 122 A / 122DA of the Drugs and Cosmetics Rules, 1945, namely :-

Name of the raw material (new bulk drug substances): (1) .....

(2) .....

(3) .....

Dated ..... *Signature* .....

Name and Designation of the Licensing Authority……

Conditions for Grant of Approval / Permission

(1) The raw material (new bulk drug substance) shall conform to the test specifications as approved by the Licensing Authority.

(2) For manufacture of raw material (new bulk drug substance) or its formulation in the country, separate approval under rule 122-B shall be obtained from the Licensing Authority.

(3) The permission to import shall not be used to convey or imply that the raw material
(new bulk drug) is categorized as "life saving or essential drug."]

1. Ins. By G.S.R. 900 (E), dt. 12.12.2001.

[1][FORM 46

(*See* rules 122 B, 122 D and 122 DA)

Permission / Approval for manufacture of new drug formulation

Number of permission and date of issue ..... ……. M/s of ..... (address) is hereby granted Permission/Approval to manufacture following new drug formulation under rule 122B/122D/122DA of the Drugs and Cosmetics Rules, 1945, namely :-

(1) Name of the formulation:

(2) Dosage form:

(3) Composition:

(4) Indications:

Dated …….. *Signature .....*

Name and designation of Licensing Athority……..

Conditions for Grant of Approval / Permission.

(1) The formulation shall conform to the specifications approved by the Licensing Authority.

(2) The proper name of the drug shall be printed or written in indelible ink and shall appear in a more conspicuous manner than the trade name, if any, which shall be shown immediately after or under the proper name on the label of he innermost container of the drug or every other covering in which the container is packed.

(3) The label of the innermost container of the drug and every other covering in which the container is packed shall bear a conspicuous red vertical line on the left side running throughout the body of the label which shall not be less than 1 mm in width and without disturbing the other conditions printed on the label to depict it as prescription drug.

(4) The label on the immediate container of the drug as well as the packing in which the container is enclosed should contain the following warning:

"WARNING : To be sold by retail on the prescription of a ..... only."

[2][(5) Post marketing surveillance study shall be conducted during initial period of two years of marketing of the new drug formulation, after getting the protocol and the names of the investigator duly approved by the Licensing Authority.] (6) All reported adverse reactions related to the drug shall be intimated to the Drugs Controller, India and Licensing Authority and regulatory action resulting from their review should be complied with.

(7) No claims except those mentioned above shall be made for the drug without the prior approval of the Licensing Authority.

(8) Specimen of the carton, labels, package insert that will be adopted for marketing the drug in the country shall be got approved from the Licensing Authority before the drug is marketed.

1. Ins. by G.S.R. 900 (E), dt. 12.12.2001.
2. Subs by G.S.R.101(E), dt. 18.2.2011.

[1][FORM 46A

(*See* rules 122 B and 122 DA)

Permission/ Approval for manufacture of raw material (new bulk drug substance)

Name of the permission/ approval and date of issue .....

M/s .....of..... (address) is hereby granted Permission/Approval to manufacture the following raw material (new bulk drug substance) under rule 122B / 122DA of the Drugs and Cosmetics Rules, 1945.

Name of the raw material (new bulk drug substance): (1) .....

(2) .....

(3) ….....

Dated ..... *Signature .....*

Name and designation of Licensing Authority.

Conditions for Grant of Permission /Approval

(1) The raw material (new bulk drug substance) shall conform to the

specifications approved by the Licensing Authority.

(2) The raw material (new bulk drug substance) can be sold to only those manufacturers who have permission, in writing, from Licensing Authority, either to use the drug for development purpose/clinical trial-bio-equivalence study or to manufacture the formulation.

(3) For manufacture of the formulation in the country, separate approval under rule 122B shall be obtained from the Licensing Authority.]

1. Ins. by No.G.S.R. 900 (E), dt. 12.12.2001.

Drugs and Cosmetics Rules 1945

[1][FORM 47

(*See* rule 160 A)

Application for grant or renewal of approval for carrying out tests on Ayurvedic, Siddha and Unani drugs or raw materials used in the manufacture thereof on behalf of licensees for manufacture for sale of Ayurvedic, Siddha and Unani drugs

1. *I/We..... of ..... hereby apply for the grant/renewal of approval for carrying out tests of identity, purity, quality and strength on the following categories of Ayurvedic, Siddha and Unani drugs or raw materials used in the manufacture thereof on behalf of licensee for manufacture for sale of Ayurvedic, Siddha and Unani drugs.

2. *Categories of Ayurvedic, Siddha and Unani drugs other than those specified in the

First Schedule to this Act for which testing will be carried out:

	AYURVEDA AND SIDDHA	UNANI
1.	Asava and Arista 1.	Nabeez, Khal (Sirka)
2.	Arka-Tinir 2.	Majoon and its sub-categories Itrifal, Jawarish, Khameera, Laooq, Halwar
3.	Avaleha and Paka-Ilakam 3.	Sufoof, Zuroor, Sunoon.
4.	Kavatha Curna-Kutinir Curanam 4.	Namak, Khar
5.	Guggulu 5.	Raughan
6.	Ghrita-Ney 6.	Zimad
7	Churna-Curanam 7.	Habb (Pill)
8.	Taila-Tailam 8.	Shiyaf
9.	Dravaka-Tiravakam 9.	Qutoor (drops)
10.	Lavana-Uppu 10.	Kohal (Surma), Kajal
11.	Kshara-Saram 11.	Satt, Usara
12.	Lepa-Pacai 12.	Kushta
13.	Vati, Gutika-Kulikai 13.	Joshanda (Single drugs)
14.	Vartti 14.	Sharbat Sikanjabeen
15.	Netrabindu (Aschyotan) 15.	Sayyal, Arq (Distillates)
16.	Anjana-Kanmai 16.	Qurs (Tablet)
17.	Sattva-Sattu 17.	Marham, Qairooti
18.	Kupipakva Rasayana-Kuppi Centuram 18.	Humool, Furzaja
19.	Parpati 19.	Bakhoor
20.	Pishti 20.	Nabati Advia
21.	Bhasma-Parpam 21.	Maadni Advia
22.	Mandura-Atai kutinir 22.	Asjad Advia
23.	Rasay oga-C entur am	23. Haiwani Advia
24.	Lauha	24. Jauhar
25.	Ghana Sattva	25. Natool
26.	Kvath Pravahi- Kutinir	26. Nashooq, Naswar
27.	Panak (Syrup)-Manappaku	27. Shamoom

28.	Tablet-Mattirai Capsule	28. Saoot (Nasal drops) 29. Mazoogh
30.	Ointment- Kalimapu Phalavarti Dhoomravarti/Doopan Sutra/Kshar Varti	30. Tila 31. Lashooq 32. Gulqand 33. Kshar Fateela
34.	Single drugs: (a) Plant based (b) Mineral based (c) Metal based	34. Ghaza, Utban, Sasbhh

(d) Animal based

(e) Synthetic

(f) Any other Ayurvedic, Siddha, Unani formulation

35. Pushp (Phool)
36. Nasya
37. Swarasa (Fresh juice)
38. Karna Bindu (Ear drops)
39. Any other dosage of Patent and Proprietary and Ayurvedic, Siddha, Unani Drug
40. Mazmazah (Mouth washer)

35. Capsule
36. Huqna
37. Naurah
38. Latookh
39. Vajoor (Throat paint)

(3) Names, qualifications and experience of experts employed for testing and the person in-charge of testing.

(4) List of testing equipment provided.

(5) *I/We enclose a plan of the testing premises showing the location and area of the different sections thereof.

(6) An inspection fee of rupees ..... has been credited to Government under the head of account .....

Dated……

Signature…….

Full address of the Applicant

*Delete which is not applicable.

1. Ins. by G.S.R. 701(E), dt. 27.9.2001 and subs. by G.S.R. 73(E), dt. 31.1.2003.

[1][**FORM 48**

(See Rule 160 B)

Approval for carrying out tests or analysis on Ayurvedic, Siddha and Unani drugs or raw materials used in the manufacture thereof on behalf of licensees for manufacture for sale of Ayurvedic, Siddha and Unani drugs

Number of approval and date of issue……

1. Approval is hereby granted to .....for carrying out tests in identity, purity, quality and strength on the following categories of Ayurvedic, Siddha or Unani drugs and the raw materials used in the manufacture thereof on the premises situated at .....

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Categories of Ayurvedic, Siddha and Unani drugs.

……
……
……

2. Name of experts employed for testing and the person-in-charge of testing

……(experts) and…… (person in-charge).

3. The approval shall be in force from ..... to.....

4. The approval is subject to the conditions stated below and such other conditions as may be specified in the rules for the time being in force under the Act.

Date ..... *Signature* .....

Place ..... *Designation* .....

Seal of State Licensing Authority

Conditions of approval

(1) This approval and any certificate of renewal in Form 49 shall be displayed in the approved premi ses and sh all be produced at the request of the Inspectors appointed under the Act.

(2) If the applicant wishes to undertake during the currency of the approval the testing of any other category of Ayurvedic, Siddha or Unani drugs it should apply to the approving authority for necessary endorsement as provided in Rule 160A. This approval will be deemed to extend to the items so endorsed.

(3) Any change in the experts or in the person in-charge of the testing shall be forthwith reported to the approving authority.

(4) The applicant shall inform the approving authority in writing in the event of any change of the constitution of the laboratory operating under this Form. Where any change in the constitution of the laboratory takes place, the current approval shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless in the meantime, a fresh approval has been taken from the approving authority in the name of the laboratory with the changed constitution.]

_

1.Ins. by G.S.R. No.702(E) dt. 27-9-2001 and subs.by.G.S.R.73(E), dt.31.01.2003.

1[**Form 49**

(See rule 160- I)

Certificate of renewal for carrying out tests or analysis on Ayurvedic, Siddha or Unani drugs or raw materials used in the manufacture thereof on behalf of licensees for manufacture for sale of Ayurvedic, Siddha or Unani drugs

1. Certified that approval number ..... gr an t ed o n th e ..... day o f ..... 20…. for carrying out tests of identity, purity, quality and strength on the following categories of Ayurvedic, Siddha or Unani, drugs and the raw materials used in the manufacture thereof at the premises situated at ..... has been renewed from ……. to..... (date).

Catagories of Ayurvedic, Siddha or Unani drugs:

…….

2. Name of experts and the person-in-charge of testing…….. (experts) and…….(person in charge)

Drugs and Cosmetics Rules 1945

Date: ..... *Signature*.....

Place *:* .....

Designation .....

Seal of State Licensing Authority]

1. Ins. by G.S.R. No.701(E) dt. 27-9-2001 and subs. by G.S.R.73(E) dt. 31.01.2003.

1[**FORM 50**

[*See* rule 160 D(f)]

Report of test or analysis by approved Laboratory

(1) Name of manufacturer from whom sample received together with his manufacturing licence number under the Act or the rules made thereunder.

……

(2) Reference number and date of the letter from the manufacturer under which the same was forwarded.

……

(3) Date of receipt of the sample

……

(4) Name of Ayurvedic, Siddha and Unani drug of raw material purporting to be contained in the sample.

……

(5) Details of raw material of final product (in bulk finished pack)* as obtained from the manufacturer:

(a) Original manufacturer's name in the case of raw materials and drugs repacked…… …….

(b) Batch number……

(c) Batch size as represented by sample……..

(d) Date of manufacture, if any .....……

(e) Date of expiry, if any…….

(6) Results of test or analysis with protocols of test or analysis applied or as per Ayurvedic, Siddha or Unani Pharmacopoeial standards.

(7) Other specific tests for identity, purity, quality and strength of Patent and Proprietary drugs.

In the opinion of the undersigned, the sample referred to above is of standard *quality/is not of standard quality as defined in the Act or the rules made thereunder for the reasons given below

……
… Date…….
Place…..

(Signature of the person-in-charge of testing)
(F. No……..)
Name and Designation and Seal……
Name and Address of the Laboratory……
License No……..

Note: Final product includes repacked material.

*Delete whichever is not applicable.

1. Ins. by G.S.R. 701(E) dt. 27-9-2001 and subs. by G.S.R.73(E) dt. 31.1.2003

1 [SCHEDULE B

(*See* rules 7 and 48)

Fees for test or analysis by the Central Drugs Laboratories or State Drugs Laboratories :

1. **I.** ***Fees for test and assay of Drugs requiring use of animals***

	Rupees
Adrenocorticotrophic hormone assay	1000
Gonadotrophic hormone for LH activity	1000
FSH Activity	1000
Posterior pituitary extract or its synthetic substitute for oxytocin activity	400

Vasopressor activity	400
Insulin and insulin in combination for hypoglycaemic activity	2000
Hyaluronidase	500
Glucagon	2000
Heparin for anticoagulant activity	600
Protamine sulphate	300
Depressor or Histamine like substane	300
Pyrogen test	500
Antigenecity or foreign protein test	300
Abnormal or undue toxicity or safety test	200
Determination of Lethal doses, LD_{10} or LD_{50} in mice	800
Skin sensitivity/eye irrigation	250
Implantation test	2000

2.*Microbiological tests and assays -*

Bioassay of Antibiotic	400
Microbiological assay of vitamins	300
Phenol coefficient	300
Preservatives – Microbial challenge test	2000
Sterility test – Parenteral preparations	100
Surgical dressings	200
Syringes and needles	300
Transfusion and infusion sets or assemblies	400
Other sterile devices	

1. Subs. by G.S.R. No.478(E), dt. 7-8-1998.

3. *Identification tests -*

(a)	Chemical Methods	50
(b)	Microscopical	50
(c)	IR Spectroscopy	150
(d)	UV Spectroscopy	100
(e)	Chromotography	
(i)	Paper	100
(ii)	Thin layer	150
(iii)	Column	100
(iv)	GLC	250
(v)	HPLC	500
(vi)	Gel Filtration	300
(f)	Electrophoresis	
	(i) Paper and Cellulose acetate	200
	(ii) Polyacrylamide Gel, starch gel, agar gel	300 each

4. *Physical tests –*

(a) Optical rotation, specific gravity, refractive index, weight per ml, fluorescence.	75 each
(b) Viscocity	100
(c) pH, Solubility, loss on drying, net content, ash, sulphated ash etc.	20 each
(d) Absorbancy, wt/unit area (surgical), foreign matter, extractive	30 each

	value, thread count etc.	
(e)	Uniformity of weight	
	(i) Tablets	15
	(i) Capsules	20
(f)	Acid value, iodine value, peroxide value, Soponification value, acetyl value.	100 each
(g)	Disintegration tests –	
	(i) Ordinary tablets	20
	(ii) Capsule	30
	(iii) Sugar Coated tablets	50
	(iv) Enteric coated tablets	100
(h)	Dissolution test	250
(i)	Uniformity of content.	500
(j)	Wt. per unit area (powder), particle size, count, methoxy value.	200 each
(k)	Limit test for impurities	100 each
(l)	Related substances	
	(i) T LC method	
	(A) Without reference standard	150
	(B) With reference standard	250
	Drugs and Cosmetics Rules 1945	
	(ii) Gas Liquid Chromatography	
	(A) Without reference standard	250
	(B) With reference standard	350
	(iii)High pressure Liquid Chromatography	100
	(A)Without reference standards	500
	(B)With reference standards	500
(m)	Water (Karl Fisher)	200
(5)	***Assays -***	
	(a) General chemical methods	100 for each ingredient
	(b) Non-aqueous/instrumental	200 for each ingredient
	(c) Chromatography	
	(i) TLC	250
	(ii) Column	200
	(iii) GLC	350
	(iv) HPLC	500
	(v) Gel filtration	400
	(d) Nitrogen determination	200
	(e) Medicinal gases	400
(6)	***Polymorph test -***	300
	(Content of polymorph A in chloramphenicol palmitate)	
	Surgical sutures (Depending on number of tests to be carried)	200-500
	Other miscellaneous tests	100-500
II	*Fees for Sera and Vaccine* –	
	Sterility test	100
	Abnormal toxicity test	400

Specific toxicity test	800
Inactivation test (Rabies)	200
Potency testing of rabies vaccine	2025
Potency testing of pertussis fraction of DPT vaccine	2025
Potency testing of tetanus fraction of DPT/DT/TT vaccine	2500
Potency testing of diphtheria Fraction of DPT/DTE vaccine.	2700
Testing of antisera for the specific titre	1000
Potency testing measles/Mumps/Rubella vaccine 760 each	
Testing of Oral Polio Vaccine (OPV) –	
Potency	4550
Identity	1000
Stability	800
Potency testing of Japanese Encephalitis Vaccine	3900
Potency testing of Snake	400
Venom serum	for each venom
Identity testing for vaccines/sera	
Cell culture (Other than OPV)	400
Other than cell culture	100

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Estimation of volume/pH/total solids/No. of organisms/Physical checking.	50 each
Estimation of total proteins/aluminium content/phenol/formaldehyde/thiomersal/moisture.	200 each
Pyrogen testing	500 Stability
test for vaccines other than Oral Polio Vaccine	4550
III *Cosmetics*	400 – 1500
(The exact amount of the fee shall be determined by the Director of Laboratory or the Government Analyst, as the case may be).	
IV *Rubber Condoms*	
	1000 IV
Homoeopathic medicines:	
1. Identification test for raw material of botanical origin (other than assay of constituents).	125
2. Identification test for raw material of chemical origin (other than assay)	100
3. Limit test for drugs of chemical origin	150 4.
Assay of total alkaloids or of drugs of chemical origin	100 5.
Identification test for drugs of animal origins or microbiological.	100
6. Fees for testing of Mother tincture, lower potencies upto 3x or equivalent.	100
7. U.V. or I.R. or H.P.C.L. defect determination	75
Determination of Biochemic drug through atomic absorbance spectrophotometer.	75

Note :-

1. For tests not listed in the Schedule, charges will be determined by the Director or the Government Analyst of the laboratory / institute as the case may be.

2. For the tests relating to Ayurvedic, Unani and Siddha medicines, charges will be determined by the Adviser (Indigenous System of Medicine), Director or Government Analyst of the Laboratory / Institute, as the cased may be.]

1. Subs by G.S.R. 478 (E), dt:7.8.1998.

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1945

[1][SCHEDULE B(1)

(See rules 163F)

FEES FOR THE TEST OR ANALYSIS BY THE PHARMACOPOEIAL LABORATORY FOR INDIAN MEDICINE (PLIM) OR THE GOVERNMENT ANALYST

	Type of testing/analysis	Cost of testing or analysis in Rupees
	(1)	(2)
1.	Test for sterlity	250.00
2.	Abnormal toxicity or undue toxicity or safety test	750.00
3.	Determination of lethal does LD 50 to 10 on mice	2500.00
4.	Chemical test for each ingredient	500.00
5.	Disinfectants	1000.00
6.	Any other test requiring animal experimentation	500.00
7.	Microbiological assay	750.00
8.	Microscopic examination of single drugs	250.00
9.	Microscopic examination of raw material of compound drug	500.00
10.	Chemical identification as per Pharmacopoeia	250.00
11.	Disintegration of tablets and capsules (a) ordinary (b) sugar coated (c) enteric coated	 100.00 200.00 400.00
12.	Psysiochemical Assays	300.00
13.	Test other than assay (limit tests for impurities, ash content, total solids, acid value, saponification value, loss on drying etc.) for each test.	100.00
14.	Optical rotation	250.00
15.	Refractive index	250.00
16.	Arsenic testing	250.00
17.	Paper chromatography	250.00
18.	Thin layer chromatography	300.00
19.	Column chromatography	2500.00
20.	Gas liquid chromatography	1000.00
21.	HPTLC restricted to single drugs qualitative	1000.00
22.	Atomical absorption spectrophotometry for Hg, Pb, As, Cd	500.00
23.	Cosmetics/ tails/ creams	500.00
24.	Identification test for raw material of plant origin (other than assay of constitutents)	125.00
25.	Identification test for raw material of chemical origin (other than assay)	100.00
26.	Limit test for drug of chemical origin	150.00
27.	Other miscellaneous tests	1000.00

Note: Sample testing charges will be determined / revised by the Director or Government Analyst of the Pharmacopoeial laboratory for Indian Medicine, as the case may be, in consultation with the Department of Ayurveda, Yoga, Unani, Siddha and Homoeopathy, Ministry of Health and Family Welfare.

[1][SCHEDULE C

(See rules 23, 61 and 76 and Part X)

Biological and Special Products

1. Sera.
2. Solution of serum proteins intended for injection.
[2][3. Vaccines for parenteral injections.
4. Toxins.
5. Antigen.
6. Antitoxins.
7. Neo-arsphenamine and analogous substances used for the specific treatment of infective diseases.
8. Insulin.
9. Pituitary (Posterior Lobe) Extract.
10. Adrenaline and Solutions of Salts of Adrenaline.
[3][11. Antibiotics and preparations thereof in a form to be administered parenterally.] [4][12 Any other preparation which is meant for parenteral administration as such or after being made up with a solvent or medium or any other sterile product and which-
(a) requires to be stored in a refrigerator; or
(b) does not require to be stored in a refrigerator.]
13. Sterilized surgical ligature and sterilized surgical suture.
[2][14. Bacteriophages.
[5][15 Ophthalmic preparations.]
[6][16 Sterile Disposable Devices for single use only.]

1. Amended by Notfn. No. F. 1-30/47-A, dt. 5-1-1950
2. Amended by Notfn. No. F. 1-8/60-D, dt. 31-8-1960
3. Subs. by No. G.S.R. 487(E) ,dt. 2.7.1984.
4. Amended by Notfn. No. F. 1-14/68-D, dt. 26-10-1968
5. Ins. by Notfn. No. G.S.R. 1242(E) ,dt. 17.9.1979
6. Ins. by Notfn. No. G.S.R. 109(E) ,dt. 22.2.1994.

[1][SCHEDULE C (1)

(*See* Rule 23, 61 and 76)

Other Special Products

1 Drugs belonging to the Digitalis group and preparations containing drugs belonging to the Digitals group not in a form to be administered parenterally.

2 Ergot and preparations containing Ergot not in a form to be administered parenterally.

3 Adrenaline and preparations containing Adrenaline not in a form to be administered parenterally.

4 Fish Liver Oil and preparations containing Fish Liver Oil.

5 Vitamins and preparations containing any vitamins not in a form to be administered parenterally.

6 Liver extract and preparations containing liver extract not in a form to be administered parenterally.

7 Hormones and preparations containing Hormones not in a form to be administered parenterally.

8 Vaccine not in a form to be administered parenterally.

[2][9. Antibiotics and preparations thereof not in a form to be administered parenterally.]

[3][10. In-vitro Blood Grouping Sera.

11. In-vitro Diagnostic Devices for HIV, HbsAg and HCV.]

1. Amended by. Notfn. No. F. 1-22/59-D, dt. 9-4-1960
2. Subs. by.G.S.R.487(E) ,dt. 2-7-1984.
3. Ins. By G.S.R. 601(E), dt. 27.8.2002.

SCHEDULE
D

[*See* Rule 43]

Class of drugs	Extent and conditions of exemption
1. Substances not intended for medicinal use	All provisions of Chapter III of the Act and rules thereunder subject to the condition that if the substance is imported in bulk, the importer shall certify that the substance is imported for non-medicinal uses, and if imported otherwise than in bulk, each container shall bear a label indicating that the substance is not intended for medicinal use or is of commercial quality. [1][Further, permission from licensing authority as defined in clause (b) of rule 21 has to be obtained for import of the substance for non-medicinal use without registration and import license.]
[2][***]	
[3][***]	
[4][5. The following substances, which are used both as articles of food as well as drugs:- (i) All condensed or powdered milk whether pure, skimmed or malted, fortified with vitamins and minerals. (ii) Farex, Oats, Lactose and all other similar cereal preparations whether fortified with vitamins or otherwise excepting those for parenteral use. (iii) Virol, Bovril, Chicken essence and all other similar predigested foods. (iv) Ginger, Pepper, Cumin, Cinnamon and all other similar spices and condiments unless they are specifically labelled as conforming to the standards in the [5][Indian Pharmacopoeia or the official pharmacopoeias and the official compendia of the drug standards prescribed under the Act and rules made thereunder].	All provisions of Chapter III of the Act and rules thereunder.

1. Ins. By G.S.R 724 (E), dt:7-11-2013.

2. Serial no 2, 3, omitted by Notfn. No. F-1-6/62-D (S.O.2889), dt: 2-7-1969.

3. Serial no 4, omitted by G.S.R.604 (E) ,dt. 24-8-2001
4. Amended by Notfn. F. 1-53/55-D, dt. 7.1.1957.
5.Amended by G.S.R. 19, dt: 15-12-1977.

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Class of drugs	Extent and conditions of exemption
[1][6. Drugs and cosmetics imported for manufacture and export by units situated in ―Special Economic Zones‖ as notified by the Government of India	The provisions of Chapter III of the Act and rules thereunder which required them to be covered by an import licence, import registration and import through notified port of entry, subject to the conditions that these drugs and cosmetics shall not be diverted for sale in the country: Provided that such imported drugs and cosmetics may be permitted to the domestic area if they meet the requirements of standard procedure for import and registration as required under Chapter III of the Act and rules thereunder. from time to time.
[2][7. Custom Made Devices	All provisions of Chapter III of the Act and the rules made thereunder, subject to the condition that the device is specifically made in accordance with a duly qualified medical practitioner‘s written prescription under his responsibility, in accordance with specific design characteristics and is intended for the sole use of a particular patient and the label should bear the word ―custom made device.‖ Explanation.—Mass produced devices which only need adoption to meet the specific requirements of the medical practitioner or any other professional user shall not be considered to be custom made devices.]

1. Ins. by G.S.R. 528(E), dt. 8.7.2003.
2. Ins. By G.S.R 690 (E) dated 25-09-2014.

Drugs and Cosmetics Rules 1945

[1][SCHEDULE D(I)

(*See* rule 21 (d) and rule 24 A)

Information and undertaking required to be submitted by the manufacturer or his authorized agent with the Application Form for a Registration Certificate. The format shall be properly filled in for each application in

Form 40. The detailed information, secret in nature, may be furnished on a Computer Floppy.

1. *Particulars of the manufacturer and manufacturing premises*

1.1 Name and address of the manufacturing premises (Telephone No., Fax No., E-mail address) to be registered.

1.2 Name(s) and address(es) of the Proprietor /Partners / Directors.

1.3 Name and address of the authorized Agent in India, responsible for the business of the manufacturer.

1.4 A brief profile of the manufacturer's business activity, in domestic as well as global market.

1.5 A copy of Plant Master File (duly notarised)

1.6 A copy of Plant Registration / approval Certificate issued by the Ministry of Health/National Regulatory Authority of the foreign country concerned (duly notarised)

1.7 A brief profile of the manufacturer's research activity.

2. *Particulars of the manufactured drugs to be registered under Registration Certificate.*

2.1 Names of drugs (Bulk/Formulation/Special product) to be registered meant for import into and use in India.

2.2 A copy of the approved list showing the bulk drugs/formulations/special products mentioned in 2.1 above are permitted for manufacturing / marketing in the country of origin (duly notarized).

2.3 [2][A copy of Good Manufacturing Practice (GMP) certificate as per WHO – GMP guidelines or Certificate of Pharmaceutical Products (CPP) or written confirmation for active substances exported to European Union which is equivalent to GMP certificate issued as per WHO – GMP guidelines, by the National Regulatory Authority of the country of origin or a copy of the certificate equivalent to GMP certificate as per WHO GMP guidelines issued by National Regulator of United States of America or Japan or Australia or Canada or the European Union for the purpose of marketing of the drugs in their country, in relation to bulk drugs or formulations or special product meant for import into India.]

2.4 The domestic prices of the drugs to be registered in India, in the currency of the country of origin.

2.5 The name(s) of the drug(s) which are original research products of the manufacturer.

1. Ins. by G.S.R. No.604(E) , dt. 24-8-2001 (w.e.f. 1-1-2003). 2. Subs. by G.S.R. No. 897(E) , dt. 21-9-2016.

3. *Undertaking to declare that: -*

3.1. We shall comply with all the conditions imposed on the Registration Certificate, read with rules 74 and 78 of the Drugs and Cosmetics rules, 1945.

3.2 We declare that we are carrying on the manufacture of the drugs mentioned in this Schedule, at the premises specified above, and we shall from time to time report any change of premises on which manufacture will be carried on and in cases where manufacture is carried on in more than one factory any change in the distribution of functions between the factories.

3.3 We shall comply with the provisions of Part IX of the Drugs and Cosmetics Rules, 1945.

3.4 Every drug manufactured by us for import under the Registration Certificate into India shall be as regard strength, quality and purity conforms with the provisions of Chapter III of Drugs and Cosmetics Act, 1940 and Part IV of the Drugs and Cosmetics Rules 1945, and their amendments from time to time.

3.5 We shall from time to time report for any change or manufacturing process, or in packaging, or in labelling, or in testing, or in documentation of any of the drugs, pertaining to the Registration Certificate, to be granted to us. Where any change in respect of any of the drugs under the Registration Certificate has taken place, in respect of any of the above matters, we shall inform the same to the licensing authority in writing within 30 days from the date of such changes. In such cases, where there will be any major change/modification in manufacturing or in processing or in testing, or in documentation, as the case may be, at the discretion of the licensing authority, we shall obtain necessary approval within 30 days by submitting a separate application, alongwith the registration fee as specified in clause (ii) of sub rule (3) of rule 24-A.

3.6 We shall from time to time report for any administrative action taken due to adverse reaction, viz. market withdrawal regulatory restriction, or cancellation of authorization and/or ―not of standard quality report‖ of any drug pertaining to the Registration Certificate declared by any Regulatory Authority of any country where the drug is marketed/sold or distributed. The despatch and marketing of the drug in such cases, shall be stopped immediately and the licensing authority shall be informed immediately. Further action in respect of stop marketing of drug shall be taken as per the directions of the licensing authority. In such cases, action equivalent to that taken with reference to the concerned drug(s) in the country of origin or in the country of marketing will be followed in India also, in consultation with the licensing authority. The licensing authority may direct any further modification to this course of action, including the withdrawal of the drug from Indian market within 48 hours time period.

3.7 We shall comply with such further requirements, if any, as may be specified, by the Government of India, under the Act and the rules made there under.

3.8 We shall allow the licensing authority and/or any person authorized by him in that behalf to enter and inspect the manufacturing premises and to examine the process/procedure and documents in respect of any drug manufactured by us for which the application for Registration Certificate has been made.

3.9 We shall allow the licensing authority or any person authorized by him in that behalf to take samples of the drugs concerned for test, analysis or examination, if considered necessary by the licensing authority.

Place:
Date:

Signature of the manufacturer
[1] [*or his authorized agent*]
Seal / Stamp

1. Ins. by G.S.R. 35(E), dt. 20.1.2005.

SCHEDULE D(II)

[*See* rule 21 (d) and rule 24 A]

Information required to be submitted by the manufacturer or his authorized agent with the Application Form for the registration of a bulk drug/formulation/special product for its import into India.

The format shall be properly filled in and the detailed information, secret in nature, may be furnished on a Computer Floppy

1. GENERAL

1.1. Name of the drug/formulation/special product, a brief description and the therapeutic class to which it belongs.

1.2 Regulatory status of the drug. Free Sale Certificate and/or Certificate of Pharmaceutical Products (CPP) issued by the Regulatory Authority of the country of origin. Free sale approval issued by the Regulatory Authorities of other major countries.

1.3 Drugs Master File (DMF) for the drug to be registered (duly notarised).

1.4 [1][GMP certificate as per WHO-GMP format, or Certificate of Pharmaceutical Products (CPP), or written confirmation for active substances exported to the European Union which is equivalent to GMP certificate issued as per WHO – GMP guidelines, by the National Regulatory Authority of the country of origin or a duly notarised copy of the certificate equivalent to GMP certificate as per WHO-GMP guidelines issued by United States of America or Japan or Australia or Canada or the European Union for the purpose of marketing of the drug in their country.]

1.5 List of countries where marketing authorization or import permission for the said drug is granted with date (respective authorisation shall be enclosed).

1.6 List of countries where marketing authorisation or import permission for the said drug is cancelled/withdrawn with date.

1.7 List of countries where marketing authorisation or import permission for the said drug is pending since (date).

1.8 Domestic price of the drug in the currency followed in the country of origin.

1.9 List of countries where the said drug is patented.

2. CHEMICAL AND PHARMACEUTICAL INFORMATION OF DRUGS.

2.1 Chemical name.

Code name or number, if any.

Non-proprietary or generic name, if any.

Structure.

Physico-chemical properties.

2.2 Dosage form and its composition.

Qualitative and Quantitative composition in terms of the active substances(s) and excipient(s). List of active substance(s) separately from the constituent(s) of excipients.

2.3 Specifications of active and inactive ingredient (s) including pharmacopoeial references.

2.4 Source of active ingredient(s), name and address.

2.5 Tests for identification of the active ingredient(s),

Method of its assays and tests for impurity profile with reference standards for the impurities (Protocol to be submitted alongwith reference standards for the impurities / relative substances).

2.6 Outline method and flow chart of manufacture of the bulk drug or finished formulation or special product.

2.7 Detailed test protocol for the drug with pharmacopoeial reference or in- house specification as approved by the registration authority, in the country of origin.

2.8 Stability data including accelerated stability and real time stability analysis.

1. Subs. by G.S.R. 897 (E), dt. 21.9.2016.

2.9 Documentation on pack size.

2.10 Numerical expression on EAN bar code on the labels and cartons,

2.11 Safety documents on containers and closures.

2.12 Documentation on storage conditions.

2.13 Three samples of medicinal product/drug and outlet packing are to be submitted with batch certificates. Additional samples as well as reference substances with batch certificates including date of manufacture, shelf life, and storage conditions of reference substance may be required both during registration procedure and during validity of registration decision.

2.14 Batch test reports/certificate of five consecutive production batches in details of the medicinal product are to be submitted for every site of manufacturing premises.

2.15 Manner of labelling as per rule 96 of the Drugs and Cosmetics Rules 1945.

2.16 Package insert.

2.17 Details of safety handling procedure of the drug.

2.18 Details of PMS study report for marketing period not exceeding five years.

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3. BIOLOGICAL AND BIOPHARMACEUTICAL INFORMATION OF DRUGS

3.1 Biological control tests applied on the starting material, if applicable.

3.2 Biological control tests applied on the intermediate products, if applicable. 3.3 Biological control tests applied on the finished medical products, if applicable. 3.4 Stability of the finished products in terms of biological potency of the drug, if applicable.

3.5 Sterility tests, if applicable, specification and protocol therein.

3.6 Pyrogen tests, if applicable, specification and protocol therein.

3.7 Acute and sub-acute toxicity tests, if applicable specification and protocol therein.

3.8 Bio-availability studies and bio-equivalence data, if applicable.

3.9 Data relating to the environmental risk assessment for r-DNA products.

3.10 Other information relevant under the section.

4. PHARMACOLOGICAL AND TOXICOLOGICAL INFORMATION OF DRUGS.

Executive summary of the product is to be submitted mentioning the specific and general pharmacological actions of the drug and pharmacokinetic studies on absorption, metabolism, distribution and excretion. A separate note is to be given on acute and sub-acute toxicity studies and long term toxicity studies. Specific studies on reproductive toxicity, local toxicity and carcinogenic activity of the drug is to be elaborated, as far as possible.

5 CLINICAL DOCUMENTATION

A new drug as defined under rule 122-E of the Drugs and Cosmetics Rules, 1945 is required to be permitted separately by the licensing authority under rule 122-A of the said rules prior to its registration. Such a new drug requires a brief summary and clinical documentation, alongwith permission under 122-A of the said rules for its Registration Certificate.

6. LABELLING AND PACKAGING INFORMATION OF DRUGS.

6.1 Labels should conform as per the specifications under the Drugs and Cosmetics

Rules 1945.

6.2 Package insert should be in English and shall indicate the following therapeutic indications: -

Posology and method of administration.

Contra-indications.
Special warnings and special precautions for use, if any.
Interaction with other medicaments and other forms of interaction.
Pregnancy and lactation, if contra-indicated.
Effects on ability to drive and use machines, if contra-indicated.
Undesirable effects/side effects.
Antidote for overdosing.

6.3 Package insert should indicate the following pharmaceutical information: -

List of excipients.
Incompatibilities.
Shelf life in the medical product as packaged for sale.
Shelf life after dilution or reconstitution according to direction.
Shelf life after first opening the container.
Special precautions for storage.
Nature and specification of the container.
Instructions for use/handling.

7 SPECIFIC INFORMATION REQUIRED FOR THE SPECIAL PRODUCTS (to be supplied, separately in Annexures, as _A', _B' and _C')

The information submitted above is true to the best of my knowledge and belief.

Place:
Date :

Signature of the manufacturer
[1] [*or his authorized agent*]
Seal/Stamp

NB: 1. Any change in the process of manufacture, method of testing, labelling, packaging, designing of the sale pack, medical literature and documentation is to be intimated to the licensing authority forthwith and permission to be obtained from him within 30 days time period.

2. Information relating to Serial No.4 and Serial No.5 are not applicable for drugs figuring in Indian Pharmacopoeia and also for the drugs figuring in United States of Pharmacopoeia, European Pharmacopoeia, and British Pharmacopoeia provided such drugs have already been approved for marketing in India for the applicant under rules 122A, 122B, 122C or 122D of the Drugs and Cosmetics Rules 1945.

1.Ins. by G.S.R. 35(E), dt. 20.1.2005.

Drugs and Cosmetics Rules 1945

ANNEXURE A

(*See* Schedule D-II, item No.7)

INFORMATION TO BE SUBMITTED IN SCHEDULE D-II

SPECIFIC INFORMATION REQUIRED FOR THE BLOOD PRODUCTS

A product dossier showing the:

1. Details of source Plasma, its viral screening, storage and transport from Collection Centres to Fractionation Centre. Regulatory status of Collection Centres.

2. Details of Fractionation Centre, Regulatory Status, Method of Fractionation and Control Processes.

3. Details of viral inactivation process for enveloped and non-enveloped virus(es) and viral validation studies to assess the viral load of the product. Testing of viral screening at any stage is to be highlighted with the details of the kits used with their respective sensitivity and specificity.

4. Bulk filtration prior to pharmaceutical packing giving the full details of Micro-filtration or nanofiltration followed.
5. Complete details of pharmaceutical processing and utilization.
6. Test protocol of the product showing the specifications and pharmacopoeial method followed for various testing parameters.

   Specific batch test report for at least 3 batches showing the specifications of each testing parameter.
7. Pack size and labelling.
8. Product insert.
9 Specimen Batch Release Certificate issued by the National Regulatory Authority of the country of origin.

   Specific processings like safe handling, material control, area control, pasteurization, stability studies, storage at quarantine stage and finished stage and packaging should be highlighted in the product dossier.

The information submitted above is true to the best of my knowledge and belief.

Place:
Date:

Signature of the manufacturer
Seal / Stamp

NB: 1. Any change in the process of manufacture, method of testing, labelling, packaging, designing of the sale pack, medical literature and documentation is to be intimated to the licensing authority forthwith and permission to be obtained from him within 30 days time period.

Drugs and Cosmetics Rules 1945

ANNEXURE-B

(*See* Schedule D-II, item No.7)

INFORMATION TO BE SUBMITTED IN SCHEDULE D-II SPECIFIC INFORMATION REQUIRED FOR THE DIAGNOSTIC KITS

A Product dossier showing the :

1. The details of source antigen or antibody as the case may be and characterization of the same. Process control of coating of antigen or antibody on the base material like Nitrocellulose paper, strips or cards or ELISA wells etc.

   Detailed composition of the kit and manufacturing flow chart process of the kit showing the specific flow diagram of individual components or source of the individual components.

2. Test protocol of the kit showing the specifications and method of testing. In house evaluation report of sensitivity, specificity and stability studies carried out by the manufacturer.

3. The report of evaluation in details conducted by the National Control Authority of country of origin.

   Specimen batch test report for at least consecutive 3 batches showing specification of each testing parameter.

4. The detailed test report of all the components used/packed in the finished kit.

5. Pack size and labelling.

6. Product insert.

Specific evaluation report, if done by any laboratory in India, showing the sensitivity and specificity of the kit.

Specific processing like safe handling, material control, area control, process control, stability studies, storage at quarantine stage and finished stage, packaging should be highlighted in the product dossier.

The information submitted above is true to the best of my knowledge and belief.

Place:
Date:

Signature of the manufacturer
Seal / Stamp

NB: 1.Any change in the process of manufacture, method of testing, labelling, packaging, designing of the sale pack, medical literature and documentation is to be intimated to the licensing authority forthwith and permission to be obtained from him within 30 days time period.

Drugs and Cosmetics Rules 1945

ANNEXURE-C

(*See* Schedule D-II, item No.7)

INFORMATION TO BE SUBMITTED IN SCHEDULE D-II

SPECIFIC INFORMATION REQUIRED FOR VACCINES

A Product dossier showing the:

1. History, source, date of receipt, storage, identity and characterization of the seed strain.
2. Detailed flow chart of manufacturing process showing all the details of in-process control on toxicity, potency study and stability data of the final bulk and the final finished product including the storage temperature.
3. Complete details of chemical and pharmaceutical data for the product.

   Composition and dosage form – method of manufacture with detailed flow chart – control of starting material – control tests on intermediate and finished products – certificate of analysis of finished products – validation of critical manufacturing steps.
4. Test protocol of the vaccines showing the specification and method of testing including pharmacopoeial specification.
5. Specimen batch test report for at least consecutive three batches showing the specification of each testing parameter.
6. The detailed test reports of all the components used / packed in the finished vaccine.
7. Pack-size and labelling.
8. Product insert
9. Specimen batch release certificates issued by the National Regulatory Authority of the country of origin.
10. Summary of pre-clinical and clinical data including :
    (a) Prescribing information.
    (b) Pharmacological and toxicological data pertaining to tests on animals Characterisation of immuno response and safety study in human use, in specific conditions.

Specific information on source of seed strain, its characterization, inactivation, etc. and processings like safe handling, material control, area control, process control, stability studies, storage at quarantine stage and finished state, packaging should be highlighted in the product dossier.

Specimen production and quality control protocols for at least three consecutive lots showing the specifications for each quality control parameter including pharmacopoeial requirement shall be submitted for study.

The information submitted above is true to the best of my knowledge and belief.

Place:

Date:

Signature of the manufacturer
Seal / Stamp

NB: 1. Any change in the process of manufacture, method of testing, labelling, packaging, designing of the sale pack, medical literature and documentation is to be intimated to the licensing authority forthwith and permission to be obtained from him within 30 days time period.

2. All vaccines shall be new drugs unless certified otherwise by the liencesing authority approved under rule 21 of the Drugs and Cosmetic Rules, 1945. A copy of approval of the vaccine issued by the said licensing authority is to be enclosed, prior to issue of Registration Certificate of the said vaccines.

[1][SCHEDULE D (III)

(See rule 129 A)

INFORMATION AND UNDERTAKING REQUIRED TO BE SUBMITiED BY THE MANUFACTURER OR HIS AUTHORISED IMPORTER/DISTRIBUTOR/AGENT WITH THE APPLICATION FORM FOR A REGISTRATION CERTIFICATE.

(The format shall be properly filled in for each application in

form 42)

1. PARTICULARS OF THE MANUFACTURER AND MANUFACTURING PREMISES.-

(a)Name and address of the manufacturer and manufacturing premises to be registered along with telephone numbers, Fax numbers and e-mail address.

(b)Name(s) and address of the Partners/Directors.

(c)Name and address of the authorised importer/distributor/agent in India, responsible for the business of the manufacturer.

(d)A brief profile of the manufacturer 's business activity, in domestic as well as global market. **2. PARTICULARS OF THE COSMETICS TO B E RE G IST E RED UNDER REGISTRATION CERTIFICATE.-**

(a)Names of cosmetics along with their brands name, category, pack sizes and variants to be registered and meant for import into and use in India.

(b)Particulars of the manufacturing licenses/registration/marketing authorizations (if any) under which the cosmetics are being manufactured in the country of origin along with the copy of the licenses/ marketing authorization/registration issued by the Regulatory Authority of that country.

(c)List of countries where marketing authorization or import permission for the said cosmetic has been granted.

3. CHEMICAL INFORMATION OF COSMETICS.-

(a)Name(s) of ingredients in the nomenclature of standard references, along with percentages contained in the cosmetic.

(b)Specification and testing method for testing of the cosmetic(s).

(c)Manner of labelling as per Drugs and Cosmetics Rules, 1945.

(d)Package insert (if any).

4. UNDERTAKINGTO DECLARETHAT.-

(a)We shall comply with all the conditions imposed on the Registration Certificate for the import of cosmetics as required under the provisions of Drugs and Cosmetics rules, 1945.

(b)We declare that we are carrying on the manufacture of the cosmetics mentioned in this Schedule, at the premises specified above, and we shall from time to time report any change of premises on which manufacture will be carried on and in cases where manufacture is carried on in more than one factory any change in the distribution of functions between the factories.

(c)We shall comply with the provisions of Part XIII of the Drugs and Cosmetics Rules, 1945.

(d)Every cosmetic manufactured by us for import under the Registration Certificate into India shall conform to the specifications given in the Drugs & Cosmetics Rules, 1945 as amended from time to time.

(e)We shall inform to the licensing authority, within 30 days in the event of any change in variants or in category or in manufacturing location or in labelling or in documentation of any of the cosmetic pertaining to the certificate to be granted to us.

1. Ins. By G.S.R. 426 (E) dated 19-05-2010, read with corrigendum G.S.R. 263(E) dated 30-05-2011, corrigendum G.S.R. dated 29-09-2011, corrigendum G.S.R. 270(E) dated 30-03-2012 and corrigendum G.S.R. 733(E), dated 29-09-2012.

(f)We shall from time to time report for any administrative action taken due to adverse reaction, viz. market withdrawals/regulatory restriction, or cancellation of authorisation and/or ―not of standard quality report‖ of any cosmetic pertaining to the Registration Certificate declared by any Regulatory Authority of any country where the cosmetic is marketed/sold or distributed. The despatch and marketing of the cosmetic in such cases, shall be stopped and the licensing authority shall be informed immediately.

(g)We shall comply with such further requirements, if any, as may be specified, by the Government of India, under the Act and the Rules, made thereunder.

(h)We shall allow the licensing authority or any person authorised by him in that behalf to take samples of the cosmetics for testing if considered necessary by the licensing authority.

The information submitted above is true to the best of my/our knowledge and belief.

Place:
Date:

Signature of the manufacturer or his authorized agent
Seal/Stamp.

[1][***]

2[SCHEDULE E(1)

[See rule 161 (2)]

List of poisonous substances under the Ayurvedic (including Siddha) and Unani Systems of Medicine

A. AYURVEDIC SYSTEM

I	*Drugs of vegetable origin*	
1	Ahipena (Except seeds)	*Papaver somniferum* Linn.
2	Arka	*Calotropis procera* (Ait.)R.Br. ex.
3	Bhallataka	*Semecarpus anacardium* Linn. F.
4	Bhanga (Except seeds)	*Cannabis sativa* Linn. (Except seeds)
5	Danti	*Baliospermum montanum* Mull. Arg.
6	Dhattura	*Datura metal* Linn..
7	Gunja (seed)	*Abrus precatorium* Linn. (seed)
8	Jaipala (seed)	*Croton tiglium* Linn.
9	Karaveera	*Rerium indicum* Mill.
10	Langali	*Gloriosa superba* Linn.
11	Parasika Yavani	*Hyoscyamus niger* Linn.
12	Vatsanabha	*Acontium chasmanthum* Stapf ex Holm.
	Vishamushti	*Strychnox nuxvomica* Linn.
13	Shringivisha	*Acontium chasmanthum* Stapf ex Holm.
II	*Drugs of Animal Origin*.	
14	Sarpa Visha	Snake poison.
III	*Drugs of Mineral Origin*	
15	Gauripashana Arsenic.	
16	Hartala	Arseno sulphide.
17	Manahashila	Arseno sulphide.
18	Parada Mercury.	
19	Rasa Karpura Hydrargyri subchloridum.	
20	Tuttha Copper sulphate.	
21	Hingula Cinnabar.	

1 —Schedule E‖ omitted No.G.S.R. 462(E),dt 22-6-1982.

2. Subs. By G.S.R. 683(E) dated 19-08-2010.

B. SIDDHA SYSTEM

1.	Abini	*Papaver somniferum* Linn.
2.	Alari	*Nerium indicum* Mill.
3.	Attru thummatti	Citrullus colocynthis (L.) Schrad
4.	Umathai	Datura stramonium Linn.
5.	Etti	Stychnos nux vomica Linn.
6.	Ganja (except seed)	Cannabis sativa Linn.
7.	Kalappaki Kizahangu	Glorisa superba Linn.
8.	Kodikkalli (exempted for external use)	Euphorbia tirucalli Linn.
9.	Kattu Thumatti	Cucumis trigonus Roxb.

10	Kunri (except root)	Arbus precatorius Linn.
11.	Cheramkottai	Semecarpus anacardium Linn f.
12.	Thillai	Exoecoria agallocha Linn.
13.	Nabi	Aconitum ferox Wall.
14.	Nervalam	Croton tiglium Linn.
15.	Pugaielai	Nicotiana tabacum Linn.
16.	Mancevikkalli	Euphorbia species

C. UNANI SYSTEM

I *Drugs of vegetable origin*

1.	Afiyun (except seed)	*Papaver somniferum* Linn.
2.	Bazrul-banj	*Hyoscyamus niger* Linn.
3.	Bish	*Aconitum chasmanthum* Strapfex Holmes.
4.	Bhang	*Cannabis sativa* Linn.
5.	Charas	*Canabis sativa* Linn.
6.	Dhatura seeds	*Datura metal* Linn (seeds).
7.	Kuchla	
8.	Shokran	*Strychnos nuxvomica* Linn.
		Conium maculatum Linn.

II *Drugs of Animal origin*

9. Sanp (head)	Snake (head).
10.Telni makkhi	*Mylabris cichori* Linn.
	Mylabaris pustulata Thund.
	Mylabris macilenta .

III *Drugs of Mineral origin*

1. Darchikna	Hydrargryi perchloridum.
2. Hira Diamond.	
3. Ras Kapoor	Hydrargryi Subchloridum (calomel).
4. Shingruf	Hydrargryi bisulphuratum.
5. Zangar	Cupri subacetas.
6. Sammul-Far	(Abyaz, Asfar, Aswad and Ahmar) (white, yellow, black and red, Arsenic).
7. Tootiya	Copper Sulphate
8. Para	Hydrargyrum.
9. Hartal	Arsenic trisulphide (yellow).]

SCHEDULE F

(See rule 78 and Part X)

[1][***]

[2][PART XII B

REQUIREMENTS FOR THE FUNCTIONING AND OPERATION OF A BLOOD BANK AND / OR FOR PREPARATION OF BLOOD COMPONENTS.

I. BLOOD BANKS / BLOOD COMPONENTS

A. GENERAL

1. *Location and Surroundings* : The blood bank shall be located at a place which shall be away from open sewage, drain, public lavatory or similar unhygienic surroundings.
2. *Building* : The building (s) used for operation of a blood bank and/or preparation of blood components shall be constructed in such a manner so as to permit the operation of the blood bank and preparation of blood components under hygienic conditions and shall avoid the entry of insects, rodents and flies. It shall be well lighted, ventilated and screened (mesh), wherever necessary. The walls and floors of the rooms, where collection of blood or preparation of blood components or blood products is carried out shall be smooth, washable and capable of being kept clean. Drains shall be of adequate size and where connected directly to a sewer, shall be equipped with traps to prevent back siphonage.
3. *Health, clothing and sanitation of staff:* The employees shall be free from contagious or infectious diseases. They shall be provided with clean overalls, head-gears, foot-wears and gloves, wherever required. There shall be adequate, clean and convenient hand washing and toilet facilities.

B. ACCOMMODATION FOR A BLOOD BANK.

A blood bank shall have an area of 100 square meters for its operations and an additional area of 50 square meters for preparation of blood components. It shall be consisting of a room each for –

(1) registration and medical examination with adequate furniture and facilities for registration and selection of donors;

(2) blood collection (air-conditioned);

1. Part I to Part XIIA omitted by G.S.R. 663 (E), dated 03-07-1992 corrected vide corrigendum G.S.R. 27(E) dated 22-01-1993.

2. Part XIIB and Part XIIC, were sub. By G.S.R. 245 (E) dated 05-04-1999, previously Part XIIB and XIIC, were substituted for Part XIIB by G.S.R. 28(E) dated 22-01-1992 and before that Part XIIB was added by notification number F 1-17/67-D, 24-06-1967.

(3) blood component preparation. (This shall be air-conditioned to maintain temperature between 20 degree centigrade to 25 degree centigrade);

(4) laboratory for blood group serology (air-conditioned);

(5) laboratory for blood transmissible diseases like Hepatitis, Syphilis, Malaria, HIV-antibodies (air-conditioned);

(6) sterilization-cum-washing;

(7) refreshment-cum-rest room (air-conditioned);

(8) store-cum-records.

NOTES :

(1) The above requirements as to accommodation and area may be relaxed, in respect of testing laboratories and sterilization-cum-washing room, for reasons to be recorded in writing by the Licensing Authority and/or the Central Licence Approving Authority, in respect of blood banks operating in hospitals, provided the hospital concerned has a pathological laboratory and a sterilization-cum-washing room common with other departments in the said hospital.

(2) Refreshments to the donor after phlebotomy shall be served so that he is kept under observation in the blood bank.

C PERSONNEL

Every blood bank shall have following categories of whole time competent technical staff:-

(a) Medical Officer, possessing the qualifications specified in condition (i) of rule 122-G.

(b) Blood Bank Technician(s) possessing –

(i) Degree in Medical Laboratory Technology (M.L.T) with six months' experience in the testing of blood and/or its components; or

(ii) Diploma in Medical Laboratory Technology (M.L.T) with one year's experience in the testing of blood and / or its components, the degree or diploma being from a University / Institution recognized by the Central Government or State Government.

(c) Registered Nurse(s);

(d) Technical supervisor (where blood components are manufactured), possessing- (i) Degree in Medical Laboratory Technology (M.L.T) with six months' experience in the preparation of blood components; or

(ii) Diploma in Medical Laboratory Technology (M.L.T) with one year's experience in the preparation of blood components,

the degree or diploma being from a University / Institution recognized by the Central Government or State Government.

Drugs and Cosmetics Rules 1945

NOTES :

(1) The requirements of qualification and experience in respect of Technical Supervisor and Blood Bank Technician shall apply in the cases of persons who are approved by the Licensing Authority and/or Central Licence Approving Authority after the commencement of the Drugs and Cosmetics (Amendment) Rules, 1999*.

(2) As regards, the number of whole time competent technical personnel, the blood bank shall comply with the requirements laid down in the Directorate General of Health Services Manual.

(3) It shall be the responsibility of the licensee to ensure through maintenance of records and other latest techniques used in blood banking system that the personnel involved in blood banking activities for collection, storage, testing and distribution are adequately trained in the current Good Manufacturing Practices/Standard Operating Procedures for the tasks undertaken by each personnel. The personnel shall be made aware of the principles of Good Manufacturing Practices / Standard Operating Procedures that affect them and receive initial and continuing training relevant to their needs.

D. MAINTENANCE

The premises shall be maintained in a clean and proper manner to ensure adequate cleaning and maintenance of proper operations. The facilities shall include:-

(1) Privacy and thorough examination of individuals to determine their suitability as donors.

(2) Collection of blood from donors with minimal risk of contamination of exposure to activities and equipment unrelated to blood collection.

(3) Storage of blood or blood components pending completion of tests.

(4) Provision for quarantine, storage of blood and blood components in a designated location, pending repetition of those tests that initially give questionable serological results.

(5) Provision for quarantine, storage, handling and disposal of products and reagents not suitable for use.

(6) Storage of finished products prior to distribution or issue.

(7) Proper collection, processing, compatibility testing, storage and distribution of blood and blood components to prevent contamination.

(8) Adequate and proper performance of all procedures relating to plasmapheresis, plateletpheresis and leucapheresis.

(9) Proper conduct of all packaging, labelling and other finishing operations.

(10) Provision for safe and sanitary disposal of –

(i) Blood and/or blood components not suitable for use, distribution or sale.

(ii) Trash and items used during the collection, processing and compatibility testing of blood and / or blood components.

*Note : 2nd Amendment Rules, 1999 (w.e.f. 5-4-1999)

Drugs and Cosmetics Rules 1945

E. EQUIPMENT

Equipment used in the collection, processing, testing, storage and sale/distribution of blood and its components shall be maintained in a clean and proper manner and so placed as to facilitate cleaning and maintenance. The equipment shall be observed, standardized and calibrated on a regularly scheduled basis as described in the Standard Operating Procedures Manual and shall operate in the manner for which it was designed so as to ensure compliance with the official requirements (the equipments) as stated below for blood and its components.

Equipment that shall be observed, standardized and calibrated with at least the following

frequencies:

EQUIPMENT	PERFORMANCE	FREQUENCY	FREQUENCY OF CALIBRATION
1. Temperature Recorder	Compare against thermometer	Daily	As often as necessary
2 Refrigerated centrifuge	Observe speed and temperature	Each day of use	As often as necessary
3 Hematocrit centrifuge	–	–	Standardise before initial use, after repair or adjustments and annually.
4, General lab. Centrifuge	–	–	Tachometer, every 6 months.

5. Automated Blood typing	Observe controls for correct results		Each day of use	–
6. Haemoglobinometer	Standardize against cyanamethemoglob ulin standard			
−ditto−	–			
7. Refractiometer or Urinometer	Standardize against distilled water		− ditto −	–
8. Blood container	Standardize against weighing device container of known weight.		− ditto –	As often as necessary
9 Water Bath	Observe temperature		− ditto −	−ditto−
10 Rh view box	–ditto–	− ditto −	− ditto−	
	(wherever necessary)			

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11 Autoclave	Observe temperature		Each day of use	As often as necessary
12 Serologic rotators	Observe controls for correct results		-- ditto--	Speed as often as necessary.
13 Laboratory thermometers	–		–	Before initial use
14 Electronic thermometers	–		Monthly	–
15 Blood agitator with	Observe weight of the		Each day of use	Standardize

	first container of blood filled for correct results	container of known mass or value before initial use, and after repairs or adjustments.

F. SUPPLIES AND REAGENTS:

All supplies and reagents used in the collection, processing, compatibility, testing, storage

and distribution of blood and blood components shall be stored at proper temperature in a safe and hygienic place, in a proper manner and in particular:–

(a) all supplies coming in contact with blood and blood components intended for transfusion shall be sterile, pyrogen-free, and shall not interact with the product in such a manner as to have an adverse effect upon the safety, purity, potency or effectiveness of the product.

(b) supplies and reagents that do not bear an expiry date shall be stored in a manner that the oldest is used first.

(c) supplies and reagents shall be used in a manner consistent with instructions provided by the manufacturer.

(d) all final containers and closures for blood and blood components not intended for transfusion shall be clean and free of surface solids and other contaminants.

(e) each blood collecting container and its satellite container(s), if any, shall be examined visually for damage or evidence of contamination prior to its use and immediately after filling. Such examination shall include inspection for breakage of seals, when indicated, and abnormal discoloration. Where any defect is observed, the container shall not be used or, if detected after filling, shall be properly discarded.

(f) representative samples of each lot of the following reagents and/or solutions shall be tested regularly on a scheduled basis by methods described in the Standard Operating Procedures Manual to determine their capacity to perform as required,

Reagents and solutions	Frequency of testing alongwith controls
Anti-human serum	Each day of use
Blood grouping serums	Each day of use
Lectin	Each day of use
Antibody screening and reverse grouping cells	Each day of use
Hepatitis test reagents	Each run
Syphilis serology reagents	Each run
Enzymes	Each day of use
HIV I and II reagents	Each run
Normal saline (LISS and PBS)	Each day of use
Bovine Albumin	Each day of use.

G. GOOD MANUFACTURING PRACTICES (GMPs) /STANDARD OPERATING PROCEDURES (SOPs):

Written Standard Operating Procedures shall be maintained and shall include all steps to be followed in the collection, processing, compatibility testing, storage and sale or distribution of blood and/or preparation of blood components for homologous transfusion, autologous transfusion and further manufacturing purposes. Such procedures shall be available to the personnel for use in the concerned areas. The Standard Operating Procedures shall *inter alia* include:

1. (a) criteria used to determine donor suitability.

(b) methods of performing donor qualifying tests and measurements including minimum and maximum values for a test or procedure, when a factor in determining acceptability;

(c) solutions and methods used to prepare the site of phlebotomy so as to give maximum assurance of a sterile container of blood;

(d) method of accurately relating the product (s) to the donor;

(e) blood collection procedure, including in-process precautions taken to measure accurately the quality of blood drawn from the donor;

(f) methods of component preparation, including any time restrictions for specific steps in processing;

(g) all tests and repeat tests performed on blood and blood components during processing;

(h) pre-transfusion testing, wherever applicable, including precautions to be taken to identify accurately the recipient blood components during processing;

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(i) procedures of managing adverse reactions in donor and recipient reactions:

(j) storage temperatures and methods of controlling storage temperatures for blood and its components and reagents;

(k) length of expiry dates, if any assigned for all final products;

(l) criteria for determining whether returned blood is suitable for re-issue;

(m) procedures used for relating a unit of blood or blood component from the donor to its final disposal;

(n) quality control procedures for supplies and reagents employed in blood collection, processing and re-transfusion testing;

(o) schedules and procedures for equipment maintenance and calibration;

(p) labelling procedures to safeguard its mix-ups, receipt, issue, rejected and in-hand;

(q) procedures of plasmapheresis, plateletphersis and leucapheresis if performed, including precautions to be taken to ensure re-infusion of donor‘s own cells;

(r) procedures for preparing recovered (salvaged) plasma if performed, including details of separation, pooling, labelling, storage and distribution;

(s) all records pertinent to the lot or unit maintained pursuant to these regulations shall be reviewed before the release or distribution of a lot or unit of final product. The review or portions of the review may be performed at appropriate periods during or after blood collection, processing, testing and storage. A thorough investigation, including the conclusions and follow-up, of any unexplained discrepancy or the failure of a lot or unit to meet any of its specification shall be made and recorded.

(2) A licensee may utilise current Standard Operating Procedures, such as the Manuals of the following organizations, so long as such specific procedures are consistent with, and at least as stringent as, the requirements contained in this Part, namely :-

(i) Directorate General of Health Services Manual.

(ii) Other Organisations or individual blood bank's manuals, subject to the approval of State Licensing Authority and Central Licence Approving Authority.

H. CRITERIA FOR BLOOD DONATION:

Conditions for donation of blood:

(1) *General* – No person shall donate blood and no blood bank shall draw blood from a person, more than once in three months. The donor shall be in good health, mentally alert and physically fit and shall not be inmates of jail, persons having multiple sex partners and drug-addicts. The donors shall fulfil the following requirements, namely: -

1[(a) the donor shall be in the age group of 18 to 65 years;]

(b) the donor shall not be less than 45 kilograms;

(c) temperature and pulse of the donor shall be normal;

(d) the systolic and diastolic blood pressure are within normal limits without medication;

(e) haemoglobin which shall not be less than 12.5 grams;

(f) the donor shall be free from acute respiratory diseases;

(g) the donor shall be free from any skin diseases at the site of phlebotomy;

(h) the donor shall be free from any disease transmissible by blood transfusion, insofar as can be determined by history and examination indicated above;

(i) the arms and forearms of the donor shall be free from skin punctures or scars indicative of professional blood donors or addiction of self injected narcotics.

(2) *Additional qualifications of donor* – No person shall donate blood, and no blood bank shall draw blood from a donor, in the conditions mentioned in column (1) of the Table given below before the expiry of the period of deferment mentioned in the column (2) of the said Table.

Table: Deferment of blood donation

CONDITIONS	PERIOD OF DEFERMENT
(1)	(2)_
(a) Abortions	6 months
(b) History of Blood transfusion	6 months
(c) Surgery	12 months
(d) Typhoid	12 months after recovery
(e) History of Malaria and duly treated	2 months (endemic) 3 years (non endemic area)
(f) Tattoo	6 months
(h) Breast feeding	12 months after delivery
(i) Immunization (Cholera, Typhoid, Diphtheria, Tetanus, Plague, Gammaglobulin)	15 days
(j) Rabies vaccination	1 year after vaccination
(k) History of Hepatitis in family or close contact	12 months
(l) Immunoglobulin	12 months

(3) No person shall donate blood and no blood bank shall draw blood from a person, suffering from any of the diseases mentioned below, namely:–

(a) Cancer

(b) Heart disease

1. Subs. By G.S.R 101 (E), dt:18-2-2011

(c) Abnormal bleeding tendencies

(d) Unexplained weight loss

(e) Diabetes-controlled on insulin

[1][(f) Hepatitis infection]

(g) Chronic nephritis

(h) Signs and symptoms, suggestive of AIDS

(i) Liver diseases

(j) Tuberculosis

(k) Polycythemia Vera.

(l) Asthma

(m) Epilepsy

(n) Leprosy

(o) Schizophrenia

(p) Endocrine disorders

I. GENERAL EQUIPMENTS AND INSTRUMENTS.

1. For blood collection room:

(i) Donor beds, chairs and tables: These shall be suitably and comfortably cushioned and shall be of appropriate size.

(ii) Bedside table

(iii) Sphygmomanometer and stethoscope

(iv) Recovery beds for donors.

(v) Refrigerators, for storing separately tested and untested blood, maintaining temperature between 2 to 6 degree centigrade with digital dial thermometer, recording thermograph and alarm device, with provision for continuous power supply.

(vi) Weighing devices for donor and blood containers.

2. For haemoglobin determination:

(i) Copper sulphate solution (specific gravity 1.053) (ii) Sterile lancet and impregnated alcohol swabs.

(iii) Capillary tube (1.3 x 1.4 x 96 mm for Pasteur pipettes) (iv) Rubber bulbs for capillary tubings.

(v) Sahli's haemoglobinometer / Colorimetric method.

3. For temperature and pulse determination.

(i) Clinical thermometers

(ii) Watch (fitted with a second-hand) and a stop-watch.

4. For blood containers:

(a) Only disposable PVC blood bags shall be used (closed system) as per specifications of IP/USP/BP.

(b) Anti-coagulants: The anti-coagulant solution shall be sterile, pyrogen-free and of the following composition that will ensure satisfactory safety and efficacy of the whole blood and/or for all the separate blood components.

(i) Citrate Phosphate Dextrose Adenine solution (CPDA) or Citrate Phosphate Dextrose Adenine – 1 (CPDA-1) – 14 ml solution shall be required for

1. Subs. by G.S.R. No. 40(E), dated 29-01-2001.

100 ml of blood.

Note 1.- (i) In case of single/double/triple/quadruple blood collection bags used for blood component preparations, CPDA blood collection bags may be used. (ii) Acid Citrate Dextrose solution (A.C.D. with Formula-A) I.P. – 15 ml solution shall be required for 100 ml of blood,

(iii) Additive solutions such as SAGM, ADSOL, NUTRICEL may be used for storing and retaining Red Blood Corpuscles up to 42 days.

Note 2.- The licensee shall ensure that the anti-coagulant solutions are of a licensed manufacturer and the blood bags in which the said solutions are contained have a certificate of analysis of the said manufacturer.

5. Emergency equipments/items:

(i) Oxygen cylinder with mask, gauge and pressure regulator. (ii) 5 per cent Glucose or Normal Saline.

(iii) Disposable sterile syringes and needles of various sizes.

(iv) Disposable sterile I.V. infusion sets.

(v) Ampoules of Adrenaline, Noradrenaline, Mephentin, Betamethasone or Dexamethasone, Metoclorpropamide injections.

(vi) Aspirin.

6. Accessories:

(i) Such as blankets, emesis basins, haemostats, set clamps, sponge forceps, gauze, dressing jars, solution jars, waste cans.

(ii) Medium cotton balls, 1.25 cm adhesive tapes.

(iii) Denatured spirit, Tincture Iodine, green soap or liquid soap. (iv) Paper napkins or towels.

(v) Autoclave with temperature and pressure indicator.

(vi) Incinerator

(vii) Stand-by generator

7. Laboratory equipment:

(i) Refrigerators, for storing diagnostic kits and reagents, maintaining a temperature between 4 to 6 degree centigrade (plus/minus 2 degrees centigrade) with digital dial thermometer having provision for continuous power supply.

(ii) Compound Microscope with low and high power objectives.

(iii) Centrifuge Table Model.

(iv) Water bath: having range between 37 degree centigrade to 56 degree centigrade.

(v) Rh viewing box in case of slide technique.

(vi) Incubator with thermostatic control.

(vii) Mechanical shakers for serological tests for Syphilis.

(viii) Hand-lens for observing tests conducted in tubes.

(ix) Serological graduated pipettes of various sizes.

(x) Pipettes (Pasteur).

(xi) Glass slides.

(xii) Test tubes of various sizes / micrometer plates (U or V type).

(xiii) Precipitating tubes 6mm x 50mm of different sizes and glass beakers of different sizes.

(xiv) Test tube racks of different specifications.

(xv) Interval timer electric or spring wound.

(xvi) Equipment and materials for cleaning glass wares adequately.

(xvii) Insulated containers for transporting blood, between 2 degree centigrade to 10 degree centigrade temperatures, to wards and hospitals.

(xviii) Wash bottles.

(xix) Filter papers.

(xx) Dielectric tube sealer.

(xxi) Plain and EDTA vials.

(xxii) Chemical balance (wherever necessary).

(xxiii) ELISA reader with printer, washer and micropipettes.

J. SPECIAL REAGENTS :

(1) Standard blood grouping sera Anti A, Anti B and Anti D with known controls. Rh typing sera shall be in double quantity and each of different brand or if from the same supplier each supply shall be of different lot numbers.

(2) Reagents for serological tests for syphilis and positive sera for controls.

(3) Anti Human Globulin Serum (Coomb's serum).

(4) Bovine Albumin 22 percent Enzyme reagents for incomplete antibodies.

[1][(5) ELISA or RPHA test kits for Hepatitis and HIV I & II.

(6) Detergent and other agents for cleaning laboratory glass wares.

K. TESTING OF WHOLE BLOOD :

(1) It shall be responsibility of the licensee to ensure that the whole blood collected, processed and supplied conforms to the standards laid down in the Indian Pharmacopoeia and other tests published, if any, by the Government.

(2) *Freedom from HIV antibodies (AIDS) Tests.* – Every licensee shall get samples of every blood unit tested, before use, for freedom from HIV 1 and HIV II antibodies either from laboratories specified for the purpose by the Central Government or in his own laboratory. The results of such testing shall be recorded on the label of the container.

(3) Each blood unit shall also be tested for freedom from [2][(Hepatitis B surface antigen and Hepatitis C Virus antibody)] VDRL and malarial parasite and results of such testing shall be recorded on the label of the container.

NOTES (a) Blood samples of donors in pilot tube and the blood samples of the Recipient shall be preserved for 7 days after issue.

(b) The blood intended for transfusion shall not be frozen at any stage.

(c) Blood containers shall not come directly in contact with ice at any stage.

1. Subs. By G.S.R. 733(E) dated 21-12-2005
2. Subs. by G.S.R. 40(E) dated 29-01-2001

RECORDS :

The records which the licensee is required to maintain shall include *inter alia* the following particulars, namely:

(1) *Blood donor record*: It shall indicate serial number, date of bleeding, name, address and signature of donor with other particulars of age, weight, haemoglobin, blood grouping, blood pressure, medical examination, bag number and patient's detail for whom donated in case of replacement donation, category of donation (voluntary / replacement) and deferral records and signature of Medical Officer In-charge.

(2) *Master records for blood and its components*: It shall indicate bag serial number, date of collection, date of expiry, quantity in ml. ABO/Rh Group, results for testing of HIV I and HIV II antibodies, Malaria, V.D.R.L. [1][(Hepatitis B surface antigen and Hepatitis C Virus antibody)] and irregular antibodies (if any), name and address of the donor with particulars, utilization issue number, components prepared or discarded and signature of the Medical Officer in charge.

(3) *Issue Register*: It shall indicate serial number, date and time of issue bag serial number, ABO/RH Group, total quantity in ml, name and address of the recipient, group of recipient, unit/institution, details of cros-matching report, indication for transfusion.

(4) *Records of components supplied*: Quantity supplied; compatibility report, details of recipient and signature of issuing person.

(5) Records of ACD/CPD/CPD-A/SAGM bags giving details of manufacturer, batch number, date of supply, and results of testing.

(6) Register for diagnostic kits and reagents used: name of the kits/reagents, details of batch number, date of expiry and date of use.

(7) Blood bank must issue the cross matching report of the blood to the patient together with the blood unit.

(8) Transfusion adverse reaction records.

(9) Records of purchase, use and stock in hand of disposable needles, syringes, blood bags, shall be maintained.

NOTE : The above records shall be kept by the licensee for a period of five years.

M. LABELS :

The labels on every bag containing blood and/or component shall contain the following particulars, namely;

(1) The proper name of the product in a prominent place and in bold letters on the bag.

(2) Name and address of the blood bank

(3) Licence number

1 Subs. by G.S.R. 40(E), dt. 29.1.2001 (w.e.f. 1.6.2001).

(4) Serial number

(5) The date on which the blood is drawn and the date of expiry as prescribed under Schedule P to these rules.

(6) A colored label shall be put on every bag containing blood. The following color scheme for the said labels shall be used for different groups of blood:

Blood Group	Colour of the label
O	Blue
A	Yellow
B	Pink
AB	White

(7) The results of the tests for [1][(Hepatitis B surface antigen and Hepatitis C Virus antibody)] syphilis, freedom from HIV I and HIV II antibodies and malarial parasite.

(8) The Rh. Group.

(9) Total volume of blood, the preparation of blood, nature and percentage of anti-coagulant.

(10) Keep continuously temperature at 2 degree centigrade to 6 degree centigrade for whole human blood and/or components as contained under III of Part XII B.

(11) Disposable transfusion sets with filter shall be used in administration equipment.

(12) Appropriate compatible cross-matched blood without atypical antibody in recipient shall be used.

(13) The contents of the bag shall not be used if there is any visible evidence of deterioration like haemolysis, clotting or discoloration.

(14) The label shall indicate the appropriate donor classification like ―Voluntary Donor‖ or ―Replacement Donor‖ in no less prominence than the proper name.

NOTES :

1. In the case of blood components, particulars of the blood from which such components have been prepared shall be given against item numbers (5), (7), (8), (9) and (14).
2. The blood and/or its components shall be distributed on the prescription of a Registered Medical Practitioner.

II. BLOOD DONATION CAMPS.

A blood donation camp may be organized by –

1. Subs. by G.S.R 40(E), dt. 29.1.2001.

(a) a licensed designated Regional Blood Transfusion Centre ; or

(b) a licensed Government blood bank; or

(c) the Indian Red Cross society; or

NOTES:

(i) ― Designated Regional Blood Transfusion Centre‖ shall be a center approved and designated by a Blood Transfusion Council constituted by a State Government to collect, process and distribute blood and its components to cater to the needs of the region and that center has also been licensed and approved by the Licensing Authority and Central Licence Approving Authority for the purpose.

(ii) The designated Regional Blood Transfusion Centre, Government blood bank and Indian Red Cross Society shall intimate within a period of seven days, the venue where the blood camp was held and details of group wise blood units collected in the said camp to the Licensing Authority and Central Licence Approving Authority.

For holding a blood donation camp, the following requirements shall be fulfilled/complied with, namely: -

(A) Premises, personnel etc.

(a) Premises under the blood donation camp shall have sufficient area and the location shall be hygienic so as to allow proper operation, maintenance and cleaning.

(b) All information regarding the personnel working, equipment used and facilities available at such a Camp shall be well documented and made available for inspection, if required, and ensuring -

(i) Continuous and uninterrupted electrical supply for equipment used in the Camp;

(ii) Adequate lighting for all the required activities;

(iii) Hand-washing facilities for staff;

(iv) Reliable communication system to the central office of the Controller/ Organizer of the Camp;

(v) Furniture and equipment arranged within the available space;

(vi) Refreshment facilities for donors and staff;

(vii) Facilities for medical examination of the donors;
(viii) Proper disposal of waste.

(B) Personnel for Out-door Blood Donation Camp:

To collect blood from 50 to 70 donors in about 3 hours or from 100 to 200 donors in 5 hours, the following requirements shall be fulfilled / complied with:

(i) one Medical Officer and two nurses or phlebotomists for managing 6-8 donor tables;
(ii) two medico social workers;
(iii) three blood bank technicians;
(iv) two attendants;

(v) vehicle having a capacity to seat 8-10 persons, with provision for carriage of donation goods including facilities to conduct a blood donation camp;

(C) Equipments :

1. BP apparatus.
2. Stethoscope.
3. Blood bags (single, double, triple, quadruple). 4. Donor questionnaire.
5. Weighing device for donors.
6. Weighing device for blood bags.
7. Artery forceps, scissors.
8. Stripper for blood tubing.
9. Bed sheets, blankets/mattress.
10. Lancets, swab stick/tooth picks.
11. Glass slides.
12. Portable Hb meter/copper sulphate.
13. Test tube (big) and 12x100mm (small).
14. Test tube stand.
15. Anti-A, Anti-B and Anti-AB, Antisera and Anti-D.
16. Test tube sealer film.
17. Medicated adhesive tape.
18. Plastic waste basket.
19. Donor cards and refreshment for donors.
20 Emergency medical kit.
21 Insulated blood bag containers with provisions for storing between 2 degree centigrade to 10 degree centigrade.
22. Dielectric sealer or portable tube sealer.
23. Needle destroyer (wherever necessary).

III. PROCESSING OF BLOOD COMPONENTS FROM WHOLE BLOOD BY A BLOOD BANK

The Blood components shall be prepared by blood banks as a part of the Blood Bank services. The conditions for grant or renewal of licence to prepare blood components shall be as follows: -

A. ACCOMMODATION:

(1) Rooms with adequate area and other specification, for preparing blood components depending on quantum of workload shall be as specified in item

B under the heading ―1. BLOOD BANKS/BLOOD COMPONENTS‘ of this Part.

(2) Preparation of Blood components shall be carried out only under closed system using single double, triple or quadruple plastic bags except for preparation of Red Blood Cells Concentrates, where single bags may be used with transfer bags.

B. EQUIPMENT :

(i) Air Conditioner;

(ii) Laminar air flow bench;

(iii) Suitable refrigerated centrifuge;

(iv) Plasma expresser;

(v) Clipper and clips and/or dielectric sealer;

(vi) Weighing device;

(vii) Dry rubber balancing material;

(viii) Artery forceps,

scissors;

(ix) Refrigerator maintaining a temperature between 2 degree centigrade to 6 degree centigrade, a digital dial thermometer with recording thermograph and alarm device, with provision for continuous power supply;

(x) Platelet agitator with incubator (wherever necessary);

(xi) Deep freezers maintaining a temperature between minus 30 degree centigrade to minus 40 degree centigrade and minus 75 degree centigrade to minus 80 degree centigrade;

(xii) Refrigerated Water bath for Plasma Thawing;

(xiii)

Insulated blood bag containers with provisions for storing at appropriate temperature for transport purposes;

C. PERSONNEL:

The whole time competent technical staff meant for processing of Blood Components (that is Medical Officer, Technical Supervisor, Blood Bank Technicians and Registered Nurse) shall be as specified in item C, under the heading ― 1. BLOOD BANKS/BLOOD COMPONENTS‖ of this Part.

D. TESTING FACILITIES:

General: Facilities for A, B, AB and O groups and Rh(D) grouping. [1][(Hepatitis B surface antigen and Hepatitis C Virus antibody)], VDRL, HIV I and HIV II antibodies and malarial parasites shall be mandatory for every blood unit before it is used for the preparation of blood components. The results of such testing shall be indicated on the label.

E. CATEGORIES OF BLOOD COMPONENTS:

(1) CONCENTRATED HUMAN RED BLOOD CORPUSCLES: The product shall be known as ―Packed Red Blood Cells‖ that is Packed Red Blood Cells remaining after separating plasma from human blood.

General Requirements:

(a) *Storage*: Immediately after processing, the Packed Red Blood Cells shall be kept at a temperature maintained between 2 degree centigrade to 6 degree centigrade.

(b) *Inspection*: The component shall be inspected immediately after separation of the plasma, during storage and again at the time of issue.
The product shall not be issued if there is any abnormality in color or physical appearance or any indication of microbial contamination.

(c) *Suitability of Donor*: The source of blood for Packed Red Blood Cells shall be obtained from a donor who meets the criteria for Blood Donation as specified in item H under the heading ―I. BLOOD BANKS/BLOOD COMPONENTS‖ of this Part.

1. Subs. by G.S.R. 40(E), dt. 29.1.2001.

(d) Testing of Whole Blood: Blood from which Packed Red Blood Cells are prepared shall be tested as specified in item K relating to Testing Of Whole Blood under the heading ―I. BLOOD BANKS/BLOOD COMPONENTS‖ of this Part.

(e) *Pilot samples*: Pilot samples collected in integral tubing or in separate pilot tubes shall meet the following specifications:

(i) One or more pilot samples of either the original blood or the Packed Red Blood Cells being processed shall be preserved with each unit of Packed Red Blood Cells which is issued.

(ii) Before they are filled, all pilot sample tubes shall be marked or identified so as to relate them to the donor of that unit or Packed Red Blood Cells.

(iii) Before the final container is filled or at the time the final product is prepared, the pilot samples tubes accompanying a unit of Packed Red Blood Cells, shall be attached in a tamper-proof manner that shall conspicuously identify removal and re- attachment.

(iv) All pilot sample tubes, accompanying a unit of packed red blood cells, shall be filled immediately after the blood is collected or at the time the final product is prepared, in each case, by the person who performs the collection of preparation.

F. Processing:

(i) *Separation*: Packed Red Blood Cells shall be separated from the whole blood, --

(a) if the whole blood is stored in ACD solution within 21 days, and

(b) if the whole blood is stored in CPDA-1 solution, within 35 days, from the date of collection. Packed Red Blood Cells may be prepared either by centrifugation done in a manner that shall not tend to increase the temperature of the blood or by normal undisturbed sedimentation method. A portion of the plasma, sufficient to ensure optimal cell preservation, shall be left with the packed Red Blood Cells.

(ii) *Packed Red Blood Cells Frozen*: Cryophylactic substance may be added to the Packed Red Blood Cells for extended manufacturer‘s storage not warmer than minus 65 degree centigrade provided the manufacturer submits data to the satisfaction of the Licensing Authority and Central Licence Approving Authority, as adequately demonstrating through in-vivo cells survival and other appropriate tests that the addition of the substance, the material used and the processing methods results in a final product meets the required standards of safety, purity and potency for Packed Red Blood Cells, and that the frozen

product shall maintain those properties for the specified expiry period.

(iii) *Testing*: Packed Red Blood Cells shall conform to the standards as laid down in the Indian Pharmacopoeia.

(2) PLATELETS CONCENTRATES:

The product shall be known as ―Platelets Concentrates‖ that is platelets collected from one unit of blood and re-suspended in an appropriate volume of original plasma.

General Requirements:

(i) *Source*: The source material for platelets shall be platelet rich plasma or buffy coat which may be obtained from the whole blood or by plateletpheresis.

(ii) *Processing* :

(a) Separation of buffy-coat or platelet-rich plasma and platelets and re-suspension of the platelets shall be in a closed system by centrifugal method with appropriate speed, force and time.

(b) Immediately after collection, the whole blood or plasma shall be held in storage between 20 degree centigrade to 24 degree centigrade. When it is to be transported from the venue of blood collection to the processing laboratory, during such transport action, the temperature as close as possible to a range between 20 degree centigrade to 24 degree centigrade shall be ensured. The platelet concentrates shall be separated within 6 hours after the time of collection of the unit of whole blood or plasma.

(c) The time and speed of centrifugation shall be demonstrated to produce an unclamped product, without visible haemolysis, that yields a count of not less than 3.5×10^{10} (3.5 x 10 raised to the power of 10) and 4.5×10^{10} (4.5 x 10 raised to the power ten) i.e. platelets per unit from a unit of 350 ml and 450 ml blood respectively. One percent of total platelets prepared shall be tested of which 75 per cent of the units shall conform to the above said platelet count.

(d) The volume of original plasma used for re-suspension of the platelets shall be determined by the maintenance of the pH of not less than 6 during the storage period. The pH shall be measured on a sample of platelets which has been stored for the permissible maximum expiry period at 20 degree centigrade to 24 degree centigrade.

(e) Final containers used for platelets shall be colorless and transparent to permit visual inspection of the contents. The caps selected shall maintain a hermetic seal to prevent contamination of the contents. The container material shall not interact with the contents, under the normal conditions of the storage and use, in such a manner as to have an adverse effect upon the safety, purity, potency, or efficacy of the product. At the time of filling, the final container shall be marked or identified by number so as to relate it to the donor.

(iii) *Storage*: Immediately after re-suspension, platelets shall be placed in storage not exceeding for a period of 5 days, between 20 degree centigrade to 24 degree centigrade, with continuous gentle agitation of the platelet concentrates maintained throughout such storage

(iv) *Testing*: The units prepared from different donors shall be tested at the end of the storage period for –

(a) Platelet count;

(b) pH of not less than 6 measured at the storage temperature of the unit;

(c) measurement of actual plasma volume;

(d) one percent of the total platelets prepared shall be tested for sterility;

(e) the tests of functional viability of the platelets shall be done by swirling movement before issue.

(f) if the results of the testing indicate that the product does not meet the specified requirements, immediate corrective action shall be taken and records maintained;

(v) *Compatibility Test*: Compatible transfusion for the purpose of variable number of Red Blood Cells, A, B, AB and O grouping shall be done if the platelets concentrate is contaminated with red blood cells.

(3) GRANULOCYTE CONCENTRATES:

(i) *Storage*: It shall be kept between 20 degree centigrade to 24 degree centigrade for a maximum period of 24 hours;

(ii) Unit of granulocytes shall not be less than 1×10^{10} (i.e. 1 x 10 raised to the power of 10) when prepared on cell separator;

(iii) Group specific tests/HLA test wherever required shall be carried out.

(4) FRESH FROZEN PLASMA:

Plasma frozen within 6 hours after blood collection and stored at a temperature not warmer than minus 30 degree centigrade, shall be preserved for a period of not more than one year.

(5) CRYOPRECIPITATE:

Concentrate of anti-hemophiliac factor shall be prepared by thawing of the fresh plasma frozen stored at minus 30 degree centigrade.

(a) Storage:

Cryoprecipitate shall be preserved at a temperature not higher than minus 30 degree centigrade and may be preserved for a period of not more than one year from the date of collection.

(b) *Activity*:

Anti-hemophiliac factor activity in the final product shall be not less than 80 units per bag. One percent of the total cryoprecipitate prepared shall be tested of which seventy five percent of the unit shall conform to the said specification.

F PLASMAPHERESIS, PLATELETPHERESIS, LEUCAPHERESIS, USING A CELL SEPARATOR.

An area of 10 square meters shall be provided for apheresis in the blood bank.

The blood banks specifically permitted to undertake the said apheresis on the donor shall observe the criteria as specified in item H relating to Criteria for blood donation—I. Blood Banks/Blood Components‖ of this Part. The written consent of the donor shall be taken and the donor must be explained, the hazards of apheresis. The Medical Officer shall certify that the donor is fit for apheresis and it shall be carried out by a trained person under supervision of the Medical Officer.

(A) PLASMAPHERESIS, PLATELETPHERESIS AND LEUCAPHERESIS:

The donors subjected to plasmapheresis, plateletpheresis and leucapheresis shall, in addition to the criteria specified in item H relating to the CRITERIA FOR BLOOD DONATION, under the heading —I. BLOOD BANKS/BLOOD COMPONENTS‖ of this Part being observed, be also subjected to protein estimation on post-pheresis/first sitting whose results shall be taken as

reference for subsequent/sitting. It shall also be necessary that the total plasma obtained from such donor and periodicity of Plasmapheresis shall be according to the standards described under validt. Standard Operating Procedures.

NOTE :

(i) At least 48 hours must elapse between successive apheresis and not more than twice in a week.

(ii) Extracoporeal blood volume shall not exceed 15% of donor's estimated blood volume.

(iii) Platelet pheresis shall not be carried out on donors who have taken medication containing Asprin within 3 days prior to donation.

(iv) If during plateletpheresis or leucapheresis, RBCs cannot be re-transfused then at least 12 weeks shall elapse before a second cytapheresis procedure is conducted.

(B) MONITORING FOR APHERESIS:

Before starting apheresis procedure, hemoglobin or haematocrit shall be done. Platelet count, WBC counts, differential count may be carried out. In repeated plasmapheresis, the serum protein shall be 6 gm./ml.

(C) COLLECTION OF PLASMA:

The quantity of plasma separated from the blood of donor shall not exceed 500 ml. per sitting and once in a fortnight or shall not exceed 1000 ml per month.

PART XII C

I. REQUIREMENTS FOR MANUFACTURE OF BLOOD PRODUCTS

The blood products shall be manufactured in a separate premises other than that meant for blood bank. The requirements that are essential for grant or renewal of licence to manufacture blood products such as Albumin, Plasma Protein Fraction, Immunoglobins and Coagulation Factor Concentrates, shall be as follows, namely: -

A. GENERAL REQUIREMENTS:

1. *Location and surroundings, buildings and water supply*:

The requirements as regards location and surrounding, buildings and water supply as contained in paragraphs 1.1.1, 1.1.2, 1.1.3 of Part 1 of Schedule M shall apply *mutatis mutandis* to the manufacture of blood products.

2. *Disposal of waste and infectious materials:*

(i) The requirements as regards disposal of waste and infectious materials as contained in paragraph 1.1.4 of Part 1 of Schedule M shall apply *mutatis mutandis* to the manufacture of blood products.

(ii) Proper facility shall also be provided for potentially infectious materials, particularly HIV I & HIV II [1][(Hepatitis B surface antigen and Hepatitis C Virus antibody)] through autoclaving, incineration or any other suitable validt. methods.

3. *Health, clothing and sanitation personnel:*

(i) The requirement as contained in paragraph 3 of Part I of Schedule M shall be complied with.

(ii) The personnel working in the manufacturing areas shall be vaccinated against Hepatitis B virus and other infectious transmitting diseases.

4. *Requirements for manufacturing area for Blood Products*:

(i) For the manufacture of blood products, separate enclosed areas specifically designated for the purpose shall be provided. These areas be provided with air locks for entry and shall be essentially dust free and ventilated with an air supply. Air supply for manufacturing area shall be filtered through bacteria retaining filters (HEPA Filters) and shall be at a pressure higher than in the adjacent areas.

The filters shall be checked for performance on installation and periodically thereafter, and records thereof shall be maintained.

(ii) Interior surfaces (walls, floors and ceilings) shall be smooth and free from cracks, they shall not shed matter and shall permit easy cleaning and disinfection. Drains shall be excluded from aseptic areas.

1. Subs. by G.S.R. 40(E) dated 29-01-2001

Routine microbial counts of the manufacturing area shall be carried out during manufacturing operations. The results of such counts shall be checked against well documented in-house standards and records maintained.

Access to the manufacturing areas shall be restricted to a minimum number of authorized personnel. Special procedures for entering and leaving the manufacturing areas shall be prominently displayed.

(iii) Sinks shall be excluded from aseptic areas. Any sink installed in other clean areas shall be of suitable material such as stainless steel, without an overflow, and be supplied with water of potable quality. Adequate precautions shall be taken to avoid contamination of the drainage system with dangerous effluents and airborne dissemination of pathogenic micro-organisms.

(iv) Lighting, air-conditioning, ventilation shall be designed to maintain a satisfactory temperature and relative humidity to minimize contamination and to take account of the comfort of personnel working with protective clothing.

(v) Premises used for the manufacture of blood products shall be suitably designed and constructed to facilitate good sanitation.

(vi) Premises shall be carefully maintained and it shall be ensured that repair and maintenance operations do not present any hazard to the quality of products. Premises shall be cleaned and, where applicable, disinfected according to detailed written validt. procedures.

(vii) Adequate facilities and equipments shall be used for the manufacture of blood products derived from blood plasma.

(viii) All containers of blood products, regardless of the stage of manufacture, shall be identified by securely attached labels. Cross contamination shall be prevented by adoption of the following measures, namely: –

(a) processing and filling shall be in segregated areas;

(b) manufacture of different products at the same time shall be avoided;

(c) simultaneous filling of the different products shall be avoided;

(d) ensure transfer, containers/materials by means of airlocks, air extraction, clothing change and careful washing and decontamination of equipment;

(e) protecting containers/materials against the risk of contamination caused by re-circulation of untreated air or by accidental re-entry of extracted air;

(f) using containers that are sterilized or are of documented low —bioburden‖,

(ix) Positive pressure area shall be dedicated to the processing area concerned; (x) Air-handling units shall be dedicated to the processing area concerned;

(xi) Pipe work, valves and vent filters shall be properly designed to facilitate cleaning and sterilization. Valves on fractionation/reacting vessels shall be completely steam sterilisable. Air vent filters shall be hydrophobic and shall be validated for their designated use.

5. Ancillary Areas :

(i) Rest and refreshment rooms shall be separated from other areas.

(ii) Facilities for changing and storing clothes and for washing and toilet purposes shall be easily accessible and appropriate for the number of users. Toilets shall not be connected directly with production or storage areas.

(iii) Maintenance workshops shall be separated from production areas. Wherever parts and tools are stored in the production area, they shall be kept in rooms or lockers reserved for that use.

(iv) Animal houses shall be well isolated from other areas with separate entrance.

B. COLLECTION AND STORAGE OF PLASMA FOR FRACTIONATION

(a) *Collection:*

(1) Plasma shall be collected from the licensed Blood Banks through a cold chain process and stored in frozen condition not warmer than minus twenty degree centigrade.

(2) Individual plasma shall remain in quarantine till it is tested for [1][(Hepatitis B and Hepatitis C Virus antibody)], HIV I and HIV II.

(3) A sample from pooled – lot plasma of about 10-12 units of different donors shall be tested for [1][(Hepatitis B and Heptitis C Virus antibody)] HIV I and HIV II and if the same sample found negative, only then it shall be taken up for fractionation.

(b) *Storage Area* :

(1) Storage areas shall be of sufficient space and capacity to allow orderly storage of the various categories of materials, intermediates, bulk and finished products, products in quarantine, released, rejected, returned, or recalled products.

(2) Storage areas shall be designed or adopted to ensure good storage conditioning. In particular, they shall be clean, dry and maintained within temperature required for such storage and where special storage conditions are required (e.g. temperature, humidity), these shall be provided, checked and monitored.

(3) Receiving and dispatch bays shall protect materials and products from the weather and shall be designed and equipped to allow containers of incoming materials to be cleaned, if necessary, before storage.

(4) Where quarantine status is ensured by storage in separate areas, these areas shall be clearly marked and their access restricted only to authorized personnel.

(5) There shall be separate sampling area for raw materials. If sampling is performed in the storage area, it shall be conducted in such a way so as to prevent contamination or cross-contamination.

(6) Segregation shall be provided for the storage of rejected, recalled, or returned materials or products.

(7) Adequate facility shall be provided for supply of ancillary material, such as ethanol, water, salts and polyethylene glycol. Separate facilities shall be provided for the recovery of organic solvents used in fractionation.

1. Subs. by G.S.R 40(E), dt. 29.1.2001 (w.e.f. 1.6.2001)

C. PERSONNEL :

(1) *Manufacture :*

The manufacture of blood products shall be conducted under the active direction and personal supervision of competent technical staff, consisting of at

least one person who shall be a whole time employee, with one year practical experience in the manufacture of blood products / plasma fractionation and possesses –-

(a) Post-graduate degree in Medicine–M.D. (Microbiology/Pathology/ Bacteriology/Immunology/Biochemistry); or

(b) Post-graduate degree in Science (Microbiology); or

(c) Post-graduate degree ib Pharmacy (Microbiology), from a recognized University or Institution.

2. Testing :

The head of the testing unit shall be independent of the manufacturing unit and testing shall be conducted under the active direction and personal supervision of competent technical staff consisting at least one person who shall be a whole time employee. The Head of the testing unit shall have eighteen months practical experience in the testing of drugs, especially the blood products and possesses –

(a) Post-graduate degree in Pharmacy or Science– (Chemistry/ Microbiology/ Bio-chemistry); or

(b) Post-graduate degree in Medicine– M.D(Microbiology/Pathology/ Biochemistry), from a recognized University or Institution.

D. PRODUCTION CONTROL :

(1) The production area and the viral inactivation room shall be centrally air- conditioned and fitted with HEPA filters having Grade C (Class 10,000) environment as given in the Table below.

(2) The filling and sealing shall be carried out under aseptic conditions in centrally air-conditioned areas fitted with HEPA Filters Grade A or, as the case may be, Grade B (Class 100) environment given in the said Table.

TABLE

AIR CLASSIFICATION SYSTEM FOR MANUFACTURE OF STERILE PRODUCTS.

Grade	*Maximum number of particles permitted per m3*		*Maximum number of Viable Micro-organism permitted per m3*
	0.5 – 5 micron	*Less than 5 micron*	

A (Class 100) (Laminar - Airflow workstation)	3500	None	Less than 1
B (Class 100)	3500	None	Less than 5
C (Class 10,000)	3,50,000	2000	Less than 100

(3) The physical and chemical operations used for the manufacture of plasma fractionation shall maintain high yield of safe and effective protein.

(4) The fractionation procedure used shall give a good yield of products meeting the in-house quality requirements as approved by the Licensing Authority and Central Licence Approving Authority reducing the risk of microbiological contamination and protein denaturation to the minimum.

(5) The procedure adopted shall not affect the antibody activity and biological half- life or biological characteristics of the products.

E. VIRAL INACTIVATION PROCESS :

The procedure used by the licensee to inactivate the pathogenic organisms such as enveloped and non-enveloped virus, especially infectivity from HIV I & HIV II, [1][(Hepatitis B surface antigens and Hepatitis C Virus antibody)], the viral inactivation and validation methods adopted by the licensee, shall be submitted for approval to the Licensing Authority and Central Licence Approving Authority.

NOTES:

(1) No preservative (except stabilizer to prevent – protein denaturation such as glycine, sodium chloride or sodium caprylate) shall be added to Albumin, Plasma Protein Fraction, Intravenous Immunoglobulins or Coagulation Factor Concentrates without the prior approval of Licensing Authority and Central Licence Approving Authority.

(2) The licensee shall ensure that the said stabilizers do not have deleterial effect on the final product in the quantity present so as not to cause any untoward or adverse reaction in human beings.

F. QUALITY CONTROL:

Separate facilities shall be provided for Quality Control such as Hematological, Bio-chemical, Physico-chemical, Microbiological, Pyrogens, Instrumental and Safety testing. The Quality Control Department shall have *inter alia* the following principal duties, namely :-

(1) To prepare detailed instructions for carrying out test and analysis.

(2) To approve or reject raw material, components, containers, closures, in-process materials, packaging material, labelling and finished products.

(3) To release or reject batch of finished products which are ready for distribution.

(4) To evaluate the adequacy of the conditions under which raw materials, semi-finished products and finished products are stored.

1. Subs. by G.S.R 40(E), dt. 29.1.2001 (w.e.f. 1.6.2001)

(5) To evaluate the quality and stability of finished products and when necessary of raw materials and semi-finished products.

(6) To review production records to ensure that no errors have occurred or if errors have occurred that they have been fully investigated.

(7) To approve or reject all procedures, or specifications impacting on the identity, strength, quality and purity of the product.

(8) To establish shelf-life and storage requirements on the basis of stability tests related to storage conditions.

(9) To establish and when necessary revise, control procedures and specifications.

(10) To review complaints, recalls, returned or salvaged products and investigations conducted there under for each product.

(11) To review Master Formula Records/Cards periodically.

G. TESTING OF BLOOD PRODUCTS:

The products manufactured shall conform to the standards specified in the Indian Pharmacopoeia and where standards of any product is not specified in the Pharmacopoeia, the standard for such product shall conform to the standard specified in the United States Pharmacopoeia or the British Pharmacopoeia. The final products shall be tested for freedom from HIV I and HIV II antibodies [1][(Hepatitis B surface antigen and Hepatitis C Virus antibody)].

H. STORAGE OF FINISHED PRODUCT :

(i) The final products shall be stored between two degree centigrade to eight degree centigrade, unless otherwise specified by the Central Licence Approving Authority.

(ii) The shelf-life assigned to the products by the licensee shall be submitted for approval to the Licensing Authority and Central Licence Approving Authority.

I. LABELLING :

The products manufactured shall be labelled as specified in the Indian Pharmacopoeia, the British Pharmacopoeia or the United Stated Pharmacopoeia which shall be in addition to any other requirement stated under Part IX or Part X of these rules. The labels shall indicate the results of test for [1][(Hepatitis B surface antigen and Hepatitis C Virus antibody)] freedom from HIV I and HIV II antibodies.

J. RECORDS:

The licensee shall maintain records as per Schedule U and also comply with Batch manufacturing records as specified in Paragraph 9 of Part -I of Schedule M and any other requirement as may be directed by Licensing Authority and Central Licence Approving Authority.

K. MASTER FORMULA RECORDS:

The licensee shall maintain Master Formula Records relating to all manufacturing and quality control procedures for each product, which shall be prepared and endorsed by the Competent Technical Staff, i.e. Head of the manufacturing unit. The Master Formula Records shall contain: –

(i) the patent or proprietary name of the product along with the generic name, if any, strength and the dosage form;

(ii) a description or identification of the final containers, packaging materials, labels and closures to be used;

1. Subs. by G.S.R 40(E), dt. 29.1.2001(w.e.f. 1.6.2001)

(iii) the identity, quantity and quality of each raw material to be used irrespective of whether or not it appears in the finished product. The permissible overage that may be included in a formulated batch shall be indicated;

(iv) a description of all vessels and equipments and the sizes used in the process; (v) manufacturing and control instructions along with parameters for critical steps such as mixing, drying, blending, sieving and sterilizing the product;

(vi) the theoretical yield to be expected from the formulation at different stages of manufacture and permissible yield limits;

(vii) detailed instructions on precautions to be taken in the manufacture and storage of drugs and of semi finished products; and

(viii) the requirements in-process quality control tests and analysis to be carried out during each stage of manufacture including the designation of persons or departments responsible for the execution of such tests and analysis.

II. REQUIREMENTS FOR MANUFACTURE OF BLOOD PRODUCTS FROM BULK FINISHED PRODUCTS

Where the blood products, such as Albumin, Plasma Protein Fraction, Immunoglobulins and Coagulation Factor Concentrates are manufactured through the manufacturing activities of filling and sealing the blood products from bulk powder or solution or both, the requirements as they apply to the manufacture of blood products from whole blood shall apply *mutatis mutandis* to such manufacture of blood products, unless other requirements have been approved by the Central Licence Approving Authority.]

[1][PART XIID

REQUIREMENTS FOR COLLECTION, PROCESSING, TESTING, STORAGE, BANKING AND RELEASE OF UMBILICAL CORD BLOOD DERIVED STEM CELLS

(A) GENERAL REQUIREMENTS

1. Location, Surroundings and Building: The building (s) for storage of Umbilical cord blood shall be so situated and shall have such measures as to avoid risk of contamination from external environment including open sewage, drain, public lavatory or any factory which produces disagreeable or obnoxious odour or fumes, excessive soot, smoke, chemical or biological emissions.

2. Buildings and premises: (1) The premises used for processing and storage shall be designed, constructed and adapted and maintained to ensure that the above operations and other ancillary functions are performed smoothly under hygienic conditions and in sterile areas wherever required. They shall also conform to the conditions laid down in the Factories Act, 1948 (63 of 1948).

The premises shall be:

(a)Adequately provided with working space to allow orderly and logical placement of equipment, material and movement of personnel so as to maintain safe operations and prevent contamination;

(b)Designed / constructed / maintained to prevent entry of insects, pests, birds, vermins and rodent. interior surfaces (walls, floors, ceilings and doors) shall be smooth and free from cracks, and permit easy cleaning, painting and disinfection, and in aseptic areas the surfaces shall be impervious, non-shedding, non-flaking and non-cracking;

(c)Flooring shall be unbroken and provided with a cove both at the junction between the wall and the floor as well as the wall and the ceiling.

1. Inserted by G.S.R. 899(E) dated 27-12-2011

(d)Provided with light fitting and grills which shall flush with the walls and not hanging from the ceiling to prevent contamination;

(e)If provided with fire escapes, these shall be suitably installed in the walls without any gaps;

(f)Provided with the furniture in aseptic areas which is smooth, washable and made of stainless steel or any other appropriate non shedding material other than wood;

(g)Provided with separate areas for processing and storage of products to prevent mix- ups, product contaminations and cross contamination;

(h)Provided with defined environmental conditions for temperature, humidity, ventilation and air filtration. Classifications shall be defined and, if appropriate, monitored.

(2) A periodical record of cleaning and renovating of the premises shall be maintained.

3. Disposal of waste and infectious materials:

(a)Waste materials awaiting disposal shall be stored safely;

(b)The disposal of sewage and effluents from the facility shall be in conformity with the requirements of the Pollution Control Board;

(c)All bio-medical waste shall be dealt with in accordance with the provisions of the Bio-medical Waste Management and Handling Rules, 1996.

4. Health, clothing and Sanitation of personnel:

(a)All personnel shall undergo medical examination prior to employment and shall be free from infectious and contagious diseases and thereafter they should be medically examined periodically at least once a year and for this purpose records shall be maintained thereof:

(b)All personnel, prior to and during employment, shall be trained in practices which ensure personal hygiene and a high level of personal hygiene shall be observed by all those engaged in the collection, processing, banking of umbilical cord blood;

(c)All persons shall wear clean body coverings appropriate for their duties before entering the Processing Zone and the Change Rooms with adequate facilities shall be provided prior to entry into any specific zone;

(d)Smoking, eating, drinking is prohibited inside the Laboratory;

(e)All personnel working in the Laboratory shall be protected against virus infections.

5. Requirements for Processing, Testing and Storage Areas for Umbilical cord blood stem cells:

(a)Separate dedicated areas specifically designed for the purpose and the workload shall be provided:

(b)There shall be separate areas for designated work purposes namely:-

(i)Cord blood Reception: cord blood reception area with space for transient storage of units and physical examination shall have adequate facilities for registration, date entry and generation of bar-coded labels. Air condition area of at lease 10.00 Sq. meters shall be provided;

(ii)Cord blood processing area: The room shall be clean and have an air handling System to provide a Class 10,000 environment. Entry to this area shall be through air lock. The room will house Class 100 biological safety cabinets for Umbilical cord blood processing. The temperature of the clean room shall be maintained 20 ºC to 25ºC and with a positive differential pressure of 10-15 pascals and Relative humidity of 50-60% Minimum area shall be 10.00 Sq. meters for the activity; (iii)Haematology and Serology Laboratory: The laboratory shall be equipped and utilized for the purpose of independently testing of Umbilical Cord Blood for ABO grouping and Rh Typing, Total Nucleated Cell Count, Progenitor cell count and

viability test. The room shall be air-conditioned and area of at least 10.00 Sq. meters shall be provided.

(iv)Transfusion Transmissible Disease Screening Laboratory: The Laboratory shall be equipped and utilized for screening tests on maternal blood for infectious diseases viz. HIV I & II; Hepatitis B & C virus, syphilis, malaria, CMV and HTLV. The room shall be air-conditioned and area of at least 10.00 Sq. meters shall be provided.

(v)Sterility Testing Laboratory: The laboratory shall be used for performing Sterility tests on Umbilical Cord blood unit. The premises may be classified depending on the testing method used. The room shall be air-conditioned with adequate and ancillary area for media prepar ation, sterilization, incubation and decontamination. Area of at least 10.00 Sq. meters shall be provided.

(vi)HLA Typing Laboratory: The Umbilical Cord blood unit shall have arrangements for HLA typing and genetic disease testing. In-house testing can be done by providing a well demarcated laboratory from the processing area for evaluation of possible genetic

disease and HLA typing. The area shall have Class 100,000 environment and air-conditioned and area of at least 10.00 Sq. meters shall be provided.

(vii) Sterilization-cum-washing: Appropriate facility shall be provided within the premises for proper washing and sterilization. This facility would be optional for laboratories using entirely disposable items.

(viii) Records and Store Rooms: There shall be designed record room(s) and store room(s) of at least 10.00 Sq. meters each. The access to record room shall be permitted only to authorized person. The room will have adequate protective facilities as the documents and records are to be preserved for long years.

(ix)Cryogenic Storage room: A minimum space of 20.00 sq. meters shall be provided by the licensee. The cryogenic storage room shall have provision for temperature monitoring of storage vessels, liquid nitrogen level in storage vessels and oxygen meter. The service space between each liquid nitrogen storage vessel, supply cylinders and connecting hose should be minimum 1.00 sq. Meters. Separate storage space for other accessories required shall be provided. The room shall be air-conditioned.

(x)General Storage area: General storage area shall be provided to store all the consumables, under conditions deemed optimum for storage by manufacturers.

B. COLLECTION AND STORAGE OF PROCESSED UMBILICAL CORD BLOOD COMPONENT

1. Collection:

(a)Umbilical Cord blood unit specific for an individual will be collected after signing an agreement with the parents, whose child‘s Umbilical Cord blood is to be collected and the cord blood bank. Private and Public Umbilical Cord blood banking to have different agreements;

(b)Umbilical Cord blood shall be collected from hospitals, nursing homes, birthing centers and from any other place where a consenting mother delivers, under the supervision of the qualified Registered Medical Practitioner responsible for the delivery;

(c)The cord blood shall be collected aseptically in a disposable PVC bag, containing adequate quantity of sterile, pyrogen free anti-coagulant and sealed effectively and such PVC Bags shall be procured from licensed manufacturer;

(d)The Umbilical Cord blood would be collected from a premises operating in hygienic condition to allow proper operation, maintenance and cleaning.

2. Transportation:

(a)Umbilical Cord blood shall be transported from the birthing center to the designated laboratory under and as per procedure prescribed by the cord blood bank;

(b)The transportation procedure shall be validated to ensure optimum survival of the Stem Cells;

(c)The transportation temperature should be between 18 to 28ºC;

(d)The time period between collection and processing shall not exceed 72 hours.

3. Storage:

(a)The Umbilical Cord blood shall be stored at room temperature between 20 to 25ºC in the reception area prior to processing;

(b)Samples pending tests for specific transfusion transmittable infectious diseases shall be stored in a segregated manner.

Note:- Temperature range between 4 to 37 degrees Celsius, for the whole time period of transit may be allowed beyond the 18ºC to 28ºC in exceptional cases. The effects of deviation of transit temperature from the optimum, on the product shall be adequately explained by the licensee in the client education booklet.

C. PERSONNEL

Cord blood bank shall have following categories of whole time competent technical staff, namely:-

1.Medical Director:- The operation of cord blood bank shall be conducted under the active directions and supervision of a Medical Director who is a whole time employee and is

possessing a Post Graduate degree in medicine – MD [Pathology/Transfusion Medicine/Microbiology] and has experience / training in cord blood processing and Cryogenic Storage.

2.Laboratory In-charge: The laboratory in-charge shall have Post Graduate qualification in Physiology or Botany or Zoology or Cell Biology or Microbiology or Biochemistry or Life Sciences or Graduate in Pharmacy and one year working experience in pathological laboratory licensed by the local health authority or any microbiology laboratory of a licensed drug manufacturing / testing unit and or experience / training in cord blood processing and cryogenic storage.

3.Technical Supervisor (cord blood processing):- The technical supervisor shall have a:

(a)Degree in Physiology or Botany or Zoology, Pharmacy or Cell Biology or Bio Sciences or Microbiology or Biochemistry or Medical Laboratory Technology (M.L.T.) with minimum of three years of experience in the preparation of blood components and / or experience or training in cord blood processing and Cryogenic Storage; or

(b)Diploma in Medical Laboratory Technology (M.L.T.) with five years experience in the preparation of blood components and experience or training in cord blood processing and Cryogenic Storage shall be essential.

4. Cord Blood Bank Technician(s):- The technicians employed shall have a:

(a)A degree in Physiology or Botany or Zoology or Pharmacy or Cell Biology or Bio Science or Microbiology or Biochemistry or Medical Laboratory Technology (M.L.T.) with six months experience and or training in cord blood processing and cryogenic storage; or

(b)Diploma in Medical Laboratory Technology (MLT) with one year experience in the testing of bloodand / or its components and / or experience or training in cord blood processing and Cryogenic Storage.

D. AIR HANDLING SYSTEM

1.Air handling for sterile areas shall be different from those for other areas. The filter configuration in the air handling system shall be suitably designed to achieve the grade of

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air as given in the Table I. The environmental microbiological monitoring of clean areas shall be in accordance to the recommended limits given in Table II.

2.The Processing area shall have HVAC system and fitted with HEPA Filters having Grade C (Class 10,000) environment as given in Table I.

3.The entire processing shall be done conforming to Grade A (Class 100) Standard of air quality.

TABLE I

AIR BORNE PARTICULATE CLASSIFICATIONS FOR MANUFACTURE OF STERILE PRODUCTS

Grade	Maximum number of permitted particles per cubic meter equal to or above			
	At rest (b)		In Operation (a)	
	0.5µm	5 µm	0.5 µm	5µm
A	3,500	0	3,500	0
B(a)	3,500	0	3,50,000	2000
C(a)	3,50,000	2000	35,00,000	20,000
D(a)	35,00,000	20,000	Not defined	Not defined

Notes:-

(a)In order to reach the B, C and D air grades, the number of air changes shall be related to the size of the room and the equipment and personnel present in the room. The air system shall be provided with the appropriate filters such as HEPA for grades A, B and C. The maximum permitted number of particles in the ―at rest‖ condition shall approximately

be as under:-

[Grade A and B corresponds with class 100 or M 3.5 or class 5]; Grade C with Class 10,000 or M 5.5 or ISO Class 7; Grade D with Class 1,00,000 or M 6.5 or ISO Class 8. (b)The requirement and limit for the area shall depend on the nature of the operation carried out.

TABLE II

RECOMMENDED LIMITS FOR MICROBIOLOGICAL MONITORING OF CLEAN AREAS ―IN OPERATION‖

Grade	Air samples Cfu/m3	Settle Plates (dia 90mm) cfu/2hrs	Contact plates (dia 55 mm) cfu per plate	Glove points (Five fingers) cfu per glove
A	Less than 1	Less than 1	Less than 1	Less than 1
B	10	5	5	5
C	100	50	25	-
D	500	100	50	-

Notes:-

(a) These are average values.

(b) Individual settle plates may be exposed for not less than two hours in Grade B, C and D areas and for not less than thirty minutes in Grade A area.

E. QUALITY CONTROL

1.Facilities shall be provided for Quality Control such as Haematological, Microbiological and Instrumental testing.

2.Following duties shall be performed under the function of quality control:

(a)To prepare detailed instructions for carrying out such tests and analysis;

(b)To approve or reject raw materials and consumables, used in any step, on the basis of approved specifications;

(c)Haematological tests like Total Nucleated Cell Counts, Mononuclear Cell Count, Enumeration of the population of Stem Cells, Stem Cell viability shall be performed on samples of processed Umbilical cord blood unit;

(d)Microbiological Tests shall be done on Maternal Blood samples for freedom from Hepatitis B Surface Antigen, Hepatitis C Virus antibody, HIV I and II antibodies. Syphilis, Malaria, CMV and HTLV. Bacterial and Fungal Culture shall be done on the umbilical cord blood samples;

(e)Instruments which would be used to process test and store the UCB unit would be validated before commissioning and calibrated from time to time to check their conformity to specific standards according to an approved and valid protocol;

(f)The environmental monitoring of the clean rooms would be done at periodic intervals according to an accepted and validated protocol;

(g)All tests mentioned above shall be done in house except tests under itme numbers (e), (f) and test for enumeration of Stem Cell Population, HLA typing and Genetic Disease Testing which may be outsourced to a competent third party approved by the licensing authority.

F. SCREENING TESTS

1. The maternal blood sample shall be tested for

(a) Hepatitis B;

(b) Hepatitis C;

(c) HIV 1 & 2;

(d) Syphilis;

(e) Malaria;

(f) CMV;
(g) HTLV

2. The Umbilical Cord Blood shall be tested for
(a) Total Nucleated Cell count;
(b) Total Mononuclear Cell Count;
(c) Progenitor Cell (CD34+) enumeration;
(d) Cell Viability;
(e) ABO Group and Rh Type;
(f) Sterility as regards Bacterial and Fungal contamination status;
(g) HLA Matching (Only for allogenic Cord Blood Units).

G. STORAGE

1.The Umbilical cord blood shall be cryopreserved using a controlled rate freezing or equivalent validated procedures. The frozen storage shall be at minus 196ºC and shall not be warmer than minus 150ºC.

2.There will be no shelf life for this class of product.

H. REFERENCE SAMPLES

1.At least two reference samples shall be collected from cord blood unit product prior to cryopreservation and stored at minus 196ºC and shall not be warmer than minus 150ºC. 2.At least one additional reference sample shall be stored at minus 76ºC or colder for the purposes other than viability analysis.

I. LABELLING

1. Initial label placed during collection shall specify:

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(a)Human Umbilical Cord Blood;
(b)Approximate Volume or weight of contents in the collection bag [UCB+ Anticoagulant];
(c)Mother ‘s name;
(d)Place of collection;
(e)Date and time of collection;
(f)Collected by;
(g)To be labeled in bold, ―ROOM TEMPERATURE ONLY– DO NOT REFRIGERATE, DO NOT IRRADIATE‖;
(h)Manufacturing license number.

2. Label at completion of processing and before issue - Cryogenic Storage Label [Statutory label] shall indicate the following:-
(a)Name of product:- Human Progenitor Cell [HPC] – Cord Blood;
(b)Volume or weight of contents;
(c)Percentage of Cryoprotectant [DMSO];
(d)Percentage of any other additive / preservant;
(e)Date of collection [birth] ……;
(f)Date of processing ……..;
(g)Name of manufacturer…….;
(h)Manufacturing license number;
(i)Storage temperature – not less than, - 196ºC and shall not be warmer than minus 150ºC,
(j)Unique Traceability Number and / or BAR Code.

3.Issue label at the time of release of Cord Blood Unit shall indicate the following namely:-
(a)Name of manufacturer;
(b)License number;
(c)All details of the Cryogenic Storage Label;
(d)The results of Total Nucleated Cells, Progenitor Cell percentage {CD34+), Viability;
(e)Results of Transfusion Transmittable diseases testing on maternal blood;
(f)ABO Group and Rh Type;

(g)Date of processing;
(h)Result of HLA typing (allogenic);
(i)Statement ―properly identify intended Recipient and Product‖;
(j)A statement indicating that leukoreduction filters should not be used;
(k)Statement ―Do not irradiate‖
(l)Name and address of receiving hospital.

J. RECORDS OR DOCUMENTATION

1. The licensee shall maintain the following records
(a)Client / donor enrolment / agreement record;
(b)Collection of unit and transportation record;
(c)Master record of stored unit;
(d)HLA Matching record;
(e)Unit Release Register;
(f)Stock Register for Blood Collection Bag Cryoprotectant and Preservant, RBC Sedimentation Enhancer;
(g)Stock Register for Diagnostic Kits, Reagents and other consumables;
(h)Record on feedback after use of cord blood / Adverse reaction record.

2. The following Standard Operating Procedures shall be maintained by the licensee, namely:-
(a)Umbilical Cord Blood collection;
(b)Transportation of the collected Umbilical cord Blood unit;
(c)Processing of Umbilical cord blood unit;
(d)Cryogenic storage of processed umbilical cord blood unit;

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(e)Testing of maternal blood for transfusion transmittable infections;
(f)Testing of Umbilical cord blood for ABO Grouping and Rh Typing;
(g)Testing of Umbilical cord blood unit for Total Nucleated Cell Count, Mononuclear Cell Count, Progenitor Cell (CD34+) enumeration, and viability;
(h)Testing of Umbilical cord blood stem cell unit for sterility;
(i)Disposal of bio medical waste;
(j)Dispensation of Umbilical cord blood unit;
(k)Preventive maintenance Protocol for all Instruments;
(l)Acceptance / Rejection procedure of consumables;
(m)Environment monitoring of classified areas;
(n)Any other standard operative procedure as per requirements.

K. CORD BLOOD RELEASE

1.There shall be designated area with adequate space for procedures and records related to cord blood unit selection and release.

2.The cord blood bank shall obtain written or electronic request from the transplant physician or designee for shipment of the cord blood unit.

3.Accompanying documentation at the time of issue from the cord blood bank shall include indications, contra-indications, caution, instruction for handling and use of the cord blood unit including short-term storage and preparation for transplantation.

4.Procedure for transportation of cryopreserved cord blood unit within the facility shall be designed to protect the integrity of the unit and the health and safety of the personnel.

5.Cryopreserved cord blood unit stored at -150ºC or colder shall be transported in a liquid nitrogen cooled dry shipper that contains adequate absorbed liquid nitrogen and has been validated to maintain temperature below -150ºC for at least 48 hours beyond the expected time of arrival at the receiving facility.

[1][PART XIII]

GENERAL

1. For the purposes of this Schedule, any test or method of testing described in the [2][Indian Pharmacopoeia] shall be deemed to be a method approved by the Licensing Authority.

2. The Licensing Authority shall publish in the Official Gazette from time to time particulars of any test or method of testing approved by him.

1. Renumbered by Notification No. F-18-1/46, dt. 18-6-48
2. Subs. by G.S.R. 19, dated 15-12-1977

[1][SCHEDULE F(I)

PART 1–VACCINES

(A) PROVISIONS APPLICABLE TO THE PRODUCION OF BACTERIAL VACCINES:

1. ***Definition.*** –(1) This part of the Schedule applies to bacterial vaccines made from any micro-organism pathogenic to man or other animal and to vaccines made from other micro-organisms which have any antigenic value.

(2) For the purposes of this part of the Schedule, a bacterial vaccine means a sterile suspension of a killed culture of the micro-organism from which the vaccine derives its name or a sterile extract or derivative of a micro-organism, or a pure suspension of living micro- organisms which have been previously made avirulent.

2. ***Staff of Establishment***.–A competent expert in bacteriology with sufficient experience in the manufacture and standardisation of biological products shall be in charge of the establishment responsible for the production of bacterial vaccine and he shall be assisted by a staff adequate for carrying out the tests required during the preparation and standardisation of the vaccines.

3. ***Proper Name***.–The proper name of any vaccine shall be the name of the micro-organism from which it is made followed by the word ―Vaccine‖ unless this Schedule otherwise provides or if there is no other special provision in this Schedule, some other name as approved by the Licensing Authority. Provided that in the case of the undermentioned preparations the proper name of the vaccine may be as follows: –

1. Anthrax Spore Vaccine (Living).
2. Blackquarter Vaccine.
3. Enterotoxaemia Vaccine.
4. Fowl Cholera Vaccine.
5. Haemorrhagic Septicaemia Adjuvant Vaccine.
6. Haemorrhagic Septicaemia Vaccine (Broth).

[2][7. Multi Component Clostridial Vaccine.

8. Hemorrhagic Septicaemia Vaccine – Alum Treated.]

4. ***Records***.–Cultures used in the preparation of vaccine before being manipulated into a vaccine, should be thoroughly tested for identity by the generally accepted tests applicable to the particular micro-organisms.

The permanent records which the licensee is required to keep shall include amongst others, a record of the origin, properties and characteristics of the cultures.

5. ***Combined Vaccines***.–Vaccines may be issued either singly or combined in any proportion in the same container. In the case of combination of vaccines, a name for the combined vaccine may be submitted by the licensee to the Licensing Authority, and if approved, may be used as the proper name of the vaccine.

1. Added by Ministry of Health F.P., W.H and U.D. Notfn. No. F.1-6/62-D (SO. 2889), dt. 2-7-1969 2. Ins. by G.S.R. 659(E) ,dt. 31.8.1994.

6. ***Preparation***– Bacterial vaccines, simple or polyvalent, are prepared from selected cultures after careful examination for their identity, specificity, purity and antigencity. They may be prepared in the following manner:.–

(a) Formal Cultures or Bacterins.– The selected pure culture strain or strain are grown in a suitable fluid medium, at an optimum temperature, for an appropriate period. The pure growth is then exposed to the action of solution of Formaldehyde I.P. in suitable concentration and temperature. The product is finally filled in suitable sterilised containers which are subsequently sealed.

(b) Vaccine of Bacterial Products or Bacterial Derivatives.–These vaccines are prepared by growing the organisms on suitable media and then deriving specific antigenic constituents of the bacteria by various special methods.

(c) Living Bacterial Vaccines.– They are prepared from non-pathogenic but fully immunogenic strains of micro-organism. Strict aseptic precautions are taken throughout the preparation against the introduction of microbial contaminants.

7. ***General Standards:***.

(a)Description.– Bacterial vaccines are colourless to yellowish brown liquids containing dead or viable bacteria in homogenous suspension.

(b) Identification.–All types of vaccines confer active immunity in the susceptible animals which can be demonstrated by injecting suitable experimental animals with the calculated doses of the product and subsequently determining the presence of the protective antibodies in their serum and/or by challenging the vaccinated animals by injecting virulent strain of the homologous organisms. The protected animals should survive the challenge.

(c) Test for Sterility.–All bacterial vaccines shall be tested for sterility in accordance with the provision of Rules 115 to 119 (both inclusive). If the vaccine contains added bactericide or bacteriostatic, a quantity of medium sufficient to render the growth inhibitor ineffective is added to the sample, or a suitable substance is added to the sample, or a suitable substance is added in concentration sufficient to render the growth inhibitor ineffective but not itself to inhibit the growth of micro-organism.

(d) Purity Tests for Living Bacterial Vaccine.–Petri dishes containing suitable media are streaked with the final product and incubated at 37˚ C for 72 hours. The vaccine passes the test if no growth of micro-organisms other than those from which the vaccine was prepared is observed. Other tests include examination for motility of the organisms, fermentation reactions and thermoagglutination test and dye-inhibitor tests in case of bruceliza vaccine.

(e) Safety Test.– The safety of the vaccine shall be assessed by injecting it in appropriate doses in suitable susceptible animals. No animal should show any untoward, general or local reaction within seven days after inoculation.

(f). Potency Test.–Wherever applicable, susceptible experimental animals are inoculated with the calculated doses of the final product. The animals are challenged after the period of immunisation, with virulent infective dose of the homologous culture along with the controls. The potency of the vaccine is assessed by the survival of the vaccinated animals and the death of the controls.

8. ***Labelling:***

(a) The label on the ampoule or the bottle shall indicate:.–

(i) Proper name.

(ii) Contents in millilitres or doses.

(iii) Potency, if any.

(iv) Batch number.

(v) Expiry date.

(b) The label on the outside container shall indicate:

(i) Proper name.

(ii) Contents in Millilitres or doses.

(iii) Batch number.

(iv) Date of manufacture.

(v) Manufacturing licence No.

(vi) Manufacturer‘s name and address.

(vii) ―For animal treatment only‖.

(viii) Storage conditions.

9. ***Storage***.―Bacterial vaccines shall be stored, protected from light at temperature between 2˚C to 4˚C and shall not be frozen.

10. ***Date of manufacture***.– The date of manufacture shall be, unless otherwise specified in the individual monograph in this part, as defined in clause (b) of sub-rule (3) of rule 109.

Anthrax Spore Vaccine (Living)

1. ***Synonyms***.―Avirulent Anthrax Spore Vaccine or Bacillus Anthracis Vaccine (Living).

2. ***Definition***.―The vaccine is a suspension of living spores of an uncapsulated avirulent strain of B anthracis in 50 per cent glycerine saline.

3. ***Preparation***.―Avirulent B, anthracis of known antigenicity is grown on suitable medium at pH 7.4 in Roux flasks. After 72 hours incubation at 37˚ C, the pure sporulated culture growth which shows 70 to 80 per cent sporulation is washed with normal saline and glycerinated to the extent of 50 per cent by weight of the culture washing and the whole suspension is kept at room temperature for twenty-one days to allow for the stabilization of the spores.

4. ***Standard***:.

(a) Description.― It is slightly opalescent or pale brown semi-viscous liquid.

(b) Identification.―Uncapsulated B anthracis which is avirulent can be isolated from the vaccine.

(c) Sterility test.― Should comply with the test for sterility described in the general monograph on ―Bacterial Vaccine‖.

(d) Purity Test.― Complies with the ―Purity Tests for Living Bacterial Vaccine‖ described under the general monograph on ―Bacterial Vaccines‖.

(e) Safety Test.―Four healthy adult guinea-pigs each weighing 300-450 g. not previously treated with any material which will interfere with the test are inoculated subcutaneously, two with 0.2 ml. each and two with 0.5 ml. each of the unglycerinated suspension respectively. Four more guinea-pigs are injected with 1:5 dilution of the glycerinated product in the same manner. No untoward reaction should be observed and none of the animals should die of anthrax during the period of observation for seven days.

(f) Safety and Potency Test in sheep and goat–Spore count of the glycerinated suspension is made after twenty-one days from the date of glycerination. Three plates for each of the three dilution 10_5, 10_6 and 10_7 are made.

Eight sheep and eight goats each weighing not less than 18 kg. are injected subcutaneously in the following manner:–

two sheep : Each subcutaneously with 10 ml. of the stock suspension (for safety).

two goats : Each subcutaneously with 5 ml. of the stock suspension (for safety).

six sheep : Each subcutaneously with one million spores suspended in 50 per cent glycerine saline solution.

six goats : Each subcutaneously with one million spores suspended in 50 per cent glycerine saline solution.

None of these animals should die of anthrax. Twenty one days after vaccination, the animals are challenged with 100 lethal doses of virulent *B. anthracis* spores along with two healthy sheep and two goats as controls.

All the controls should die of anthrax within 72 hours after challenge and at least 66 per cent of the vaccinated animals should survive. The animals shall be observed for a minimum of ten days from the date of challenge.

[1][*(g) Viable Count.*– The vaccine when plated on suitable media should show 10 million viable spores per cattle dose and 5 million spores per sheep dose.]

5. ***Labelling and Storage***.– Should comply with the requirements for ―Labelling‖ and ―Storage‖ as laid down in the general monograph on ―Bacterial Vaccines‖.

[2]**[6**. ***Expiry Date***.– The date of expiry of the potency of the vaccine shall be not more than two years from the date of manufacture if stored in 4o C and six months, if stored at room temperature.]

Blackquarter Vaccine

1. ***Synonym***.–Blackleg vaccine or Quarter Evil Vaccine.

2. ***Definition***.– Blackquarter Vaccine is a culture of *Clostridium chauvoei* grown in a suitable anaerobic fluid medium and rendered sterile and toxic by the addition of Solution of Formaldehyde I.P. in such a manner that it retains its immunising properties.

3. ***Preparation***.–Cultures of *Cl. Chauvoei* are grown in a suitable anaerobic fluid medium and killed by the addition of a suitable concentration of Solution of Formaldehyde I.P. The final product shall be adjusted to pH.7.0.

4. ***Standards:***.

(a) Description.–It is a yellowish brown liquid containing dead bacteria in suspension.

(b) Identification.–It protects susceptible animals against infection with *Cl. Chauvoei*.

(c) Sterility Test.–Should comply with the test for sterility described in the general monograph on ―Bacterial Vaccine‖.

1. Subs. by. G.S.R 659 (E) ,dt.. 31-8-1994.

2. Ins. by. G.S.R 659 (E) ,dt.. 31-8-1994.

(*d*) *Safety and Potency Tests.*–At least six adult healthy guinea-pigs each weighing 300 g to 450 g are injected subcutaneously each with 3 ml. of the product followed a week later by a second injection with the same dose. They should not show any systemic reaction but may show only a minimum of local reaction. Fourteen days after the second injection six of the vaccinated guinea-pigs are challenged intramuscularly with 25 viable spores of *Cl. Chauvoei* equivalent to 5 c.h.d. along with 0.2 ml. of a 5 per cent solution of calcium chloride. Two controls are used. The controls

should die of the specific injection and at least 4 of the six vaccinated animals should survive before the product is passed for issue.

5. ***Labelling and Storage***.– Should comply with the requirements of ―Labelling‖ and ―Storage‖ as laid down in the general monograph on ―Bacterial Vaccines‖.

6. ***Expiry Date***.—- The date of expiry of the potency of the vaccine shall not be more than twenty-four months from the date of manufacture.

Brucella Abortus (Strain 19 Vaccine) (Living)

1. ***Synonym***.–Contagious Abortion Vaccine, (Strain 19) (Living).

2. ***Definition***.–Brucella Abortus (Strain 19) Vaccine (Living) is a suspension of a pure smooth living culture of *Br. Abortus* of low virulence in normal saline solution.

3. ***Preparation***.–Forty eight to seventy-two hour old growth of *Br. Abortus* (Strain 19) on potato agar medium in Roux flasks washed with buffered normal saline solution pH 6.4 and the pure growth from the flasks are pooled together, 0.5 ml. of the pooled product is mixed with 4.5 ml. of normal saline solution at pH 6.4 in graduated centrifuge tube and centrifuge at 3000 r.p.m for one hour. The percentage of cell deposit is assessed by reading the amount of cell deposit obtained.

The concentrated suspension is then diluted with buffer normal saline solution so that the final product contains 0.72 per cent bacterial cell deposit.

4. ***Standard****:*

(a) Description.–It is an almost white turbid liquid containing live bacteria in suspension.

(b) Identification.–It consists of Gram-negative bacilli capable of protecting susceptible animals against Brucellosis.

(c) Sterility Test.–Should comply with the test for sterility described in the general monograph on ―Bacterial Vaccine‖.

(d) Purity Test.–A smear of the finished products is examined microscopically after staining by Gram‘s method for evidence of any contamination. When grown on suitable media, *Br. Abortus* should be obtained in a pure state.

(e) Safety Test.–Two healthy guinea-pigs each weighing 300 g. to 450g. are inoculated subcutaneously each with 1.0 ml. of the final product. The guinea-pigs should not show excessive reaction of a toxic nature during the period of observation of ten days.

(f) Potency Test.–Each of a group of four healthy guinea-pigs, drawn from a uniform stock and each weighing 300 g. to 450 g. is injected intra-muscularly with 1 ml. of the vaccine, and is challenged nine weeks after vaccination by the intramuscular injection of 1 ml. of a suspension containing 5,000 fully virulent *Br. Abortus* organisms. Each of a group of two unvaccinated guinea-pigs is similarly injected. After a further six weeks, the guinea-pigs are killed and cultures are made from their spleens. More than half of the vaccinated guinea-pigs contain no demonstrable *Br. Abortus* in the spleen; all the controls are infected.

(g) Viable Count.–The vaccine when plated on suitable media should show between 14, 000 million and 18,000 million *Br. Abortus* organisms per ml. At least 80 per cent brucella organisms should be in the smooth phase.

4. ***Labelling and storage***.– Should comply with the requirements of ―Labelling‖ and ―Storage‖ as laid down in the general monograph on ―Bacterial Vaccines‖. The liquid vaccine shall be issued fresh as far as possible without allowing any period of storage after manufacture.

5. ***Expiry Date***–The date of expiry of the vaccine shall be not more than five weeks from the date of manufacture.

Enterotoxaemia Vaccine

1. ***Synonyms***.–Clostridium Welchii, Type D, Formal Culture: Pulpy Kidney Vaccine.

2. ***Definition***.–Enterotoxaemia Vaccine is a culture of a highly toxigenic strain of *Clostridium* type D, group is an anaerobic medium rendered sterile and toxic by the addition of Solution of Formaldehyde I.P in such a manner that it retains its immunising properties.

3. ***Preparation***.– Selected toxigenic strain of *Cl. Welchii* type D, is grown in a liquid medium under conditions which ensure maximum epsilon toxin production. The culture is checked for purity and toxicity as tested in mice. Solution of Formaldehyde I.P. is added in suitable concentration and the formolised culture is kept at 37° C till the production is sterile and non-toxic.

4. ***Standard***:

(a) *Description*- It is a yellowish brown liquid containing dead bacteria in suspension.

(b) *Identification*- When injected into susceptible animals it stimulates the production of epsilon antitoxin of *Cl. Welchii*, type D.

(c) *Sterility Test*- Complies with the test for sterility described in the general monograph on ‗Bacterial Vaccines'.

(d) *Safety and Potency Tests*- At least eight sheep each weighing not less than 18 kg. or twelve rabbits each weighing 1 kg. to 1.5 kg. are used for testing the safety and potency of each brew of the vaccine. Two sheep receive subcutaneously 10 ml. each and the other six sheep receive each 2.5 ml. of the product subcutaneously. The rabbits are given subcutaneously a dose of 5 ml. each. The sheep and rabbits are observed for five days. They should show only a minimum local reaction and no systemic reaction.

The sheep receiving 10 ml. are withdrawn from experiments after five days. Each of the other six sheep is inoculated with a second dose of 2.5 ml. fourteen days after the first injection. The rabbits are inoculated with 5 ml. as a second dose, after one month of the first inoculation. Ten days after the second inoculation the sera of sheep or rabbits are pooled separately. The pooled serum of each group of animal shall contain in each ml. not less than two international units of *Cl. Welchii* epsilon antitoxin which is determined by testing on mice as follows:

One ml. of the pooled serum is mixed with one ml. of the epsilon toxin of *Cl. Welchii* type D, containing 300 mouse-minimum-lethal-doses (mouse m.l.d.) and kept at room temperature for half an hour. At least two mice each weighing not less than 18 g. are each given intravenously 0.2 ml. of the mixture. As control two mice each weighing not less than 18 g. should each receive 0.2 ml. of the toxin containing 300 mouse m.l.d per ml. diluted with equal volume of normal saline. The control mice should die within 1 to 2 hours while the mice receiving the mixture of serum and toxin should survive for at

least two days. Sera containing one International Unit of epsilon antitoxin per ml. will be able to neutralise 150 mouse m.l.d. of epsilon toxin of *Cl. Welchii*, type D.

5. ***Labelling and Storage***.–Should comply with the requirements regarding ―Labelling‖ and ―Storage‖ as laid down in the general monograph on ―Bacterial Vaccines‖.

6. ***Expiry Date***.–The expiry date of potency of the vaccine shall be not more than twelve months from the date of manufacture.

Fowl Cholera Vaccine (Polyvalent)

1. ***Synonym***.–Pasteurella Septica Vaccine (Avian).

2. ***Definition***.–Fowl Cholera Vaccine is a formolised pure broth culture of virulent strains of *Pasteurella Septica* (Avian).

3. ***Preparation***.–The strains are grown separately in nutrient broth for 48 hours at 37˚ C. The pure growth is killed by the addition of a Solution of Formaldehyde I.P in a suitable concentration. The cultures are then mixed in equal proportions and the final vaccine is bottled in suitable containers.

4. ***Standard-***

(a) Description.–It is a light yellow liquid containing dead bacteria in suspension.

(b) Identification.–It protects susceptible birds against *P. aviseptica* infection.

(c) Sterility test.–Complies with the test for ―Sterility‖ described under the general monograph on ―Bacterial Vaccines‖..

(d) Safety Test.–Two healthy young fowls each weighing not less than 400 g. or twelve healthy mice are inoculated subcutaneously each with 1 ml. of the final product. The birds should not show any untoward reaction during the period of observation for seven days.

5. ***Labelling and Storage***.–Should comply with the requirements of ―Labelling‖ and ―Storage‖ as laid down in the general monograph on ―Bacterial Vaccines‖.

6. ***Expiry Date***.–The date of expiry of potency of the Vaccine shall be not more than six months from the date of manufacture.

Hemorrhagic Septicaemia Adjuvant Vaccine

1. ***Synonym***.– Pasteurella Septica Adjuvant Vaccine.

2. ***Definition***.–The vaccine is a homogenous suspension of formolised agar-washed *Pasteurella septica* with liquid paraffin and lanolin.

3. ***Preparation***.–Pure growth of a highly antigenic strain of *P. Septica* in phase 1 grown on nutrient agar medium containing 0.5 per cent yeast extract is washed with 0.5 per cent formol saline. The pooled suspension is diluted with normal saline to contain approximately 2100 million *P. Septica* organisms per ml. The safety test of this adjusted suspension is conducted on four white mice each weighing not less than 18 g. and observed for three days before it is mixed with liquid paraffin and lanolin in suitable proportion.

The mixture is blended until a homogenous emulsion is obtained which is filled in suitable containers.

4. *Standard:*

(a) Description– It is a white thick oily liquid containing dead bacteria in suspension.

(b) Identification.–It protects susceptible animals against infection with *P. Septica.*

(c) Sterility Test.–It complies with the test for ―Sterility‖ described in the general Monograph on ―Bacterial Vaccines‖.

(d) Safety Test.– Six white mice each weighing not less than 18 g. are inoculated intraperitoneally each with 0.5 ml. of the vaccine. None of the mice should die of pasteurellosis during the observation period for seven days.

(e) Potency Test.–Three susceptible calves in good condition between the ages of nine months to three years are injected intramuscularly, each with 2 ml. of the vaccine, in the case of animals weighing upto 140 kg. and 3 ml. for heavier ones.

Three weeks later these animals along with two healthy animals of the same type and species are challenged subcutaneously with 18 hours old broth culture of *P. Septica* equivalent to at least 50 million mouse minimum infective dose. Both the controls should die of

pasteurellosis and at least two out of the three protected animals should survive the challenge dose for a period of seven days.

5. ***Labelling and storage-*** Should comply with the requirements for ―Labelling‖ and ―Storage‖ as laid down in the general monograph on ―Bacterial Vaccines‖.

6. ***Expiry Date-*** The date of expiry of potency of the vaccine shall be not more than twelve months from the date of manufacture.

Haemorrhagic Septicaemia Vaccine (Broth)

1. *Synonym.*–Pasteurella Septica Vaccine (Broth).

2. *Definition.*–Haemorrhagic Septicaemia Vaccine is formolised culture of a virulent strain of Pasteurella septica in nutrient broth.

3. *Preparation.–.Septica* culture is grown in nutrient broth at 37˚C. The pure growth is killed by the addition of a solution of Formaldehyde I.P. in a suitable concentration.

4. ***Standard:***

(a) Description.–It is a pale yellow liquid containing dead bacteria in suspension.

(b) Identification.–It protects susceptible animals against infection with *P.Septica.*

(c) Sterility Test.–Complies with the test for ―Sterility‖ described under the general monograph on ―Bacterial Vaccines‖.

(d) Safety Test.–Four healthy rabbits each weighing 1 kg. to 1.5 kg. are inoculated subcutaneously each with 5 ml. of the product. There should be no untoward reaction during the period of observation for seven days. Alternately two rabbits and six mice may be employed. The dose for mice will be 0.5 ml.

5. *Labelling and Storage.*–Should comply with the requirements of ―Labelling‖ and ―Storage‖ as laid down in the general monograph on ―Bacterial Vaccines‖.

6. *Expiry Date.*–The date of expiry of potency of the vaccine shall be not more than six months from the date of manufacture.

Salmonella Abortus Equi Vaccine

1. ***Synonym***.–Equine Abortion Vaccine.

2. ***Definition***.– Equine Abortion Vaccine is a mixture of equal parts of pure formolised cultures of smooth laboratory strains of *Salmonella abortus equi*.

3. ***Preparation***.–The strains are grown separately on plain agar in Roux flasks, for 24- 28 hours at 37˚ C. The pure growth is washed with normal saline solution and the washings are pooled together. The suspension is standardised to contain approximately 600 million *Sal.Abortus equi* organisms per ml. using normal saline solution as diluent. The culture is killed by the addition of sufficient quantity of solution of Formaldehyde I.P in a suitable

concentration and the product is kept at 37˚C for seven days. Potassium alum is added to give a final concentration of 1 per cent

4. ***Standard****:*

(a) Description.–It is an opalescent liquid containing dead bacteria in suspension.

(b) Identification.–It protects susceptible animals against infection with *Sal. Abortus equi*.

(c) Sterility Test.–Complies with the test for sterility described in the general monograph on ―Bacterial Vaccines‖.

(d) Safety Test- Six white mice each weighing not less than 18 g. are inoculated intraperitoneally each with 0.5 ml. of the product. None of the mice should die of salmonellosis. The mice are observed for ninety-six hours.

5. ***Labelling and Storage***- Should comply with the requirements for ―Labelling‖ and ―Storage‖ as laid down in the general monograph on ―Bacterial Vaccines‖.

6. ***Expiry Date***- The date of expiry of potency of the vaccine shall be not more than six months from the date of manufacture.

Streptococcus Equi vaccine

1. ***Synonym***.– Strangles Vaccine

2. ***Definition***.– *Streptococcus equi* Vaccine is a phenolised culture of a number of different isolates of Streptococcus equi in glucose serum broth.

3. ***Preparation***.– Equal proportions of forty-eight hours old pure cultures of different isolates of *Str. Equi* in serum glucose both are mixed together. The suspension is centrifuged and the deposit is washed with normal saline solution after removing the supernatant. The washed cells are suspended in normal saline and heated in a water bath 65˚C for two hours. Phenol and normal saline are added to give a final concentration of 1200 million *Str. Equi* organisms per ml. and 0.5 per cent of phenol in the vaccine.

4. ***Standard-***

(a) Description.– It is a slightly opalescent liquid containing dead bacteria in suspension.

(b) Identification.–It protects susceptible animals against infection with *Str. Equi*.

(c) Sterility Test.–Complies with the test for ―Sterility‖ described in the general monograph on ―Bacterial Vaccines‖, the nutrient broth being replaced by glucose broth.

(e) Safety Test.–Two ponies and two rabbits (each weighing not less than 1 kg.) are inoculated each with 10 ml. and 2 ml. respectively of the final product. The animals should not show any untoward reaction during the period of observation of seven days.

5. ***Labelling and Storage***.–Should comply with the requirements for ―Labelling‖ and ―Storage‖ as laid down in the general monograph on ―Bacterial Vaccines‖

6. ***Expiry Date***.– The date of expiry of potency of the vaccine shall be not more than six months from the date of manufacture.

Old Adjuvant Vaccine against Pasteurellosis in Sheep and Goats.

1. ***Synonym-*** Pasteurella Septica Adjuvant Vaccine for ovines and Caprines.

2. ***Definition***- The vaccine is a homogenous suspension of formolised agarwashed Pasteurella septica of ovine origin with liquid paraffin and lanolin.

3. ***Preparation***― Pure growth of highly antigenic strains (R1, R2, R4) in phase I grown separately on nutrient agar medium containing 0.5 per cent yeast extract is washed with 0.5 per cent Normal saline. Equal quantities of the suspension of three strains diluted with Normal saline to contain approximately 2100 million organisms per ml. is pooled together. The safety test of this adjusted pooled suspension is conducted in for white mice each weighing not less than 18 g. and observed for three days before it is mixed with liquid paraffin and lanolin in suitable proportion.

The mixture is blended until a homogenous emulsion is obtained which is filled in suitable containers.

4. ***Standards:***

(a) Description- It is a white thick oily liquid containing dead bacteria in suspension.

(b) Identification- It protects susceptible animals against infection with *P. Septica*.

(c) Sterility Test- Complies with the test for sterility described in the general monograph on ―Bacterial Vaccines‖.

(*d) Safety Test*- Six white mice each weighing not less than 18 g. are inoculated intra-peritoneally each with 0.5 ml. of the vaccine. None of the mice should die of Pasteurellosis druing the observation period of seven days.

The vaccine is also inoculated into six sheep and six goats in a dose of 3 ml. each intramuscularly and are observed for a period of seven days. During this period none should die of Pasteurellosis.

(e) Potency Test- Not being done at present.

5. ***Labelling and Storage***- Should comply with the requirements for ―Labelling‖ and ―Storage‖ as laid down in the general monograph on ―Bacterial Vaccines.

6. ***Expiry Date***- The expiry date of Potency of the Vaccine shall be not more than twelve months from the date of manufacture.

[1]*Multicomponent of Clostridial Vaccine*

1. ***Synonyms***. – Combined anaculture of *Clostridium perfringens* type C and D, C1. septicum and CI.oedematiens.

2. ***Definition*** – It consists of four highly antigenic components containing the toxoids of *C. perfringens* type D, *CI. Perfringens* type C, *Cl. oedematiens* and CI. septicum which are prepared in double strength and then combined in such a proportion that would invoke adequate anti-toxin response in the vaccinated sheep against each antigen incorporated in the vaccine

3. ***Preparation*** – The above strains are grown separately in suitable liquid media under conditions which ensure maximum toxin production. The cultures are checked for purity and toxicity in mice. Solution of Formaldehyde I.P. of analytical grade is added to a 0.5 per cent final concentration and formalized cultures are kept at 37°C till the product is sterilized and atoxic. The formalized anacultures are pooled, precipitated by the addition of Aluminium Chloride, 20 per cent solution in distilled water to have a final concentration of the chemical to 10 per cent and pH adjusted to 6.0.the sedimented toxoid is reconstituted to have its original volume in normal saline.

1. Ins. by G.S.R. No. 659(E) ,dt. 31-8-1994

4 ***Standards*** *:*

(a) Description – It is whitish liquid when shaken thoroughly to contain killed bacteria and toxoid in suspension.

(b) Identification – When injected to susceptible animals it stimulates the production of epsilon and beta antitoxins against *CI. perfrigens* type D and C and also antitoxins against *CI. septicum* and toxin of *CI. Oedematiens*.

(c) Sterility Test – Complies with the test of sterility described in general monograph on ―Bacterial Vaccines.‖

(d) Safety Test – Four sheeps each are inoculated with 10 ml. S/C of the product and these are observed for 7 days during which period animals shall not show any local or systemic reaction.

(e) Potency Test – Eight sheep each are inoculated with 2 doses of vaccines S/C at an interval of 21 days and bled on 10th day after 2nd inoculation for collection of serum for assessing the antitoxin titre against each antigen incorporated in the vaccine. The post-

inoculation serum should contain not less than 2 i.u. of epsilon and beta antitoxins of *CI. perfringens* and 2.5 i.u. of *CI. septicum* antitoxin and 4 i.u. of *CI. oedematiens* antitoxin.

5. ***Labelling and storage*** - Shall comply with the requirements regarding labelling and storage as laid down in the general monograph on ―Bacterial Vaccine‖.

6. ***Expirty date*** – The expiry date of potency of vaccine shall not be more than 6 months from the date of manufacture.

Haemorrhagic Septicaemia Vaccine – Alum Treated

1. ***Synonyms*** – Pasterulla multocida/(Yersinia Multocida) vaccine – Alum treated.

2. ***Definition*** -- The vaccine is a formalized culture of a virulent strain of *Pasteurella multocida* in nutrient broth treated with potash alum.

3. ***Preparation*** -- A highly potent strain of *Pasteurella multocida* type I in Phase I is grown on nutrient broth at 37°C. The pure growth is killed by the addition of a solution of Formalin I.P in suitable concentration (0.5 per cent). This is treated with Potassium Alum I.P to give a final concentration of 1 per cent.

4. ***Standard*** *:*

(a) Description – It is a white suspension containing dead bacteria and alum.

(b) Identification – It protects susceptible animals against infection with *P. multocida*.

(c) Sterility Test -- It complies with the test for sterility described under general monograph on ―Bacterial Vaccines‖.

(d) Safety Test -- Four healthy rabbits each weighting 1 to 1.5 kg. are inoculated subcutaneously each with 5 ml. of the product. There shall be no untoward reaction during the period of observation for 7 days except slight local swelling. Alternatively two rabbits and six mice may be employed. The dose for mice will be 0.5 ml.

5. ***Labelling and Storage*** *:*-- Shall comply with the requirements of labelling and storage as laid down in the general monograph on ―Bacterial Vaccines‖.

6. ***Expiry date*** – The date of expiry of potency of the vaccine shall be not more than six months from the date of manufacture.]

(B) PROVISIONS APPLICABLE TO THE PRODUCTION OF VIRAL VACCINES

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1. ***Definition-*** (***i***) This part of the Schedule applies to viral vaccines live or inactivated made from any virus pathogenic to domestic animals and poultry and made from other modified viruses which have any antigenic value.

(ii) For the purpose of this Part of the Schedule, a virus vaccine means a sterile suspension or a freeze dried powder containing the modified living or inactivated virus particles, which in its original unaltered stage, causes disease from which the vaccine derives its name and which has been prepared from the blood or tissues of a suitable host in which it has been grown *in vivo* or from tissue culture.

2. ***Staff of Establishment-*** The establishment in which viral vaccines are prepared must be under the direction and control of an expert in bacteriology with specialized training in virology and sufficient experience in the production of viral vaccines, and he shall be assisted by a staff adequate for carrying out the tests required during the preparation and standardisation of the vaccines.

3. ***Proper Name-*** The proper name of any viral vaccine shall be the name of the disease which is caused by the particular virus from which the vaccine is produced followed by the word ―vaccine‖ unless the Schedule otherwise provides, if there is no special provision in the Schedule

such other name as is approved by the Licensing Authority. Provided that in the case of the undermentioned preparations the proper name of the vaccine shall be as follows:

(i) Fowl Pox Vaccines, Chick Embryo Virus (Living).

(ii) Fowl Pox Vaccine, Pigeon Pox Virus (Living).

(iii) Horse Sickness Vaccine (Living)

(iv) Ranikhet Disease Vaccine (Living)

(v) Ranikhet Disease Vaccine F Strain (Living)

(vi) Rinderpest Goat Adapted Tissue Vaccine (Living)

(vii) Rinderpest Lapinised Vaccine (Living)

(viii) Rinderpest Lapinised Avianised Vaccine (Living)

(ix) Sheep and Goat Pox Vaccine (Living)

(x) Swine fever vaccine (crystal violet)

(xi) Swine fever vaccine lapinised (Living).

[1][(xii) Foot and Mouth Dieseas Vaccine (Inactivated).

(xiii) Canine Hepatitis Vaccine (Living).]

[2][**4.** ***Records***- The seed virus used in the preparation of vaccine shall, before being used for preparing a batch, be thoroughly tested for purity, safety, sterility and antigenicity by the generally accepted tests applicable to a particular virus. It shall not be more than five passages away from the stock seed virus, unless otherwise prescribed for a particular virus. The stock seed virus shall be maintained by seed-lot system at specified passage level and tested for bacterial, mycoplasmal and extraneous viral contamination. The permanent record which the licensee is required to keep shall include a record of the origin, properties and characteristics of the seed virus from which the vaccines are made.]

5. ***Tests***- Viral vaccine shall be tested for sterility, safety and potency on suitable test animals and for viability in the case of live vaccines.

(a) *Sterility Test*- All vaccines shall be tested for sterility in accordance with rules 115 to 119. If the vaccine contains added bactericides or bacteriostatic, a quantity of medium sufficient to render the growth inhibitor ineffective is added to the sample or a suitable substance is added in a concentration sufficient to render the growth inhibitor ineffective but not itself to inhibit the growth of micro-organisms.

(b) *Safety Test*- Suitable laboratory animals or large animals or birds may be employed to test the vaccine for safety. Details of the safety test are given in the individual monograph.

1. Ins. by G.S.R. 659(E) ,dt. 31-8-1994.

2. Subs. by G.S.R. 659(E) ,dt. 31-8-1994.

(c) *Potency Test*- All virus vaccines for which potency test has been prescribed shall be tested for potency and only those which pass the potency test shall be issued. Details of the potency test are given in the individual monograph.

6. ***Storage***- Live viral vaccines shall be stored, protected from light at sub-zero temperature as required. Other viral vaccines shall be stored at 2 ˚ C to 4 ˚ C but shall not be frozen.

7. ***Condition of housing of animals***- (***i***) The animals used in the production of vaccine must be housed in hygienic conditions in premises satisfactory for this purpose.

(ii) Only healthy animals may be used in the production of vaccine. Each animal intended to be used as a source of vaccine must, before being passed for the production of vaccine be subjected to a period of observation in quarantine for at least seven days. During the period of quarantine the animal must remain free from any sign of disease and must be well kept.

1[(***iii***) The poultry birds from which eggs and cell culture for production of vaccines are obtained should be housed in a manner so as to keep them free from extraneous infection and shall be screened at frequent intervals for common bacterial, mycoplasmal and viral infection. The record of the tests and their results shall be maintained by the manufacturers.]

8. ***Labelling***- The provisions of ―Labelling‖ as laid down for Bacterial Vaccines shall also apply to Viral Vaccines. The following additional information shall also be included on the label of the outside container:

(*i*) The name and percentage of bacteriostatic agent contained in the vaccine.

(ii) If the vaccine as issued for sale contains any substance other than the diluent, the nature and strength of such substances.

9. ***Date of Manufacture***- For the purpose of this part of the Schedule, the date of manufacture shall be what is given unless otherwise stated in the individual monograph, as defined in sub-clause (b) of sub-rule (3) of rule 109.

Fowl Pox Vaccine Chick- Embryos Virus (Living)

1. ***Synonym***- Egg adapted Fowl Pox Vaccine (Living).

2. Definition- Fowl-pox Vaccine, Chick-Embryo Virus (Living) is a suspension of a modified living virus (e.g. Mukteswar Strain) prepared from the chorioallantoic membrane (CAM) of the infected embryo and is either freeze dried or is issued as glycerinated liquid vaccine.

3. ***Preparation***- Active chick-embryos obtained from Salmonella pullorum free flock, are used. 1[Twelve to thirteen days old embryos are injected with a suitable dilution of the suspension of the infected membrane (seed virus) of chick embryo adopted fowl pox virus.] The suspension of the stock seed virus is dropped on the CAM. After an incubation at 37˚C for a suitable period membranes showing discrete or confluent lesions (pocks) are harvested. These are homogenised with adequate quantity of antibiotics (penicillin and streptomycin) ampouled in 0.5 ml. quantities and freeze dried.

4. ***Standard-***

(a) Description- Light mauve coloured scales.

(b) Identification- When reconstituted vaccine is applied to scarified area of the skin of a fowl it produces characteristic lesions of fowl pox. This product should afford protection against fowl pox.

1. Ins. by. GSR 659(E) , dt. 31-8-1994.

(c) Moisture Content- Moisture Content in the finished product should not exceed 1.0 per cent.

(d) Safety Test- For testing each batch of fowl pox vaccine twelve healthy cockerels, or other suitable young chicken each weighing not less than 400 g. from the same source are taken. This group of twelve birds is immunized at least twenty-one days previous to the test, with fowl pox vaccine. The vaccine under test is reconstituted in 5 ml. of 50 per cent glycerine saline and administered to fowls as follows:-

Three of the test birds are injected subcutaneously with 0.8 ml. or 10 times the field doses of the vaccine under test. This group serves to indicate whether the product is free from other viruses and bacteria causing septicaemia or not.

Three of the test birds are injected intratrecheally with 0.3 ml. or 10 times the field dose of vaccine under test. This group serves to indicate whether the product is free from the virus of infectious laryngotracheitis and similar disease.

1[Three of the test birds are injected intranasally with 0.2 ml. of 10 times of the field dose of the vaccine under test. This group serves to indicate whether the product is free from the virus of infectious laryngotracheitis and similar disease.]

The three remaining birds serve as controls. They are isolated and kept under observation for twenty-one days. The birds that succumb during the period of twenty-one days are subjected to a careful postmortem examination. The product is withheld from issue until the vaccine and the test birds are shown to be free from the causative agents of any extraneous disease.

(*e*) *Sterility test*- Complies with the tests for sterility as described under the general monograph on ―Viral Vaccines‖.

(f) Potency Test- For testing of potency three unsusceptible birds each weighing not less than 400 g. are vaccinated using the field dose by the stick method and examined for ―takes‖. Three weeks after vaccination these birds along with two unvaccinated controls are exposed to challenged virus and observed for fourteen days. The vaccinated birds should not manifest any reaction, while the controls should show active ―takes‖.

5. ***Labelling***- Should comply with the requirement for ―Labelling‖ as laid down in the general monograph on ―Viral Vaccines‖.

6. ***Storage and Expiry date***- Freeze dried vaccine shall be expected to retain its potency for periods at temperatures as specified below:-

-15 ˚ C to - 20˚ C–Twenty-four months.

2˚ C to 4˚ C–Twelve months.

Room temperature– upto one month.

The liquid vaccine shall be expected to retain its potency for periods and temperatures as specified below:

2˚ C to 4 ˚C – six months.

Room temperature– seven days.

1. Ins. by. GSR 659(E) , dt. 31-8-1994.

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Fowl- Pox Vaccine, Pigeon Pox Virus (Living)

1. ***Synonym***- Fowl Pox Vaccine (Pigeon pox scab).

2. ***Definition-*** Fowl Pox Vaccine, Pigeon-pox Virus (living) consists of pigeon pox virus in scabs collected from artificially infected pigeons and dried.

3. ***Preparation-*** Healthy pigeon are scarified on the legs and breast, with a suitable dilution of the suspension of pigeon-pox virus. The pigeons reacting satisfactorily and showing good takes are selected and the superficial skin layer scraped by means of sharp scalpel. The material so collected is freed from feathers, homogenised and dried or freeze dried. The dried pulp is powdered, sieved and ampouled in 0.3 g. quantities and sealed

4. ***Standard-***

(a). Description- Light cream coloured powder.

(b) Identification- When applied to feather follicles by vigorous rubbing, it produces mild reaction in fowls. The product should afford protection to fowls upto six weeks against fowl pox.

(c) Safety Test- For testing a batch of vaccine, twelve healthy cockerels, or other suitable young chicken from the same source are made available at the same time. This group of twelve birds is immunised at least twenty-one days previous to the test with fowl pox vaccine. The vaccine under test is reconstituted in 10 ml. of 50 per cent glycerine saline and administered to fowls as follows: -

Three of the test birds are injected subcutaneously with 0.3 ml. or 10 times the field dose of the vaccine to be tested. This group serves to indicate whether the product is free from organisms of septicaemia disease.

Three of the test birds are injected intranasally with 0.2 ml. of the vaccine to be tested. This group serves to indicate whether the product is free from virus of Coryza and similar diseases.

1[Three of the test birds are injected intratricheally with 0.2 ml or 10 times of the field dose of vaccine under test. This group serves to indicate whether the product is free from the virus of infectious laryngotracheitis and similar diseases.]

The three remaining birds serve as controls. All the birds under test are isolated and held under observation for twenty-one days. All those that succumb are subjected to careful post-mortem examination. The product is withheld from issue until the vaccine and test birds are shown to be free from the causative agents of any extraneous diseases.

(d) Sterility Test- Complies with the tests for sterility described under the general monograph on ―Viral Vaccines‖.

(e) Potency Test- For testing the potency of a batch of vaccines three susceptible birds each weighing not less than 400 g. are vaccinated using the field dose by the follicular method and examined for _takes'. Three weeks after vaccination these birds and two healthy susceptible controls are exposed to challenge virus and are observed for fourteen days. The vaccinated birds shall manifest no reaction, while the controls must have active ―takes‖.

5. ***Storage and Labelling***- Should comply with the requirements of _Labelling' as laid down in the general monograph on _Viral Vaccines'.

6. ***Expiry date***- The vaccine shall be expected to retain its potency for periods at temperature as *specified below:-*

-15 ˚ C to - 20 ˚C-- two years.
2˚ C to 4 ˚C-- twelve months.
Room temperature- Upto one month.

1.Ins. by. GSR 659(E) , dt. 31-8-1994.

Fowl Pox Vaccine- Pigeon Pox- Chick Embryos Virus (Living)

1. ***Synonym***- Chick embryo adapted pigeon pox vaccine (Living).

2. ***Definition-*** Fowl pox vaccine (Pigeon Pox virus) chick embryo adapted virus (living) is a suspension of a modified living virus prepared from the chorioallantoic membranes of the infected embryos and is freeze dried.

3. ***Preparation***- Active chick embryos obtained from Salmonella Pullorum free stock are used. Twelve to thirteen days old embryos are injected with a suitable dilution of the suspension of the infected membrane (stock seed virus) of chick embryo adapted pigeon pox virus. The suspension of the stock seed virus is dropped on the membrane. The inoculated eggs are incubated at 37 ° C for four days. One of the fourth day embryos that are living, are removed to a refrigerator for chilling for about one hour. Membranes showing discrete lesions (Pocks) are harvested. These are homogenised with adequate quantities of antibiotics, ampouled in 0.5 ml. quantities and freeze dried.

4. ***Standards-***

(a) Description- Light mauve coloured scales.

(b) Identification- When reconstituted vaccine is applied to scarified area of the skin of a fowl, it produces characteristics lesions of Fowl Pox. This product should afford protection against pox.

(c) Moisture content- Moisture content in the finished product should not exceed 1.0 per cent.

(d) Safety test- For testing each batch of chicks aged four to six weeks from the same source are taken. This groups of twelve birds is immunised at least twenty-one days

previous to the test, with fowl-pox vaccine. The vaccine under test is reconstituted in 3 ml. of normal saline solution and administered as under:-

Three of the test chicks are injected subcutaneously with 0.3 ml. or 10 times the field dose of the vaccine under test. This group serves to indicate whether the product is free from other viruses and bacteria causing of septicaemia or not.

Three of the test chicks are injected intratracheally with 0.3 ml. or ten times the field dose. This group serves to indicate whether the product is free from the viruses of infections laryngeotracheitis and similar diseases.

Three of the test chicks are injected with 0.2 ml 1/N of the vaccine under test. This group serves to indicate whether the product is free from the virus of coryza and similar diseases.

The remaining three chicks serve as controls. They are isolated and kept under observation for twenty-one days. The birds that succumb during the period of observation are subjected to careful post-mortem examination. The product is withheld from issue until the vaccine and the test birds are shown to be free from the causative agents of any extraneous disease.

In addition to the above, similar groups of pigeons aged six to nine months old are also injected in a similar way to eliminate psittacosis.

(e) Sterility Test- Should comply with the tests for sterility described under the general monograph on _Viral Vaccine‘.

(f) Potency test- For testing potency of a batch of vaccine three susceptible chicks of three to four weeks of age are vaccinated by feather forthicle method (a few forthicles on one leg are injected) and these are examined for _takes‘.

Three weeks after vaccination these chicks along with two unvaccinated chicks are exposed to challenge virus (virulent fowl pox virus) and observed for fourteen

days. The vaccinated chicks should not manifest any reaction while controls should show active _takes‘.

5. ***Labelling***- Should comply with the requirements for _Labelling‘ as laid down in the general monograph on _**Viral Vaccines‘**.

6 ***Storage***- The freeze dried product is expected to retain its potency for periods at temperatures as specified below:

-15 ° C to 20 ° C–two years.

2° C to 4 ° C–twelve months.

Room temperature- up to one month.

Sheep Pox Vaccine (Living)

1. ***Synonym-*** Sheep Pox vaccine; Goat pox vaccine.

2. ***Definition-*** Sheep pox vaccine consists of sheep pox virus collected from sheep artificially infected with sheep pox virus and freeze dried.

3. ***Preparation-*** Healthy yearling sheep are infected artificially by subcutaneous infection on the undersurface of the previously shaved abdomen with 200- 300 cc. of the freeze dried sheep pox virus (seed material) diluted in 1 : 1 Normal saline solution. On the sixth or seventh day after injection oedematous swelling develops in the injected area with thermal reaction. The sheep which develop good swelling are slaughtered and the gelatinous material present under the skin in the infected area is collected under sterile conditions. This material is mixed with 2 parts by volume of sterile peptone broth of pH 7.2 and homogenised.

The homogenised suspension is filtered, ampouled in 0.5 ml. quantities and freeze dried.

4. ***Standard:***

(a) Description- White scales.

(b) Identification- Reconstituted vaccine when applied over the scarified area of the skin of the abdominal region of sheep will produce characteristic local lesion of pox.

(c) Moisture content- The moisture content should not exceed 1.0 per cent.

(d) Safety test- Two rabbits each weighing not less than 1 kg. are injected subcutaneously each with 1 ml. of 1 : 100 dilution of the vaccine in normal saline solution. These animals are observed for fourteen days. The animals should remain normal.

(e) Sterility Test- Complies with the tests for sterility described under the general monograph on ‗Viral Vaccines'.

(f) Potency Test- Four yearling sheep are vaccinated on the inner surface of the ear by scarification method. The contents of one ampoule of F.D. Sheep Pox vaccine are constituted in 10 cc. of 50 % glycerin saline solution, characteristic ‗takes' develop in the scarified area with ulceration and scab formation. Three weeks later these and two more susceptible sheep (Controls) are challenged by scarifying with a suspension of the previous brow of the vaccine of the undersurface of the abdomen. The controls should develop typical lesions of pox and the vaccinated should remain normal.

5.*Labelling*- Should comply with the requirements of ‗labelling' as laid down in the general monograph in ‗Viral Vaccine'.

6. *Storage and expiry date*- The vaccine is expected to retain potency for period and temperature as specified below:-

-15 ° C to – 20 ° C– two years

2 ° C to 4 ° C–three months.

Room temperature- Fifteen days.

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Horse Sickness Vaccine (Living)

1. ***Synonym-*** African Horse Sickness Vaccine, Mouse adapted Polyvalent Horse Sickness Vaccine (Living).

2. ***Definition-*** Horse sickness vaccine is a suspension of live mouse adapted strains of Horse Sickness Virus (Onderstepoort) prepared from the brains of infected mice and is freeze dried.

3. ***Preparation***- Thirty to thirty-five days old white mice are infected intracerebrally with 0.05 ml. of a suitable dilution of the seed virus (6 or 7 types, as the case may be). Groups of large numbers of mice are injected separately with each type of the virus and are housed at 27 ° C to 32 ° C. A majority of these become paralytic on the third and fourth day when they are sacrificed and their brains collected and stored at – 15 ° C to – 20 ° C till the day of processing. For preparing the polyvalent vaccine, equal number of brains collected from mice infected with different types of the virus are homogenised with 5-10 times its volume of sterile lactose buffer medium (pH 7.2) containing antibiotics. The suspension is centrifuged at 1500 r.p.m. for five minutes. The supernatant liquid is distributed in ampoules in suitable quantities and freeze dried.

4. ***Standard:***

(a) *Description*- White scaly material.

(b) Identification- This product affords protection to horse against horse sickness.

(c) Safety Test- Four healthy mice thirty to thirty-five days old are injected intraperitoneally with 0.2 ml. of 10:1 dilution of the vaccine and kept under observation for ten days. All the mice should remain normal throughout the period of observation.

(d) Sterility Test- Should comply with the test for sterility described under the general monograph on _Viral Vaccines‘.

(e) Viability Test- Each batch of vaccine is titrated in tenfold dilutions using four mice of thirty to thirty-five days old for each dilution. Each mouse is injected intracerebrally with 0.05 ml and kept under observation for ten days. Mortality and survival ratios are noted and LD_{50} ml is determined. The minimum acceptable titre is 10–4 LD_{50} per 0.05 ml.

(5) ***Labelling*** - Should comply with the requirements of _labelling‘ as laid down in the general monograph in _Viral Vaccines‘.

(6) Storage- The vaccine may be expected to retain its potency for twelve months if stored – 15 ° C to 20° C and about six months if stored in refrigerator at 2 ° C to 4° C.

Rabies Vaccine (Inactivated)

1. ***Synonym***- Antirabic Vaccine (Inactivated)

2. ***Definition***- Rabies vaccine is a suspension of the brain tissue of animals, that have been infected with a suitable strain of rabies fixed virus, inactivated with phenol or some other suitable agent.

3. The following particulars relating to this vaccine are the same as those relating to Antirabic vaccine described in Part D of Schedule F to these rules, namely:-

(i) Strain of fixed Rabies Virus to be used;

(ii) Staff of Establishment;

(iii) Condition and housing of animals;

(iv) Precaution to be observed in preparation;

(v) Records;

(vi) Issue.

4. ***Preparation***- Healthy sheep or any other suitable species of animal are inoculated subdurally or intracerebrally with an appropriate dose of suspension of a suitable strain of rabbit brain passaged rabies fixed virus. The sheep or animals which get paralysed from the sixth day onwards after the inoculation are sacrificed and their brains collected aseptically. Brain tissue is weighed individually and a suspension of suitable concentration of brain tissue prepared in buffered saline is strained through gauze. The suspension treated with phenol or some other suitable inactivating agent is incubated for an appropriate period.

5. ***Standard-***

(a) Description- A grey to pale yellow opalescent suspension.

(b) Identification- Appropriate doses protect mice against subsequent intracerebral inoculation with suitable strain of fixed rabies virus.

(c) Safety test- Not less than five mice, each weighing at least 18 gm., are inoculated intracerebrally with not less than 0.03 ml. of the suitably diluted vaccine. None of the animals should show symptoms of rabies or die of the disease during period of observation of three weeks.

(d) Sterility Test- Should comply with the test for sterility described under the general monograph on _Viral Vaccine‘.

6. ***Labelling-*** Should comply with the requirements of _Labelling‘ as laid down in the general monograph on _Viral Vaccines‘. In addition the label on the container shall indicate the percentage of brain tissue present in the vaccine.

7. ***Storage***- The vaccine may be expected to retain its potency for about six months if stored in refrigerator at 2˚ to 4 ° C.

Rabies Vaccine (Living)

1. ***Definition-*** Rabies vaccine (living) is a freeze-dried suspension of chick-embryo tissue infected with a suitable attenuated strain of rabies virus.

2. ***Preparation-*** It may be prepared by the following method. Seed virus consisting of a suspension of the Flury or other suitable strain of chick adapted virus that has been maintained by passage in chick embryos is injected into the yolk-sacs of fertile eggs incubated for a suitable period. After incubation for a further ten days, the embryos are harvested and grind in water for injection to give 33 percent suspension. The suspension is centrifuged to remove coarse particles and the supernatant fluid is distributed into ampoules in 3 millilitre quantities, and freeze dried. The vaccine is reconstituted immediately before use by adding 3 millilitres of water for injection to the contents of an ampoule.

3. ***Standard-*** It complies with the requirements of general standard of viral vaccines for abnormal toxicity, sterility, and labelling with the following additions.

(a) Description- Dry honey-coloured flakes or powder, readily dispersible in water.

(b) Identification- It protects guinea pig against a subsequent inoculation of rabies street virus. It is distinguished from the inactivated Rabies vaccine by its ability to produce rabies encephalitic on intracerebral injection into mice.

(c) *Safety-* The guinea pigs used in the test for potency should not show any marked local or systemic reaction during the three weeks following injection with the vaccine.

(d) Sterility Test- Complies with the tests for sterility described under the general monograph on _Viral Vaccines'.

(e) *Potency Test-* The contents of an ampoule are dispersed in water for injection to give a 5 per cent suspension and not fewer than twenty guinea pigs, drawn from a uniform stock and each weighing 350 g. to 500 g., are each injected intramuscularly with 0.25 ml. of this suspension. Three weeks later, these guinea pigs and an equal number of similar unvaccinated control guinea pigs are each inoculated with 0.1 ml. of a suitable dilution of canine salivary gland suspension of street virus which is maintained as a 20 per cent suspension at 70 ° C or lower. The guinea pigs are observed for thirty days; not less than 80 per cent of the control guinea-pigs die of rabies and not less than 70 per cent of the vaccinated guinea-pigs are protected.

4. ***Storage-*** Freeze-dried vaccine should be stored at refrigeration temperatures of 2 ° C to 4 ° C.

5. ***Labelling-*** The life of the vaccine at room temperature and at refrigeration temperature should be stated on the label.

6. ***(a) Action and uses-*** Rabies vaccine (living) is used for the prophylactic inoculation of dogs against rabies; one injection should provoke a serviceable immunity lasting for at least a year. The vaccine has been used to a limited extent on cattle.

(b) Dose- By intramusclar *injection:* Dogs, the contents of one ampoule reconstituted in 3 ml. of water for injection; cattle five times the dog dose.

Ranikhet Disease Vaccine (Living)

1. ***Synonym-*** New Castle Disease Vaccine (Living); pheumoenteritis Vaccine (Living).

2. ***Definition-*** Ranikhet Disease vaccine is a suspension of a modified living virus e.g. (Mukteswar strain) prepared from infected embryos and fluids and is freeze dried.

3. ***Preparation-*** Good fertile eggs obtained from *Salmonella pullorum* free flock are incubated in an egg incubator. Ten days old vigorous embryos are infected with 0.1 ml. of a suitable dilution of a suspension of the virus. Inoculation is done in the allantoic cavity. Embryos are incubated at a suitable temperature. Eggs showing dead embryos twenty-four hours after incubation are discarded. After forty-eight hours incubation the eggs are candled and those

showing dead embryos are chilled for a suitable period of time, while embryos alive beyond forty-eight hours are discarded. The fluids and embryos are then collected and spot haemogglutination carried out. The material is homogenised in a blender and ampouled in aliquots of 0.5 ml. quantities and freeze-dried.

4. ***Standards-***

(a) Description- Light brown scales.

(b) Identification- This product affords protection to fowls against Ranikhet Disease.

(c) *Safety Test-* For testing each batch of freeze dried Ranikhet Disease Vaccine, twelve healthy young chickens, all from the same source each weighing not less than 100 g. are taken and immunised against Ranikhet Disease. Fourteen days later, these birds, are tested as follows with the contents of one ampoule suspended in 100 ml. of normal saline.

Three of the test birds are injected subcutaneously with 0.1 ml. equivalent to ten times the field dose of the vaccine to be tested. This group serves to indicate whether the product is free from viruses or organisms of speticaemia disease.

Three of the test birds are injected intratracheally with 0.1 ml. equivalent to ten times the field dose of he vaccine to be tested. This group serves to indicate whether the product is free from the virus of infectious laryngotracheitis, [1][***] and similar diseases.

The three remaining birds serve as controls.

[2][Three of the test birds are injected intranasally with 0.2 ml of the vaccine to be tested. This group serves to indicate whether the product is free from virus of Coryza and similar diseases.]

All the treated birds and controls are observed daily for fourteen days. All the test birds that succumb are subjected to careful postmortem examination. The product is not issued until the birds under test are shown to be free from the causative agents of any extraneous diseases.

(e) Sterility Test- Should comply with the test for sterility described in the general monograph on _Viral Vaccine‘.

1. The word —Coryzal omitted by. GSR 659(E) ,dt.. 31-8-1994. 2.
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(f) Potency Test- Four susceptible birds eight to twelve weeks old and each weighing not less than 400 g. are vaccinated by injecting subcutaneously 1 ml. of a 10^{-5} dilution of the product. Two weeks after vaccination these birds and four non-protected birds are challenged by injecting subcutaneously each with 1.0 ml. of a 1: 100 dilution of virulent virus (liver and spleen suspension) or 1.0 ml. of a 1 : 100 dilution of fluid from the embryo infected with virulent Ranikhet Disease virus. The non-protected birds should show symptoms of Ranikhet Disease and die and all the protected birds should remain normal during an observation period of fourteen days.

5. ***Labelling-*** Should comply with the requirements of _Labelling as laid down in the general monograph on _Viral Vaccines‘.

6. ***Storage-*** The vaccine when stored at – 15° C to 20° C. may be expected to retain the potency for about one year and about three months if stored in a refrigerator at 2° C to 4° C. The product should not be used if stored for more than ten days outside the refrigerator.

Ranikhet Disease Vaccine F strain (Living)

1. ***Synonyms-*** New castle disease vaccine F Strain (Living).

2. ***Definition-*** Ranikhet disease vaccine F. strain is a suspension of a naturally modified living virus (F strain) prepared from the infected embryos, devoid of beaks and eyes and fluids in a frozen state.

3. ***Preparation-*** Good fertile eggs obtained from Salmonella pullorum free flock are incubated in an egg incubator. Eight days old vigorous embryos are infected with 0.1 ml. of 1 : 100 suspension of Ranikhet disease vaccine F strain virus. Inoculation is done via the allantoic cavity. Embryos are incubated at 37° C. Eggs are candled every day upto four days and the dead

ones are discarded. Final candling of the embryos is carried out on the fourth day and only the living ones are chilled in a refrigerator for one hour. The fluids embryos are collected separately. The fluids are tested for spot haemagglutination and sterility test is carried out. The beaks and eye balls of the embryos are removed. The materials are homogenised with adequate quantities of antibiotics in a cool warning blender and ampouled in aliquots of 0.5 ml. quantity and freeze dried.

4. ***Standard-***

(a) *Description*- Light brown scales.

(b) Identification- This product affords protection to baby chicks against Ranikhet disease.

(c) Moisture content- The moisture content should not exceed [1][1.0] per cent.

(d) *Potency test*- For testing each batch of the vaccine twelve one-day old chicks are given two drops 1/N o the field dose of the vaccine (5 ampoules selected at random may be reconstituted in 50 ml.) of cold normal saline solution. These are observed for fourteen days and the vaccinated chicks should remain normal throughout the period of observation. This serves the safety test also.

On the fourteenth days the vaccinated chicks are challenged two drops with 1:50 virulent Ranikhet disease virus alongwith 8 control chicks. Four of the controls receive two drops 1/N of the virulent virus while the rest of the four receive 0.5 ml. of the virulent virus. The control chicks should succumb to the challenge virus showing symptoms of Ranikhet Disease while the protected chicks should remain normal throughout the observation period of fourteen days.

(e) Sterility Test- Should comply with the tests for sterility described in the general monograph on _Viral Vaccines‘

5. ***Labelling***- Should comply with the requirements of ―Labelling‖ as laid down in the general monograph on _Viral Vaccines‘.

6. ***Storage***- The vaccine when stored at – 15 ° C to –20 ° C may be expected to retain the potency for about one year and about three months if stored in a refrigerator at 2 ° C to 4° C. When removed from the refrigerator, the product should not be used later than ten days.

1. Ins. by G.S.R. 659(E) ,dt.. 31-8-1994

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Rinderpest Goat adapted Tissue Vaccine (Living)

1. ***Synonym-*** Goat-adapted Cattle Plague Vaccine; Goat Tissue Vaccine (Living).

2. ***Definition-*** Rinderpest Goat-adapted Tissue Vaccine is the homogenised freeze dried preparation of spleen pulp of goats artificially infected with the suitable strain of rinderpest virus.

3. ***Preparation***- Healthy susceptible goats are quarantined for a period of ten days. After this period a batch of selected goats are injected subcutaneously with 2 ml. of a suitable dilution of the suspension of the seed virus. The donor goats are sacrificed after a suitable period when the titre of the virus in the animal body is expected to be maximum, usually four days, and the spleen from animals free from any pathological change or signs are collected under sterile conditions. Smear from each spleen is examined microscopically to exclude spleen which are contaminated from the production batch.

The spleen is freed from fat and fascia and is blended into a smooth pulp in a grinder. The pulp is spread on a shallow dish of glass or stainless steel and is freeze dried.

The freeze dried pulp is then ground into a fine powder and sieved. The powder is ampouled in 0.25 g. or 0.125 g. quantities and freeze dried.

4. ***Standard:***

(a) Description- Dark brown or chocolate coloured scales or powder.

(b) Identification- The product affords protection to susceptible animals against rinderpest.

(c) Moisture content- Not more than 1.0 per cent.

(d) Safety Test- Each batch of vaccine shall be tested for safety in laboratory animals and cattle or buffalo calves as follows:-

(i) Small animals- At least two guinea pigs each weighing 300 g. to 450 g. and two adult rabbits each weighing 1 kg. to 1.5 kg. should be injected each with 1 ml. of 1: 100 suspension of the vaccine subcutaneously and kept under observation for seven days. None of the animals should die. Alternatively, a batch of six white mice each weighing not less than 18 g. may be used, each mouse receiving 0.5 ml. of a dilution 1 : 100 suspension subcutaneously. None of the animals should die.

(ii) Large animals- Either cattle of good grade of susceptibility (hill cattle) or buffalo calves may be employed. For each batch of vaccine, three animals should be injected subcutaneously with 1 ml. of 1 : 8000 dilution of the vaccine. These animals should be kept under observation for twelve to fourteen days. None of the animals should show any untowards reactions.

(e) Sterility Test- Complies with the tests for sterility described under the general monograph in _ Viral Vaccines‘.

(f) Potency Test- The animals receiving 1 ml. of 1 : 8000 dilution of vaccine used under safety test mentioned above and kept under observation for fourteen days, should be challenged with 1 ml. of 1 per cent suspension of stock Rinderpest Virulent virus. None of the animals should die of rinderpest within a period of ten days. This test serves as a short potency test for each of the batches.

For conducting a detailed potency test the following procedure may be followed:-

Dilution 1: 8000, 1: 12,000 and 1 : 16,000 shall be tested and for each dilution three susceptible cattle or buffalo calves should be used. Each animal is inoculated subcutaneously with 1 ml. of a dilution of the vaccine, followed twelve to fourteen days later with a standard challenge dose of virulent rinderpest bull virus containing

in 1 ml. of a 1 : 100 suspension of spleen tissue. Two unvaccinated bovines, each receiving the same quantity of the challenge dose acts as controls. These are kept under observation for fourteen days. The end point of protection titre is assessed on the death or survival rate and the dose contained in one gramme of vaccine calculated on the basis of 20 to 40 minimum protective doses being equivalent to one vaccinating dose.

(g) Virulence and Viability Test- Two to four goats each weighing not less than 18 kg. are injected with 2 ml. of 1 : 100 suspension of the vaccine and kept under observation for ten days. These animals should show reaction characterised by pyrexia (rise of about 2˚ C) *anorexia and dullness.*

5. *Labelling*- Should comply with the requirement of _Labelling‘ as laid down in the general monograph on _ Viral Vaccines‘.

6. *Storage*- The vaccine may be expected to retain its potency for twelve months if stored at -15˚ C to -20˚ C or about three months if stored at 2˚C to 4 ˚ C.

Rinderpest Lapinised Vaccine (Living)

1. ***Synonym-*** Rabbit Adapted Cattle Plague Vaccine (Living) Lapinised Vaccine (Living).

2. ***Definition***- Rinderpest lapinised vaccine is a suspension of a modified living virus (e.g. Nakamura III Strain) prepared with the blood, spleen and mesenteric lymph glands of infected rabbits and is freeze dried.

3. ***Preparation-*** Adult rabbits possibly from a known stock, each weighing not less than 1 kg. free from cocidiosis and snuffles, are injected intravenously with 1 ml. of a suitable dilution of a

suspension of the stock seed virus. Donor rabbits are sacrificed after a suitable period when the titre of the virus in the animals is expected to be the maximum usually the third day.

Ten millilitres of blood is collected from each rabbit in a defibrinating flask under aseptic condition. Later the animals are sacrificed and the spleen and mesenteric lymph glands collected. Each rabbit is subjected to a thorough post-mortem examination to observe lesions of rinderpest infection.

After harvesting, the blood and the organs (spleen and glands) are homogenised in a suitable proportion if necessary. Adequate quantities of penicillin and streptomycin may be added. The homogenized material is ampouled in suitable quantities and freeze dried.

4. ***Standard-***

(a) Description- Dark chocolate coloured mass.

(b) Identification- This product affords protection to susceptible animals against rinderpest.

(c) Moisture content- Not more than 1.0 per cent.

(d) Safety Test- For testing a batch 2 guinea pigs each weighing not less than 300 g. are injected subcutaneously with 1 ml. of a 1 : 100 suspension of the vaccine. Alternatively, a group of six white mice each weighing not less than 18 g. is used. Each animal receives subcutaneously 0.5 ml. of 1 : 100 suspension of the vaccine. None of the test animals should die within a period of seven days.

(e) Sterility Test- Should comply with the tests for sterility described in the general monograph on _Viral Vaccines‘. If antibiotics have been added the inoculum should be neutralised before doing the test.

(f) Potency Test- Dilution 1: 100, 1 : 200, 1 : 400 and 1 : 800 shall be tested and for each dilution 2 susceptible cattle (hill bulls) or buffalo calves should be used. Each animal is inoculated subcutaneously with 1 ml. of a dilution of the vaccine, followed twenty-one days later with a standard challenge dose of a virulent rinderpest bulls virus contained in 1 ml. of a 1 : 100 suspension of spleen tissue. Two unvaccinated bovines each receiving the same quantity of the challenge virus serve as controls. These animals are kept under observation for fourteen days. The end point of the protecting titre is assessed on the death or survival rate and the dose contained in one gramme of vaccine calculated on the basis of twenty minimum protective doses being equivalent to one vaccinating dose.

(g) Virulence and Viability Test- Four rabbits each weighing 1 to 1.5 kg. are injected subcutaneously with 1 ml. of 1 : 100 suspension of the vaccine. The animals should react typically showing all the symptoms of rinderpest in rabbits.

5. ***Labelling-*** Should comply with the requirements of _Labelling‘ as laid down in the general monograph on _Viral Vaccines‘.

6. ***Storage-*** The vaccine may be expected to retain its potency for six months if stored at 15 ˚C to –20 ˚C or about a month if stored at 2 ˚C to 4 ˚C.

Rinderpest Lapinised Avianised Vaccine (Living)

1. ***Synonym-*** Lapinised Avianised Vaccine (Living).

2. ***Definition-*** Rinderpest Lapinised Avianised Vaccine is a suspension of a modified live rinderpest virus of low virulence prepared either with the whole chick embryo or the viscera of the infected chick embryo.

3. ***Preparation-*** Twelve or thirteen days old active chick embryos from a flock free from Salmonella pullorum infection are injected intravenously with a suitable dilution of the suspension of the stock seed virus in six per cent glucose solution. The embryos are incubated at

38.5˚ C for five days. At the end of this incubation period, eggs which show living embryos are selected for the preparation of the vaccine. The viscera of the chicks are harvested, care being taken to reject the gizzard and gall bladders. The material is homogenised in a blender with adequate quantities of antibiotics (penicillin and streptomycin added if necessary), and primary freeze dried done. This freeze dried material is ground into a fine powder, ampouled in suitable quantities and finally subjected to secondary freeze drying and sealed under vacuum.

4. ***Standard-***

(a) Description- Pale cream or yellow coloured sterile powder.

(b) Identification- This product affords good grade of immunity to susceptible animals against rinderpest.

(c) Moisture content- Not more than 1.0 per cent.

(d) Safety Test- For testing each batch, a group of six mice each weighing not less than 18g. is used. Each mouse is injected subcutaneously with 0.5 ml. of a 1 : 100 suspension. Alternatively, two guinea pigs each weighing not less than 300 g. and two rabbits each weighing not less than 1 kg. are injected with 1 ml. of 1 : 100 suspension subcutaneously. These animals should not show any untoward reaction during the period of observation for seven days.

(e) Sterility Test- Should comply with the test or sterility as laid down in the general monograph on _Viral Vaccines‘.

(f) Potency Test- Healthy highly susceptible cattle (hill bulls) or buffalo calves should be used for testing the potency of each batch of vaccine in suitable dilution. For each dilution two highly susceptible animals should be used. Each animal is inoculated

subcutaneously with 1 ml. of a dilution of the vaccine, followed twenty-one to twenty- eight days after with a standard challenge dose of a virulent rindepest bull virus contained in 1 ml. of a 1 : 100 suspension of spleen tissue. Two unvaccinated bovines, each receiving the same quantity of the challenge virus serve as controls. All these animals are kept under observation for fourteen days. The end point of protective titre is assessed on the death or survival rate and the dose contained in one gramme of vaccine calculated on the basis of forty minimum protective doses being equivalent to one vaccinating dose.

5. ***Labelling***- Should comply with the requirements of _Labelling‘ as laid down in the general monograph on _Viral Vaccines‘.

6. ***Storage and Expiry date***- The vaccine shall be expected to retain its potency for the period at temperatures as specified below:-

-15˚ C to – 20˚ C .. Six months.

2˚ C to 4˚ C . .. One month.

Sheep and Goat Pox Vaccine (Living)

1. ***Synonym***- Sheep Pox Vaccine. Goat Pox Vaccine (Living).

2. ***Definition-*** Sheep and Goat Pox Vaccine consists of the virus contained in the scabs collected from sheep artificially infected with the virus.

3. ***Preparation-*** Healthy yearling sheep are infected artificially on the shaved portion of the abdomen with a suitable dilution of the suspension of the stock seed virus 50 per cent glycerine saline solution. The material from the semi-dried areas where the pock lesions are evident is collected and dried over calcium chloride or phophorus pentoxide under vacuum. Dry scabs are powdered, sieved, ampouled in suitable quantities and sealed.

4. ***Standard:***

(a) Description- Light cream coloured powder.

(b) Identification- This product when applied to scarified area of the skin of the sheep or goats produces characteristic local lesions of pox and should afford protection to sheep and goat against Sheep and Goat Pox.

(c) Safety Test- Two rabbits each weighing not less than 1 kg. are injected subcutaneously each with 1 ml. of a 1 : 100 dilution of the vaccine in normal saline solution. These animals are observed for fourteen days. The animals should remain normal.

(d) Sterility Test- Complies with the tests for sterility described under the general monograph on ‗Viral Vaccines'.

(e) Potency Test- Four yearling sheep are inoculated with 1 : 100 suspension of the vaccine in 50 per cent glycerine saline on a scarified area on the abdomen. Fourteen days later, these and two more susceptible sheep are inoculated by the same method with stock virus and observed for a period of fourteen days. The control animals should develop typical lesions of pox and vaccinated animals should remain normal.

5. ***Labelling***- Should comply with requirement of ‗Labelling' as laid down in the general monograph on ‗Viral Vaccines'.

6. ***Storage and Expiry date***- The vaccine shall be expected to retain its potency for period at temperatures as specified below:-

-15˚ C to – 20˚ C	**:**	Twenty months.
2˚ C to 4˚ C	**:**	Three months.
Room Temperature	**:**	Fifteen days.

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Fowl Spirochaetosis Vaccine (Chick Embryo Origin)

1. *Synonym*- Tick Fever Vaccine.

2. *Definition*- The vaccine consists of a merthiolated suspension of chorioallantoic membrane, internal viscera and blood of chick embryos infected with a vaccine strain of spirochaetes and freeze dried.

3. *Preparation*- Eleven days old developing chick embryos are infected with 0.2 ml. of sterile fresh blood containing spirochaetosis via the chorioallantoic membrane. The inoculated embryos are incubated at 37 ˚C and candled daily and the dead one are discarded. On the seventh day the living embryos are chilled in the refrigerator for two hours. The chilled embryos are harvested separately and necrotic lesions in liver noted. Representative samples of blood should be examined for teaming spirochaetes. The internal viscera, chorio-allantoic membranes and the blood are collected. The material is pooled, weighed and held in deep freeze at – 15 ˚C to –20 ˚C for a period of one week. Thereafter the material is blended with equal quantity of Merthiolate (final concentration of merthiolate in the suspension should be 1 : 10, 000) thoroughly for three times, each time the motor running at full speed and the vaccine is ampouled in 2 ml. quantities and freeze dried.

4. *Standard*-

(a) Description- Light brownish scales.

(b) Identification- The vaccine affords protection when inoculated into the fowls against spirochetosis.

(c) Moisture content- The moisture content should not exceed 1.0 per cent.

(d) Safety and potency test- Six healthy cockerals ten to twelve weeks old are used for this purpose. Each ampoule of vaccine is reconstituted in 10 ml. of cold distilled water and the six cockerals are injected intramuscularly each with 1 ml. of the reconstituted vaccine and the birds are observed for a period of ten days and the vaccinated birds should remain

normal throughout the period of observation. The vaccinated birds are challenged with 0.2 ml. intramuscularly with virulent spirochaete blood along with two susceptible controls. Temperature and blood smear examination of the challenged birds and controls should be carried out daily for a period of ten days. The blood smears of vaccinated birds should remain negative for spirochaetes during the entire period of observation. The controls should react and show spirochaetes in the blood.

(e) Sterility Test- Complies with the tests for sterility described in the general monograph on _ Bacterial Vaccine‘.

5. ***Labelling***- Should comply with the requirement of _Labelling‘ as laid down in the general monograph on _Viral Vaccines‘.

6. ***Storage***- The vaccine when stored at –15 ˚C to – 20 ˚C may be expected to retain the potency for about one year and about two months if stored in refrigerator at 2 ˚C to 4 ˚C.

Swine Fever Vaccine Crystal Violet

1. *Synonym*- Crystal Violet Swine fever vaccine, Hog Cholera Vaccine.

2. *Definition*- Swine fever vaccine, crystal violet is a suspension of blood of swine that have been infected with a suitable virulent antigenic strain of swine fever virus, inactivated with 0.25 per cent crystal violet ethylene glycol at 37 ˚C for fourteen days.

3. *Preparation*- Susceptible healthy pigs of six to seen months of age belonging to a well established strain or bred are used. Body weight of these animals at this age may vary according to the breed but optimum weight is considered as between 75 to 100 kg. Animals used for production may be procured from well established farms and kept under quarantine

for fourteen days. These are injected intramuscularly with a suitable dilution of the suspension of the virulent blood viruses. Bleeding of the clinically injected animals is carried out on the sixth day. The defibrinated blood from each animal is strained and stored separately in sterile glass containers. To the four parts of defibrinated blood, one part of 0.25 per cent crystal violet- ethylene glycol is added and the suspension after thorough mixing, is stored at 37˚ C (+0.5) for two weeks. The product is filled in 20 ml. volumes in sterile vials and labelled on the completion of tests.

4. ***Standard-***

(a) Description- Very dark violet suspension.

(b) Identification- This product affords protection against swine fever but not against African Swine Fever.

(c) Safety Test- Two young pigs weighing about 15 to 30 kg. are injected subcutaneously each with 40 ml. of the vaccine batch to be tested. In addition, one unvaccinated susceptible pig is placed in contact.

(d) Sterility Test- Should comply with the test for sterility described under general monograph on _Viral Vaccines‘.

(e) Abnormal toxicity test- Two guinea pigs are given 1 ml. of vaccine intramuscularly.

Two guinea pigs are given 2 ml. of the vaccine intraperitoneally.

Two mice are given 0.5 ml. of the vaccine subcutaneously.

(f) Potency Test- Four susceptible pigs weighing between 20-30 kg. are injected with 5 ml. of the vaccine subcutaneously. After twenty-one days these are challenged with 1 ml. of suitable dilution of the challenge virus subcutaneously. The dose must contain at least 1000 minimum infective doses. At least two control pigs should be used.

5. ***Labelling***- - Should comply with requirement of _Labelling‘ as laid down in the general monograph on _Viral Vaccines‘.

6. ***Storage***- The vaccine may be expected to retain its potency for twelve months if stored in refrigerator at 2 ˚C to 4 ˚C.

Swine Fever Vaccine Lapinised (Living)

1. ***Synonym***- Lapinised swine fever vaccine, freeze dried lapinised swine fever vaccine.

2. ***Definition-*** Swine fever lapinised vaccine consists of the suspension of a modified live swine fever virus prepared from spleens of infected rabbits and is freeze dried.

3. ***Preparation-*** Healthy adult rabbits weighing approximately 1000 gms. or over, free from coccidiosis snuffles etc. are injected intravenously with a suitable dose of a dilution of the modified rabbit adapted virus. Rabbits are sacrificed at the height of reaction and spleens are collected with sterile precautions. The collection is later homogenised in a blender using ten per cent yolk phosphate buffer as a diluent. The suspension is ampouled in 0.5 ml. quantities and freeze dried.

4. ***Standard-***

(a) Description- Light scales.

(b) Identification- This product affords protection against swine fever.

(c) Moisture content- The moisture content should not exceed 1.0 per cent.

(d) Safety Test- Six mice are injected each with 0.5 ml. of a 1 : 100 suspension of the vaccine. These are kept under observation for seven days. Non should die.

(e) Viability Test- Two healthy rabbits are injected intramuscularly with 1 ml. of 1 : 100 suspension of the vaccine. These animals show thermal reaction.

(f) Sterility Test- Should comply with the test for sterility described under the general monograph on _Viral Vaccines‘.

(g) Potency Test- The vaccine batch under test should be tested on susceptible healthy pigs weighing between 20-30 kg. Two animals for each dilution may be used. The dilutions tested are 1 : 10, 1 : 25, 1 : 50 and 1 : 100. One millilitre of each of these dilutions is injected subcutaneously. One healthy, susceptible, unvaccinated in contact animal should be kept along with the vaccinated animals.

Fourteen to twenty-one days later these animals along with two controls are injected subcutaneously with 1 ml. of the challenge virus containing at least 1000 minimum infective doses.

5. ***Labelling-*** Should comply with requirements of _Labelling‘ as laid down in the general monograph on _Viral Vaccines‘.

6. ***Storage***- The vaccine may be expected to retain its potency for six months if stored at temperature ranging between – 10˚ C to - 15˚ C and for seven days at 2˚ C to 4˚ C in the refrigerator.

[1]*Foot and Mouth Disease Vaccine (Inactivated)*

1. ***Synonym***. – Inactivated Tissue culture mono or polyvalent Foot and Mouth Disease Vaccine.

2 ***Definition.*** – Foot and Mouth Disease Vaccine is a liquid product or preparation containing one or more types of foot and mouth disease virus which have been inactivated in such a way that its immunogenic property is maintained. It may also contain an adjuvant. The vaccine is described as monovalent, bivalent, trivalent or polyvalent depending on the number of types of virus used.

3. ***Preparation.*** – The virus is propagated in suitable cell culture. The cell culture is infected with an appropriate inoculum of virus and incubated at a suitable temperature for multiplication of virus. The virus is harvested and cellular debris removed by filteration. Inactivation is carried out by a suitable agent such as formaldehyde solution or aziridine compound. The adjuvant may be aluminium hydroxide and/or saponin. In case of inactivated gel vaccine the antigen is concentrated by sedimentation at plus 4 degree C. For preparing a polyvalent vaccine, monovalent

antigens are mixed in appropriate quantities to give the final mixture which is the formulated vaccine.

4. ***Standards*** *:*

(a) Description :- Aluminium hydroxide gel vaccines settle down to variable degree on storage leaving the supernatant clear.

1. Ins. by G.S.R. No. 659(E) ,dt.. 31-8-1994.

(b) Identification – It protects cattle against Foot and Mouth Disease due to homologous type/subtype of virus.

(c) Sterility test – It shall comply with the tests for sterility as prescribed under the ―general monograph on ―Viral Vaccines‖.

(d) Safety test - The test is carried out on fully susceptible cattle not less than 12 months of age and which have not been sensitized either by vaccination or previous infection. Inoculate 3 susceptible cattles each with 2 ml. of finished product at multiple sites on tongue by intradermal route and observe for 4 days. The same animals are inoculated on 4th day with 3 cattle doses subcutaneously and are observed for a further period of 6 days. The animals should not develop any signs of FMD and remain normal.

(e) Potency test – Each batch of the vaccine is to be tested in susceptible cattle of not less than 15 months of age. The potency test in cattle can be done either by :–

(*i*) PD_{50} Method : The vaccine shall be tested by the determination of PD_{50} in susceptible cattle by challenging animals vaccinated with appropriate dilution of the vaccine made in adjuvanted or non-adjuvanted diluent as appropriate.

A minimum of 5 animals should be used per dilution and 2 unvaccinated animals to be included as controls to the challenge. All animals are needle challenged with 10,000 ID_{50} of the homologous strain of virus by inoculation on the tongue on the 21_{st} day of post-vaccination.

The control animals are to be similarly challenged. Animals are observed for 10 days for the development of lesions. Unprotected animals show generalised lesions due to FMD. Control animals must shown generalized lesions. From the number of animals protected in each group the PD_{50} content of the vaccine is calculated. The vaccine passes the test if an observed PD_{50} value of 3 or greater is obtained in the test.

(*ii*) Percentage protection method in which groups of ten health susceptible cattle are each injected subcutaneously with the vaccinating dose and 14 – 21 days later the cattle are challenged by intradermal injection into three separate sites on the tongue with 10,000 ID_{50} of the strain of virus used in the preparation of the vaccine. The vaccine can be passed if atleast seven out of the ten in the group are protected against the development of generalized infection whereas all the controls should react by developing primary and secondary lesions observable in the mouth and feet.

For other reasons if cattle testing is not possible then the potency of the vaccine may be assed in guineapigs either by Lucam ‗C‘ index or PD_{50} method by challenging those which have been previously vaccinated, provided that the correlation has been established between guinea pig challenge test and cattle challenge results.

The estimation of the serum neutralizing antibody titre cattle may be considered as a supportive test to evaluate potency of vaccine.

However, potency testing of vaccines, in cattle, of batches whenever by other accepted methods of testing is in doubt, at aleast one out of every five batches, be undertaken.

5 ***Labelling*** :- It is labelled as described under the requirements of ‗labelling' as laid down in the general monograph, with the additional requirements that the label on the container states the virus types used in the preparation.

6. ***Storage :-*** It should be protected from the light and stored between 4_o C to 8_o C. Under these conditions it may be expected to retain its potency for not less than 12 months. Freezing of aluminium hydroxide vaccine must be avoided. The frozen product will not be fit for use.

Canine Hepatitis Vaccine (Living)

1. ***Synonyms*** : Infectious Canine Hepatitis Vaccine (Living), Canine Hepatitis Cell Culture Vaccine.

2. ***Definition :*** Canine Hepatitis Vaccine (Living) is a freeze dried preparation of tissue culture fluid containing the cell culture adopted canine hepatitis virus.

3. ***Preparation*** *:* Canine hepatitis vaccine shall be prepared from virus bearing cell culture fluid.

Only stock seed virus which has been established as pure, safe and immunogenic shall be used in the preparation of the vaccine.

Immunogenicity test *:* Each lot of stock seed virus shall be tested for immunogenicity as follows *:*

Thirteen canine hepatitis susceptible dogs, 8-14 weeks old shall be used for the test (10 vaccinates and 3 controls). Blood samples may be drawn from these animals and individual serum samples tested for the presence of antibodies, against canine hepatitis virus. Ten dogs shall be injected subcutaneously with predetermined quantity of the virus and remaining 3 dogs are kept as unvaccinated controls. The dose calculation will be based on virus titration in suitable cell culture system. Not less than 14 days post vaccination, the vaccinated and control shall each be challenged intravenously with virulent infectious canine hepatitis virus and observed daily for 14 days. At least 2 out of 3 controls should die and the survivors shall show the clinical signs of canine hepatitis. Nine out of ten vaccinated dogs shall survive and shall not show any signs of infectious canine hepatitis during the observation period.

The stock seed virus shall be tested once in 5 years and maintained under standard conditions as prescribed.

The stock seed virus may be inoculated on a suitable tissue culture system and may be incubated for five to seven days.

The tissue culture fluid is then harvested and titrated in cell culture system for virus content. After appropriate dilution and pooling, the material is stored at minus 20_o C until freeze dried. Each vaccine dose shall contain not less than $10^{3.5}$ $TCID_{50}$ dose.

4. ***Standards :-***

(a) Description. – The dried product is a pinkish cream material readily dispersible in water. The reconstituted vaccine is a pinkish liquid.

(b) Identification.- It causes characteristic cytopathic effect in dog, pig and ferret kidney monolayers. This can be neutralized by specific antiserum. When inoculated into dogs, the development of specific neutralizing antibodies can be demonstrated by suitable serological tests.

(c) Moisture content.- In the finished product moisture content shall not exceed 1.0 per cent.

(d) Sterility Test.-- Shall comply with the tests of sterility as described under the general monograph on ―Viral Vaccines‖.

(e) Safety Test.-- Mouse safety test – Vaccine prepared for use as recommended on

the label shall be tested. Eight mice shall be inoculated intracerebrally with 0.03 ml and 8 mice shall be inoculated intraperitoneally with 0.5ml. Both the groups shall be observed for seven days. If unfavourable reaction attributable to the product occurs in two or more mice in either group during their observation period, the batch is unsatisfactory.

(f) Dog Safety Test.-- Each of the two susceptible pups aged 8 – 14 weeks shall be injected with vaccine equivalent of 10 vaccinating doses from the batch reconstituted with sterile diluent and administered in the manner recommended on the label and observed for 21 days. None of the pups shall show any unfavourable reaction during the period of observation.

(g) Potency test, Virus Titration: – Samples of finished product shall be tested for virus titre in suitable cell culture system. The batch shall have a virus titre of not less than $10^{3.5}$ $TCID_{50}$ dose.

(h) Potency test in dog:– Two healthy susceptible dogs of 8-14 weeks of age shall be injected subcutaneously with one Vaccine dose. 14 days after vaccination, specific neutralizing antibodies from both the dogs shall be demonstrable by serological tests.

5 *Labelling:* Shall comply with the requirement for labelling as laid down in the general monograph on ―Viral Vaccines‖.

6 *Storage:* The dry product shall be stored at temperature of minus 20° C or below. . The vaccine is expected to retain its potency for about 6 months in the freezing chamber of the refrigerator (temperature) approximately minus 8°C

Duck Plague Vaccine

1 *Definition.-* Duck plague vaccine is a suspension of modified living virus prepared from infected chick embryos.

2 *Preparation*.- Fresh fertile hen‘s eggs obtained from salmonella free flocks are . incubated in an incubator. Nine days old embryos are injected with 0.2 ml of the suitable dilution (1 in 100) of the suspension of the virus on the CAM and incubated at 37° C for 5 days post-inoculation. Dead embryos of the 3rd, 4th and 5th days post-inoculation are harvested.

The embryos (devoid of head and legs). Clear fluid and the membranes are collected and homogenized in a Blender, ampoulded in 0.5ml quantities and freeze dried.

3 *Standards:-*

(a) Description.- Light brown scales.

(b) Identification.- This product affords protection to the ducks against duck plague.

(c) Safety Test.- Four healthy, 8 to 12 weeks old ducks weighting not less than 600 gms are inoculated subcutaneously with 1ml of 10^{-1} dilution of the vaccine and observed for a period of 14 days. During the period of observation, the ducks shall not show any untoward reaction.

(d) Sterility test.- Shall comply with the test for sterility described in the general monograph on ―Viral Vaccines‖.

(e) Potency Test.- Six susceptible ducks 8 to 12 weeks old each weighing not less than 600 gms are inoculated subcutaneously with 1 ml of 10^{-3} dilution of the vaccine. The minimum virus contents in 1 ml. dose of the vaccine shall be $10^{3.5}$ $EID_{50.}$ 14 days later these ducks are challenged subcutaneously each with 1 ml. of 10^{-2} dilution of the virulent duck plague virus (1000 $DEID_{50}$) along with 2 unprotected young ducks of about 8-12 weeks age. The unprotected ducks shall show symptoms of duck plague and die within 10 days, while the protected ducks shall remain normal during the observation period of 14 days.

4. ***Labelling***.- Should comply with the requirements of labelling as laid down in the general monograph on ―Viral Vaccine‖.

5. ***Storage.-*** Vaccine when stored at minus 15o C to minus 20o C may be expected to retain its potency for one year and about three months if stored in the freezing chamber of Refrigerator i.e. minus 5o C.

Avian Encephalomyelitis Vaccine (Living)

1. ***Synonyms.-*** Avin-encephalomyelitis Vaccine Freeze dried.

2. ***Definition.-*** A virus bearing tissue and fluid suspension from embryonated hen‘s legs.

3. ***Preparation.-*** The stock seed virus which has been established as pure, safe and immunogenic shall be used for preparing the vaccine.

(i) Each lot of stock seed virus shall be tested for pathogenicity by chicken embryo inoculation test:

(*a*) One dose of the seed lot shall be mixed with 9 volume of sterile heat inactivated specific, antiserum to neutralize vaccine virus in the product.

(b) After neutralization, 0.2 ml of serum vaccine mixture shall be inoculated into each of at least 20 fully susceptible chicken embryos (0.1ml of the inoculum shall be inoculated on CAM of 9-11 days old embryos and 0.1 ml in the allantoic sac).

(*c*) Eggs shall be candled for 7 days. Deaths occurring during first 24 hours shall be discarded but at least 18 viable embryos shall survive 24 hours post inoculation for a valid test. All embryos and CAMs from embryos which die after the first day shall be examined.

(*d*) If the death or abnormality attributable to inoculums occur, the seed lot is unsatisfactory.

(ii) ***Immunogenicity test***.- Avian encephalomyelitis susceptible chicks, all of same age 8 weeks old) shall be used 20 chickens shall be inoculated with the field dose of the virus by prescribed route. Ten additional chickens of same age and flock shall be held as unvaccinated controls.

At least 21 days post vaccination, the controls and vaccinates shall be challenged intracerebrally with Virulent avian encephalomyelitis virus and observed each for 21 days. At least 80 percent of controls shall show signs of avian encephalomyelitis or die. At least 19 to 20 vaccinates shall remain free from clinical avian encephalomyelitis during the observation period for the stock seed virus to be satisfactory

4. ***Standards:-***

(a) Description:- Greyish white flakes easily dispersible in the diluent.

(b) Identification:- At least 5–6 days old embryonated eggs (from hens with no history of infection with avian encephalomyelitis) shall be inoculated with 0.1 ml of undiluted vaccine into the yolk sac and kept in incubator and then transferred to the brooder where they are allowed to hatch. The hatched chicks shall be raised for 7 days. More than 5 per cent of hatched chicks shall manifest the typical symptoms (weak-leg, leg paralysis tremor etc.) at the end of this period.

(c) Moisture Content: - Shall not exceed 1.0 per cent.

(d) Sterility Test: - Shall comply with the test for sterility described under general monograph on ―Viral Vaccines‖.

(e) Safety Test: - At least 25 avian encephalomyelitis susceptible birds (6-10 weeks of age) shall be vaccinated with 10 field doses by the recommended route and observed

each day for 21 days. If unfavourable reactions attributable to the vaccine occur during the observation period, the batch of vaccine is unsatisfactory.

(f) Potency Test: -

(i) The vaccine shall be titrated for virus content. To be eligible for release, the batch shall have a virus titre of at least $10^{2.5}$ EID_{50} per dose.

(ii) At least 10 susceptible chickens shall be vaccinated with the field dose of the vaccine by prescribed route and 10 chickens from same batch and source shall be kept as unvaccinated controls.

At least 21 days post-vaccination, both the groups shall be challenged intracerebrally with Virulent avian encephalomyelitis virus and observed for 21 days. At least 8 out of 10 controls shall develop recognizable signs or lesions of avian encephalomyelitis and at least 8 out of 10 vaccines should remain normal

5. *Labelling:* Shall comply with the requirement of labelling as laid down in general monograph on ―Viral Vaccines‖.

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Marek's Disease Vaccine (Living)

1. *Synonyms.-* Herpes virus of Turkey Vaccine HVT vaccine (Living).

2. *Definition:-* Marek's disease vaccine is a suspension of cell free fluid containing live virus.

3. *Preparation.-* The stock seed virus which has been established as pure, safe and immunogenic in avian species shall be used for preparing the seed virus for vaccine production.

(i) Safety Test – The stock seed virus shall be non-pathogenic for chickens as determined by the following procedure:

The groups of at least 25 chickens each at one day of age shall be used. These chickens shall be of the same source and batch be susceptible to Marek's disease and be kept in isolated group.

Group 1: Each chicken shall be injected with 0.2 ml of 10 times as much viable virus as will be contained in one dose of vaccine by intramuscular route.

Group II : Shall serve as controls. At least 20 chickens in each group shall survive for four days postinjection. All chickens that die shall be necropsied and examined for lesions of Marek's disease and cause of death. The test shall be judged according to the following :

At 120 days o age, the remaining chicken in both the groups shall be weighted, killed and necropoised. If at least 15 chicken in each of these two groups have not survived the 120 days period if any of the chicken of Group-I have gross lesions of Marek's disease at necroposy or if the average body weight of the chickens in Group-I is significantly (statistically) different from the average of Group-II at the end of 120 days, the lot of stock seed virus is unsatisfactory.

(ii) Purity test – Shall conducted in chickens and no lesions other than those typical of Turkey Herpes virus shall be evidenced.

(iii) Immunologenicity test – Sixty susceptible day old chicks are used. Thirty of them inoculated with the seed virus in a dose corresponding to the field dose of the final vaccine and 14-21 days later challenged by intrabdominal route with virulent Marek's diseas virus, alongwith the other 30 non-vaccinated control chicks. At the end of the observation period when the chicks are 20 weeks old, the surviving chickens are examined for the presence of antibody against Marek's disease by serological tests and postmortem inspection for lesions of Marek's disease.

Any bird dead is thoroughly examined and the cause of death ascertained by necropsy/histopathological examination. All the surviving birds are killed and necropsied.

The protection index (P1) is determined by following procedure :

1. Percent MD = $\frac{\text{No. with MD lesions}}{\text{No. with MD lesions + No. of –ve Surviviours (effective No.)}} \times 100$

2. P.I. = $\frac{\text{Percent MD in controls – Percent MD in vaccinated}}{\text{Percent MD controls}} \times 100$

Master seed virus should have P.1 of at least 80 per cent.

Eighty per cent of the chicks in the control group must fall ill specifically. If more than 80 per cent of the vaccinated chickens do not show symptoms or signs of Marek‘s disease, the seed virus is regarded as sufficiently effective and can be used for production of vaccine.

The seed virus is propagated in duck embryo fibro-blast cell culture, chick embryo fibroblast or any other suitable cell culture (specific pathogen free SPF flock) and when the peak passage level is attained the cell monolayer is suspended in cold diluent of the following composition:

SPGA Stablizer

0.218% Sucrose.

0.0038% monosodium phosphate.

0.0072% dipotassium phosphate.

L Monosodium glutanate 0.0049 M.

1 per cent bovine albumin fraction (V).

0.25 per cent EDTA (Sterilised by Seitz filteration and stored at minus 10_{o} C). The virus is freed from cell by ultrasonication for 3 minutes interrupted after every 30 seconds) at 100 MA and freeze dried at times 60_{o} C preferably in shelf freeze dried in convenient volumes. The doses per ampoule vial is calculated after titrating the freeze dried product in terms of plaque

forming units (PFU) in the corresponding cell monolayers.

4. *Standards:*

(a) Description: - The cell free freeze dried HVT vaccine look uniformly grayish in colour and easily dispersible in the specified diluent.

(b) Identification. - The vaccine on inoculation in suitable cell culture system shall cause cytopathic effect typical of Herpes virus of Turkey. Specific antiserum of Herpes virus of Turkey shall neutralize the cytopathic effect.

(c) Moisture content. - Moisture content shall not exceed one per cent.

(d) Sterility test. - Shall comply with the test prescribed in general monograph on ―Viral Vaccines‖.

(e) Safety Test.- At least 25 one day old chickens shall be injected with ten times of the field dose of vaccine by intramuscular route. The chickens shall be observed each day for 21 days. Chickens dying during the period shall be examined, cause of death determined and the results recovered as follows :

(i) If at least 20 chickens do not survive the observation period, the test is inconclusive.

(ii) If lesions of any disease or cause of death are directly attributable to the vaccine the vaccine is unsatisfactory.

(f) Potency test. - The sample shall be titrated in the cell culture system. A satisfactory batch shall contain at least 1500 plaque

forming units (PFU) as per dose at the time of release

and maintain at least 1000 PFU till the end of expiry period.

5. ***Labelling.*** - Shall comply with the requirements of labelling as laid down in general monograph on ―Viral Vaccines‖.

6. ***Storage and expiry date***. - The freeze-dried cell free HVT vaccine may be stored at 4°C for 6 months.

Goat Pox Vaccine (Living Cell Culture)

1. ***Synonym.*** - Goat Pox Vaccine (living), Attenuated Goat Pox Vaccine.

2. ***Definition.*** - Goat Pox vaccine is freeze-dried preparation, prepared by growing attenuated goat pox virus in kid kidney/testicular cell culture.

3. ***Preparation.*** - Primary kidney/testicular cell cultures of disease free kid are used. The monolayers infected with the seed virus are incubated at 37° C. The cultures are harvested by three cycles of freezing and thawings 6 to 7 days post infection when more than 80 per cent cells show CPE. The suspension is centrifuged at 1000 rpm for 10 minutes to remove cellular debris being stored at minus 20° C. The suspension is freeze dried after addition of 5 per cent Lactalbumin hydrolysate and 10 per cent sucrose.

4. ***Standards****:*

(a) Description. - Light yellow colour.

(b) Identification - The product affords protection to goat against goat pox.

(c) Moisture content. - The moisture content shall not exceed 1.0 per cent.

(d) Safety tests.-

(i) Laboratory animals. - Six mice, 3 guinea pigs and 3 rabbits are inoculated with 0.2ml intraperitoneally, 0.5 ml and 1.0 ml subcutaneously, respectively with 10 field doses of the vaccine. The inoculated animals during the observation period of 80 days shall remain normal.

(ii) *Goat*. - Two susceptible goats of 6 to 8 months of age are inoculated in postaxillary region by subcutaneous route with one-hundred field doses of the vaccine. The inoculated animals shall not develop more than a local reaction of 2 to 3 cms. These animals shall be observed for 10 days.

(e) Sterility test.- Shall comply with the test for sterility described under the general monograph on ―Viral Vaccines‖.

(f) Titration in cell culture.- Four randomly selected samples are inoculated in kid kidney cell cultures using 5 tubes for each dilution. The titration shall be repeated thrice. One thousands $TCID_{50}$ is used as a field dose.

(g) Potency Test.- The three susceptible goats (8-10 months) are inoculated with 1/10th field dose and 3 susceptible goats (8-10 months) with one field dose, subcutaneously. Three in contract controls are also kept with the inoculated goats. These animals are observed for a period of 14 days and their body temperature recorded daily. The vaccinated

animals shall not show any termal, local or generalized reaction. Twenty one days post infection, the vaccinated and controls and challenged with 10,000 $TCID_{50}$ of virulent goat pox virus by intradermal route. The temperature of these goats are recorded for a period of 14 days. The vaccinated goats shall not develop localized or generalized reaction while control goats shall develop high fever, localized reaction or even generalized reaction in some cases.

5. ***Labelling*** .- Shall comply with requirements of labelling as laid down in the general monograph on ―Viral Vaccines‖.

6. ***Storage and expiry date***.- The vaccine is expected to retain its potency for 12 months if stored at minus 15° C to minus 20° C and for three months at 2° C to 4° C.

Sheep Pox Vaccine (Inactivated)

1. ***Synonym*** .- Formal gel sheep pox vaccine.

2. ***Definition*** .- Sheep pox vaccine is a formaline inactivated gel treated tissue vaccine.

3. ***Preparation.-*** Healthy susceptible sheep of 8-12 months of age are inoculated subcutaneously with 500 ml of the 1:100 dilution of the Russian Virulent Sheep Pox Virus. Seven to eight day post inoculation skin of the abdomen alongwith the oedema is collected. The infected tissues are homogenized in 10 percent concentration in phosphate buffer (pH 7.4-7.6) which after the extraction of the virus is mixed with sterile gel and buffer in the following proportion :-

6 percent aluminium hydroxide gel-50 per cent.

Phosphate Buffer (pH 7.6)- 35 per cent.

10 per cent suspension – 15 per cent

This is later formalized and kept at 20-25°C/10°C for varying periods.

4. ***Standards.-***

(a) Description .- It is a greyish white suspension. During storage the gel settles at the bottom, upper layer of the suspension is clear.

(b) Identification.- This product affords protection to sheep against sheep pox.

(c) Safety test.- This is carried out by inoculating 2 white mice with 0.2 ml., one guinea pig with 1.0 ml and one rabbit with 3,0 ml of vaccine. The animals should remain clinically healthy for 10 days.

(d) Sterility test.- This is done by seeding the vaccine on usual bacterial media. The plates and tubes are incubated for 10 days at 37° C. If the pathogenic bacteria are found, the vaccine is rejected while with non-pathogenic bacteria the vaccine is passed for field use.

(e) Potency test.- This is done by inoculating 4 non immune susceptible sheep preferably exotic breed of 1-2 years with 3 ml of vaccine in the thigh, subcutaneously.

The vaccinated sheep are challenged 15 days after inoculation alongwith 3 controls each with 0.1 ml of virulent virus containing 200 infective doses intradermally under the tail.

The sheep are observed for 10 days and their skin reaction recorded. The vaccine is considered potent if all the vaccinated, sheep do not show thermal or local skin reaction. Vaccine is also potent if 3 vaccinated animals do not develop any reaction and one shows abortive skin reaction, while at least 2 of the 3 controls develop typical sheep pox reaction at the site of inoculation.

5. ***Labelling.***- Shall comply with the requirements of labelling as laid down in the general monograph on ― Viral Vaccines‖.

6. ***Storage.-*** The vaccine shall be stored at 4° C to 5°C. it keeps well at above temperature upto 12 months.

Sheep Pox Vaccine (Living Cell Culture)

1. ***Synonym.***- Sheep pox vaccine (Living), attenuated sheep pox vaccine.

2. ***Definition.***- Sheep pox vaccine is freeze dried preparation prepared by growing attenuated sheep pox virus in lamb kidney/testicular cell cultures.

3. ***Preparation***.- Primary cell cultures prepared from kidney/testicles of disease free lambs are used. The mono layers infected with the seed virus are incubated at 37° C. The cultures are harvested by 3 cycles of freezing and thawing 6 to 7 days post infection when more than 80 per cent Cells show C.P.E. The suspension is centrifuged at 1000 r.p.m. for 10 minutes to

remove cellular debris before being stored at minus 20o C. The suspension is freeze dried after addition of 5 per cent Lactalbumin hydrolysate and 10 per cent sucrose.

4. *Standards:-*

(a) Description.- Light yellow colour.

(b) Identification.- The product affords protection to sheep against sheep pox.

(c) Moisture contents.- The moisture contents should not exceed 1.00 per cent.

(d) Safety tests.-

(i) Six mice, 3 guinea pig and 3 rabbits are inoculated with 0.2 ml intraperitoneally 0.5ml and 1.0 ml subeutaneously, respectively containing 10 field doses of the vaccine. The inoculated animals during the observation period of 10 days should remain normal.

(ii) One hundred field doses of the vaccine are inoculated subcutaneously into each of 2 susceptibles sheep in postaxillary region. Inoculated animals shall not develop more than a local reaction of 2 to 3 cms.

(e) Sterility test. - Shall comply with the test for sterility as described under the general monograph on ―Viral Vaccines‖.

(f) Titration in cell culture. - Four randomly selected samples reconstituted in a maintenance medium are inoculated in lamb kidney cell cultures using 5 tubes for each dilution. The titrations shall be repeated thrice. The $TCID_{50}$ to be calculated by Read and Muonch method. One thousand $TCID_{50}$ is calculated as one field dose.

(g) Potency test. - Three susceptible sheep 8-10 months old are inoculated with 1/10th, field dose and 3 susceptible sheep with one field dose, subcutaneously. Three in contact controls are also kept with the inoculated sheep. These animals are observed for a period

of 14 days and their temperature is recorded daily. The vaccinated animals should not show any thermal, local or generalize reactions. Twenty-one days post infection the vaccinated and controls are challenged with 10,000 ID_{50} of virulent sheep poxvirus by intradermal route. The temperature of these sheep are recorded for a period of 14 days. The vaccinated sheep should not develop localised or generalized reaction while control sheep should develop high fever, localized reaction or even generalized reaction in some cases.

5. *Labelling.*- Shall comply with requirements of labelling as laid down in the general monograph on ―Viral Vaccines‖.

6. *Storage and expiry date*.- The vaccine is expected to retain its potency for 12 months if stored at minus 15o C to minus 20o C and three months at 2 o C to 4 o C

Tissue Culture Rinderpest Vaccine

1. *Synonyms*.- Cell Culture Rinderpest Vaccine.

2. *Definition.*- Tissue Culture Rinderpest Vaccine is a freeze dried preparation of live modified rinderpest virus adapted to and propagated in cell culture.

3. *Preparations.*- Primary or secondary monolayer cultures of the kidney cells (Bovine or any other suitable animals) taken from kidney from healthy animals free from any pathological changes shall be used. When secondary cultures are used they shall have retained their original morphology and Karyotype. Kabete ‗O‘ stain of Rinderpest virus developed by East African veterinary Research Organisation (Plowrights strain between the passage levels of 99th and 100th passages) shall be used. The virus harvested from cell monolayer culture prepared from the kidneys of a single calf or serially cultivated bovine kidneys cells (Not more than 10 passages away from the Primary) inoculated with the same seed and harvested together, will be freeze dried with stabilizers in suitable quantities.

4. *Standards.*- It complies with the requirements of general standards of viral vaccines:

(a) Description.- Dry light yellow coloured flakes readily soluble in chilled and saline or buffered saline.

(b) Identifications.-

(i) Protects cattle against a subsequent challenge with virulent or caprinised rinderpest virus.

(ii) It is titrable in tissue culture systems capable of supporting the multiplication of this virus. The test shall be made on at least three separate occasions using a cell culture derived from different animals.

(iii) Specificity test shall be performed using an appropriate scrum neutralization test.

(c) Sterility test. - Each batch shall be tested for bacterial and mycotic sterility as given in general monograph on ―Viral Vaccines‖.

(d) Innocuity test.- Shall be made on each batch in at least two guinea pigs and six mice. These animals shall be observed for at least two weeks for any untoward reaction.

(e) Safety and efficacy test.- The test for safety and efficacy shall be performed using the pooled reconstituted contents of not less than 4 ampoules taken at random. The vaccine

shall be injected subcutaneously into each of at least two susceptible cattle free from specific antibodies using the quantity containing not less than 100 fields doses and two further cattle and using 1/10th of the field dose (calculated on the basis of 1000 $TCID_{50}$ one field dose). The animals shall be housed with at least two unvaccinated animals and observed for a period of three weeks. The vaccine passes the safety test if the cattle show no signs of unusual clinical reactions.

At the end of three weeks all the four animals will be challenged alongwith two in contact cattle with a challenge dose of not less than $10^4 ACID_{50}$ of virulent Rinderpest virus. The vaccine passes the potency/efficacy test if the in contact animals develop rinderpest and all the vaccinated animals remain normal.

5 *Labelling.-* Shall comply with general monograph on ―Viral Vaccines‖. Each ampoule or at least 50 percent ampoules in a lot shall contain at least following print :

(i) TCRP Volume.

(ii) Batch No. with year.

(iii) General instructions for use.

6 *Storage .-* The vaccine when stored at minus 20_o C and plus 4 degree C will maintain its titre for 2 years and 6 months respectively.

Canine Distemper Vaccine

1. ***Synonyms.***- Cannine Distemper Vaccine (Living)- Freeze-dried.

2. ***Definition.-*** It is freeze dried preparation of either tissues from chick embryo containing eggs adapted strain of cannine distemper virus or the cell culture in which modified virus has been cultivated.

3. ***Preparation***.- Canine distemper vaccine shall be prepared from virus bearing cell culture, fluid or infected chroioalantoic membrane. Only stock seed virus which has been established as pure, safe and immunogenic shall be used for preparation of vaccine. Stock seed virus propagated in chicken embryo shall be tested for pathogen by chicken embryo test. One volume of the virus shall be mixed with 9 volume of specific sterile heat inactivated serum to neutralize the virus. Mixture shall be inoculated into twenty (9 to 11 days old) chicken embryo (with 0.1 ml on CAM and 0.1 ml in alantoic sac). Embryonated eggs shall be candled for 7 days daily. Death occurring in the first 24 hours shall be discarded. CAMS of embryos which die after 24 hours shall be examined. When necessary embryo sub-culture shall be made to determine the cause of death. The test should be concluded on the 7th day post inoculation.

The surviving embryos and their CAMS are examined. If deaths or abnormality due to the inoculums occur, the seed virus is unsatisfactory.

Immunogenicity test: Thirteen susceptible dogs 8-14 weeks old shall be used for the test (ten vaccinates and 3 controls). Blood samples are drawn from these animals and individual sample is tested for antibodies against canine distemper. Ten dogs shall be injected with a predetermined quantity of the virus and remaining 3 dogs are used as unvaccinated controls. The dose shall be based on the virus tiltration. At least 21 days post infection the vaccinated and controls shall be challenged intramuscularly with the same dose of virulent canine distemper virus and the animals are observed each day for 21 days. At least 2 out of 3 controls should die and survivor should show the symptoms typical of canine distemper. At least 9 out of 10 vaccinated animals should survive and should not show any clinical signs of canine distemper during the observation period. The stock seed

virus should be tested for immunogenicity at least once in 5 years, if maintained under suitable conditions of storage. Eight days old chicken embryos from a healthy flock are inoculated on their chorioallantoic membrane with bacteriologically sterile virus suspension of egg adapted strain. After incubation for a period of five days, infected membrane and embryos are harvested. The individual embryo is tested for bacterial sterility. Those free from bacterial contamination are made into a 20 percent suspension in a suitable medium. The suspension is distributed in a single dose quantity into the ampoules of vials and freeze-dried.

The ampoules are sealed under vacuum or with pure dry sterile nitrogen before sealing. Alternatively, the virus may be grown on the suitable cell culture. Cells along with the suspending fluid is harvested, distributed in single dose quantity in ampoules and freeze dried.

4. ***Standard.-***

(a) *Description.* - It is a dry product, pinkish cream material, readily dispersible in water or a suitable solvent.

(b) *Identification*. - It infects CAM of fertile eggs. This is neutralized by canine distemper antiserum. It does not cause distemper after injection into susceptible ferrets or dogs but immunizes them against the disease.

(c) *Moisture content.* - Moisture content in the finished product shall not exceed more than 1.0 per cent.

(d) *Sterility test.* - Shall comply with the test for sterility as described in the general monograph on ―Viral Vaccines.‖

(e) *Safety tests. - (i) Mice safety test:* Reconstituted vaccine as recommended on the label shall be tested.

Eight mice, 4 weeks old shall be inoculated intracerebally with 0.03 ml and 8 mice shall be inoculated intraperitoneally with 0.5ml. Both groups shall be observed for 7 days, if unfavourable reaction attributable to the product in either 2 or more mice in either group is observed during observation period, the batch is unsatisfactory.

(*ii*) Dog *Safety test.*-Inject two healthy dogs eight to fourteen weeks old that have previously been shown to be free from distemper virus-neutralising antibodies by the recommended route with twice the dose stated on the label and observe for 21 days. No significant local or general reaction develops.

(i) *Potency test. - (i) Titration :* Final samples of finished product shall be tested for virus titre, and when tested at any time within the expiry period, it should contain not less than 10^3 ID_{50} per dose.

(*ii*) It shall be carried out in dogs. Two healthy susceptible dogs each of 8-14 weeks of age free from distemper neutralizing antibodies are injected subcutaneously each with one vaccination dose. Serum samples shall be

collected from each dog 14 days after vaccination and these shall have specific neutralizing antibodies at a dilution of 1: 100.

6. ***Labelling.***- Shall comply with the requirements of labelling as laid down in the general monograph on ―Viral Vaccines‖.

7. ***Storage and expiry date.*** - For the freeze-dried product the expiry date is one year when stored at minus 20$_o$C.

Avian Infectious Bronchitis Vaccine (Living)

1. ***Synonyms***. - Avian Infectious Bronchitis Vaccine (Living) freeze-dried.

2. ***Definition***. - It is a freeze-dried product of low virulent Avian Infectious Bronchitis Virus grown in embryonated hen‘s eggs of cultivated in cell culture.

3. ***Preparation***. - Only stock seed virus which has been established as pure, safe and immunogenic shall be used. Each jot of stock seed virus shall be tested for other pathogens by chicken embryo inoculation tests as follows: -

A lot of seed virus shall be mixed with 9 volumes of sterile heat inactivated specific anti-serum to neutralize and the vaccine virus serum mixture shall be inoculated into each of at least 20 fully susceptible chicken embryos of 9-11 days old (0.1 ml on CAM and 0.1 ml in the allantoic sac). Eggs are candled daily for 7 days. Deaths occurring during first 24 hours shall be discarded but at least 18 viable embryos shall survive 24 hours post inoculation for a valid test. All embryo and CAMS from embryos shall be examined which die after 24 hours. If necessary embryo subcultures shall be made to determine the cause of death. The test shall be concluded on the 7th day post inoculation and surviving embryos including the CAM shall be examined. If death and or abnormality attributable to the stock seed virus occur, the seed lot is unsatisfactory.

Each lot of stock seed virus shall be tested for immunogenicity as below: -

Bronchitis susceptible chickens of the same age and source shall be used. For each method of administration recommended on the label and for each serotype against which protection is claimed, 20 chicks shall be used as vaccinates. Ten additional chickens for each serotypes against which protection is claimed shall be held as unvaccinated controls.

21 to 28 days post vaccination all vaccinates and controls shall be challenged by eye drops with virulent Bronchitis virus. A separate set of vaccinates and controls shall be used for each serotype against which protection is claimed. The challenge virus shall have a titre of at least $10^{4.6}$ EID_{50} per ml. Trachea swabs shall be taken once 5 days post challenge from each vaccinated and controls. Each swab shall be placed in test tube containing 3 ml of tryptose phosphate broth and antibiotics. The tubes and swabs shall be swirled thoroughly and stored at minus 40$_o$ C pending egg inoculation. For each chicken swabs at least 5 chicken embryos, 9-11 days old shall be inoculated in the allantoic cavity with 0.2 ml of broth from each tube. All the embryos surviving 3rd day post inoculation shall be used in evaluation. A tracheal swab shall be positive for virus recovery when any of the embryos show typical infections bronchitis virus lesions such as stunting, curling, kidney urates, clubbed down or death during 4-7 days post inoculation period.

90 percent of the controls should prove positive for virus recovery. If less than 90 per cent of the controls are negative for virus recovery, the stock seed is unsatisfactory. The stock seed virus should be tested for immunogenicity once in 5 years provided it is maintained under standard conditions of the bronchitis virus storage.

4. ***Standards.*** **-**

(a) Descriptio: It is greyish-white product easily dispersible in the diluent.

(*b*) *Identification*: (i) The contents of the ampoule are suspended as per the instructions for the field use. The 0.2ml of the suspension shall be inoculated in the allantoic cavity of 9-11 days old chicken embryo and are incubated for 7 days. The lesions typical of

infectious bronchitis shall be observed in the embryos at the end of incubation period. The allantoic fluid shall not agglutinate the chicken RBC's.

(ii) Specific antisera against avian infectious bronchitis virus should neutralize the vaccine virus.

(*c*) *Moisture content.* - Moisture content in the finished product should not exceed 1.0 per cent.

(d) Sterility test. - Complies with the test for sterility as described under the general monograph on ―Viral Vaccines‖.

(e) Safety test. - Ten healthy susceptible chickens 5-10 days old from the same source batch shall be vaccinated with ten field dose of the vaccine and along with five chicks from same batch as unvaccinated controls by the prescribed route and observed 7 or 21 days post vaccination. Neither severe respiratory symptoms nor death shall occur to more than one experimental chicks, none of the unvaccinated control shall show any clinical symptoms.

(*f*) *Potency test.* - The minimum virus content of the freeze-dried product shall not be less than $10^{3.5}$ EID_{50} per bird. The virus content of the vaccine shall be titrated as below:

Serial ten-fold dilution of the freeze-dried material will be made in tryptose phosphate broth. Three to five embryonated eggs (9-11 days old) shall be in inoculated with 0.1 ml of each dilution into the allantoic cavity and observed daily for 7 days.

Deaths occurring during the first 24 hours shall be discarded. The surviving embryos are examined for the evidence of infection and EID_{50} shall be calculated by the Reed and Muench Method/spearman and Karber method.

5. ***Labelling*** .- Shall comply with the requirement of labelling as laid down in the general monograph on ―Viral Vaccine‖.

6. ***Storage and expiry date***.- Shall be stored at 4° C for six months].

PART II –ANTISERA

Provisions applicable to the production of all Sera from Living Animals

1. ***Definitions***- (i) This Part of the Schedule applies to antibacterial sera, anti-viral sera and anti-toxic sera which are prepared by injecting bacteria or viruses or their products into buffalo-bulls or other suitable animals so as to produce active immunity which is manifested by the formation of anti-body.

(ii) For the purpose of this Part of the Schedule an anti-serum means sterile liquid anti- serum concentrated and unconcentrated, solutions of globulins or their derivatives or solid forms which can be reconstituted when necessary.

2. ***Staff of Establishment***- The establishment shall be under the direction and control of a competent expert in bacteriology and serology with adequate training in immunology and standardisation of biological products and knowledge of animal management. He shall be assisted by a staff adequate for carrying out the tests required during the course of preparation of the sera and standardisation of the finished products.

3. ***Proper Name***- The proper name of he antiserum shall be the recognised scientific name of the diseases or its causative organism or some generally recognised abbreviations thereof preceded by the prefix ‗anti‘, and followed by the word ‗serum; as for example, ‗Anti-Anthrax serum‘. The proper name of any antitoxin may be formed from the word ‗Anti-toxin‘ preceded by the name of the organism from which the toxin was prepared, and followed, if desired, by a term indicating the source or the strain of that organism provided where there is no special provision in the Schedule, the name as approved by the Licensing Authority may be adopted.

Records-

(1) The permanent records which the licensee is required to keep shall include the following particulars: -

(a) As to the culture- Evidence of the identity and specificity of the cultures.

(b) As to the procedure used in immunising the animals;

(*i*) The method of preparing the cultures or antigen used for immunisation.

(*ii*) The dosage and methods employed in administering the culture or antigen.

(*iii*) The period in the course of immunisation at which blood is withdrawn for the preparation of the serum.

(c) Any test which may have been applied to the serum to determine its content of specific antibodies or its specific therapeutic potency and purity.

(2) If the licensee desired to treat the performance of any tests recorded under sub-paragraph (i) (c) of this paragraph as determining the date of completion of manufacture for the purpose of rule 109 he shall submit full particulars of the proposed test to the Licensing Authority and obtain his approval.

5. ***Cultures***- The cultures used in immunising the animals shall be at all times open to inspection, and specimens shall be furnished for examination at the request of the Licensing Authority.

6. ***Quantity -***

(a) Any antiserum shall be issued for veterinary use in the form of either.

(i) Actual serum, i.e., the liquid product of decantation of the coagulated blood or plasma without any addition, other than antiseptic or subtraction, or

(ii) A solution of the purified serum proteins containing the specific antibodies.

(b) At the time of issue, the liquid shall be clear or show at the most a slight opalescence or precipitate. Preparations of the natural serum shall not contain more than 10 per cent of solid matter. A solution of serum protein shall not contain more than 20 per cent of solid matter.

1. *Precautions to be observed in preparations-*

(i) Laboratories where sera are exposed to the air in the course of the process of preparation must be separated by a sufficient distance from stables and animals houses to avoid the risk of aerial contamination with bacteria from animal excreta, and must be rendered fly proof to prevent such contamination by insects. Such laboratories must have impervious walls and floors and must be capable of being readily disinfected when necessary.

(ii) A special room with impervious walls must be provided for the collection of blood from the living animals.

(iii) An efficient system of manure removal must be used which will prevent its accumulation in the vicinity of any room where blood or serum is collected or handled.

(iv) An adequate number of sterilizers must be provided for the sterilization of all glassware or other apparatus with which the serum may come into contact in the course of its preparation.

(v) All processes to which the serum is subjected during and after the collection from the animals, must be designed to preserve its sterility, but in the case of a artificially concentrated sera, it shall suffice that the process of concentration is

conducted with scrupulous cleanliness and in such a manner as to avoid unnecessary dangerous contamination.

(vi) The laboratories in which the testing of sera for potency, sterility and freedom from abnormal toxicity are carried out must be adequate for the purpose. An adequate supply of animals for use in such tests and suitable housing for such animals must be provided.

(vii) Provision must be made for complying with any special conditions which may be laid down in the Schedule relating to the production and issue of the particular serum, in respect of which the licence is granted.

8. ***Unhealthy or Infected Animals***- If an animal used in the production of sera is found to be suffering from an infection except one produced by living organisms against which it is being immunized, or shows signs of serious or persistent ill health not reasonably attributable to the process of immunisation, the licensee shall immediately report the matter to the Licensing Authority and shall, if the authority orders an inspection and the Inspectors so directs, cause such animals to be killed and a postmortem examination of it to be made, and take steps to prevent any serum obtained from the animal being sold or offered for sale until permission is given by the Licensing Authority. If the result of the postmortem is such as to bring under suspicion, the health of any of the other animals used for the production of sera, the Licensing Authority may prohibit the use of those animals for the production of sera or may take such other steps as may be necessary to prevent the issue of sera which may be dangerous to animal health.

Provided in the case of emergency, the person in charge of the establishment may order the destruction of an animal used in the production of sera and suspected of infection, and shall in that case given notice forthwith to the Licensing Authority and shall permit an Inspector to be present at the postmortem examination.

9. ***Conditions and Housing of animals:***

(i) The animals used in the production of sera should be adequately housed under hygienic environments.

(ii) Only healthy animals free from disease should be used in the preparation of sera.

(iii) Every animal intended to be used as the source of serum must be subjected to a period of observation in quarantine for at least seven days before being admitted to the animal sheds in which the serum yielding animals are housed.

(iv) In case of horses and other equidae, every animal used as source of serum shall either be actively immunized against tetanus or shall be passively immunized against the disease by injection of tetanus antitoxin in such doses as to ensure the constant presence of that antitoxin in the blood during the whole period of the use of the animals as a source of serum.

Anti-Sera and their General Standard

Anti-sera contain the immune substances that have a specific prophylactic or therapeutic action when injected into animals exposed to or suffering from a disease due to a specific microorganism or its toxin. Anti-sera are classified into three groups.

(i) Antitoxic sera (Antitoxin)

(ii) Antibacterial sera.

(iii) Antiviral sera.

Antisera are usually issued in an unconcentrated form for animal use but may be concentrated and also freeze dried. However, for the purpose of the Schedule the word _antisera‘ is also used for the unconcentrated liquid sera only. A suitable bacteriostatic agent in a concentration sufficient to prevent the growth of microorganisms is added to the liquid serum.

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General Standard

1. ***Description***- Liquid native or unconcentrated antisera are yellow or yellowish brown in colour. They are initially transparent but may become turbid with age. They are almost odourless except for the odour of any bacteriostatic agent that may have been added.

2. ***Identification***- The test for identity is described in the individual monograph.

3. ***Acidity or Alkalinity***- All native antisera have a pH of 7.0 to 8.5.

4. ***Abnormal Toxicity***- All anti-sera shall comply with the following tests or freedom from abnormal toxicity.

(a) Two healthy mice each weighing not less than 18 g. are injected subcutaneously each with 0.5 ml. of the sample and observed for five days. None of the mice should show any abnormal reaction or die.

(b) Two healthy guinea pigs each weighing 300 g. to 450 g. are injected subcutaneously each with 5 ml. of the sample and observed for seven days. None of the guinea-pigs should show any abnormal reaction or die.

5. ***Sterility***- All anti-sera shall comply with the tests for sterility described in rules 115 to 119.

6. ***Potency***- The potency of each preparation, when the available methods permit, is determined by the appropriate biological assay, and it is described under the individual monograph.

7. ***Total Solids***- Native antisera should not contain more than 10 per cent solid matter.

8 ***Labelling***- Should comply with the provisions for _Labelling‘ as laid down for _Bacterial Vaccines. ‘

9. ***Storage***- Liquid preparations of antisera shall be stored, protected from light at temperature between 2 ˚C to 4 ˚C and shall not be frozen.

10 ***Date of Manufacture***- The date of manufacture shall be unless otherwise specified in the individual monograph in this part is as defined in clause (b) of sub-rule (3) of rule 109.

11. ***Containers***- All antisera are distributed in sterilised containers of a material which is inert towards the substance and which are sealed to exclude micro-organisms.

12. ***Expiry Date***- The expiry date of potency of all sera shall not be more than twenty- four months after the date of a manufacture.

Anti-Anthrax Serum

1. ***Synonym***- Bacillus Anthracis Anti-serum.

2. ***Definition-*** Anti-anthrax serum is the serum of animals that confers a specific protection against *Baccillus anthracis.*

3. ***Preparation***- The antiserum may be prepared in buffalo bulls after repeated injections of cultures of *B. anthracis* of a virulent strain.

4. ***Standard***- It complies with the requirements in the general provisions for antisera under Description, Acidity or Alkalinity, Abnormal Toxicity, Sterility, Solids, Labelling, Storage and Expiry date.

Identification – It protects animals against infection with *B. Anthracis*

Anti-Blackquarter Serum

1. ***Synonym***- Blackleg Antiserum, Clostridium Chauvoei-Anti serum

2. ***Definition***-Anti-Blackquarter serum is the serum of suitable animals containing the Substances that have a specific neutralising effect on *Clostridium Chauvoei*.

3. ***Preparation***- It is prepared by injecting subcutaneously or intramuscularly increasing doses of formolised cultures of *Cl. Chauvoei* into buffalo bulls.

4. ***Standards***- It complies with the requirements described in the general provisions for antisera under Description, Acidity or Alkalinity, Abnormal Toxicity, Sterility, Solids, Labelling, Storage and Expiry date.

Identification- It protects susceptible animals against infection with virulent strains of *Cl. Chauvoei.*

Anti-Fowl-Cholera Serum

1. ***Synonym-*** Pasteurella Septica Antiserum (Avian).

2. ***Definition-*** Fowl Cholera Antiserum is the serum of animals containing the substances that confer a specific protection to fowls against virulent strain of Pasteurella Septica (Avian).

3. ***Preparation***- Antiserum is prepared from buffalo bulls after they have been subjected to an injection of killed cultures of virulent strain of *Pasteurella Septica* (Avian) followed by injections of living cultures of the same organism.

4. ***Standard-*** It complies with the requirements described in the general provision for anti-sera under Description, Acidity or Alkalinity, Abnormal Toxicity, Sterility, Solids, Labelling, Storage and Expiry date.

Identification- It protects susceptible fowls against infection with Pasteurella Septica (Avian) and its homologous strains.

Anti- Haemorrhagic Septicaemia Serum

1. ***Synonym-*** Pasteurella Septica Antiserum.

2. ***Definition***- Anti-Haemorrhagic Septicaemia Serum is the serum of animals containing the substances that confer a specific protection to susceptible animals against virulent strains of *Pasteurella Septica.*

3. ***Preparation*** – The antiserum is prepared from buffalo bulls after they have been subjected to repeated injections of formolised cultures of standard strain *Pasteurella Septica* with adjuvants, followed by suitable doses of virulent culture of the organism.

4. ***Standard***.-It complies with the requirements described in the general provisions for antisera under Description, Acidity or Alkalinity, Abnormal Toxicity, Sterility, Solids, Labelling, Storage and Expiry date.

Identification- It protects susceptible animals against infection with homologous strains of *Pasteurella Septica.*

Anti-Rinderpest Serum

1. ***Synonym***- Cattle Plague Antiserum

2 ***Definition***- Anti-Rinderpest Serum is the serum of buffalo bulls containing the substances that confer a specific immunity to susceptible animals against virulent strains of the virus of *rinderpest*

3. ***Preparation*** – The antiserum is prepared from buffalos who have reacted to a dose of virulent rinderpest virus, which is injected simultaneously with a predetermined quantity of anti rinderpest serum so as to control the severity of the reaction (serum-simultaneous- method).

4 ***Standard***- It complies with the requirements described in the general provisions for antisera under Description, Acidity or Alkalinity, Abnormal Toxicity, Solids, Labelling, Storage and Expiry date.

(i) ***Identification***- It protects susceptible animals against rinderpest.

(ii) ***Potency***-Five Buffalo-calves of about one year of age in good condition are used for the test. Three are injected subcutaneously with the anti-rinderpest serum under test at the rate of 10 ml. per 46 kg. body weight, subject to a minimum of 20 ml. per animal. These together with the two remaining, are simultaneously injected subcutaneously at a different site with 1 ml. of a 1: 100 dilution of spleen suspension of virulent bull-virus.

The animals should be observed for fourteen days during which time the serum treated animals should exhibit no symptoms of rinderpest other than rise in temperature and slight intestinal disturbances, while the controls develop more severe symptoms or die.

Salmonella Pullorum Anti Serum

1. ***Synonym***- Salmonella Pullorum Anti Serum.

2. ***Definition-*** Salmonella Pullorum anti-serum is the sera from fowls and contains antibodies against Salmonella Pullorum. It is used for standardizing batches of Salmonella Pullorum antigens and also used as a control along with the sera suspected for pullorum disease.

3. ***Preparation***- The serum is prepared after intravenous inoculation with smooth culture suspension of Salmonella Pulloram in healthy birds.

4. ***Standards***- It complies with the requirements in the general provisions for anti- sera under Description, Acidity, Alkalinity, Sterility, Solids, Labelling, Storage and Expiry date.

5 . ***Identification-*** It should give positive agglutination with Salmonella pullorum antigen.

Standard Anti-Brucella Abortus Serum

1. ***Synonym***- National counterpart of standard anti-Brucella Abortus serum.

2. ***Definition-*** Standard Anti-Brucella abortus serum is the serum which contains 1000 International Units (I.U) per ml. and is used for standardizing batches of brucella antigens and is also used as a control along with the sera suspected for brucellosis.

3. ***Preparation***- The serum is prepared after intravenous inoculation of suspension of smooth culture of B. abortus (strain 99) in rabbits or cattle and subsequently diluting it suitably with brucella-free healthy serum so that when tested with standardized Brucella abortus tube test antigen, it gives 50% agglutination at 1/500 final serum dilution.

4. ***Standard***- It complies with the requirements in the general provision for anti- sera under Description, Acidity, Alkalinity, Sterility, Solids, Labelling, Storage and Expiry date.

Identification- It should give agglutination with Brucella antigen.

PART III- DIAGNOSTIC ANTIGENS

Provisions Applicable to the Manufacture and Standardisation of Diagnostic Agents (Bacterial Origin)

1 ***Definition-*** This Part of the Schedule applies to reagents of bacterial origin employed for various tests.

2 ***Staff of establishment***- A competent expert in bacteriology with sufficient experience in the manufacture and standardisation of veterinary biological products shall be in charge of the establishment responsible for the production of various diagnostic agents of bacterial origin and he may be assisted by a staff adequate or carrying out the tests required during the preparation and standardisation of various diagnostic agents.

3 ***Proper Name***- The proper name of any diagnostic agent is the name of micro-oraganism from which it is made, followed by the word _antigen‘ unless the Schedule

otherwise provides, or, it may be derived from the name of the organism responsible for the causation of the disease or if there is no special provision in the Schedule, the name approved by the Licensing Authority. In the case of the undermentioned preparations the proper name of the diagnostic agent may be as follows:

1. Abortus Bang Ring (A.B.R.) Antigen.
2. Brucella Abortus Coloured Antigen.
3. Brucella Abortus Plain Antigen.
4. Johnin.
5. Mallein.
6. Salmonella Abortus Equi —H‖ Antigen.
7. Salmonella Pullorum Coloured Antigen.
8. Salmonella Pullorum Plain Antigen.
9. Tuberculin.

4. ***Records***- Cultures used in the preparation of diagnostic agents of bacterial origin must, before being manipulated into an agent be thoroughly tested for identity by the generally accepted tests applicable to the particular micro-organism. The permanent record which the licensee is required to keep shall amongst other include a record of the origin, properties and characteristics of the cultures.

5. ***Preparation***- Diagnostic agents of bacterial origin are prepared from selected cultures after their careful examination for the identity, specificity, purity and antigenicity. They may be prepared in the following manner:

(a) Formolised Antigens- The selected pure culture strain grown in a suitable medium at an optimum temperature for an appropriate period. The pure growth is then exposed to the action of a solution of Formaldehyde I.P. in a suitable concentration and at an appropriate temperature for a suitable period.

(b) In some cases, the diagnostic agents are prepared by growing the organisms on suitable media and then deriving specific protein constituents of the bacteria by various methods.

6. ***General Standard:-***

(a) Description- Diagnostic agents may be clear opalescent or coloured liquids.

(b) Identification- Some exhibit specific agglutination when mixed with the serum of the animals infected with homologous organisms and others when injected into the animal body in appropriate doses cause specific reactions like hypersensitiveness, local and general reaction, if the animal is infected with homologous organisms.

(c) Sterility Test- All antigens shall be tested for sterility in accordance with rules 114 to 119.

(d) Standardisation- It is carried out either by determining the definite concentration in the product or by observing the general and local reactions in healthy and artificially infected animals with various standard dilutions of the product.

7. ***Labelling***- As under general provisions for the bacterial vaccines with the addition that it is meant for diagnostic purposes only.

8. ***Storage***- All antigens are stored, protected from light at a temperature between 2 ˚ C to 4 ˚ C.

9. ***Date of manufacture***- The date of manufacture shall be unless otherwise specified in the individual monograph in this part as defined in clause (b) of sub- rule (3) of rule 109.

Abortus Bang Ring (A.B.R.) Antigen

1. ***Synonym***- Milk Ring Test Antigen.

2. ***Definition-*** The antigen is a suspension of pure growth culture of standard strain of Brucella abortus strain 99 strained supravitally with 2,3,5, triphenyl tetrazolium chloride suspended in 0.85 per cent saline containing 1 per cent glycerol and 1 per cent phenol.

3. ***Preparation***- Smooth strain of Brucella abortus strain 99 is grown in potato infusion agar for 48 to 72 hours in Roux flasks, at 37 ˚ C. Condensation fluid if any is pipetted off before washing. Each flask is washed with about 20 ml. of normal saline. The pooled washing is filtered through a gauze and the filtrate is collected in a measuring cylinder. To every 500 ml. of the filtrate 1 g. of 2, 3, 5, triphenyl tetrazolium chloride is added immediately. The container is shaken for thirty minutes till the tetrazolium salt is dissolved.

The product is taken out and kept at 37 ˚ C for two hours. After incubation the product is heated at 65˚ C in a water bath for thirty minutes. It is cooled and centrifuged at 3000 r.p.m for one hour. The supernatant is pipetted off and sediment is suspended in normal saline containing 1 per cent glycerol and 1 per cent phenol and filtered through sterile cotton wool. This forms concentrated antigens.

Standardization of the Strained Antigen

An aliquot portion of the microbial suspension stained with phenylte-trazolium is taken, representing the initial undiluted suspension. 1 ml. per tube of this initial undiluted stained suspension is added to six test tubes, followed by increasing quantities of the glycerolphenol diluent as follows:-

Tube	Undiluted Stained Suspension	Diluent
1	1	0.6 2
	1	0.8 3
	1	
	1.0 4	1
	1.2 5	1
	1.4 6	1
	1.6	

The contents of each tube are then diluted tenfold with the same diluent and serve as antigen for a tube agglutination test with the Standard Serum (or its national counterpart). In this way, six sero-reactions will be carried out. During this procedure, the concentrated strained microbial suspension should be kept in the refrigerator at 4 ˚ C.

The agglutination reactions are read after forty-eight hours at the agglutination titre of the Standard Serum, previously determined with the usual unstained antigen in the tube test, corresponding to the correct dilution of the standard antigen.

The next step, therefore, is to dilute the concentrated stained suspension to the same extent as the tube whose tenfold dilution has given the correct agglutination titre, i.e. the concentration of antigen in the tube before the tenfold dilution had been made.

4. ***Standard:***

(a) Description- It is a red colour liquid containing dead bacteria in suspension.

(b) Identification- It shows formation of a specific cherry red coloured ring in the cream layer when mixed with pooled samples of milk taken from animals suffering from burcellosis.

(c) Sterility Test- Should comply with tests for sterility described in the general monograph on _Diagnostic Antigen‘. The test shall, however, be done before colouring.

5. ***Labelling and Storage***- Should comply with the requirements of _Labelling‘ and _Storage‘ as laid down in the general monograph on _Diagnostic Antigens‘.

6. ***Expiry Date***- The date of expiry of potency shall be not more than nine months from the date of manufacture when stored 2 ° C to 4° C.

Brucella Abortus Coloured Antigen

1. ***Synonym***- Brucella abortus Cotton Strain 99 coloured Antigen.

2. ***Definition***- Brucella Abortus colured Antigen, is a suspension of pure smooth cultures of Brucella abortus strain 99 in phenolised glycerine saline, the bacteria being coloured by the addition of crystal violet and brilliant green. This antigen is used for plate test for serological diagnosis of brucella infection.

3. ***Preparation***- Seventy-two hours old growth of Brucella Abortus strain ninety-nine in smooth form on potato infusion agar medium in Roux flasks is washed with phenolised glycerine saline (containing 12 per cent sodium chloride, 20 per cent glycerine and 0.5 per cent phenol). The washed growth is filtered through a pad of absorbent cotton wool and the suspension is coloured by the addition of 1 ml. each of 1 per cent aqueous solution of crystal violet and brilliant green for very 250 ml. of the suspension. The product is heated for sixty minutes in a water bath at 60° C before it is standardised.

4. ***Standard****:*

(a) *Description*- It is a greenish violet liquid containing dead bacteria in suspension.

(b) Identification-It gives specific agglutination when mixed with the serum of the animal infected with brucella organism.

(c) *Sterility Test*- Should comply with the tests for sterility described in the general monograph on _Diagnostic Antigens‘

(d) Standardisation- 0.5 ml. of the antigen is mixed with 4.5 ml of normal saline solution in Hopkins graduated tube. The mixture is centrifuged at 3000 r.p.m. for sixty minutes and the percentage of bacterial cells present in the original antigen is assessed by noting the height of the cell deposit. The antigen is then standardised so as to contain 10 per cent cell deposit.

5. ***Labelling and Storage***- Should comply with the requirements of _Labelling‘ and _Storage‘ as laid down in the general monograph on _Diagnostic Antigens‘.

6. ***Expiry Date***- The date of expiry of potency shall be not more than nine months from the date of manufacture when stored at 2 ° C to 4°C.

Brucella Abortus Plain Antigen

1. ***Synonym***- Brucella Abortus Strain 99 Plain Antigen.

2. ***Definition-*** Brucella Abortus Plain Antigen is a suspension of a pure smooth culture of Brucella abortus strain 99 in phenol-saline.

3. ***Preparation***- Seventy-two hours old growth of Br. Abortus strain 99 in smooth form on potato infusion agar medium in Roux flasks is washed with normal saline solution. The washed growth is filtered through a pad of absorbent cotton wool and the suspension is

kept at 60 ° C per cent. for sixty minutes on a water bath to kill the organisms. It is then preserved by the addition of phenol in a final concentration of 0.5 per cent.

4. ***Standard:***

(a) Description- An opalescent liquid containing dead bacteria in suspension. *(b) Identification* –It gives specific agglutination when mixed with the serum of animals infected with brucella organism.

(c) Sterility Test- Should comply with the tests for sterility described in the general monograph in _Diagnostic Antigen‘.

(d) Standardisation- Mix the concentrated antigen well and dilute 1 ml. with 0.5 per cent phenol saline until it corresponds to about Tube 4 of Brown‘s opacity tubes. Further dilutions of the antigen adjusted to opacity tube No. 4 are made. The particular dilution that gives 50 per cent agglutination with anti-brucella abortus serum (containing 1000 International Units) at 1 : 500 final serum dilution, is assessed as the diluting factor for the concentrated antigen. The bulk of the concentrated antigens is accordingly diluted for issue as standard antigen.

5. *Labelling and Storage*- Should comply with the requirements of _Labelling and Storage‘ as laid down in the general monograph on _Diagnostic Antigen‘.

6. *Expiry Date-* The date of expiry of potency shall be not more than nine months from the date of manufacture when stored at 2° C to 4° C.

Johnin

1. *Definition*- Johnin is a preparation of a fluid medium in which *Mycobacterium Paratuberculosis* has been grown in artificial culture and which has been freed by filtration from the bacilli.

2. ***Preparation***- Young culture of selected strain of *Myco-Paratuberculosis* of bovine origin is grown on synthetic medium and incubated at 37 ° C for ten to twelve weeks. Flasks showing lucurient and pure growth are steamed for three hours thereafter kept at room temperature overnight. The contents are filtered through fine meshed sieve. The filtrate is concentrated over a steam bath to one-tenth of its original volume and kept in cold storage for fourteen days before being filtered through Seitz filter. The product is dispensed in ampoules and hermetically sealed.

3. *Standards:-*

(a) Description- A yellowish brown to brownish liquid.

(b) Identification- It produces hot, painful and oeodemateus swelling at the site of inoculation in animals infected with *Myco-paratuberculosis* organism.

(c) Sterility Test- Should comply with the test for sterility described in the general monograph on _Diagnostic Antigens‘.

(d) Potency Test- Two animals, previously infected with *Myco-paratuberculosis* and two healthy animals are each injected intrademally in the neck region with 0.1 ml. of the product. Forty-eight hours later, the injection is repeated at the same site. The product should produce a typical reaction in the infected animals in the form of a hot painful and oedemetous swelling at the site of inoculation persisting for at least forty-eight hours after the second injection. Control animals should not show such reaction.

4. *Labelling and Storage*- Should comply with the requirements of _Labelling‘ and _Storage‘ as laid down in general monograph on _Diagnostic Antigens‘.

5. *Expiry Date*- The date of expiry of potency shall be not more than two years from the date of manufacture when stored at 2 ˚ C to 4 ˚ C.

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Malleins

1. *Definition*- ***(i)*** Malleins are preparations of fluids media in which the *Actinobacillus mellei* has been grown in artificial culture and which have been freed by filtration from the bacilli.

(ii) For the purposes of this Schedule malleins are classified into (a) Mallein-subcutaneous and (b) Mallein intradermo-palpebral (I.D.P.)

2. *Preparation:-*

(a) Mallein Subcutaneous- Three to four weeks old pure growth of standard strain of *A. mallei* grown on synthetic medium is steamed for one hour in Koch‘s steam sterilizer. One

part of 5 per cent phenol solution is added to every nine part of the dead culture which is then filtered through Seitz filter.

(b) Mallein Concentrated. - The procedure is the same as for Mallein Subcutaneous except, that the filtrate is evaporated in porcelain dish over steam to half the original volume before addition of phenol. Five per cent phenol solution is added in sufficient quantity to the concentrated product, to give a final concentrated of 0.5 per cent.

3. *Standards:*

(a) Description- A yellowish to brown viscous liquid.

(b) Identification- It produces hot tense, painful swelling when injected into the animals infected with *A. mallei* organisms.

(c) Sterility Test- Should comply with the tests for sterility described in the general monograph on _Diagnostic Antigens'.

(d) Potency Test: -

(i) Mallein subcutaneous- Two ponies, previously sensitised with *A. Mallei* and controls, are injected each with 1 ml. of the product subcutaneously in the neck region. The animals are observed for local reaction and rise in temperature. Local reaction is manifested by a hot tense, painful swelling becoming prominent within twenty-four hours. The rise in temperature is observed by recording the body temperature at the time of inoculation and subsequently at short intervals. A rise in temperature of 1˚ C or more above normal is indicative of infection.

(ii) Mallein Intra-dermo-Palpebral (I.D.P.)- Two ponies, previously sensitized with *A. mallei* and two healthy ponies are injected intradermally with 0.2 ml. of the product near the rim of the lower eye lid of one eye. Typical reactions such as painful swelling of the palpebral tissue with mucopurulent discharge from the eye is indicative of infection. The two healthy ponies should not show such reactions.

Similar test in other eye is performed with a previously determined patient mallein using as a standard. When the local reactions produced by intradermo palpebral infections of the two preparations are comparable the batch is passed for issue.

4. *Labelling and Storage-* Should comply with the requirement of _Labelling' and _Storage' as laid down in the general monograph on _Diagnostic Antigen'.

5. *Expiry Date-* The date of expiry of potency shall be not more than two years from the date of manufacture when stored at 2 ˚ C to 4 ˚ C.

Salmonella Abortus Equi 'H' Antigen

1. *Synonym-* Equine Abortion Diagnostic Antigen.

2. *Definition-* Salmonella Abortus Equi Antigen is suspension of a pure smooth culture of actively *motile Salmonella Abortus equi* in formal saline.

3. *Preparation-* Standard strain of *S.abortus equi* is grown on nutrient agar in Roux flasks at 37 ˚ C for twenty-four hours. The pure growth in Roux flasks is washed with normal saline and diluted to contain approximately 800 million organisms per ml. Solution of Formaldehyde I.P. is added to give a final concentration 0.5 per cent and the formolised product is incubated at 37 ˚ C for twenty-four hours. The final product is dispensed in suitable containers.

4. *Standards:-*

(a) Description- A slightly opalescent liquid containing dead bacteria in suspension.

(b) Identification- It gives specific agglutination when mixed with the serum of the animals infected with *S.abortus equi* organisms.

(c) Sterility Test- Should comply with the test for sterility described in the general monograph on _Diagnostics Antigens‘.

5. ***Labelling and storage***- Should comply with the requirements of _Labelling‘ and _Storage‘ as laid down in the general monograph on _Diagnostic Antigens‘.

6. ***Expiry Date***- The date of expiry of potency shall be not more than nine months from the date of manufacture when stored at 2 ˚ C to 4 ˚ C.

Salmonella Pullorum Coloured Antigen

1. ***Synonym***- Bacillary White Diarrhoes (B.W.D) Antigen.

2. ***Definition***- The antigen is a suspension in a solution containing 1 per cent Formaline, 1 per cent KH_2PO_4 and 0.85 per cent Sodium Chloride of pure smooth culture of standard strain of *Salmonella Pullorum.*

3 ***Preparation***- Standard strain of *S. Pullorum* is grown on sulphur agar medium in Roux flasks for five days at 37 ˚ C. The pure growth is washed with 1.0 per cent Formal Saline.

Standardisation

The antigenic cell suspension is then centrifuged (preferably in cold centrifuge) for half an hour at 4000 rotations per minute and the packed cell volume determined. The packed cell is then re-suspended in a solution containing 1 per cent formalin, 1 per cent KH_2PO_4 and 0.85 per cent sodium chloride, 1 ml. of packed cell is suspended in 10 ml. of the resuspendiary solution, mixed thoroughly and is passed through a cotton wool pad. The turbidity of the antigenic suspension is usually between 100 to 125 times Mac Farland scale standard and optimum 3 cc. of a 1 per cent aqueous solution of crystal violet are added to 100 ml. of the antigenic suspension. After making the dye the antigen is allowed to stand forty-eight hours before use. The average yield per Roux flasks of culture medium is about 50 ml. The antigen should be bottled in 10 ml. or 20 ml. quantity in amber-coloured bottles and corked with rubber caps and paraffin sealed and preserved until required for use within the expiry period. This antigen reacts instantly with the blood of all carrier birds and remains permanently negative with that of non-infected birds.

This antigen gives good reactions with positive sera whose titre is even as low as 1 : 20.

4. Standard:-

(a) Description- Violet coloured liquid containing dead bacteria in suspension.

(b) Identification- It gives specific agglutination when mixed with the serum of birds in infected with *S. Pullorum* infection. It is used for carrying out plate agglutination tests for serological diagnosis for *S. Pullorum* infection in birds.

(c) Sterility Test- Should comply with the test for sterility described in the general monograph on _ Diagnostic Antigen‘. The tests shall be done before addition of _Crystal Violet ‘.

5. ***Labelling and Storage***- Should comply with the requirements of _Labelling‘ and _Storage‘ as laid down in the general monograph 0n _Diagnostic Antigens‘.

6. ***Expiry Date-*** A six month expiration date for this antigen is recommended. However, it is advisable to use fresh ones as far as possible. This antigen should be preserved at 4 ˚ C to 6 ˚ C in dark place in the refrigerator and should not be exposed to hot weather condition for longer than necessary before use in the field.

Salmonella Pullorum Plain Antigen

1. ***Synonym***- Bacillary White Diarrhoes (B.W.D) Plain Antigen.

2. ***Definition***- The antigen is a suspension of pure smooth culture of Salmonella pullorum in phenol saline.

3. ***Preparation***- Forty-eight hours old pure culture of smooth strain of *S. Pullorum* is washed with 0.5 percent phenol saline and the pooled suspension is adjusted to contain approximately 800 million organisms per ml. by the addition of more carbol saline. The suspension is kept at room temperature of twenty-four hours, and dispensed in suitable containers.

4. ***Standard: -***

(a) Description- An opalescent liquid containing dead bacteria in suspension.

(b) Identification- It gives specific agglutination when mixed with the serum of birds infected with *S. Pullorum*.

(c) Sterility Test- Should comply with the tests for sterility described in the general monograph on _Diagnostic Antigen‘.

5. ***Labelling and Storage***- Should comply with the requirments of _Labelling‘ and _Storage‘ as laid down in the general monograph on _Diagnostic Antigens‘.

6. ***Expiry Date***- The date of expiry of potency shall be not more than nine months from the date of manufacture when stored at 2 ˚ C to 4 ˚ C.

Tuberculin

1. ***Definitions:***

(i) Tuberculins are preparations of fluid media on which *Mycobacterium tuberculosis* has been grown in artificial culture and which has been freed by filtration from the bacilli.

(ii) For the purposes of the Schedule tuberculins are classified in (a) Tuberculin-Subcutaneous (b) Heat Concentrated Synthetic Medium (H.C.S.M) Tuberculin (c) Avian tuberculin.

2. ***Preparation:-***

(*a) Tuberculin subcutaneous*- Flasks containing Henley and Dorset synthetic medium are inoculated with standard human strains of Myco-Tuberculosis previously grown on glycerol- beef broth medium for ten days. After ten to twelve weeks of incubation at 37 ˚ C, flasks containing pure growth are steamed for three hours. The contents are filtered through fine meshed sieve and the volume is made up to its original with phenolised distilled water such that the final concentration of phenol is 0.5 per cent. It is then filtered through Seitz filter.

(*b) Heat Concentrated Sythetic Medium (H.C.S.M) Tuberculin*- To the strained liquid obtained after sieving as in the method of preparation of Tuberculin subcutaneous, glycerol is added in the proportion of 122 ml. per litre of the original volume of medium used. The mixture is evaporated to one-fifth of the original volume on a steam bath. An equal volume of 1 per cent phenol in distilled water is added after the mixture is cooled. The product is stored at 47 ˚ C for fourteen days before it is filtered through Seitz filter. It is then dispensed in ampoules.

(c) *Avian Tuberculin Concentrated*- The procedure is the same as for Tuberculin Concentrated (H.C.S.M) except that standard strain of *Myco-tuberculosis (Avian)* is used in its preparation.

Standard:-

(*a*) *Description*- A yellowish brown viscous liquid.

(*b*) *Identification*- When injected intradermally into the animal infected with tuberculosis diffused swelling occurs depending upon the allergic status of the animal, the magnitude of dose and specificity of the product. In non-infected animals this reaction is not observed.

(*c*) *Sterility Test*- Should comply with the test for sterility described in the general monograph on _Diagnostic Antigens‘.

(*d*) *Potency Test*- (i) *Tuberculin subcutaneous*-Six large white guinea-pigs each weighing not less than 300-450 g. are individually inoculated intramuscularly with 0.5 mg. (Moist growth from solid plants) of Mycobacterium tuberculosis three weeks prior to test of each batch of tuberculin; the following dilutions of (a) test tuberculin and (b) standard tuberculin are used:-

1 in 200, 1 in 400, 1 in 800 and 1 in 1600.

The six sensitized guinea pigs are depilated on one flank and after about twenty- four hours each animal inoculated intradermally with 0.2 ml. of each dilution of the two tuberculins in two rows. The reactions are read after twenty-four and forty-eight hours. When the local reactions produced by the graded inter-dermal injections of the two preparations are comparable the brew is passed for issue.

(ii) *Heat Concentrated Synthetic Medium (H.C.S.M) Tuberculin*-Six adult white guinea-pigs each weighing not less than 300-450 g. and sensitized three weeks previously with 0.5 mg. (moist growth from solid plants) of *Myco-Tuberculosis* bovine type, injected intramuscularly are used for test of each batch. The following dilutions of (a) test tuberculin and (b) standard tuberculin are used: -

1 in 500, 1 in 1000, 1 in 2000 and 1 in 4000.

The six sensitized guinea pigs are depilated on one flank and after about twenty- four hours each animal is inoculated intradermally with 0.2 ml. of each dilution of the two tuberculins in two rows. The reactions are read after twenty-four and forty-eight hours. When the local reactions produced by the graded inter-dermal injections of the two preparations are comparable, the test tuberculin is passed for issue. The tuberculin is dispensed in ampoules.

(iii) *Avian Tuberculin*- Six adults fowls, with well developed wattles, sensitized at least three weeks previously by intramuscular injection with 10 mg. moist weight (from solid plants) of twenty-one days old culture of *Mycobacterium tuberculosis* (Avian Type) are used for potency test of each batch. In each fowl, one wattle is inoculated with 0.2 ml. of undiluted test tuberculin and the other wattle with similar quantity of undiluted standard tuberculin. The reactions in each fowl are read after twenty-four hours and forty-eight hours and if comparable the product is passed for issue.

4. ***Labelling and Storage***- Should comply with the requirments of _Labelling‘ and _Storage‘ as laid down in the general monograph on _Diagnostic Antigens‘.

5. ***Expiry Date***- The date of expiry of potency shall be not more two years months from the date of manufacture when stored at 2 ˚ C to 4 ˚ C.

PART IV

GENERAL

1. For the purpose of this Schedule any test or method of testing described in the [1][British Pharmacopoeia (Veterinary)] shall be deemed to be a method approved by the Licensing Authority.

2. The Licensing Authority shall publish in the official Gazette from time to time particulars of any test or method of testing approved by him.]

1. Subs. by G.S.R. 647(E) dated 28-10-1998.

Drugs and Cosmetics Rules 1945

[1][SCHEDULE F (II)

(See Rule 124-C)

STANDARDS FOR SURGICAL DRESSINGS

Synonyms:

Bandage Cloth, Bleached Bandage Cloth, Rolled Bandage, Open Wove Bandage, Cotton Bandage Cloth.

Bandage Cloth consists of cotton cloth of plain weave made from machine spun yarn of suitable count to comply with a bleached count between 20 tex and 25 tex for warp and between 25 tex and 30 tex for weft. The fabric contains no filling, sizing or dressing material. It may be supplied uncut and folded or cut to suitable size and rolled.

Description for uncut bandages:

Uncut bandages are cotton cloth of plain weave, in one continuous length showing no joints or seams, with well-formed selvedges. The cloth is bleached to a good white, is clean and odourless and reasonably free from weaving defects and from seed and leaf debris.

Description for cut bandage:

Same as for uncut bandages, except for selvedges which shall not be included in cut bandages. In addition, both the extremes and edges of cut bandages shall be straight and evenly cut, with reasonable freedom and loose threads.

Threads per dm: – Warp not less than 150 and weft not less than 85.

Weight in g/m2: - 57 ± 5.

Length and Width: - The length and width shall not be less than 99 per cent each of the length and width stated on the label. For cut bandages, each of the bandages in a packing complies with this requirement.

Foreign matter: - Not more than 2 per cent.

Fluorescence:

When viewed under screened ultra-violet light, not more than occasional points of fluorescence are observed.

***Packing, Labelling and Storage*:**

Bandage Cloth shall be packed securely so as to allow normal handling and transport without tearing and exposing the contents. In packages of cut and rolled bandages, each bandage shall also individually be wrapped in a suitable paper. The net content is stated on the label in terms of length and width. Bandage Cloth must be stored in packed condition protected from dust. The packings of Bandage Cloth shall be labelled prominently with the words ―Non-Sterile‖.

Absorbent Gauze.

Synonyms.- Gauze; Unmedicated Gauze; absorbent Cotton Gauze.

Absorbent Gauze is cotton fabric of plain weave, supplied in various widths and lengths. The Gauze is bleached and free from any sizing, dressing or filling material. The yarn used is machine spun cotton yarn, of suitable count to comply with a bleached count between 17 and 25 tex in the finished fabric.

1. Ins. by G.S.R. No.318(E), dt.. 1-5-1985.

Description:

Cotton cloth, plain weave, with a simple selvedge present on both sides to prevent unravelling of yarn. The cloth is bleached to a good white, is clean, odourless, reasonably free from fabric defects and adhering sand debris from cotton seeds and leaves, or any other foreign matter.

Threads per dm:.- Warp not less than 75 and weft not less than 55.

Weight in g/m2: - 30 ± 5.

Length and widt:- Not less than 98 per cent each of the length and width stated on the label.

Absorbency:- Average sinking time not more than 10 seconds.

Fluorescence:- When viewed under screened ultra-violet light not more than occasional points of fluorescence are observed.

Foreign matter:- Not more than 1 per cent.

Sterility:- If sterile, the contents comply with the test for sterility.

Packing, Labelling and Storage:

Absorbent Gauze is folded and packed with such materials and so securely as to protect its absorbency and allow normal handling and transport without tearing and exposing the contents. The net content is stated on the label in terms of length and width. The packages shall be labelled prominently with the words ―Non-Sterile‖. If sterile, it shall be so stated on the label, and the packing method and material shall be such as to maintain the sterility. The Absorbent Gauze must also comply with the Sterility Test. Absorbent Gauze must be stored in packed conditions protected from moisture and dust.

METHODS OF TEST

Defect in fabric:.

The sample is unfolded, opened and held against diffused daylight or spread on black topped table to locate and identify prominently visible defects in yarn and fabric construction. The fabric shall be reasonably free from holes, slubs, snarls and naps as well as the following: -

Odour.- Misty odour, or any objectionable smell like that of chemicals or materials used in sizing and bleaching.

Skewness.- (For Bandage Cloth only) A condition where warp and weft do not keep at right angles to each other.

Defective Selvedge. - The selvedge tearing and allowing yarn to unravel and loop formation at selvedge.

Cracks.- Prominent steaks of space or gaps between warp or weft yarns.

Double ends.- More warp threads woven as one, due to wrong draw.

Sloughing.- Entanglement in the fabric of a bulk of yarn that has slipped off the weft yarn due to loose widing.

Measurement of length and width.

Length is the distance from end to end, along one edge of the fabric, and width is the perpendicular distance from one edge to the opposite edge.

Length. - Fix a meter scale to a table or mark off the division of one metre on a table edge. Starting from one end, spread the fabric flat on that table in a single layer keeping one

selvedge parallel to the scale; smoothen the fabric without stretching it, to avoid creases, and mark off with a coloured pencil, on the selvedge exactly one metre. Shift the fabric and measure the same way the second metre and so on for the entire length of the fabric making a mark at each metre. Note down the total length in metres. Repeat this at the opposite selvedge, as well as on the fabric folded approximately about the middle. The average of the three readings is the length. For cut bandages, one measurement at the middle of the bandages by folding it length-wise will suffice.

Width. - Lay the portion of the fabric to be measured flat and smooth on the tables, but do not stretch fabric except sufficiently to render it creaseless. At the place where mark had been made on the selvedge in measuring the length measure the perpendicular distance to the opposite selvedge with a metre scale. Note the width, repeat this at every mark made in measuring the length. The average of all the readings is the width of the fabric. For cut bandages, width shall be measured at every 50 cms., and average reported as width.

Threads per dm.- (For examples not less than 15 m. in length).

Weft. - At the third metre from one extreme locate three places one at about 5 cm. below the top selvedge, a second in the middle and third at about 5 cm. below the top selvedge, a second in the middle and third about 5 cm. above the bottom selvedge, all three in a vertical row. Take a rectangular plate (made of suitable material such as plastic or aluminium) with the rectangular opening of 5 cm. x 10 cm. cut in it. Keep the plate on the fabric horizontally so that the left 5 cm. side and bottom (10 cm. side) edges of the opening coincides with a weft and warp yarns respectively; count the number of weft yarns within the opening for the length of 10 cm.. Repeat this at the other two selected places, and note down the average of three readings. Repeat this at every third metre in the sample and calculate the average weft per dm.

Warp.- Keep the rectangular plate, this time vertically with left (10 cm. side) and bottom (5 cm. side) edge of opening coinciding with a weft and warp yarn respectively. Count the number of warp yarns within the opening for 10 cm. and note down. Repeat this for about 10 selected places in the samples taking care that the same set of warp yarns is not counted more than twice and calculate the average warp per dm. Magnifying glass mounted on stand may be used for counting.

For samples less than 15 m. in length, locate as many different places as the dimension of the fabric permits, the total being not less than 10 for each sample and calculate the warp and weft per dm. as above.

For cut bandages, all the warp threads in the samples are counted, taking care to leave 5 mm at the cut edge, and weft is counted at every 50 cm. at any place about the middle of the bandage.

Weight per unit area.

For samples not less than 15 m. in length, cut out pieces of fabric from the entire length of sample, representative places being taken from areas at every third or fourth metre so that the total area of all the pieces so collected is not less than 3 sq. metre. Weigh the pieces accurately, measure the dimension of each of the pieces and calculate the area and weight of all the pieces. From the average area and average of weight thus obtained, calculate the area per sq. metre.

For samples less than 15 m. length, take pieces in such a manner that the total area of the selected pieces is not less than 20 per cent of the total area of the sample.

For cut bandages, pieces of 50 cm. in length, cut from 5 different cut bandages in a packing should be taken and weight calculated as an average of 5 readings.

Absorbency. - Take a glass trough of approximate size length 30 cm. x width 30 cm. x depth 25 cm. with straight thick walls and flat bottom. Fill it almost full with distilled water leaving only about 5 cm. from the top rim of trough. Maintain the water at 27_{o} C ± 1_{o} C.

Cut out from any five places located equidistant down the length of the entire sample, square pieces, each weighting one gm. (±10 per cent). Fold each piece in such a manner that a square of approximately 5 cm. x 5 cm. is obtained. Keep one of the folded test specimen between two glass plates and place 1 kg weight on the top for 10 minutes. Remove the weight. Lift the specimen with forceps and gently place it on to the surface of water (the specimen should be lightly pinched in the middle with a blunt forceps having no serrations). As soon as the specimen touches the water surface start a stopwatch which is stopped when the entire sample disappears

below the surface of the water. Record the time taken. Repeat the test with the other four-test specimens. Calculate the average time in seconds.

Foreign Matter

Dry about 5 g. of the sample to constant weight at 105° C and weigh the dried sample accurately. Extract the dried sample with chloroform for one hour in an apparatus for the continuous extraction of drugs. Remove the extracted sample to a beaker and allow the evaporation of residual chloroform. Wash the material 12 times with hot water, using about 1000 ml. for each washing and wringing the material by hand after each washing; pass all water through a fine sieve (100 mesh). Place the washed material and any loose threads or fibres from sieve in a beaker, cover with a 0.5 per cent aqueous solution of diastase and maintain at 50°C until free from starch. Allow to cool, filter the solution through a sieve; return sample and loose fibre to a beaker. Repeat the washing process as before with hot water. Dry the material to constant weight at 105°C, and determine the loss in weight. Calculate the percentage of foreign matter, which is equal to the loss in weight, with reference to the sample dried to constant weight, at 105° C.

If the sample is tested with iodine and is known to be free from starch, the treatment with solution of diastase and the second series of washing with hot water may be omitted.

Cloth for manufacture of Plaster of Paris Bandages, cut and uncut.

Synonyms.- Bleached Bandage Cloth for Plaster of Paris, Rolled Bandage for Plaster of Paris.

Cloth for Plaster of Paris Bandages shall consist of cotton cloth of leno weave made from yarn of suitable count. It may be supplied cut or uncut of various widths and lengths.

Description

(a) For *uncut bandages*.- Cotton cloth of leno weave, in one continuous length showing no joints or seams, and with selvedges. The cloth is bleached to a good white, is clean and odourless and reasonably free from weaving defects as well as from seed and leaf debris; the cloth may be dressed if necessary and if so, shall not dust off when unrolled.

(b) *For cut bandages.* - Same as for uncut bandages except for selvedges which shall not be included and the bandages shall be cut evenly with straight edges and be reasonably free from loose threads.

Threads per dm:

Warp. - Average not less than 150/dm; and *Weft.*- average not less than 75/dm.

Weight in gm/m2: - 35 ± 5

Length and width:

The length and width for uncut bandages shall not be less than 98 per cent each of the length and width stated. For cut bandages a tolerance of ±5 cm. in length and ±0.5 cm. in width may be allowed, and each of the bandages in packing complies with these requirements.

Fluorescene

When viewed under screened ultra-violet light not more than occasional points of fluorescence are observed.

Packing, Labelling and Storage

Bandage Cloth for Plaster of Paris shall be packed securely so as to allow normal handling and transport without tearing and exposing the contents. In packages of cut and rolled bandages, each bandage shall also individually be warpped in suitable paper. The package shall be labelled as ―Cloth for Plaster of Paris Bandage‖. The net content is stated on the label in terms of number

of rolls and length and width. Bandage Cloth for Plaster of Paris must be stored in packed condition protected from dust.

[1][SCHEDULE F (III)

(*See r*ule 124-D)

STANDARDS FOR UMBILICAL TAPES

(A) Standards for Sterilised Umbilical Polyster Tape.

Description. - A uniform strand of Polyester yarn prepared by braiding and may be finished with a suitable silicone finishing material, white to yellowish-white in colour. Tape shall be sterilized by Gamma Radiation or other suitable method approved by the Licensing Authority.

Other requirements. - The Umbilical Polyester Tape shall conform to the claims made on the label in respect of length and width.

Tensile strength. - The Umbilical Polyester Tape shall have Tensile strength of not less than 4 kg. on straight pull.

Packing and labelling. - The Umbilical Polyester Tape shall be packed in sealed Polythene bags or sealed plastic containers which ensure that when packed, the tape is sterile. The packing shall protect the tape from contamination and damage. Every packing offered for sale shall bear a clear and permanent marking with the following particulars: -

(i) The proper name of the drug i.e. Umbilical Polyester Tape ‗Sterile'

(ii) Manufacturer's name and address.

(iii) Batch number.

(iv) Licence number under which the tape is manufactured. (v) Date of manufacture and date of expiry.

(vi) Length and width of the Tape.

Storage condition. - It should be stored in a cool place protected from light.

(B) Standards for Sterilised Umbilical Cotton Tape–

Description. - A uniform strand of cotton yarn prepared by braiding and may be finished with a suitable silicone finishing material, white to yellowish-white in colour. The tape shall be sterilized by Gamma Radiation or by any other suitable method approved by the Licesing Authority.

Other Requirement. - The Umbilical Cotton Tape shall conform to the claims made on the label in respect of length and width.

Tensile strength. - The Umbilical Cotton Tape shall have a Tensile strength of not less than 4 kg. on straight pull.

Packing and labelling. - The Umbilical Cotton Tape shall be packed in sealed Polythene bags or sealed plastic containers which ensure that when packed the tape is sterile. The packing shall protect the tape from contamination and damage. Every packing offered for sale shall bear a clear and permanent marking with the following particulars:-

(i) The proper name of drug i.e. Umbilical Cotton Tape ―Sterile‖.

(ii) Manufacturer's name and address.

1. Ins. by G.S.R. No.1115(E), dt.. 30-9-1986.

(iii) Batch number.

(iv) Licence number under which the tape is manufactured.

(v) Date of manufacture and the date of expiry.

(vi) Length and width of the Tape.

Storage condition.- It should be stored in a cool place protected from light.]

[1][SCHEDULE FF

(See rule 126-A)

Standards for ophthalmic preparations.

Part-A. Ophthalmic Solutions and suspensions.

Ophthalmic Solutions and Suspensions shall-

(a) be sterile when dispensed or when sold in the unopened container of the manufacturer, except in case of those ophthalmic solutions and suspensions which are not specifically required to comply with the test for _Sterility' in the Pharmacopoeia;

(b) contain one or more of the following suitable substances to prevent the growth of micro-organisms:-

(i) Benzalkonium Chloride, 0.01 per cent (This should not be used in solutions of nitrates or salicylates).

(ii) Phenyl mercuric nitrate, 0.001 per cent.

(iii) Chlorbutanol 0.5 per cent.

(iv) Phenyl ethyl alcohol 0.5 per cent.

Provided that solutions used in surgery shall not have any preservative and be packed in single dose container.

Provided further that the Licensing Authority may in his discretion authorise the use of any other preservative or vary the concentration prescribed on being satisfied that its use affords equal guarantee for preventing the growth of micro-organisms:-

(c) be free from foreign matter;

(d) be contained in bottles made of either neutral glass or soda glass specially treated to reduce the amount of alkali released when in contact of aqueous liquids, or in suitable plastic containers which would not in any way be incompatible with the solutions;

The droppers to be supplied with the containers of ophthalmic solutions and suspensions shall be made of neutral glass or of suitable plastic material and when supplied separately shall be packed in sterile cellophane, or other suitable packings;

(e) In addition to complying with the provisions of labelling laid down in the rules the following particulars shall also be shown on the label:-

1. Added by Notification No. F-1-13/69-D , dt.. 3-1-1970.

(1) *of the containers*

(i) The statement _Use the solution within one month after opening the container'.

(ii) Name and concentration of the preservative, if used.

(iii) The words _NOT FOR INJECTION'.

(2) of container or carton or package leaflet

(i) Special instructions regarding storage, wherever applicable.

(ii) A cautionary legend reading as

—WARNING (i) if irritation persists or increases, discontinue the use and consult the phycian.

(ii) Do not touch the dropper tip or other dispensing tip to any surface since this may contaminate solutions‖.

Part B: Ophthalmic Ointments

Ophthalmic Ointments shall-

(a) be sterile when dispensed or when sold in the unopened container of the manufacturer;

(b) be free from foreign matter;

(c) in addition to complying with the provisions for labelling laid down in the rules the following particulars shall be shown on the container or carton or package leaflet-

(i) Special instructions regarding storage wherever applicable;

(ii) A cautionary legend reading

—Warning :- If irritation persists or increases discontinue the use and consult Physicians‖].

[1][SCHEDULE G]

(See Rule 97)

Aminopterin
L-Asparaginase
Bleomycin
Busulphan; its salts
Carbutamide
Chlorambucil;its salts
Chlorothiazide and other derivatives of 1, 2, 4 benzothiadiazine
Chlorpropamide; its salts
Chlorthalidone and other derivatives of Chlorobenzene compound.
[2][(Cis-Platin)]
Cyclophosphamide; its salts
[2][(Cytarabine)]
Daunorubicin
Di-Isopropyl Eluorophosphate
Disodium Stilboestrol Diphosphate
Doxorubicin Hydrochloride
Ethacrynic Acid, its salts
Ethosuximide
Glibenclamide
Hydantoin; its salts; its derivatives, their salts
Hydroxyurea
Insulin, all types
[2] [(Lomustine Hydrochloride)]
Mannomustine; its salts
Mercaptopurine; its salts
Metformin; its salts
Methsuximide
Mustine, its salts
Paramethadione
Phenacemide

Phenformin; its salts
5-Phenylhydantoin; its alkyl and aryl derivatives; its salts
Primadone
[1][(Procarpazine Hydrochloride])

1. Subs.. by G.S.R. No.462(E) , dt. 22-6-1982 (w.e.f. 22.6.1982). 2. Ins. by G.S.R. No.626(E) , dt. 2-7-1987 w.e.f. 2-7-1987.

Quinthazone
Sarcolysine
[1][(Sodium-2-
Mercaptoethanesulfonate]
Tamoxiten Citrate
Testolactone
Thiotepa Tolbutamide
Tretamine; its salts
Troxidone

Antihistaminic substances the following, their salts, their derivatives, salts of their derivatives

Antazoline
Bromodiphenhydramine
Buclizine
Chlorcyclizine
Chlorpheniramine Clemizole
Cyproheptadine
Diphenhydramine
Diphenylpyraline Doxylamine
Succinate Isothipendyl
Mebhydrolin Napadisylate
Meclozine
Phenindamine
Pheniramine
Promethazine
Thenalidine
Triprolidine
Substances being tetra-N-Subs. derivatives of Ethylene Diamine or Prophylenediamine.

***Note* .–** Preparations containing the above substances excluding those intended for topical or external use are also covered by this Schedule.]

1. Subs.. by G.S.R. No.462(E) , dt. 22-6-1982 (w.e.f. 22.6.1982).

[1][SCHEDULE - H

(SeeRules 65 and 97)

PRESCRIPTION DRUGS

1. Abacavir
2. Abciximab
3. Acamprosate calcium
4. Acebutolhydrochloride
5. Aclarubicin
6. Albendazole
7. Alclometasone dipropionate
8. Actilyse
9. Acyclovir
38. Artesunate
39. Articaine hydrochloride
40. Atenolol
41. Atracurium besylate injection
42. Atorvastatin
43. Auranofin
44. Azathioprine
45. Aztreonam
46. Bacampicillin

10. Adenosine
11. Adrenocorticotrophic hormone (acth)
12. Alendronate sodium
13. Alopurinol
14. Alphachymotrypsin
15. [2][Alprazolam
16. Alprostadil
17. Amantadine hydrochloride
18. Amifostine
19. Amikacin sulphate
20. Amiloridehydrochloride
21. Amineptine
22. Aminoglutethimide
23. Amino salicylicacid
24. Amiodarone hydrochloride
25. Amitriptyline
26. Amlodipine besylate
27. Amoscanate
28. Amoxopine
29. Amrinonelactate
30. Analgin
31. Androgenic anabolic, oestrogenic & progestational substances
32. Antibiotics
33. Apraclonidine
34. Aprotinin
35. Organic compound of arsenic
36. Arteether
37. Artemether
47. Baclofen
48. Balsalazide
49. Bambuterol
50. Barbituric acid
51. Basiliximab
52. Benazeprilhydrochloride
53. Benidipine hydrochloride
54. Benserazide hydrochloride
55. Betahistine dihydrochloride
56. Bethanidine sulphate
57. Bezafibrate
58. Bicalutamide
59. Biclotymolmonohydrate /lactate
60. Bifonazole
61. Bimatoprost
62. Biperiden hydrochloride
63. Biphenylacetic acid
64. Bitoscanate
65. Bleomycin
66. Primonidine tartrate
67. Bromhexine hydrocloride
68. Bromocriptine mesylate
69. Budesonide
70. Bulaquine
71. Bupivacaine hydrochloride
72. Bupropion
73. Buspirone
74. Butenafine hydrochloride
75. Butorphanoltartrate

1. Subs. by G.S.R. No.160(E), dated 16.3.2006 .
2. Omitted by G.S.R 588(E) dated 30-8-2013
3. Omitted by G.S.R 602(E) dated 19-7-2010
4. Omitted by G.S.R 724(E) dated 7-11-2013

76. Cabergoline
77. Calcium dobesilate
78. Candesartan
79. Capecitabine
80. Captopril
81. Carbidopa
82. Carbocisteine
83. Carboplatin
84. Carboquone
85. Carisoprodol
86. L-carnitine
87. Carteolol hydrochloride
88. Carvedilol
89. Cefadroxyl
90. Cefatoximesodium
91. Cefazolin sodium
92. [2][Cefdinir
93. Cefepime hydrochloride
122. Clobetasone 17-butyrate
123. [2][Clofazimine]
124. Clofibrate
125. Clonazepam
126. Clonidine hydrochloride
127. Clopamide
128. Clopidogrelbisulphate
129. Clostebolacetate
130. Clotrimazole
131. Clozapine
132. [2][Codeine]
133. Colchicine
134. Corticosteroids
135. Cotrimoxazole
136. Cyclandelate
137. Cyclosporins
138. Daclizumab
139. Danazole

94. Cefetamet pivoxil
95. Cefpirome
96. Cefpodoximepoxetil
97. Ceftazidimepentahydrate
98. Ceftizoximesodium]
99. Cefuroxime
100. Celecoxib
101. Centchroman
102. Centbutindole
103. Centpropazine
104. Cetirizinehydrochloride
105. [2][Chlordiazepoxide
106. Chlormezanone
107. [3][* * *]
108. Chlorpromazine
109. Chlorzoxazone
110. Ciclopiroxolamine
111. Cimetidine
112. Cinnarizine
113. Ciprofloxacin hydrochloride
114. Cisplatin
115. Citalopram hydrobromide
116. Clarithromycin
117. Clavulanic acid
118. Clidiniumbromide
119. Clindamycin
120. Clobazam
121. Clobetasolpropenate
140. Dapsone
141. Desloratadine
142. Desogestrol
143. Dexrazoxane
144. Dextranomer
145. [2][* * *]
146. Dextropropoxyphene
147. [2][Diazepam]
148. Diazoxide
149. Diclofenacsodium/potassium/acid
150. Dicyclomin hydrochloride
151. Didanosine
152. Digoxine
153. Dilazep hydrochloride
154. Diltiazem
155. Dinoprostone
156. [2][Diphenoxylate, itssalts]
157. Dipivefrin hydrochloride
158. Di-sodiumpamidronate
159. Disopyramide
160. Docetaxel
161. Domperidone
162. Donepezil hydrochloride
163. Dopamine hydrochloride
164. Dothiepin hydrochloride
165. Doxapram hydrochloride
166. Doxazosin mesylate
167. Doxepin hydrochloride

1. Subs. by G.S.R. No.160(E), dated 16.3.2006 .
2. Omitted by G.S.R 588(E) dated 30-8-2013
3. Omitted by G.S.R 602(E) dated 19-7-2010
4. Omitted by G.S.R 724(E) dated 7-11-2013

168. Doxorubicin hydrochloride
169. Drotrecogin-alpha
170. Ebastine
171. Econozole
172. Efavirenz
173. Enalaprilmeleate
174. Enfenamicacid
175. Epinephrine quaternary compound
176. Epirubicine
177. Eptifibatide
178. Ergot, alkaloids of whether hydrogenated or not, their homologoues, salts
179. Esomeprazole
180. Estradiolsuccinate
181. Estramustinephosphate
182. Etanercept
183. Ethacridine lactate
184. [2][Ethambutol hydrochloride]
185. Ethamsylate
213. Fosfestril sodium
214. Fosinopril sodium
215. Fossphenytoin sodium
216. Fotemustine
217. Gabapentin
218. Galanthamine hydrobromide
219. Galamine, itssalts, its
220. Gancyclovir
221. Ganirelix
222. Gatifloxacin
223. Gemcitabine
224. Gemfibrozil
225. Gemtuzumab
226. Genodeoxycholic acid
227. Gliclazide
228. Glimepiride
229. Glucagon
230. Glycopyrrolate
231. Glydiazinamide

186. Ethinyloestradiol
187. [2][Ethionamide]
188. Etidronate disodium
189. Etodolac
190. Etomidate
191. Etoposide
192. Exemestane
193. Famciclovir
194. Famotidine
195. Fenbendazole
196. Fenofibrate
197. Fexofenadine
198. Finasteride
199. Flavoxate hydrochloride
200. 5-fluorouracil
201. Fludarabine
202. Flufenamic acids
203. Flunarizinehdrochloride
204. Fluoxetine ydrochloride
205. Flupenthixol
206. Fluphenazine enanthate and decanoate
207. Flurazepam
208. Flurbiprofen
209. Flutamide
210. Fluticasone propionate
211. Fluvoxaminemaleate
212. Formestane
232. Goserelinacetate
233. Granisetron
234. Guanethidine
235. Gugulipid
236. Halogenated hydroxyquinolines
237. Haloperidol
238. Heparin
239. Hepatitis b. Vaccine
240. Hyaluronidase
241. Hydrocorisone 17-butyrate
242. Hydrotalcite
243. Hydroxizine
244. Ibuprofen
245. Idebenone
246. Indapamide
247. Imipramine
248. Indinavir sulphate
249. Indomethacin
250. Insulin human
251. Interferon
252. Intravenous fat emulsion
253. Iobitridol
254. Iohexol
255. Iopamidol
256. Iomeprol
257. Iopromide
258. Irbesartan
259. Irinotecan hydrochloride

1. Subs. by G.S.R. No.160(E), dated 16.3.2006 .
2. Omitted by G.S.R 588(E) dated 30-8-2013
3. Omitted by G.S.R 602(E) dated 19-7-2010
4. Omitted by G.S.R 724(E) dated 7-11-2013

260. Iron preparation for parenteral use
261. Isepamicine
262. Isocarboxside
263. Isoflurane
264. Isonicotnic acid hydrazine and other-hydragine derivatives of isonicotinic acid
265. Isosorbide dinitrate/ mononitrate
266. Isotretinoin
267. Isoxsuprine
268. Itopride
269. [4][***]
270. Ketoconazole
271. Ketoprofen
272. Ketorolactromethamine
273. Labetalol hydrochloride
274. Lacidipine
275. Lamivudine
276. Lamotrigine
277. Latanoprost
278. Lefunomide
279. Lercanidipine hydrochloride
304. Megestrolacetate
305. Meglumine iocarmate
306. Melagenina
307. Elitracenhydrochloride
308. Meloxicam
309. Mephenesin, itsesters
310. Mephentermine
311. [2][Meropenam]
312. Mesterolone
313. Metaxalone
314. Methicillin sodium
315. Methocarbamol
316. Methotraxate
317. Metoclopramide
318. Metoprololtartrate
319. Metrizamide
320. Metronidazole
321. Mexiletine hydrochloride
322. Mianserin hydrochloride
323. Miconazole
324. [2][Midazolam]
325. Mifepristone

280. Letrozole
281. Leuprolideacetate
282. Levamesole
283. Levarterenol
284. Levobunolol
285. Levocetirizine
286. Levodopa
287. [2][Levofloxacin]
288. Levovist
289. Lidoflazine
290. Linezplid
291. Lithiumcarbonate
292. Lofepraminedecanoate
293. Loperamide
294. Lorazepam
295. Losartan potassium
296. Loteprednol
297. Lovastatin
298. Loxapine
299. Mebendazole
300. Mebeverine hydrochloride
301. Medroxyprogesterone acetate
302. Mefenamic acid
303. Mefloquine hydrochloride
326. Milrinonelactate
327. Miltefosine
328. Minocycline
329. Minoxidil
330. Mirtazapine
331. Misoprostol
332. Mitoxantrone hydrochloride
333. Mizolastine
334. Moclobemide
335. Mometasone furoate
336. Montelukast sodium
337. Morphazinamide hydrochloride
338. Mosapride
339. [2][Moxifloxacin]
340. Mycophenolate mofetil
341. Nadifloxacin
342. Nadolol
343. Nafarelin acetate
344. Nalidixicacid
345. Naproxen
346. Narcotics drugs listed in Narcotic Drugs & Psychotropic Substances Act, 1985

1. Subs. by G.S.R. No.160(E), dated 16.3.2006 .
2. Omitted by G.S.R 588(E) dated 30-8-2013
3. Omitted by G.S.R 602(E) dated 19-7-2010
4. Omitted by G.S.R 724(E) dated 7-11-2013

347. Natamycin
348. Nateglinide itsderivatives
349. N-butyl-2-cyanoacrylate
350. Nebivolol
351. Nebumetone
352. Nelfinavir mesilate
353. Netilmicin sulphate
354. Nevirapine
355. Nicergoline
356. Nicorandil
357. Nifedipine
358. Nimesulide salts of itsderivatives
359. Nimustine hydrochloride
360. [2][Nitrazepam]
361. Nitroglycerin
362. Norethisteroneenanthate
363. Norfloxacin
364. Octylonium bromide
365. Ofloxacin
366. Olanzapine
367. Omeprazole
368. Ornidazole
369. Orphenadrine
370. Orthoclone sterile
388. Parp-amino salicylicacid, itssalts,
389. Parecoxib
390. Paroxetine hydrochloride
391. D-penicilamine
392. [2][Pentazocine]
393. Pentoxifylline
394. Pepleomycin
395. Phenelzineh sulphate
396. Phenobarbital
397. Phenothiazine, derivatives of and
398. Phenylbutazine
399. Pimozide
400. Pindolol
401. Pioglitazone hydrochloride
402. Piracetam
403. Piroxicam
404. Pituitory gland, active principles of, not otherwise specified in this schedule and their salts
405. Polidocanol
406. Polyestradiol phosphate
407. Poractant alfa
408. Praziquantel

371. Oxazepam
372. Oxazolidine
373. Oxcarbazepine
374. Oxethazaine hydrochloride
375. Oxiconazole
376. Oxolinicacid
377. Oxprenololhydrochloride
378. Oxybutynin chloride
379. Oxyfedrine
380. Oxymetazoline
381. Oxyphenbutazone
382. Oxytocin
383. Ozothine
384. Paclitaxel
385. Pancuronium bromide
386. Pantoprazole
387. Para-amino benzene sulphonamide, itssalts & derivatives
409. Prednimustine iothalamates
410. Prednisolone stearoylglycolate
411. Prenoxdiazinhydro-chloride
412. Promazine hydrochloride
413. Promegestone
414. Propafenon hydrochloride
415. Propanolol hydrochloride
416. Propofol
417. Protristyline hydrochloride
418. [2][Pyrazinamide]
419. Pyrvinium
420. Quetiapine fumerate
421. Quinapril
422. Quinidine sulphate
423. Rabeprazole
424. Racecadotril
425. Raloxifenehydrochloride

1. Subs. by G.S.R. No.160(E), dated 16.3.2006 .
2. Omitted by G.S.R 588(E) dated 30-8-2013
3. Omitted by G.S.R 602(E) dated 19-7-2010
4. Omitted by G.S.R 724(E) dated 7-11-2013

426. Ramipril hydrochloride
427. Ranitidine
428. Rauwolfia,alkaloids of, their salts, derivatives of the alkaloids or rauwolfia
429. Reboxetine
430. Repaglinide
431. Reproterol hydrochloride
432. Rilmenidine
433. Riluzone
434. Risperidone
435. Ritonavir
436. Ritodrine hydrochloride
437. Rituximab
438. Rivastigmine
439. Rocuronium bromide
440. Ropinirole
441. Rosoxacin.
442. Rosiglitazone meleate
443. Salbutamolsulphate
444. Salicyl-azo-sulphapyridine
445. Salmon calcitonin
446. Saquinavir
447. Satranidazole
448. Secnidazole
449. Septopalbeads & chains
450. Serratiopeptidase
451. Sertraline hydrochloride
452. Sibutramine hydrochloride
453. Sildenafilcitrate
454. Simvastatin
467. Spectinomycinhydrochloride
468. Spironolactone
469. Stavudine
470. Sucralfate
471. Sulphadoxine
472. Sulphamethoxine
473. Sulphamethoxypyridazine
474. Sulphaphenazole
475. Sulpiride
476. Sulprostone hydrochloride
477. Sumatriptan
478. Tacrine hydrochloride
479. Tamsulosin hydrochloride
480. Trapidil
481. Tegaserod maleate
482. Teicoplanin
483. Telmisartan
484. Temozolamide
485. Terazosin
486. Terbutalinesulphate
487. Terfenadine
488. Terizidone
489. Terlipressin
490. Testosteroneun decoanoate
491. Teratolol hydrochloride
492. Thalidomide
493. [2][Thiacetazone]
494. Thiocolchicoside
495. Thiopropazate,itssalts
496. Thymogene
497. Thymosin-alpha1

455. Sirolimus
456. Sisomicin sulphate
457. S-neominophagen
458. Sodiumpico sulphate
459. Sodium cromoglycate
460. Sodium hyaluronate
461. Sodium valproate
462. Sodium and maglumine iothalamates
463. Somatostatin
464. Somatotropin
465. Sotalol
466. [2][Sparfloxacin]
498. Tiaprofenic acid
499. Tibolone
500. Timololmaleate
501. Tinidazole
502. Tizanidine
503. Tabramycin
504. Tolfenamic acid
505. Topiramate
506. Topotecan hydrochloride
507. [2][Tramadolhydrochloride]
508. Tranexamic acid
509. Tranylcypromine, itssalts
510. Trazodone

1. Subs. by G.S.R. No.160(E), dated 16.3.2006 .
2. Omitted by G.S.R 588(E) dated 30-8-2013
3. Omitted by G.S.R 602(E) dated 19-7-2010
4. Omitted by G.S.R 724(E) dated 7-11-2013

511. Tretinoin
512. Trifluperazine
513. Trifluperidol hydrochloride
514. Triflusal
515. Trimetazidine dihydrochloride
516. Trimipramine
517. Tripotassium dicitrate bismuthate
518. Tromantadine hydrochloride
519. Urokinase
520. Valsartan
521. Vasopressin
522. Vecuronium bromide
523. Venlafaxine hydrochloride
524. Verapamil hydrochloride
525. Verteporfin
526. Vincristine sulphate
527. Vinblastine sulphate
528. Vindesine sulphate
529. Vinorelbinetatrate
530. Xipamide
531. Zidovudine hydrochloride
532. Ziprasidone hydrochloride
533. Zoledronic acid
534. [2][Zolpidem]
535. Zopiclone
536. Zuclopenthixol

1. Subs. by G.S.R. No.160(E), dated 16.3.2006 .
2. Omitted by G.S.R 588(E) dated 30-8-2013
3. Omitted by G.S.R 602(E) dated 19-7-2010
4. Omitted by G.S.R 724(E) dated 7-11-2013

Note:- 1. Preparations exempted under proviso to para 2 of Note to Schedule X shall also be covered by this Schedule.

2. The salts, esters, derivatives and preparations containing the above substances excluding those intended for topical or external use (except ophthalmic and ear / nose preparations con- taining antibiotics and/ or steroids) are also covered by this Schedule.

3. The inclusion of a substance in this Schedule does not imply or convey that the substance is exempted from the provisions of Rule 122A/122B."

[1][SCHEDULE H1

(*See* Rules 65 and 97)

Alprazolam Doripenam
Balofloxacin Ertapenem
Buprenorphine Ethambutol Hydrochloride
Capreomycin Ethionamide
Cefdinir Feropenam
Cefditoren Gemifloxacin
Cefepime Imipenem
Cefetamet Isoniazide
Cefixime Levofloxacin
Cefoperazone Meropenem

Cefotaxime Midazolam
Cefpirome Moxifloxacin
Cefpodoxime Nitrazepam
Ceftazidime Pentazocine
Ceftibuten Prulifloxacin
Ceftizoxime Pyrazinamide
Ceftriaxone Rifabutin
Chlorodiazepoxide Rifampicin
Clofazimine Sodium Para-aminosalicylate
Codeine Sparfloxacin
Cycloserine Thiacetazone
Diazepam Tramadol
Diphenoxylate Zolpidem

Note:- Preparations containing the above drug substances and their salts excluding those intended for topical or extrenal use (except ophthalmic and ear or nose preparations) containing above substances are also covered by this Schedule.

1. Ins. by G.S.R 588(E) , dt. 30.8.203.

[1]SCHEDULE I

(Omited)

[2][SCHEDUL E J

(See rule 106)

DISEASES AND AILMENTS (BY WHATEVER NAME DESCRIBED) WHICH A DRUG MAY NOT PURPORT TO PREVENT OR CURE OR MAKE CLAIMS TO PREVENT OR CURE.

1. AIDS
2. Angina Pectoris
3. Appendicitis
4. Arteriosclerosis
5. Baldness
6. Blindness
7. Bronchial Asthma
8. Cancer and Benign tumour
9. Cataract
10. Change in colour of the hair and growth of new hair.
11. Change of foetal sex by drugs.
12. Congenital malformations
13. Deafness
14. Diabetes
15. Diseases and disorders of uterus.
16. Epilepticfits and psychiatric disorders
17. Encephalitis
18. Fairness of the skin
19. Form, structure of breast
20. Gangrene
21. Genetic disorders
22. Glaucoma
23. Goitre

24. Hernia
25. High/low Blood Pressure
26. Hydrocele
27. Insanity
28. Increase in brain capacity and improvement of memory.
29. Improvement in height of children/adults.
30. Improvement in size and shape of the sexual organ and in duration of sexual performance
31. Improvement in the strength of the natural teeth.
32. Improvement in vision
33. Jaundice/Hepatitis/Liver disorders
34 Leukaemia
35. Leucoderma
36. Maintenance or improvement of the capacity of the human being for sexual pleasure.
37 Mental retardation, subnormalities and growth
38. Myocardial infarction
39. Obesity
40. Paralysis

1. Schedule I omitted by G.S.R 462(E) , dt. 22.6.1982
2. Subs. by G.S.R. 21(E) , dt. 11.1.1996.

41. Parkinsonism
42. Piles and Fistulae
43. Power to rejuvinate
44. Premature ageing
45. Premature greying of hair
46. Rheumatic Heart Diseases
47. Sexual Impotence, Premature ejaculation and spermatorrhoea
48. Spondylitis
49. Stammering
50. Stones in gall-bladder, kidney, bladder
51. Vericose Vein.]

SCHEDULE K

(See rule 123)

Class of Drugs

1. Drugs falling under clause (b) (i) of Section 3 of the Drugs and Cosmetics Act, not intended for medicinal use.

Extent and Conditions of Exemption

All the provisions of Chapter IV of the Act and the Rules thereunder, subject to the conditions that the drug is not sold for medicinal use or for use in the manufacture of medicines and that each container is labelled conspicuously with the words ―NOT FOR MEDICINAL USE.‖

[1][2.* * *]

[2][2A. Quinine and other antimalarial drugs.

[3][Persons selling the drugs by retail under arrangements made by State Government for sale and distribution of the drugs will be exempted from the requirement to take out licences for retail sale under clause (c) of Section 18 of the Act.]

[4][3.* * *]

[4][4.* * *]

[5][5. Drugs supplied by a registered medical practitioner to his own patient or any drug specified in Schedule C supplied by a registered medical practitioner at the request of another such practioner if it is specially prepared with reference to the condition and for the use of an individual patient provided the registered medical practitioner is not (a) keeping an open shop or (b) selling across the counter or (c) engaged in the importation, manufacture, distribution or sale of drugs in India to a degree which render him liable to the provisions of Chapter IV of the Act and the rules thereunder.

All the provisions of Chapter IV of the Act and the Rules made thereunder, subject to the following conditions :

[5][1. The drugs shall be purchased only from a dealer or a manufacturer licensed under these rules, and records of such purchases showing the names and quantities of such drugs, together with their batch numbers and names and addresses of the manufacturers shall be maintained. Such records shall be open to inspection by an Inspector appointed under the Act, who may, if necessary, make enquiries about purchases of the drugs and may also take samples for test.]

2. In the case of medicine containing a substance specified in [6][Schedule G, H or X] of the following additional conditions shall be complied with:-

a. the medicine shall be labelled with the name and address of the registered medical practitioner by whom it is supplied;

b. if the medicine is for external application it shall be labelled with the words [7][***] ―For external use only‖ or, if it is for internal use with the dose;

c. the name of the medicine or ingredients of the preparation and the quantities thereof, the dose prescribed, the name of the patient & the date of supply and the name of the person who gave the prescription shall be entered at the time of supply in register to be maintained for the purpose;

d. the entry in the register shall be given a

number and that number shall be entered on the label of the container;

e.the register and the prescription, if any, on which the medicines are issued shall be preserved for not less than two years from the date of the last entry in the register or the date of the prescription, as the case may be.

[8][3. The drug will be stored under proper storage conditions as directed on the label.]

[9][4. No drug shall be supplied or dispensed after the date of expiration of potency recorded on its container, label or wrapper or in violation of any statement or direction

[10][5A. Drugs supplied by a hospital or dispensary maintained or supported by Government or local body [11][***]
recorded on such container, label or wrapper.] The provisions of Chapter IV of the Act and the Rules thereunder which require them to be covered by a sale licence, subject to the following conditions :

(1)The dispensing and supply of drugs shall be carried out by or under the supervision of a qualified person;

(2)The premises where drugs are supplied or stocked shall be open to inspection by an Inspector appointed under the Drugs and Cosmetics Act who can, if necessary, take samples for test;

(3)The drugs shall be stored under proper storage conditions.

(4)[12][The drugs shall be purchased from a manufacturer or a dealer licensed under these rules or received as transferred stocks from hospital stores for distribution.
Records of such purchases or receipts shall be maintained.]

(5)[13][No drug shall be supplied or dispensed after the date of expiration of potency recorded on its container, label or wrapper

or in violation of any statement or direction recorded on such container, label

[14][5B. Whole Human Blood IP and / or its components stored for transfusion by a First Referral Unit, Community Health Centre, Primary Health Centre and a Hospital.
or wrapper.]

The provisions of Chapter IV of the Act and the rules made thereunder which require obtaining of a licence for operation of a Blood Ban k or processing Whole Human Blood and / or its components, subject to the following conditions, namely: -

(1)The First Referral Unit, Community Health Centre, Primary Health Centre and / or any Hospital shall be approved by the State / Union Territory Licensing Authority after satisfying the conditions and facilities through inspection.

(2)The captive consumption of Whole Human Blood IP or its components in the First Referral Unit, Community Health Centre, Primary Health Centre and / or any Hospital shall not be more than 2000 units annually.

(3)The Whole Human Blood an d / or its components shall be procured only from Government Blood Bank and / or Indian Red Cross Society Blood Bank and / or Regional Blood Transfusion Centre duly licensed.

(4)The approval shall be valid for a period of two years from the date of issue unless sooner suspended or cancelled and First Referral Unit, Community Health Centre, Primary Health Centre and / or any Hospital shall apply for renewal to the State Licensing Authority three months prior to the date of expiry of the approval.

(5)The First Referral Unit, Community Health Centre, Primary Health Centre and / or any Hospital shall have the following technical staff for storage of blood or its components:

(a)A trained Medical Officer for proper procurement, storage and cross matching of blood and / or its components. He / she shall also be responsible for identifying haemolysed blood and ensure non-supply of date expired blood or its components.

(b)A blood bank Technician with the qualification and experience as specified in Part XII B of Schedule F or an experienced laboratory technician trained in blood grouping and cross matching.

(6)The First Referral Unit, Community Health Centre, Primary Health Centre and / or any Hospital shall have an area of 10 sq. metres. It shall be well lighted, clean and preferably air- conditioned. Blood bank refrigerator of appropriate capacity fitted with alarm device and temperature indicator with regular temperature monitoring shall be provided to store blood units between 2° C to 8° C and if the components are proposed to be stored, specialized equipment‘s as specified in Part XII B of Schedule F shall also be provided.

(7)The First Referral Unit, Community Health Centre, Primary Health Centre and / or any Hospital shall maintain records and registers including details of procurements of Whole Human Blood IP and / or blood components, as required under Part XII B Schedule F.

(8)(8) The First Referral Unit, Community Health Centre, Primary Health Centre and / or any Hospital shall store samples of donors blood as well as patients sera for a period seven days after transfusion.

15[6.* * *]

7.Quinine Sulphate

16[8.* * *]

17[9. Magnesium Sulphate

18[10. The following substances which are

The provisions of sub-section (a) (i) of Section 18 of the Act to the following extent-

(i)the colour of the drug may be pink, owing to its being coloured with an edible pink colouring matter;

(ii)the B. P. tests for readily carbonisable substances produce a yellow colour of an intensity about four times the colour produced with quinine sulphate conforming to the B.P. standard;

(iii)other Cinchona alkaloids present shall not exceed six per cent; and

(iv)the residue on incineration shall not exceed 0.14 per cent.

The provisions of sub-clause (i) of clause (a) of Section 18 of the Act to the following extent:-

Chlorides present in the salt shall not exceed 0.12 per cent in the case of the produce prepared from

sea water.]

All provisions of Chapter IV of the Act and the Rules thereunder

used both as articles of food as well as drugs -

(i)all condensed or powdered milk whether pure, skimmed or malted, fortified with vitamins and minerals or otherwise.

(ii)Farex, Oats, 19[***] and all other similar cereal preparations whether fortified with vitamins or otherwise excepting those for parenteral use.

(iii)Virol, Bovril, Chicken essence and all other similar predigested foods.

(iv)20[Ginger, Pepper, Cumin, Cinnamon and all other similar spices and condiments unless they are specially labelled as conforming to the standards in the Indian Pharmacopoeia or the Official Pharmacopoeia and official compendia of drug standards prescribed under the Act and Rules made thereunder.]

21[11.* * *]

22[12. Substances intended to be used for destruction of vermin or insects which cause disease in human beings or animals, viz.

Insecticides and Disinfectants.]

24[13. The following household remedies, namely-

(1) 25[Aspirin tablets.]

(2) 26[Paracetamol Tablets.]

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The provision of Chapter IV of the Act and Rules thereunder, which require them to be covered by a sale licence [23][subject to the condition that provision of condition (17) of Rule 65 of the Drugs and Cosmetics Rules, 1945 are complied with by the person stocking or selling such substances.]

The provisions of Chapter IV of the Act and the Rules thereunder which require them to be covered with a sales licence in

Form 20-A subject to the following conditions—

(3)	Analgesic Balms.	(a) The drugs are sold only in a village having population of not more than one thousand persons and where there is no licensed dealer under the Drugs and Cosmetics Act;
(4)	Antacid preparations.	
(5)	Gripe Water for use of infants.	
(6)	Inhalers, containing drugs for treatment of cold and nasal congestion.	
(7)	Syrups, lozenges, pills and tablets for cough.	(b) The drugs do not contain any substance specified in [27][Schedules G, H or X];
(8)	Liniments for external use.	(c) The drugs are sold in the original unopened containers of the licensed manufacturers;
(9)	Skin ointments and ointments for burns.	
(10)	Absorbent cotton wool, bandages	absorbent guaze and adhesive plaster.
(11)	Castor Oil, liquid Paraffin and Epsom	Salt.
(12)	Eucalyptus Oil	
(13)	Tincture Iodine, Tincture Benzoi n	C o. and Mercurochrome in containers not exceeding 100 ml.
(14)	Tablets of Quinine Sulphate I.P.	

(d) When the drugs are sold under clause (a) condition 3 under ―Conditions of licence‖ of

Form 20-B shall not apply.

(15)Tablets of Iodochlorohydroxy quinoline-250 mg.

[28][14. Mechanical Contraceptives

The provisions of Chapter IV of the Act and Rules thereunder, which require them to be

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covered by a sale licence [29][subject to the condition that the provisions of condition (17) of Rule 65 of the Drugs and Cosmetics Rules, 1945, are complied with by the person stocking or selling mechanical contraceptives.]

[30][14A. Vaginal contraceptive pessaries containing Nonoxynol. The provisions of Chapter IV of the Act and

[31][15. Chemical contraceptive having the following composition per tablet :

(1)DL-Norgestrel-0.30 mg. Ethinyloestradiol-0.03 mg.

(2)Levonorgestrel-0.15 mg. Ethinyloestradiol-0.03 mg. (3)Centchroman-30mg.

(4)[32][Desogestrel -0.150mg. Ethinyloestradiol 0.030mg.

(5)Levonorgestrel 0.1mg. Ethinyloestradiol 0.02mg [33][16. Cosmetics

[34][17. Ophthalmic ointments of the Tetracycline group of drugs

the Rules made thereunder which require them to be covered by a sale licence subject to the condition that the provisions of clause (17) of Rule 65 of the Drugs and Cosmetics Rules, 1945 are complied with by the person stocking or selling this contraceptive.]

The provisions of Chapter IV of the Act and the rules made thereunder which required them to be covered by a sale licence.]

The provisions of Chapter IV of the Act and the Rules made thereunder, which require them to be covered by a licence for sale provided that the cosmetics sold, if of Indian origin, are manufactured by licensed manufacturers.]

Persons authorised by the Government to distribute or sell the drugs under the National Trachoma Control Programme shall be exempted from the provisions of Chapter IV of the Act and the Rules made thereunder, which require the drugs to be covered by a sale licence.]

[35][18.* * *]

[36][19. Hair Fixers, namely mucilaginous preparations containing gums, used by men for fixing beard.

[37][20. Radio Pharmaceuticals.

[38][21. Tablets of Chloroquine Salts.

The provisions of Chapter IV of the Act and the rules thereunder.]

All the provisions of Chapter IV of the Act and the rules made thereunder.]

The provisions of Chapter IV of the Act and Rules thereunder, which require them to be covered by a sale licence, provided the drug in strip pack is sold under the Commercial Distribution Scheme of the National Malaria Eradication Programme and duly labelled as

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—National Malaria Eradication Programme-

Ministry of Health and Family Welfare,

Government of India.‖]

[39][22. Sales from restaurant cars of trains and from coastal ships of household remedies, which do not require the supervision of a qualified person for their sale.

[40][23. Drugs supplied by (i) Multipurpose

The provisions of Chapter IV of the Act and the rules thereunder which require them to be covered by a sale licence, subject to the following conditions, namely -

(a) the records of purchase and sale of drugs shall be maintained by the person in charge of sale of such drugs, which shall be available for inspection by an Inspector appointed under the Act;

(b) the place where such drugs are stocked shall be open to inspection by a n Inspector appointed under the Act who can, if necessary, takes samples for test.]

		All The provisions of Chapter IV of the Act
Workers attached to Primary Health Centres/Sub- Centres, (ii) Community Health Volunteers under the Rural Health Scheme, (iii) Nurses, Auxiliary Nurses, Midwives an d Lady Health Visitors attached to Urban Family Welfare Centres/Primary Health Centres/Sub-Centres and [41][(iv) Anganwadi Workers].	be covered by a sale licence, provided the drugs are supplied under the Health or Family Welfare Programme of the Central or State Government.]	
[42][24. Homoeopathic medicines supplied by a registered Homoeopathic medical practitioner to his own patient or Homoeopathic medicines supplied by a registered Homoeopathic medical practitioner at the request of another such practitioner provided the registered Homoeopathic medical practitioner is not (a) keeping an open shop, or (b) selling across the counter or, (c) engaged in the importation, manufacturer licensed under the Drugs and Cosmetics Rules, 1945. (2) The premises where the Homoeopathic Medicines are stocked shall be open to inspection by an Inspector appointed under the manufacture, distribution or sale of Homoeopathic medicines in India to a degree which renders him liable to the provisions of Chapter IV of the Act and the rules made thereunder	All the provisions of Chapter IV of the Act and the rules made thereunder subject to the following conditions:— (1) The Homoeopathic medicines shall be purchased only from a dealer or a	
[43][25. Preparations applied to human body for the purpose of repelling insects like mosquitoes.	The provisions of Chapter IV of the Act and Rules thereunder which require them to be covered by a sale licence subject to the conditions that such a product has been manufactured under a valid drug manufacturing licence.	
[44][26. Medicated Dressing and Bandages for First Aid.	The provisions of Chapter IV of the Act and Rules thereunder which require them to be covered by a sale licence subject to the conditions that such a product has been manufactured under a valid drug manufacturing licence.]	

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[45][27. Oral Rehydration Salts (Manufactured as per the following formula) : o Sodium chloride 3.5 g/litre. o Trisodium citrate dehydrate 2.9 g/litre o Potassium Chloride 1.5 g/ litre.	The provisions of Chapter IV of the Act and Rules thereunder which required them to be covered by a sale licence, subject to the conditions that such a product has been manufactured under a valid drug	

May be replaced by Sodium bicarbonate(Sodium hydrogen Carbonate) 2.5 g/ litre, when citrate salt is not available. manufacturing Licence.]

[46][28. White or Yellow Petroleum Jelly I.P. (Non-perfumed).

[47][29. Morphine Tablets

30. Whole Human Blood collected and transfused by Centres r un by Armed Forces Medical Services in border areas, small mid-zonal hospitals including peripheral hospitals, Field Ambulances, Mobile medical units and other field medical units including blood supply units in border, sensitive and field areas.

The provisions of Chapter IV of the Act and Rules thereunder which required them to be covered by a sale licence, subject to the condition that such a product has been manufactured under a valid drug manufacturing Licence.

The provisions of Chapter IV of the Act and the rules made thereunder which require them to be covered by a sale licence, subject to the following conditions, namely: -

(i) The drug shall be supplied by the Palliative Care Centres approved by the State Government to terminally ill cancer patients

(ii) The drug shall be kept under the custody of the Medical Officer in charge of the said Centre.

(iii) The drug shall be purchased from a dealer or a manufacturer who holds licence under these rules and records of such purchases showing the names and quantities together with their batch numbers and names and addresses of the manufacturers or dealers and the names and addresses of the patients to whom supplies have been made shall be maintained. Such records shall be open to inspection by an inspector appointed under the Act, who may also take samples for test.

All the provisions of Chapter IV of the Act and rules made thereunder which require them to be covered by a licence to operate a Blood Bank for collection, storage and processing of whole human blood for sale or distribution subject to the following conditions:-

(i) These Centres shall collect, process and transfuse blood in emergent situations which require lifesaving emergency surgeries/or transfusion.

(ii) These Centres shall be under the active direction and personal supervision of a qualified Medical Officer, possessing the

qualifications and experiences specified in condition (i) of rule 122-G.

(iii) Each blood unit shall be tested before use for freedom from HIV I and II antibodies, Hepatitis B surface antigen, malarial parasites and other tests specified under the monograph ―Whole Human Blood‖ in current edition of Indian Pharmacopoeia

(iv) These Centres shall have adequate infrastructure facilities for storage and transportation of blood.

(v) The blood collected and tested by such Centres shall be transfused by the Centre itself and may be made available for use of other peripheral Armed Forces hospitals or Centres during operational circumstances.]

[48][31. The following Homoeopathic Medicines, namely: -

The provisions of Chapter IV of the Act and the rules made thereunder which require them

***

(b) Homoeopathic Ointments, each [50][in 25gm. Tube]:

(i) Arnica Montana
(ii) Calendula Officinalis
(iii) Cantharis
(iv) Rhus Toxicodendron

(c) Biochemic tissue remedies in tablet forms, in generic names only, each in 20gm. Packing in 3X and 6X trituration-

(i) Calcarea Phosphorica
(ii) Calcarea Sulphurica
(iii) Ferum Phosphoricum
(iv) Kali Muriaticum (v) Kali Phosphoricum (vi) Kali Sulphuricum
(vii) Magnesium Phophoricum
(viii) Magnesia Sulphurica (ix) Natrum Muriaticum (x) Natrum Phophoricum (xi) Natrum Sulphuricum (xii) Silica

(d) Homoeopathic medicines, mentioned below, in pills, each in 30C potency, in sealed original packing of manufacturer of 8 gms:

(i) Arnica Montana
(ii) Aconitum Napellus
(iii) Arsenicum Album

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(iv) Aloe Socotrina
(v) Apis Mellifica
(vi) Allium Cepa
(vii) Bryonia Alba
(viii) Borax
(ix) Belladonna
(x) Cantharis
(xi) Carbo Vegatabilis
(xii) Cina
(xiii) Colocythis
(xiv) Calendula Officinalis
(xv) Caulophyllum Thalictroides
(xvi) Cocculus Indicus
(xvii) Chamomilla
(xviii) Drosera Rotundifolia
(xix) Hypeicum Perforatum
(xx) Hepar Sulphur
(xxi) Ipecacuanha
(xxii) Ledum Palustre
(xxiii) Millefolium
(xxiv) Mercurius Solubilis

to be covered with a sale licence in Form 20-[49][(a) C, subject to the following conditions: -

(i) These homoeopathic medicines shall be sold in the original sealed small quantity packings of the licensed manufacturers.

(ii) These medicines may be stocked and sold by retail of medicines licensed under rule 61.

(iii) These medicines shall be stored separately from other allopathic drugs.

(iv) These medicines shall be purchased from a manufacturer or a dealer licensed under these rules.

(v) The purchase and sale records of these medicines shall be maintained by the dealer for minimum period of three years.

(vi) These medicines shall be labelled in generic / pharmacopoeial names only.

(xxv) Nux Vomica
(xxvi) Pulsatilla Nigricans
(xxvii) Podophyllum Peltatum
(xxviii) Plantago Major
(xxix) Rhus Toxicodendron
(xxx) Ruta Graveolens
(xxxi) Symphytum Officinalis
(xxxii) Veratrum Album

51[(e) All biochemic and its combinations (1 to 28), in tablet forms, in sealed original packing of the manufacture.]

52[32. First Aid kit supplied along with motor vehicle by the manufacturer or its distributors at the time of first sale of vehicle.

53[33. Nicotine gum 54[and Lozenges] containing upto 2 mg of nicotine

55[34. Production of Oxygen 93 per cent USP, produced from air by the molecular sieve process, by a hospital or Medical Institute for their captive consumption.

The provisions of Chapter IV of the Act and rules made thereunder which require them to be covered by a sale licence, subject to the condition that the drug items are procured from a manufacturer or a dealer licensed under the rules.]

The provisions of Chapter IV of the Act and the Rules made thereunder which require them to be covered by a sale license subject to the condition that such a product has been manufactured under a valid drug manufacturing license.]

The provisions of Chapter IV of the Act and the Rules made thereunder which require them to be covered by manufacturing licence under the rules, provided that the production facilities shall be open to inspection by an Inspector appointed under the Act, who can, if necessary, take samples For test‖.]

56[35. Homoeopathic hair oils having active ingredients up to 3X potency only

58[36. Custom made devices

The provisions of Chapter IV of the Act and the rules made thereunder which require them to be covered with a sale licence 57[***] subject to the condition that such a product has been manufactured under a valid manufacturing licence and sold in the original sealed packing of the licensed manufacturers.] All provisions of Chapter IV of the Act and the rules made thereunder, subject to the condition that the device being specifically made in accordance with a duly qualified medical practitioner‘s written prescription under his responsibility, in accordance with specific design characteristics and is intended for the sole use of a particular patient and the label should bear the word ―custom made device.‖

Explanation.— Mass produced devices which only need adoption to meet the specific requirements of the medical practitioner or any other professional user shall not be considered to be custom made devices.]

1. Item 2 omitted by Government of India Notification No. F.1-56/47-D, dt. 16.1.1950). 2. Added by Notification No .F. I-2/47-D dt. 13-2-1950.
3. Amended by Notification No. F. I-22/59-D dt.. 9-4-1960.
4. Item 3 and 4 omitted by Notification No. F.I-6/62-D dt. 2-7-1969.
5. Subs. by G.S.R. 1074, dt: 19.8.1978.
6. Subs. by G.S.R. 462 (E), dt: 22.6.1982.
7. Certain words omitted by G.S.R. 462 (E), dt: 22.6.1982.
8. Ins. by G.S.R. 460 (E), dt: 20.6.1984.
9. Ins. by G.S.R. 592 (E), dt: 13.8.2008.
10. Added by notification No. F.1-22/59-D, dt: 9.4.1960.
11. Certain words omitted by G.S.R. 812 (E), dt: 14.11.1994.
12. Ins. by G.S.R. 648 (E), dt: 16.9.2002.
13. Ins. by G.S.R. 592 (E), dt: 13.8.2008.
14. Ins. by G.S.R. 909 (E), dt: 20.12.2001.
15. Item 6 omitted by G.S.R. 681 (E), dt: 5.12.1980.

16. Item 8 omitted by G.S.R.1185 (E), dt: 18.8.1964.
17. Added by notification No. F.1-19/50-D.S, dt: 30.3.1953.
18. Added by notification No. DR/Sch.Ddk/F.1-40/54-D.S., dt: 27.1.1955.
19. Omitted by G.S.R. 665 (E), dt: 6.5.1977.
20. Subs. by G.S.R. 19, dt: 15.12.1977.
21. Item 11 omitted by notification No. F.1-36/64-D (G.S.R 1188), dt: 17.8.1964. 22. Amended by notification No. F.1-20/60-D (S.O.400), dt: 24.1.1964.
23. Added by G.S.R. 926, dt: 24.6.1977.
24. Added by notification No. F.1-19/59-D, dt: 13.6.1961.
25. Subs by S.O. 2139, dt: 5.6.1972.
26. Subs. by G.S.R. 1060(E), dt: 5.9.1986.
27. Subs. by G.S.R. 462 (E), dt: 22.6.1982.
28. Added by notification No. F.1-39/61-D (S.O. 1057), dt: 23.3.1964.
29. Added by G.S.R. 926, dt: 24.6.1977.
30. Ins. by G.S.R. 784 (E), dt: 28.8.1989.
31. Subs by G.S.R. 730 (E), dt: 10.12.1991.
32. Ins. by G.S.R. 648 (E), dt: 16.9.2002.
33. Added by notification No. F.1-36/64-D (G.S.R 1183), dt: 17.8.1964.
34. Added by notification No. F.1-21/63-D (G.S.R 70), dt: 4.1.1965.
35. Item 18 is omitted by G.S.R. 1594, dt: 28.10.1976.
36. Added by S.O. 2139, dt: 5.6.1972.
37. Added by G.S.R. 926, dt: 24.6.1977.

38. Added by G.S.R. 697 (E), dt: 11.11.1977.
39. Ins. by G.S.R. 1241, dt: 15.9.1979.
40. Ins. by G.S.R. 540 (E), dt: 22.9.1980.
41. Ins. by G.S.R. 784 (E), dt: 28.8.1989.
42. Ins. by G.S.R. 680 (E), dt: 5.12.1980.
43. Ins. by G.S.R. 1060 (E), dt: 5.9.1989.
44. Ins. by G.S.R. 371 (E), dt: 24.3.1988.
45. Ins. by G.S.R. 677 (E), dt: 2.6.1988.
46. Ins. by G.S.R. 753 (E), dt: 4.11.1999.
47. Ins. by G.S.R. 6 (E), dt: 4.1.2001.
48. Ins. by G.S.R. 218 (E), dt: 28.3.2001.
49. Sub-item (a) relating to ―Arnica Montana Hair Oil‖ omitted by G.S.R. 917 (E), dt: 22.12.2009. 50. Subs. by G.S.R. 592 (E), dt: 13.8.2008.
51. Ins. by G.S.R. 592 (E), dt: 13.8.2008.
52. Ins. by G.S.R. 648 (E), dt: 16.9.2002.
53. Ins. by G.S.R. 549 (E), dt: 16.7.2003.
54. Ins. by G.S.R. 101 (E), dt: 18.2.2001.
55. Ins. by G.S.R. 734 (E), dt: 21.12.2005.
56. Ins. by G.S.R. 917 (E), dt: 22.12.2009.

57. The words —in

Form 20C‖ omitted by G.S.R. 107 (E), dt: 17.2.2015.

58. Ins. By G.S.R. 890 (E), dt: 25.9.2014.

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[1][SCHEDULE L

(Omitted)

[2][SCHEDULE L-I

(see rules 74, 78 and 150E)

GOOD LABORATORY PRACTICES AND REQUIREMENTS OF PREMISES AND EQUIPMENTS

1.General Requirements:-

(a)The laboratory or the organisation of which it is a part must be an entity that is legally authorised to function and can be held legally responsible.

(b)It is the responsibility of the management to ensure that the laboratory carry out its testing, calibration, validation, and all other technical activities in such a way as to meet Good Laboratory Practices (GLP) requirements.

(c)Laboratory management shall have a qualified individual to be known as quality manager or technical manager for carrying out all technical activities and for the implementation of documented quality system and shall report to the top management directly.

(d)The quality manager shall prepare a schedule for technical audit of the laboratory for GLP compliance by an expert or experts appointed by the top-management other than the in-charge of the laboratory and shall ensure the maintenance of documented quality system as per quality manual.

2.Premises:-

(a)(i) the laboratories shall be designed, constructed and maintained so as to prevent entry of insects and rodents besides cross contamination;

(ii) interior surface (walls, floor, and ceilings) shall be smooth and free from cracks, and permit easy cleaning and disinfection;

(iii) adequate provision is made not only for space and equipment for carrying out necessary test but also for utilities like water, power and gas;

(iv) air ventilation system shall ensure dust free environment.

(b)The laboratories shall be provided with adequate lighting and ventilation and if necessary, air-conditioning to maintain satisfactory temperature and relative humidity that will not adversely affect the testing and storage of drugs or the accuracy of the functioning of the laboratory equipments or instruments.

(c)The drainage system facilities shall be such as to facilitate proper maintenance and prevent water logging in the laboratory.

(d)Tabletops shall be constructed with acid, alkali and solvent resistant material and shall be smooth and free from crevices as far as possible.

(e)All bio-medical laboratory waste shall be destroyed as per the provisions of the Bio-- Medical waste (Management and Handling) Rules, 1996.

(f)Adequate space with proper storage conditions in the laboratory shall be provided for keeping reference and working standards and be maintained by the quality control department. Standard Operating Procedure (SOP) for the maintenance of reference standards and evaluation of Working and Secondary standards shall be prepared by the laboratory.

(g)The air circulation is maintained in the area where sterility test is carried out as per Schedule‘M‘.

(h)Bio-burden shall be routinely maintained in the controlled and uncontrolled area, (e.g. air locks)

1. Schedule L omitted by G.S.R. 462 (E), dt: 22.6.1982.
2. Ins. by G.S.R. 780 (E), dt: 10.11.2008.

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(i)Animals House:-

(i) Animal House shall have the approval of the Committee for the Purpose of Control and Supervision on Experiments on Animals (CPCSEA).

(ii) Designed in such a way that there is an arrangement to quarantine the new animals procured or purchased and have a provision for clean corridor and dirty corridor.

(iii) In case of a diseased animal proper diagnosis shall be done and proper record of treatment shall be maintained.

(iv) Different types of animals shall be housed separately with proper identification.

(v) A Standard Operating Procedure shall be prepared for breeding and care of animals, maintenance, cleaning or sanitation with suitable schedule for cleaning of animal cages, racks, floor and other equipments.

(vi) The animal house shall have proper air-conditioning (temperature and humidity) with proper lighting and be monitored regularly and documented periodically.

3.Personnel-

(a)Staff in the laboratory shall possess necessary qualification, proper training and shall have adequate, experience for the assigned duties.

(b)A training record of all the personnel shall be maintained.

(c)Head of the laboratory must be of high professional standing with experience in drug analysis and laboratory management who is responsible for.

(i)ensuring the control and maintenance of documents including the quality system as per the requirements of regulatory authorities which involves all raw data, SOPs, documentation exhibits, protocols, training charts, etc;

(ii)planning and organising the audit of the quality system and initiation as well as follow up action of the corrective actions, if any;

(iii)investigation of technical complaints;

(iv)taking finai responsibilities for recommending any regulatory action in the event of noncompliance of tested samples.

4.Equipments:-

(a)The laboratory shall be furnished with all types of equipments as may be necessary for carrying out the different activities within the laboratory.

(b)The analytical instruments shall be housed in dust-free environment and whenever required, conditions of temperature and humidity shall be maintained and periodic checks on temperature and humidity be made and recorded.

(c)The instruments, instrument bench and surrounding areas shall be kept clean and tidy at ail times.

(d)Instruments requiring calibration shall be calibrated at regular intervals and records of such calibration or maintenance be maintained and there shall be written instructions in the form of Standard Operating Procedures for the operation, maintenance and calibration of instruments.

(e)Equipment records shall be maintained and such records shall contain the following:-

(i)name of equipment or machine or apparatus;

(ii)manufacturer ‘s name, model number and type of identification;

(iii)serial number;

(iv)date on which equipment was received in laboratory;

(v)current location;

(vi)condition when received (e.g. new, used, re-conditioned);

(vii)copy of the manufacturer ‘s operating instructions;

(viii)frequency of calibration;

(ix)frequency of maintenance;

(x)log Book (day to day entry including status of the equipment)

(xi)staff responsible for monitoring the calibration and maintenance status of the equipment;

(xiii)list of authorised users or operators, if any;

(xiv)history of any damage, malfunction, modification or upgradation, repair and calibration;

(xv)list of spares and accessories, if any.

(f)A progress register for non-functional equipments and action for procurement of spares and accessories, monitoring thereof, shall be maintained.

(g)A Standard Operating Procedure for preventive maintenance of machine or equipment or apparatus shall be prepared by the laboratory.

(h)Other equipments such as burettes, pipettes, volumetric flasks, weight boxes, thermometers, etc., shall be thoroughly checked for accuracy of calibration before acceptance for use.

(i)Maintenance procedure in the form of Standard Operating Procedures must be prepared and regular servicing must be performed by the maintenance engineer or specialist

(j)Equipments, instruments giving anomalous results or defective must be labeled as _out- of-order' till they are repaired and after instrument is repaired it should be calibrated before use.

(k)The maintenance of equipments for services like electricity, gas, water, steam, and compressed gas shall be handled by competent person.

(l)Autoclaves must meet the requirements described for operations, safety and validation procedures, and the validation carried out by the laboratory shall be recorded.

(m)Fume Cupboards.-

Work involving the evolution of harmful and obnoxious vapours shall be carried out in a fume cupboard. The exhaust system of the fume cupboard shall be checked frequently to ensure that it is in order. There should be a water drainage system inside the fume cupboard and shall be checked frequently to ensure that there is no water logging and it is in order.

5. Chemicals and Reagents:

(a)The storage and handling of chemicals and reagents shall be done in a manner considering the physicochemical properties of these substances and the hazards involved in their use.

(b)All reagents and solutions in the laboratory shall be properly identified with a label.

(c)A standardisation register shall be maintained by the laboratory along with its raw data and Standard Operating Procedure for preparation and standardisation on stock solutions, standard solutions, volumetric solutions must be prepared for the guidance of staff.

(d)Containers of stock solutions and of standard solutions shall bear the following details:-

(i) name of analytical chemist who prepared the solution;

(ii) date of preparation;

(iii) Each volumetric solution shall have ―use before date‖ depending upon the stability of the solution; and

(iv) standardization records.

(e)The transfer of hazardous chemicals and regents from one container to another container shall be carried out with suitable equipment by taking the care of safety and no make-shift or hazardous methods must be resorted to.

6.Good house keeping and safety.-

(a)General and specific written down instructions for safety shall be circulated to each staff member and the instructions be revised periodically as appropriate (e.g., poster displays, audio- visual material and by seminars/conferences)

(b)Standard Operating Procedure for safety, house-keeping and loss prevention shall be prepared in accordance with the various rules, and regulations of the Government of India and include the following requirements, namely:-

(i)safety data sheets must be made available to staff before testing is carried out;

(ii)drinking, eating and smoking shall not be permitted in the laboratories; food for human consumption shall not be kept in working or storage areas; food meant for test animals shall be handled by the workers under the guidance of a veterinary doctor or qualified person. In the animal house, the facilities for collection and

disposal of animal waste or safe sanitary storage of waste before removal from testing be provided;

(iii)staff must wear laboratory coats or other protective clothing including gloves and face masks and eye protection wherever required;

(iv)the laboratories shall have adequate first aid kit and fire fighting equipments located at the right places and the staff must be familiar and trained with the use of fire fighting equipment including fire extinguishers, fire blankets and gas masks,

(v)operators carrying out sterility tests shall wear sterilised garments including headgear, face masks and shoes;

(vi)the staff must be educated in the first aid techniques, emergency care and use of antidotes; and

(vii)safety rules in handling cylinders of compressed gases must be observed and staff must be familiar with relevant colour identification codes;

(c)Protective Precautions to be taken in Laboratories:

(i) water showers shall be installed at appropriate places in the laboratory;

(ii) rubber suction bulbs must be used on manual pipettes and siphons;

(iii) warnings, precautions, and written instructions must be given for work with violent, uncontrollable or dangerous reactions (e.g. mixing water and acids, biological such as infectious agents, etc.); .

(iv) appropriate facilities for the collection, storage, and disposal of wastes shall be made available;

(v) staff must be aware of methods for safe disposal of corrosive or dangerous products by neutralisation or deactivation and of the need for complete disposal of mercury and its salts.

(vi) staff must also be aware about the safety precautions to be adopted while handling potassium cyanide and cyanogen bromide.

(vii) a Standard Operating Procedure for handling, collection, disposal of chemical and biological wastes be prepared.

7.Maintenance, calibration, and validation of equipments:-

(a)All equipments, instruments and other devices used in the laboratory shall use appropriate methods and procedures for all tests or calibrations and they shall be regularly calibrated and validated. The frequency of calibration may differ from instrument to instrument.

(b)The original equipment manufacturer ‘s recommendations along with the experience of the laboratory staff and the use of equipment per day may also be considered while fixing the frequency of calibration.

(c)For most of the equipments and instruments, Standard Operating Procedures for calibration and calibration schedule be prepared by the laboratory and a logbook shall also be prepared by each laboratory for proper documentation of calibration results.

8.Reference materials:-

(a)Reference materials are necessary for the testing and, or calibration, validation or verification of a sample or of equipment, instruments or other devices and all such materials shall be traceable to agency authorised by Government of India or any other International body .

(b)The laboratory shall prepare working standard by comparing with the reference standards and shall be routinely checked for their purity by selecting parameters such as identity, loss on drying or on water, impurity and assay, etc.

(c)Whenever, any new reference material is received by the laboratory, a code number shall be assigned and this code number shall be quoted on the laboratory note book and analytical work sheet. The working standard shall also be provided with identification

(d)A register pertaining to reference and working materials must be maintained by the laboratory. The following details may be mentioned in the register:

(i) source of supply;
(ii) code number of the reference material;
(iii) date of receipt;
(iv) batch number or identification number of the supplying agency;
(v) details like assay value, water content or any other information provided;
(vi) storage condition of the material; and
(vii) date of expiry, if any and date of manufacturing if possible

(e)All working standards shall be checked at appropriate intervals or before use to ensure that it has not deteriorated or decomposed during storage. These observations be recorded in a register: All the reference and working standards shall be stored at appropriate storage condition; those requiring storage between 2-8°C shall be stored in a refrigerator. Wherever recommended the material may not be allowed to be frozen.

9.Microbiological Cultures:-

(a)Standard Operating Procedure for maintenance of microbial culture and sub-culture must be prepared by the laboratories.

(b)If the cultures have become non-viable or mutant, proper procedure shall be followed to destroy these cultures by autoclaving under an authorised personnel for biological testing. Preferably not more than five passages may be prepared.

(c)All activities be carried out in a aseptic area by authorised person.

(d)The laboratories shall perform standard biochemical tests on the sub-culture as given in literature to ensure their viability.

10.Quality system.-

The quality system shall be designed to ensure the following objectives:-

(a)The measurements and calibrations shall fully conform to the compendial requirements and the methods demonstrably based on validation protocols are followed.

(b)It shall be effective in providing necessary assurance that the activities or processes or techniques or practices comply with planned arrangements.

(c)It helps in early detection and correction of non conformities.

(d)Remedial action on the observations by internal and external audits are taken appropriately and

(e)It shall have a documented quality policy for the organisation.

11.Internal quality system audits.-

(a)Internal audits are done to assure the integrity of the analysis‘ and such audits shall be conducted periodically with a predetermined schedule and procedure with appropriate checklist, to verify that the operations continue to comply with the requirements of quality system and requirements of regulatory authorities. Internal quality audits shall be carried out by trained and qualified personnel who are independent of the activity to be audited.

(b)The periodicity of quality audit shall be fixed by the Head of the laboratory so that each activity is audited at least once in a year.

(c)Head of the laboratory will be responsible for initiation of the corrective action arising from audits and verification of corrective action.

(d)Whenever any non-compliance or any diversion is noticed by the team in implementing quality policy or quality system, protocols, the same will be attended by the Quality Manager. The problem will be analysed and necessary actions will be taken with proper documentation.

(e)The Quality Manager shall maintain all the records of the analysis being conducted which includes test system, the type of analysis, date on which analysis is done, etc and quality Manager shall also maintain copies of all protocols pertaining to different activities being checked by the audit team.

12.Management review –

Quality system reviews shall be conducted by the top management at least once in every

twelve months and the agenda of review shall generally cover the following:- (i) report or input of internal audits;

(ii) matter arising from previous reviews;
(iii) report of external audits, if any;
(iv) surveillance report, if any;
(v) result of proficiency testing;
(vi) complaints or feedback received from users of laboratory services;
(vii) details of in-house quality control checks;
(viii) need of amendment of the quality system and documentation;.
(ix) induction training of new staff; and
(x) any other requirements of the laboratory.

13.Standard Operating Procedures:-

(a)Standard Operating Procedures are written procedures for different activities being conducted in a laboratory and shall include the following characteristics:

(i)they shall be written in a chronological order listing different steps leading to an analysis of drugs or calibration of an instrument:

(ii)testing laboratories shall have Standard Operating Procedure manuals and have its periodic review;

(iii)it shall be user friendly documents and shall include designation of the person responsible for intended activity.

(b)Standard Operating Procedures in addition to those recommended under various activities shall also be prepared to the minimum in respect of the following:

(i) sample handling and accountability;
(ii) receipt identification, storage, mixing and method sampling of the test and control articles;
(iii) record keeping, reporting, storage and retrieval of data;
(iv) coding of different studies, handling of data including use of computerized data system;
(v) operation of technical audit personnel in performing and reporting audits, inspections and final report reviews;
(vi) routine inspection of cleaning, maintenance, testing, calibration and standardisation of instruments;
(vii) action to be taken in respect of equipment failure;
(viii) analytical data methods;
(ix) the raw data;
(x) data handling and storage retrieval;
(xi) health and safety protection;
(xii) animal room preparations;
(xiii) animal care;
(xiv) storage and maintenance of microbial cultures;
(xv) maintenance of sterility room (i.e. constant maintenance and monitoring of Aseptic condition of sterility room);
(xvi) use and storage of reference standards;
(xvii) procurement of stores and equipment; (xviii) monitoring of testing of samples;
(xix) method of retention of unexpended samples, their location, maintenance and disposal;
(xx) document control;
(xxi) redressal of technical complaints;
(xxii) housing-keeping;

(xxiii) corrective and preventing action;
(xxiv) working procedure (test methods);
(xxv) calibration Manual; and
(xxvi) training manual.

14.Protocols and specifications archive.-

(a)Every laboratory shall have a specification archive and. current versions of all necessary specifications shall be kept as per the requirements of the Act and the rules made thereunder and the National Pharmacopoeia (Indian Pharmacopoeia).

(b)All updates and corrections must be noted in the master volumes of Pharmacopoeias to prevent the use of obsolete sections; supplement and addendum shall also be made available in the laboratory.

(c)The specification archive shall contain the following :-

(i) list of all the pharmacopoeias;

(ii) a file on patent and proprietary medicines (non-pharmacopoeial) test methods to specifications prepared and validated by the manufacturer or by the laboratory itself. The test methods shall be submitted to the ·concerned Drug Control Authority. The validated test methods developed by the manufacturer or the laboratory shall stand to the requirements of compendial parameters in regard to its precision, accuracy, reproducibility, specificity, linearity, and ruggedness etc.

15.Raw data:-

(a)Raw data refers to the laboratory work sheet, note books or analysis sheet, records, and other activities and such raw data shall include hand written notes, photographs, software, drawings, computer printouts, spectral charts, dictated observations or recorded data from automated equipments. The raw data also includes record on receipt of animals, result of environmental monitoring, calibration, records of equipments, integrator output from analytical equipment, including work-sheet used to read a note, information from Light Emitting Diode (LED) display of any equipment. (b)A single line shall strike through the data being changed; the correct information shall be recorded along with the old data and the reason of change. The analyst making the change shall be identified by his signature with date. In case of automated data collection system, the person responsible shall be identified at the time of data output. The original entry must be saved and the system have audit trial for all the data.

(c)Data integrity and security shall be maintained and the data shall not be accessible to any unauthorised person.

16.Storage and archival.-

(a)The residual sample shall be retained in proper storage condition for a period of one year after the final report.

(b)The laboratory must establish and maintain procedures for the identification collection, indexing, retrieval, storage, maintenance, and disposal of all quality documents.

(c)All the raw data, documentation, Standard Operating Procedures, protocols, and final reports are to be retained and there shall be archives for orderly storage and expeditious retrieval of all raw data, documentation, protocols, interim and final report. The archive shall provide a suitable environment that will prevent modification, damage, or deterioration and/or loss.

(d)The condition under which the original documents are stored must ensure their security and confidentiality,

(e)Paper documents shall not be kept for long periods under high humidity and raw data in the form of tape and discs are to be preserved with care,

(f)In case of storage of only optical disc, the life of disc shall be longer than the storage time,

(g)Raw data on thermal paper might fade away with time; therefore, a photocopy of the thermal paper shall also be retained in the archive.

(h)Time for which records are retained shall be prescribed in the documents.

[1][SCHEDULE M

(*See* Rules 71, 74, 76 and 78)

GOOD MANUFACTURING PRACTICES AND REQUIREMENTS OF PREMISES, PLANT AND EQUIPMENT FOR PHARMACEUTICAL PRODUCTS

Note: *To achieve the objectives listed below, each licensee shall evolve appropriate methodology, systems and procedures which shall be documented and maintained for inspection and reference; and the manufacturing premises shall be used exclusively for production of drugs* [2][*and no other manufacturing activity shall be undertaken therein except in respect of units licensed prior to 11th December, 2001*].

PART 1

GOOD MANUFACTURING PRACTICES FOR PREMISES AND MATERIALS

1 GENERAL REQUIREMENTS:

1.1. *Location and surroundings.*- The factory building(s) for manufacture of drugs shall be so situated and shall have such measures as to avoid risk of contamination from external environment including open sewage, drain, public lavatory or any factory which produce disagreeable or obnoxious odour or fumes, excessive soot, dust, smoke, chemical or biological emissions.

1.2. *Buildings and premises.*- The building(s) used for the factory shall be designed, constructed, adapted and maintained to suit the manufacturing operations so as to permit production of drugs under hygienic conditions. They shall conform to the conditions laid down in the Factories Act, 1948 (63 of 1948).

The premises used for manufacturing, processing, warehousing, packaging, labelling and testing purposes shall be –

(i) compatible with other drug manufacturing operations that may be carried out in the same or adjacent area / section;

(ii) adequately provided with working space to allow orderly and logical placement of equipment, materials and movement of personnel so as to:

(a) avoid the risk of mix-up between different categories of drugs or with raw materials, intermediates and in-process material;

(b) avoid the possibilities of contamination and cross- contamination by providing suitable mechanism;

(iii) designed / constructed / maintained to prevent entry of insects, pests, birds, vermins and rodents. Interior surface (walls, floors and ceilings) shall be smooth and free from cracks, and permit easy cleaning, painting and disinfection;

1. Subs. by G.S.R. 894(E) , dt. 11.12.2001.- applicable to manufacturers licensed to manufacture drugs, for the period up to 31.12.2003.

2. Subs. by Act 431(E), dt. 30.6.2005.

(iv) air-conditioned, where prescribed for the operations and dosage forms under production. The production and dispensing areas shall be well lighted, effectively ventilated, with air control facilities and may have proper Air Handling Units (wherever applicable) to maintain conditions including temperature and, wherever necessary, humidity, as defined for the relevant product. These conditions shall be appropriate to the category of drugs and nature of the operation. These shall also be suitable to the comforts of the personnel working with protective clothing, products handled, operations undertaken within them in relation to the external environment. These areas shall be regularly monitored for compliance with required specifications;

(v) provided with drainage system, as specified for the various categories of products, which shall be of adequate size and so designed as to prevent back- flow and/or prevent insects and rodents entering the premises. Open channels shall be avoided in manufacturing areas and, where provided, these shall be shallow to facilitate cleaning and disinfection;

(vi) the walls and floors of the areas where manufacture of drugs is carried out shall be free from cracks and open joints to avoid accumulation of dust. These shall be smooth, washable, coved and shall permit easy and effective cleaning and disinfection. The interior surfaces shall not shed particles. A periodical record of cleaning and painting of the premises shall be maintained.

1.3 *Water System.* - There shall be validt. system for treatment of water drawn from own or any other source to render it potable in accordance with standards specified by the Bureau of Indian Standards or Local Municipality, as the case may be, so as to produce Purified Water conforming to Pharmacopoeial specification. Purified Water so produced shall only be used for all the operations except washing and cleaning operations where potable water may be used. Water shall be stored in tanks, which do not adversely affect quality of water and ensure freedom from microbiological growth. The tank shall be cleaned periodically and records maintained by the licensee in this behalf.

1.4. *Disposal of waste.* -

(i) The disposal of sewage and effluents (solid, liquid and gas) from the manufactory shall be in conformity with the requirements of Environment Pollution Control Board.

(ii) All bio-medical waste shall be destroyed as per the provisions of the Bio-Medical Waste (Management and Handling) Rules, 1996.

(iii) Additional precautions shall be taken for the storage and disposal of rejected drugs. Records shall be maintained for all disposal of waste.

(iv) Provisions shall be made for the proper and safe storage of waste materials awaiting disposal. Hazardous, toxic substances and flammable materials shall be stored in suitably designed and segregated, enclosed areas in conformity with Central and State Legislations.

2. ***Warehousing Area****:*

2.1 Adequate areas shall be designed to allow sufficient and orderly warehousing of various categories of materials and products like starting and packaging materials, intermediates, bulk and finished products, products in quarantine, released, rejected, returned or recalled, machine and equipment spare parts and change items.

2.2 Warehousing areas shall be designed and adapted to ensure good storage conditions. They shall be clean, dry and maintained with acceptable temperature limits. Where special storage conditions are required (e.g. temperature, humidity), these shall be provided, monitored and recorded. Storage areas shall have appropriate house-keeping and rodent, pests and vermin control procedures and records maintained. Proper racks, bins and platforms shall be provided for the storage of materials.

2.3 Receiving and dispatch bays shall protect materials and products from adverse weather conditions.

2.4. Where quarantine status is ensured by warehousing in separate earmarked areas in the same warehouse or store, these areas shall be clearly demarcated. Any system replacing the physical quarantine, shall give equivalent assurance of segregation. Access to these areas shall be restricted to authorized persons.

2.5. There shall be a separate sampling area in the warehousing area for active raw materials and excipients. If sampling is performed in any other area, it shall be conducted in such a way as to prevent contamination, cross-contamination and mix-up.

2.6. Segregation shall be provided for the storage of rejected, recalled or returned materials or products. Such areas, materials or products shall be suitably marked and secured. Access to these areas and materials shall be restricted.

2.7. Highly hazardous, poisonous and explosive materials such as narcotics, psychotropic drugs and substances presenting potential risks of abuse, fire or explosion shall be stored in safe and secure areas. Adequate fire protection measures shall be provided in conformity with the rules of the concerned civic authority.

2.8. Printed packaging materials shall be stored in safe, separate and secure areas.

2.9. Separate dispensing areas for β (Beta) lactum, Sex Hormones and Cytotoxic substances or any such special categories of product shall be provided with proper supply of filtered air and suitable measures for dust control to avoid contamination. Such areas shall be under differential pressure.

2.10. Sampling and dispensing of sterile materials shall be conducted under aseptic conditions conforming to Grade A, which can also be performed in a dedicated area within the manufacturing facility.

2.11. Regular checks shall be made to ensure adequate steps are taken against spillage, breakage and leakage of containers.

2.12. Rodent treatments (Pest control) should be done regularly and at least once in a year and record maintained.

3. ***Production area:***

3.1. The production area shall be designed to allow the production preferably in uni-flow and with logical sequence of operations.

3.2. In order to avoid the risk of corss-contamination, separate dedicated and self-contained facilities shall be made available for the production of sensitive pharmaceutical products like penicillin or biological preparations with live micro-organisms. Separate

dedicated facilities shall be provided for the manufacture of contamination causing and potent products such as Beta-Lactum, Sex Hormones and Cytotoxic substances.

3.3. Working and in-process space shall be adequate to permit orderly and logical positioning of equipment and materials and movement of personnel to avoid cross- contamination and to minimize risk of omission or wrong application of any manufacturing and control measures.

3.4. Pipe-work, electrical fittings, ventilation openings and similar service lines shall be designed, fixed and constructed to avoid [1][accumulation of dust]. Service lines shall preferably be identified by colours and the nature of the supply and direction of the flow shall be marked/indicated.

4. ***Ancillary Areas:***

4.1 Rest and refreshment rooms shall be separate from other areas. These areas shall not lead directly to the manufacturing and storage areas.

4.2 Facilities for changing, storing clothes and for washing and toilet purposes shall be easily accessible and adequate for the number of users. Toilets, separate for males and females, shall not be directly connected with production or storage areas. There shall be written instructions for cleaning and disinfection of such areas.

4.3 Maintenance workshops shall be separate and away from production areas. Whenever spares, changed parts and tools are stored in the production area, these shall be kept in dedicated rooms or lockers. Tools and spare parts for use in sterile areas shall be disinfected before these are carried inside the production areas.

4.4. Areas housing animals shall be isolated from other areas. The other requirements regarding animal houses shall be those as prescribed in rule 150-C(3) of the Drugs and Cosmetics Rules, 1945 which shall be adopted for production purposes.

5. ***Quality Control Area.***

5.1. Quality Control Laboratories shall be independent of the production areas. Separate areas shall be provided each for physico-chemical, biological, microbiological or radio-isotope analysis. Separate instrument room with adequate area shall be provided for sensitive and sophisticated instruments employed for analysis.

5.2 Quality Control Laboratories shall be designed appropriately for the operations to be carried out in them. Adequate space shall be provided to avoid mix-ups and cross-contamination. Sufficient and suitable storage space shall be provided for test samples, retained samples, reference standards, reagents and records.

5.3. The design of the laboratory shall take into account the suitability of construction materials and ventilation. Separate air handling units and other requirements shall be provided for biological, microbiological and radioisotopes testing areas. The laboratory shall be provided with regular supply of water of appropriate quality for cleaning and testing purposes.

5.4. Quality Control Laboratory shall be divided into separate sections i.e. for chemical, microbiological and wherever required, biological testing. These shall have adequate area for basic installation and for ancillary purposes. The microbiology section shall have arrangements such as airlocks and laminar air flow work station, wherever considered necessary.

1. Subs. by G.S.R. 431(E), dt. 30.6.2005.

6. ***Personnel:***

6.1. The manufacture shall be conducted under the direct supervision of competent technical staff with prescribed qualifications and practical experience in the relevant dosage form and / or active pharmaceutical products.

6.2 The head of the Quality Control Laboratory shall be independent of the manufacturing unit. The testing shall be conducted under the direct supervision of competent technical staff who shall be whole time employees of the licensee.

6.3. Personnel for Quality Assurance and Quality Control operations shall be suitably qualified and experienced.

6.4. Written duties of technical and Quality Control personnel shall be laid and followed strictly.

6.5. Number of personnel employed shall be adequate and in direct proportion to the workload.

6.6. The licensee shall ensure in accordance with a written instruction that all personnel in production area or into Quality Control Laboratories shall receive training appropriate to the duties and responsibility assigned to them. They shall be provided with regular in-service training.

7. ***Health, clothing and sanitation of workers****:*

7.1 The personnel handling Beta-lactum antibiotics shall be tested for Penicillin sensitivity before employment and those handling sex hormones, cytotoxic substances and other potent drugs shall be periodically examined for adverse effects. These personnel should be moved out of these sections (except in dedicated facilities), by rotation, as a health safeguard.

7.2 Prior to employment, all personnel, shall undergo medical examination including eye examination, and shall be free from Tuberculosis, skin and other communicable or contagious diseases. Thereafter, they should be medically examined periodically, at least once a year. Records shall be maintained thereof. The licensee shall provide the services of a qualified physician for assessing the health status of personnel involved in different activities.

7.3 All persons prior to and during employment shall be trained in practices which ensure personnel hygiene. A high level of personal hygiene shall be observed by all those engaged in the manufacturing processes. Instructions to this effect shall be displayed in change- rooms and other strategic locations.

7.4 No person showing, at any time, apparent illness or open lesions which may adversely affect the quality of products, shall be allowed to handle starting materials, packaging materials, in-process materials, and drug products until his condition is no longer judged to be a risk.

7.5 All employees shall be instructed to report about their illness or abnormal health condition to their immediate supervisor so that appropriate action can be taken.

7.6 Direct contact shall be avoided between the unprotected hands of personnel and raw materials, intermediate or finished, unpacked products.

7.7 All personnel shall wear clean body coverings appropriate to their duties. Before entry into the manufacturing area, there shall be change rooms separate for each sex

with adequate facilities for personal cleanliness such as wash basin with running water, [1][clean towels or hand dryers], soaps, disinfectants, etc. The change rooms shall be provided with cabinets for the storage of personal belongings of the personnel.

7.8 Smoking, eating, drinking, chewing or keeping plants, food, drink and personal medicines shall not be permitted in production, laboratory, storage and other areas where they might adversely influence the product quality.

8. ***Manufacturing Operations and Control:***

8.1 All manufacturing operations shall be carried out under the supervision of technical staff approved by the Licensing Authority. Each critical step in the process relating to the selection, weighing and measuring of raw material addition during various stages shall be performed by trained personnel under the direct personal supervision of approved technical staff.

The contents of all vessels and containers used in manufacture and storage during the various manufacturing stages shall be conspicuously labelled with the name of the product, batch number, batch size and stage of manufacture. Each label should be initialled and dt. by the authorised technical staff.

Products not prepared under aseptic conditions are required to be free from pathogens like *Salmonella, Escherichia coli, Pyocyanea, etc.*

8.2. ***Precautions against mix-up and cross-contamination:***

8.2.1. The licensee shall prevent mix-up and cross-contamination of drug material and drug product (from environmental dust) by proper air-handling system, pressure differential, segregation, status labelling and cleaning. Proper records and Standard Operating Procedures thereof shall be maintained.

8.2.2 The licensee shall ensure processing of sensitive drugs like Beta-Lactum antibiotics, sex hormones and cytotoxic substances in segregated areas or isolated production areas within the building with independent air-handling unit and proper pressure differentials. [1][The effective segregation of these areas shall be validated with adequate records of maintenance and services].

8.2.3 To prevent mix-ups during production stages, material under process shall be conspicuously labelled to demonstrate their status. All equipment used for production shall be labelled with their current status.

8.2.4 Packaging lines shall be independent and adequately segregated. It shall be ensured that all left-overs of the previous packaging operations, including labels, cartons and caps are cleared before the closing hour.

8.2.5 Before packaging operations are begun, steps shall be taken to ensure that the work area, packaging lines, printing machines, and other equipment are clean and free from any

products, materials and spillages. The line clearance shall be performed according to an approximate check list and recorded.

8.2.6 The correct details of any printing (for example of batch numbers or expiry dates) done separately or in the course of the packaging shall be rechecked at regular intervals. All printing and overprinting shall be authorized in writing.

1. Subs. by G.S.R. 431(E), dt. 30.6.2005.

8.2.7 The manufacturing environment shall be maintained at the required levels of temperature, humidity and cleanliness.

8.2.8 Authorised persons shall ensure change-over into specific uniforms before undertaking any manufacturing operations including packaging.

8.2.9 [1][There shall be segregated secured areas for recalled or rejected material and for such material which are to be reprocessed or recovered.]

9. ***Sanitation in the Manufacturing Premises:***

9.1 The manufacturing premises shall be cleaned and maintained in an orderly manner, so that it is free from accumulated waste, dust, debris and other similar material. A validt. cleaning procedure shall be maintained.

9.2 The manufacturing areas shall not be used for storage of materials, except for the material being processed. It shall not be used as a general thoroughfare.

9.3 A routine sanitation program shall be drawn up and observed, which shall be properly recorded and which shall indicate–

(a) specific areas to be cleaned and cleaning intervals;

(b) cleaning procedure to be followed, including equipment and materials to be used for cleaning; and

(c) personnel assigned to and responsible for the cleaning operation.

9.4 The adequacy of the working and in-process storage space shall permit the orderly and logical positioning of equipment and materials so as to minimize the risk of mix- up between different pharmaceutical products or their components to avoid cross contamination, and to minimise the risk of omission or wrong application of any of the manufacturing or control steps.

9.5 Production areas shall be well lit, particularly where visual on-line controls are carried out.

10. ***Raw Materials:***

10.1 The licensee shall keep an inventory of all raw materials to be used at any stage of manufacture of drugs and maintain records as per Schedule U.

10.2 All incoming materials shall be quarantined immediately after receipt or processing. All materials shall be stored under appropriate conditions and in an orderly fashion to permit batch segregation and stock rotation by a ‗first in/first expiry' – ‗first-out' principle. All incoming materials shall be checked to ensure that the consignment corresponds to the order placed.

10.3 All incoming materials shall be purchased from approved sources under valid purchase vouchers. Wherever possible, raw materials should be purchased directly from the producers.

10.4 Authorized staff appointed by the licensee in this behalf, which may include personnel from the Quality Control Department, shall examine each consignment on receipt and shall check each container for integrity of package and seal. Damaged containers shall be identified, recorded and segregated.

1. Subs. by G.S.R. 431(E), dt. 30.6.2005.

10.5 If a single delivery of material is made up of different batches, each batch shall be considered as a separate batch for sampling, testing and release.

10.6 Raw materials in the storage area shall be appropriately labelled. Labels shall be clearly marked with the following information:

(a) designated name of the product and the internal code reference, where applicable, and analytical reference number;

(b) manufacturer‘s name, address and batch number;

(c) the status of the contents (e.g. quarantine, under test, released, approved, rejected); and

(d) the manufacturing date, expiry date and re-test date.

10.7 There shall be adequate separate areas for materials ―under test‖, ―approved‖ and ―rejected‖ with arrangements and equipment to allow dry, clean and orderly placement of stored materials and products, wherever necessary, under controlled temperature and humidity.

10.8 Containers from which samples have been drawn shall be identified.

10.9 Only raw materials which have been released by the Quality Control Department and which are within their shelf-life shall be used. It shall be ensured that shelf life of formulation product shall not exceed with that of active raw materials used.

10.10 It shall be ensured that all the containers of raw materials are placed on the raised platforms/racks and not placed directly on the floor.

11. ***Equipment:***

11.1 Equipment shall be located, designed, constructed, adapted and maintained to suit the operations to be carried out. The layout and design of the equipment shall aim to minimise the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination, build-up of dust or dirt and, in general, any adverse effect on the quality of products. Each equipment shall be provided with a logbook, wherever necessary.

11.2 Balances and other measuring equipment of an appropriate range, accuracy and precision shall be available in the raw material stores, production and in-process control operations and these shall be calibrated and checked on a scheduled basis in accordance with Standard Operating Procedures and records maintained.

11.3 The parts of the production equipment that come into contact with the product shall not be reactive, additive or adsorptive to an extent that would affect the quality of the product.

11.4 To avoid accidental contamination, wherever possible, non-toxic/edible grade lubricants shall be used and the equipment shall be maintained in a way that lubricants do not contaminate the products being produced.

11.5 Defective equipment shall be removed from production and Quality Control areas or appropriately labelled.

12. ***Documentation and Records:–*** Documentation is an essential part of the Quality assurance system and, as such, shall be related to all aspects of Good Manufacturing Practices (GMP). Its aim is to define the specifications for all materials, method of manufacture and control, to ensure that all personnel concerned with manufacture know the information necessary to decide whether or not to release a batch of a drug for sale and to provide an audit trail that shall permit investigation of the history of any suspected defective batch.

12.1 Documents designed, prepared, reviewed and controlled, wherever applicable, shall comply with these rules.

12.2 Documents shall be approved, signed and dt. by appropriate and authorized persons.

12.3 Documents shall specify the title, nature and purpose. They shall be laid out in an orderly fashion and be easy to check. Reproduced documents shall be clear and legible. Documents shall be regularly reviewed and kept up to date. Any alteration made in the entry of a document shall be signed and dt..

12.4 The records shall be made or completed at the time of each operation in such a way that all significant activities concerning the manufacture of pharmaceutical products are traceable. Records and associated Standard Operating Procedures (SOP) shall be retained for at least one year after the expiry date of the finished product.

12.5 Data may be recorded by electronic data processing systems or other reliable means, but Master Formulae and detailed operating procedures relating to the system in use shall also be available in a hard copy to facilitate checking of the accuracy of the records. Wherever documentation is handled by electronic data processing methods, authorized persons shall enter or modify data in the computer. There shall be record of changes and deletions. Access shall be restricted by ‗passwords' or other means and the result of entry of critical data shall be independently checked. Batch records electronically stored shall be protected by a suitable back-up. During the period of retention, all relevant data shall be readily available.

13. ***Labels and other Printed Materials***:– Labels are absolutely necessary for identification of the drugs and their use. The printing shall be done in bright colours and in a legible manner. The label shall carry all the prescribed details about the product.

13.1 All containers and equipment shall bear appropriate labels. Different colour coded labels shall be used to indicate the status of a product (for example under test, approved, passed, rejected).

13.2 To avoid chance mix-up of printed packaging materials, product leaflets, relating to different products, shall be stored separately.

13.3 Prior to release, all labels for containers, cartons and boxes and all circulars, inserts and leaflets shall be examined by the Quality Control Department of the licensee.

13.4 Prior to packaging and labelling of a given batch of a drug, it shall be ensured by the licensee that samples are drawn from the bulk and duly tested, approved and released by the quality control personnel.

13.5 Records of receipt of all labelling and packaging materials shall be maintained for each shipment received indicating receipt, control reference numbers and whether accepted or rejected. Unused coded and damaged labels and packaging materials shall be destroyed and recorded.

13.6 The label or accompanying document of reference standards and reference culture shall indicate concentration, lot number, potency, date on which containers was first opened and storage conditions, where appropriate.

14. ***Quality Assurance:–***This is a wide-ranging concept concerning all matters that individually or collectively influence the quality of a product. It is the totality of the arrangements made with the object of ensuring that products are of the quality required for their intended use.

14.1 The system of quality assurance appropriate to the manufacture of pharmaceutical products shall ensure that: –

(a) the pharmaceutical products are designed and developed in a way that takes account of the requirements of Good Manufacturing Practices (hereinafter referred as GMP) and other associated codes such as those of Good Laboratory Practices (hereinafter referred as GLP) and Good Clinical Practices (hereinafter referred as GCP);

(b) adequate arrangements are made for manufacture, supply and use of the correct starting and packaging materials.

(c) adequate controls on starting materials, intermediate products and bulk products and other in-process controls, calibrations, and validations are carried out.

(d) the finished product is correctly processed and checked in accordance with established procedures;

(e) the pharmaceutical products are not released for sale or supplied before authorized persons have certified that each production batch has been produced and controlled in accordance with the requirements of the label claim and any other provisions relevant to production, control and release of pharmaceutical products.

15. ***Self Inspection and Quality audit:–*** It may be useful to constitute a self-inspection team supplemented with a quality audit procedure for assessment of all or part of a system with the specific purpose of improving it.

15.1 To evaluate the manufacturer‘s compliance with GMP in all aspects of production and quality control, concept of self-inspection shall be followed. The manufacturer shall constitute a team of independent, experienced, qualified persons from within or outside the company, who can audit objectively the implementation of methodology and procedures evolved. The procedure for self-inspection shall be documented indicating self-inspection results, evaluation, conclusions and recommended corrective actions with effective follow up program. The recommendations for corrective action shall be adopted.

15.2 The program shall be designed to detect shortcomings in the implementation of Good Manufacturing Practice and to recommend the necessary corrective actions. Self-inspections shall be performed routinely and on specific occasions, like when product recalls or repeated rejections occur or when an inspection by the licensing authorities is announced. The team responsible for self-inspection shall consist of personnel who can evaluate the implementation of Good Manufacturing Practice objectively; all recommendations for corrective action shall be implemented.

15.3 Written instructions for self-inspection shall be drawn up which shall include the following: -

(a) Personnel.
(b) Premises including personnel facilities.
(c) Maintenance of buildings and equipment
(d) Storage of starting materials and finished products.
(e) Equipment.
(f) Production and in-process controls.
(g) Quality control.
(h) Documentation.
(i) Sanitation and hygiene.
(j) Validation and revalidation programmes.
(k) Calibration of instruments or measurement systems.
(l) Recall procedures.
(m) Complaints management.
(n) Labels control.
(o) Results of previous self-inspections and any corrective steps taken.

16. *Quality Control System.* - Quality control shall be concerned with sampling, specifications, testing, documentation, release procedures which ensure that the necessary and relevant tests are actually carried and that the materials are not released for use, nor products released for sale or supply until their quality has been judged to be satisfactory. It is not confined to laboratory operations but shall be involved in all decisions concerning the quality of the product. It shall be ensured that all quality control arrangements are effectively and reliably

carried out.The department as a whole shall have other duties such as to establish, evaluate, validate and implement all Quality Control Procedures and methods.

16.1 Every manufacturing establishment shall establish its own quality control laboratory manned by qualified and experienced staff.

16.2 The area of the quality control laboratory may be divided into Chemical, Instrumentation, Microbiological and Biological testing.

16.3 Adequate area having the required storage conditions shall be provided for keeping reference samples. The quality control department shall evaluate, maintain and store reference samples.

16.4 Standard operating procedures shall be available for sampling, inspecting and testing of raw materials, intermediate bulk finished products and packing materials and, wherever necessary, for monitoring environmental conditions.

16.5 There shall be authorized and dt. specifications for all materials, products, reagents and solvents including test of identity, content, purity and quality. These shall include specifications for water, solvents and reagents used in analysis.

16.6 No batch of the product shall be released for sale or supply until it has been certified by the authorized person(s) that it is in accordance with the requirements of the standards laid down.

16.7 Reference/retained samples from each batch of the products manufactured shall be maintained in quantity which is at least twice the quantity of the drug required to conduct all the tests, except sterility and pyrogen/Bacterial Endotoxin Test performed on the active material and the product manufactured. The retained product shall be kept in its final pack or simulated pack for a period of three months after the date of expiry.

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16.8 Assessment of records pertaining to finished products shall include all relevant factors, including the production conditions, the results of in-process testing, the manufacturing (including packaging) documentation, compliance with the specification for the finished product, and an examination of the finished pack. Assessment records should be signed by the in-charge of production and countersigned by the authorised quality control personnel before a product is released for sale or distribution.

16.9 Quality control personnel shall have access to production areas for sampling and investigation, as appropriate.

16.10 The quality control department shall conduct stability studies of the products to ensure and assign their shell life at the prescribed conditions of storage. All records of such studies shall be maintained.

16.11 The in-charge of Quality Assurance shall investigate all product complaints and records thereof shall be maintained.

16.12 All instruments shall be calibrated and testing procedures validt. before these are adopted for routine testing. Periodical calibration of instrument and validation of procedures shall be carried out.

16.13 Each specification for raw materials, intermediates, final products, and packing materials shall be approved and maintained by the Quality Control Department.

Periodic revisions of the specifications shall be carried out whenever changes are necessary.

16.14 Pharmacopoeia, reference standards, working standards, references, spectra, other reference materials and technical books, as required, shall be available in the Quality Control Laboratory of the licensee.

17. *Specification*

17.1 *For raw materials and packaging materials.* - They shall include-

(a) the designated name and internal code reference;
(b) reference, if any, to a pharmacopoeial monograph;
(c) qualitative and quantitative requirements with acceptance limits;
(d) name and address of manufacturer or supplier and original manufacturer of the material;
(e) specimen of printed material;
(f) directions for sampling and testing or reference to procedures;
(g) storage conditions; and
(h) maximum period of storage before re-testing.

17.2 *For product containers and closures:–*

17.2.1 All containers and closures intended for use shall comply with the pharmacopoeial requirements. Suitable validt. test methods, sample sizes, specifications, cleaning procedure and sterilization procedure, wherever indicated, shall be strictly followed to ensure that these are not reactive, additive, absorptive, or leach to an extent that significantly affects the quality or purity of the drug. No second hand or used containers and closures shall be used.

17.2.2 Whenever bottles are being used, the written schedule of cleaning shall be laid down and followed. Where bottles are not dried after washing, they should be rinsed with de-ionised water or distilled water, as the case may be.

17.3. *For in-process and bulk products.* - Specifications for in-process material, intermediate and bulk products shall be available. The specifications should be authenticated.

17.4 *For finished products.* - Appropriate specifications for finished products shall include: -

(a) the designated name of the product and the code reference;
(b) the formula or a reference to the formula and the pharmacopoeial reference;
(c) directions for sampling and testing or a reference to procedures;
(d) a description of the dosage form and package details;
(e) the qualitative and quantitative requirements, with the acceptance limits for release;
(f) the storage conditions and precautions, where applicable, and
(g) the shelf-life.

17.5 *For preparation of containers and closures.* - The requirements mentioned in the Schedule do not include requirements of machinery, equipments and premises required for preparation of containers and closures for different dosage forms and categories of drugs. The suitability and adequacy of the machinery, equipment and premises shall be examined taking into consideration the requirements of each licensee in this respect.

18. ***Master Formula Records:***

There shall be Master Formula records relating to all manufacturing procedures for each product and batch size to be manufactured. These shall be prepared and endorsed by the competent technical staff i.e. head of production and quality control. The Master Formula shall include: -

(a) the name of the product together with product reference code relating to its specifications;
(b) the patent or proprietary name of the product along with the generic name, a description of the dosage form, strength, composition of the product and batch size;
(c) name, quantity, and reference number of all the starting materials to be used. Mention shall be made of any substance that may ‗disappear' in the course of processing.
(d) a statement of the expected final yield with the acceptable limits, and of relevant intermediate yields, where applicable.

(e) a statement of the processing location and the principal equipment to be used. (f) the methods, or reference to the methods, to be used for preparing the critical equipments including cleaning, assembling, calibrating, sterilizing;

(g) detailed stepwise processing instructions and the time taken for each step;

(h) the instructions for in-process control with their limits;

(i) the requirements for storage conditions of the products, including the container, labelling and special storage conditions where applicable;

(j) any special precautions to be observed;

(k) packing details and specimen labels.

19. ***Packing Records:***

There shall be authorised packaging instructions for each product, pack size and type. These shall include or have a reference to the following: -

(a) name of the product;

(b) description of the dosage form, strength and composition;

(c) the pack size expressed in terms of the number of doses, weight or volume of the product in the final container;

(d) complete list of all the packaging materials required for a standard batch size, including quantities, sizes and types with the code or reference number relating to the specifications of each packaging material.;

(e) reproduction of the relevant printed packaging materials and specimens indicating where batch number and expiry date of the product have been applied;

(f) special precautions to be observed, including a careful examination of the area and equipment in order to ascertain the line clearance before the operations begin.

(g) description of the packaging operation, including any significant subsidiary operations and equipment to be used;

(h) details of in-process controls with instructions for sampling and acceptance; and (i) upon completion of the packing and labelling operation, a reconciliation shall be made between number of labelling and packaging units issued, number of units labelled, packed and excess returned or destroyed. Any significant or unusual discrepancy in the numbers shall be carefully investigated before releasing the final batch.

20. ***Batch Packaging Records:***

20.1 A batch packaging record shall be kept for each batch or part batch processed. It shall be based on the relevant parts of the packaging instructions, and the method of preparation of such records shall be designed to avoid transcription errors.

20.2 Before any packaging operation begins, check shall be made and recorded that the equipment and the work stations are clear of the previous products, documents or materials not required for the planned packaging operations, and that the equipment is clean and suitable for use.

21. ***Batch Processing Records***

21.1 There shall be Batch Processing Record for each product. It shall be based on the relevant parts of the currently approved Master Formula. The method of preparation of such records included in the Master Formula shall be designed to avoid transcription errors.

21.2 Before any processing begins, check shall be performed and recorded to ensure that the equipment and work station are clear of previous products, documents or materials not required for the planned process are removed and the equipment is clean and suitable for use.

21.3 During processing, the following information shall be recorded at the time each action is taken and the record shall be dt. and signed by the person responsible for the processing operations: -

(a) the name of the product,
(b) the number of the batch being manufactured,
(c) dates and time of commencement, of significant intermediate stages and of completion of production,
(d) initials of the operator of different significant steps of production and where appropriate, of the person who checked each of these operations,
(e) the batch number and/or analytical control number as well as the quantities of each starting material actually weighed,
(f) any relevant processing operation or event and major equipment used,
(g) a record of the in-process controls and the initials of the person(s) carrying them out, and the results obtained,

(h) the amount of product obtained after different and critical stages of manufacture (yield),
(i) comments or explanations for significant deviations from the expected yield limits shall be given,
(j) notes on special problems including details, with signed authorization, for any deviation from the Master Formula,
(k) addition of any recovered or reprocessed material with reference to recovery or reprocessing stages.

22. ***Standard Operating Procedures (SOPs) and Records, regarding:***

22.1 Receipt of materials:

22.1.1 There shall be written Standard Operating Procedures and records for the receipt of each delivery of raw, primary and printed packaging material.

22.1.2 The records of the receipts shall include;

(a) the name of the material on the delivery note and the number of containers;
(b) the date of receipt;
(c) the manufacturer‘s and/ or supplier‘s name;
(d) the manufacturer‘s batch or reference number;
(e) the total quantity, and number of containers, quantity in each container received;
(f) the control reference number assigned after receipt;
(g) any other relevant comment or information.

22.1.3 There shall be written standard operating procedures for the internal labelling, quarantine and storage of starting materials, packaging materials and other materials, as appropriate.

22.1.4 There shall be Standard Operating Procedures available for each instrument and equipment and these shall be placed in close proximity to the related instrument and equipment.

22.2 ***Sampling:***

22.2.1 There shall be written Standard Operating Procedures for sampling which include the person(s) authorized to take the samples.

22.2.2 The sampling instructions shall include:

(a) the method of sampling and the sampling plan,
(b) the equipment to be used,
(c) any precautions to be observed to avoid contamination of the material or

any deterioration in its quality,

(d) the quantity of samples to be taken,

(e) instructions for any required sub-division or pooling of the samples,

(f) the types of sample container to be used,

(g) any specific precautions to be observed, especially in regard to sampling of sterile and hazardous materials.

22.3. *Batch Numbering:*

22.3.1 There shall be Standard Operating Procedures describing the details of the batch

(lot) numbering set up with the objective of ensuring that each batch of intermediate, bulk or finished product is identified with a specific batch number.

22.3.2 Batch numbering Standard Operating Procedures applied to a processing stage and to the respective packaging stage shall be same or traceable to demonstrate that they belong to one homogenous mix.

22.3.3 Batch number allocation shall be immediately recorded in a logbook or by electronic data processing system. The record shall include date of allocation, product identity and size of batch.

22.4. *Testing:*

22.4.1 There shall be written procedures for testing materials and products at different stages of manufacture, describing the methods and equipment to be used. The tests performed shall be recorded.

22.5 *Records of analysis:*

22.5.1 The records shall include the following data:

(a) name of the material or product and the dosage form,

(b) batch number and, where appropriate the manufacturer and/ or supplier,

(c) references to the relevant specifications and testing procedures,

(d) test results, including observations and calculations, and reference to any specifications (limits),

(e) dates of testing,

(f) initials of the persons who performed the testing,

(g) initials of the persons who verified the testing and the detailed calculations,

(h) a statement of release or rejection, and

(i) signature and date of the designated responsible person.

22.5.2 There shall be written standard operating procedures and the associated records of actions taken for:

(a) equipment assembly and validation

(b) analytical apparatus and calibration,

(c) maintenance, cleaning and sanitation;

(d) personnel matters including qualification, training, clothing, hygiene; (e) environmental monitoring;

(f) pest control;

(g) complaints;

(h) recalls made; and

(i) returns received.

23. *Reference Samples*:-

23.1 Each lot of every active ingredient, in a quantity sufficient to carry out all the tests, except sterility and pyrogens/Bacterial Endotoxin Test, shall be retained for a

period of 3 months after the date of expiry of the last batch produced from that active ingredient.

23.2. Samples of finished formulations shall be stored in the same or simulated containers in which the drug has been actually marketed.

24. ***Reprocessing and Recoveries:***

24.1. Where reprocessing is necessary, written procedures shall be established and approved by the Quality Assurance Department that shall specify the conditions and limitations of repeating chemical reactions. Such reprocessing shall be validt..

24.2. If the product batch has to be reprocessed, the procedure shall be authorized and recorded. An investigation shall be carried out into the causes necessitating re- processing and appropriate corrective measures shall be taken for prevention of recurrence. Re-processed batch shall be subjected to stability evaluation.

24.3. Recovery of the product residue may be carried out, if permitted, in the master production and control records by incorporating it in subsequent batches of the product.

25. ***Distribution records:***

25.1. Prior to distribution or dispatch of given batch of a drug, it shall be ensured that the batch has been duly tested, approved and released by the quality control personnel. Pre-dispatch inspection shall be performed on each consignment on a random basis to ensure that only the correct goods are dispatched. Detailed instructions for warehousing and stocking of Large Volume Parenterals, if stocked, shall be in existence and shall be complied with after the batch is released for distribution. Periodic audits of warehousing practices followed at distribution centers shall be carried out and records thereof shall be maintained. Standard Operating Procedures shall be developed for warehousing of products.

25.2. Records for distribution shall be maintained in a manner [1][so as] to facilitate prompt and complete recall of the batch, if and when necessary.

26. ***Validation and process validation:***

26.1. Validation studies shall be an essential part of Good Manufacturing Practices and shall be conducted as per the pre-defined protocols. These shall include validation of processing, testing and cleaning procedures.

26.2. A written report summarizing recorded results and conclusions shall be prepared, documented and maintained.

26.3. Processes and procedures shall be established on the basis of validation study and undergo periodic revalidation to ensure that they remain capable of achieving the intended results. Critical processes shall be validt., prospectively or retrospectively.

26.4. When any new Master Formula or method of preparation is adopted, steps shall be taken to demonstrate its suitability for routine processing. The defined process, using the materials and equipment specified shall be demonstrated to yield a product consistently of the required quality.

26.5. Significant changes to the manufacturing process, including any change in equipment or materials that may affect product quality and/or the reproducibility of the process, shall be validt..

1. Subs. by G.S.R. 431(E), dt. 30.6.2005. for ― such that finished batch of a drug can be traced to the retail level‖.

27. ***Product Recalls:***

27.1 A prompt and effective product recall system of defective products shall be devised for timely information of all concerned stockists, wholesalers, suppliers, upto the retail level within the shortest period. The licensee may make use of both print and electronic media in this regard.

27.2. There shall be an established written procedure in the form of Standard Operating Procedure for effective recall of products distributed by the licensee. Recall operations shall be capable of being initiated promptly so as to effectively reach at the level of each distribution channel.

27.3 The distribution records shall be readily made available to the persons designated for recalls.

27.4 The designated person shall record a final report issued, including reconciliation between the delivered and the recovered quantities of the products.

27.5 The effectiveness of the arrangements for recalls shall be evaluated from time to time.

27.6 The recalled products shall be stored separately in a secured segregated area pending final decision on them.

28. ***Complaints and Adverse Reactions:.***

28.1 All complaints thereof concerning product quality shall be carefully reviewed and recorded according to written procedures. Each complaint shall be investigated/evaluated by the designated personnel of the company and records of investigation and remedial action taken thereof shall be maintained.

28.2. Reports of serious adverse drug reactions resulting from the use of a drug along with comments and documents shall be forthwith reported to the concerned licensing authority.

28.3 There shall be written procedures describing the action to be taken, recall to be made of the defective product.

29. ***Site Master File.*** –The licensee shall prepare a succinct document in the form of _Site Master File‘ containing specific and factual Good Manufacturing Practices about the production and/or control of pharmaceutical manufacturing preparations carried out at the licensed premises. It shall contain the following: -

29.1 ***General information:***

(a) brief information of the firm;
(b) pharmaceutical manufacturing activities as permitted by the licensing authority;
(c) other manufacturing activities, if any, carried out on the premises;
(d) type of products licensed for manufacture with flow charts mentioning procedure and process flow;
(e) number of employees engaged in the production, quality control, storage and distribution;
(f) use of outside scientific, analytical or other technical assistance in relation to manufacture and analysis;
(g) short description of the Quality Management System of the firm; and
(h) products details registered with foreign countries.

29.2 ***Personnel:***

(a) organisational chart showing the arrangement for quality assurance including production and quality control;
(b) qualification, experience and responsibilities of key personnel;

(c) outline for arrangements for basic and in-service training and how the records are maintained;

(d) health requirements for personnel engaged in production; and

(e) personnel hygiene requirements, including clothing.

29.3 ***Premises:***

(a) simple plan or description of manufacturing areas drawn to scale;

(b) nature of construction and fixtures/fittings;

(c) brief description of ventilation systems. More details should be given for critical areas with potential risk of airborne contamination (schematic drawing of systems). Classification of the rooms used for the manufacture of sterile products should be mentioned;

(d) special areas for the handling of the highly toxic, hazardous and sensitizing materials;

(e) brief description of water system (schematic drawings of systems), including sanitation;

(f) description of planned preventive maintenance programs for premises and of the recording system.

29.4 ***Equipment:***

(a) brief description of major equipment used in production and Quality Control Laboratories (a list of equipment required);

(b) description of planned preventive maintenance programs for equipment and of the recording system; and

(c) qualification and calibration including the recording systems and arrangements for computerized systems validation.

Sanitation:

29.5

(a) availability of written specifications and procedures for cleaning manufacturing areas and equipment.

29.6 ***Documentation. -***

(a) arrangements for the preparation, revision and distribution of;

(b) necessary documentation for the manufacture;

(c) any other documentation related to product quality that is not mentioned elsewhere (e.g. microbiological controls about air and water).

29.7 ***Production*:.**

(a) brief description of production operations using, wherever possible, flow sheets and charts specifying important parameters;

(b) arrangements for the handling of starting materials, packaging materials, bulk and

finished products, including sampling, quarantine, release and storage;

(c) arrangements for the handling of rejected materials and products;

(d) brief description of general policy for process validation.

29.8 ***Quality Control:***

(a) description of the quality control system and of the activities of the Quality Control Department. Procedures for the release of the finished products.

29.9 ***Loan licence manufacture and licensee*:**

(a) description of the way in which compliance of Good Manufacturing Practices by the loan licensee shall be assessed.

29.10 ***Distribution, complaints and product recall:***

(a) arrangements and recording system for distribution;

(b) arrangements for the handling of complaints and product recalls.

29.11 *Self inspection.* -

(a) short description of the self-inspection system indicating whether an outside, independent and experienced external expert was involved in evaluating the manufacturer‘s compliance with Good manufacturing Practices in all aspects of production.

29.12 ***Export of drugs.*** **-**

(a) products exported to different countries;

(b) complaints and product recall, if any.

PART IA

SPECIFIC REQUIREMENTS FOR MANUFACTURE OF STERILE PRODUCTS, PARENTERAL PREPARATIONS (SMALL VOLUME INJECTABLES AND LARGE VOLUME PARENTERALS) AND STERILE OPHTHALMIC PREPARATIONS.

Note. - The general requirements as given in Part 1 of this Schedule relating to Requirements of Good Manufacturing Practices for Premises and Materials for pharmaceutical products shall be complied with, *mutatis mutandis*, for the manufacture of sterile products, Parenteral preparations (Small Volume Injectables and Large Volume Parenterals) and Sterile Ophthalmic Preparations. In addition to these requirements, the following specific requirements shall also be followed, namely: -

1. ***General :***

Sterile products, being very critical and sensitive in nature, a very high degree of precautions, prevention and preparations are needed. Dampness, dirt and darkness are to be avoided to ensure aseptic conditions in all areas. There shall be strict compliance in the prescribed standards especially in the matter of supply of water, air, active materials and in the maintenance of hygienic environment.

2. ***Buildings and Civil Works:***

2.1 The buildings shall be built on proper foundation with standardized materials to avoid cracks in critical areas like aseptic solution preparation, filling and sealing rooms.

2.2 Location of services like water, steam, gases etc. shall be such that their servicing or repair shall not pose any threat to the integrity of the facility. Water lines shall not pose any threat of leakage to aseptic area.

2.3. The manufacturing areas shall be clearly separated into support areas (e.g. washing and component preparation areas, storage areas etc.), preparation areas (e.g. bulk manufacturing area, non-aseptic blending areas etc.) change areas and aseptic areas. Operations like removal of outer cardboard wrappings of primary packaging materials shall be done in the de-cartoning areas which are segregated from the washing areas. Wooden pallets, fiber board drums, cardboard and other particle shedding materials shall not be taken inside the preparation areas.

2.4. In aseptic areas –

(a) walls, floors and ceiling should be impervious, non-shedding, non-flaking and non-cracking. Flooring should be unbroken and provided with a cove both at the junction between the wall and the floor as well as the wall and the ceiling.

(b) walls shall be flat, and ledges and recesses shall be avoided. Wherever other surfaces join the wall (e,g, sterilizers, electric sockets, gas points etc.) these shall flush the walls. Walls shall be provided with a cove at the joint between the ceiling and the floor;

(c) ceiling shall be solid and joints shall be sealed. Light-fittings and air-grills shall flush with the walls and not hanging from the ceiling, so as to prevent contamination;

(d) there shall be no sinks and drains in Grade A and Grade B areas;

(e) doors shall be made of non-shedding material. These may be made preferably of Aluminium or Steel material. Wooden doors shall not be used. Doors shall open towards the higher-pressure area so that they close automatically due to air pressure;

(f) Windows shall be made of similar material as the doors, preferably with double panel and shall be flush with the walls. If fire escapes are to be provided, these shall be suitably fastened to the walls without any gaps;

(g) The furniture used shall be smooth, washable and made of stainless steel or any other appropriate material other than wood.

2.5. The manufacturing and support areas shall have the same quality of civil structure described above for aseptic areas, except the environmental standards which may vary in the critical areas.

2.6 Change rooms with entrance in the form of air-locks shall be provided before entry into the sterile product manufacturing areas and then to the aseptic area. Separate exit space from the aseptic areas is advisable. Change rooms to the aseptic areas shall be clearly demarcated into _black‘. _grey‘, and _white rooms‘ with different levels of activity and air cleanliness. The _black‘ change room shall be provided with a hand-washing sink. The sink

and its drain in the un-classified (first) change rooms may be kept clean all the time. The specially designed drain shall be periodically monitored to avoid presence of pathogenic micro-organisms. Change room doors shall not be opened simultaneously. An appropriate inter-locking system and a visual and/or audible warning system may be installed to prevent the opening of more than one door at a time.

2.7. For communication between aseptic areas and non-aseptic areas, intercom telephones or speak-phones shall be used. These shall be minimum in number.

2.8 Material transfer between aseptic areas and outside shall be through suitable airlocks or pass-boxes. Doors of such airlocks and pass-boxes shall have suitable interlocking arrangements.

2.9. Personal welfare areas like rest rooms, tea room, canteen and toilets shall be outside and separated from the sterile product manufacturing area.

2.10 Animal houses shall be away from the sterile product manufacturing area and shall not share a common entrance or air handling system with the manufacturing area.

3. ***Air Handling System (Central Air-Conditioning):***

3.1 Air Handling Units for sterile product manufacturing areas shall be different from those for other areas. Critical areas, such as the aseptic filling area, sterilized components unloading area and change room conforming to Grades B, C and D respectively shall have separate air handling units. The filter configuration in the air handling system shall be suitably designed to achieve the Grade of air as given in Table1. Typical operational activities for clean areas are highlighted in Table II and Table III.

3.2 For products which are filled aseptically, the filling room shall meet Grade B conditions at rest unmanned. This condition shall also be obtained within a period of about 30 minutes of the personnel leaving the room after completion of operations.

3.3. The filling operations shall take place under Grade A conditions which shall be demonstrated under working of simulated conditions which shall be achieved by providing laminar air flow work stations with suitable HEPA filters or isolator technology.

3.4. For products, which are terminally sterilized, the filling room shall meet Grade C conditions at rest. This condition shall be obtainable within a period of about 30 minutes of the personnel leaving the room after completion of operations.

3.5. Manufacturing and component preparation areas shall meet Grade C conditions.

3.6. After completion of preparation, washed components and vessels shall be protected with [1][Grade D background and should be handled in such a way that they are not recontaminated].

3.7. The minimum air changes for Grade B and Grade C areas shall not be less than 20 air changes per hour in a room with good air flow pattern and appropriate HEPA filters. For Grade A laminar air flow work stations, the air flow rate shall be 0.3 meter per second ± 20% (for vertical flows) and 0.45 meter per second ± 20% (for horizontal flows).

3.8. Differential pressure between areas of different environmental standards shall be at least 15 Pascal (0.06 inches or 1.5 mm water gauge). Suitable manometers or gauges shall be installed to measure and verify pressure differential.

1. Subs. by G.S.R. 431(E), dt. 30.6.2005

3.9 The final change room shall have the same class of air as specified for the aseptic area. The pressure differentials in the change rooms shall be in the descending order from _white' to _black'.

3.10 Unless there are product specific requirements, temperature and humidity in the aseptic areas [1][shall be 27 ± 2 degree centigrade and relative humidity 55% ± 5, respectively].

[1][TABLE I

AIR BORNE PARTICULATE CLASSIFICATION FOR MANUFACTURE OF STERILE PRODUCTS

Grade	Maximum number of permitted particles per cubic metre equal t to or above			
	At rest (b)		In operation (a)	
	0.5µm	5µm	0.5µm	5µm
A	3500	0	3500	0
B (a)	3500	0	3,50,000	2,000
C (a)	350,000	2,000	35,00,000	20,000
D (a)	35,00,000	20,000	Not defined (c)	Not defined (c)]

Notes :

(a) In order to reach the B, C and D air grades, the number of air changes shall be related to the size of the room and the equipment and personnel present in the room. The air system shall be provided with the appropriate filters such as HEPA for Grades A, B and C. The maximum permitted number of particles in the —at rest‖ condition shall approximately be as under:

[1][*Grade A and B corresponds with class 100 or M 3.5 or class 5*]*; Grade C with Class 10,000 or M 5.5 or ISO Class 7; Grade D with Class 1,00,000 or M 6.5 or ISO Class 8.*

(b) *The requirement and limit for the area shall depend on the nature of the operation carried out.*

(c) *Type of operations to be carried out in the various grades are given in Table II and Table III as under:*

TABLE II

TYPES OF OPERATIONS TO BE CARRIED OUT IN THE VARIOUS GRADES FOR ASEPTIC PREPARATIONS

Grade	Types of operations for aseptic preparations
A	Aseptic preparation and filling
B	Background room conditions for activities requiring Grade A
C	Preparation of solution to be filtered
D	Handling of components after washing

1. Subs. by G.S.R. 431(E), dt. 30.6.2005.

TABLE III

TYPES OF OPERATIONS TO BE CARRIED OUT IN THE VARIOUS GRADES FOR TERMINALLY STERILIZED PRODUCTS

Grade	Types of operations for terminally sterilized products.
A	Filling of products, which are usually at risk.
C	Placement of filling and sealing machines, preparation of solutions when [1][unusually at risk]. Filling of product when unusually at risk.
D	Moulding, blowing (pre-forming) operations of plastic containers, preparations of solutions and components for subsequent filling.

4. ***Environmental Monitoring:***

4.1 All environmental parameters listed under para 3.1 to 3.10 shall be verified and established at the time of installation and thereafter monitored at periodic intervals. The recommended frequencies of periodic monitoring shall be as follows :-

(a) Particulate monitoring in air – 6 Monthly.

(b) HEPA filter integrity testing (smoke testing) – Yearly

(c) Air change rates – 6 Monthly.

(d) Air pressure differentials – Daily.

(e) Temperature and humidity – Daily

(f) Microbiological monitoring by settle plates and/or swabs in aseptic areas– Daily, and at decreased frequency in other areas.

`***Note****:* The above frequencies of monitoring shall be changed as per the requirements and load in individual cases.

4.2 There shall be a written environmental monitoring program and microbiological results shall be recorded. Recommended limits for microbiological monitoring of clean areas ―in operation‖ are as given in the table below:

TABLE

RECOMMENDED LIMITS FOR MICROBIOLOGICAL MONITORING OF CLEAN AREAS ― IN OPERATION‖

Grade	Air sample Cfu/m^2	Settle plates (dia. 90mm. Cfu/2 hrs.	Contact plates (dia. 55mm) cfu per plate	Glove points (five fingers) cfu per glove
A	< 1	< 1	< 1	< 1
B	10	5	5	5
C	100	50	25	--
D	500	100	50	--

Notes:

(a) These are average values.

(b) Individual settle plates may be exposed for not less than two hours in Grade B, C and D areas and for not less than thirty minutes in Grade A area.

1. Subs. by G.S.R. 431(E), dt. 30.6.2005.

4.3 Appropriate action shall be taken immediately if the result of particulate and microbiological monitoring indicates that the counts exceed the limits. The Standard Operating Procedures shall contain corrective action. After major engineering modification to the HVAC system of any area, all monitoring shall be re-performed before production commences.

5. ***Garments.***

5.1 This section covers garments required for use by personnel working only in aseptic area. Outdoor clothing shall not be brought into the sterile areas.

5,2 The garments shall be made of non-shedding and tight weave material. Cotton garments shall not be used. The garments shall shed virtually no fibres or particulate matter.

5.3 The clothing and its quality shall be adopted to the process and the work place and worn in such a way as to protect the product from contamination. Garments shall be single piece with fastenings at cuffs, neck and at legs to ensure close fit. Trouser legs shall be tucked inside the cover boots. Suitable design of garments shall either include a hood (head- cover) or a separate hood which can be tucked inside the over-all. Pockets, pleats and belts shall be avoided in garments. Zips (if any) shall be of plastic material. Garments with damaged zips shall not be used.

5.4. Only clean, sterilized and protective garments shall be used at each work session where aseptic filtration and filling operations are undertaken and at each work shift for products intended to be sterilized, post-filling. The mask and gloves shall be changed at every work session in both instances.

5.5 Gloves shall be made of latex or other suitable plastic materials and shall be powder-free. These shall be long enough to cover wrists completely and allow the over-all cuff to be tucked in.

5.6. The footwear shall be of suitable plastic or rubber material and shall be daily cleaned with a bactericide.

5.7. Safety goggles or numbered glasses with side extension shall be used inside aseptic areas. These shall be sanitized by a suitable method.

5.8. Garment changing procedures shall be documented and operators trained in this respect. A full size mirror shall be provided in the final change room for the operator to verify that he is appropriately attired in the garments. Periodic inspection of the garments shall be done by responsible staff.

6. ***Sanitation:***

6.1. There shall be written procedures for the sanitation of sterile processing facilities. Employees carrying out sanitation of aseptic areas shall be trained specifically for this purpose.

6.2. Different sanitizing agent shall be used in rotation and the concentrations of the same shall be as per the recommendations of the manufacturer. Records of rotational use of sanitizing agents shall be maintained.

6.3. Distilled water freshly collected directly from the distilled water plant or water maintained above 70 degree centigrade from the re-circulation loop shall be used for dilution of disinfectants. Alternatively, distilled water sterilized by autoclaving or membrane filtration shall be used. The dilution shall be carried out in the _white‘ change room.

6.4. 1[Where alcohol or isopropyl alcohol is used for dilution of disinfectants for use as hand sprays, the preparation of the same shall be done in the bulk preparation area in grade C.]

6.5. Diluted disinfectants shall bear the label _use before', based on microbiological establishment of the germicidal properties. The solutions shall be adequately labelled and documents maintained.

6.6. Formaldehyde or any other equally effective fumigant is recommended for the fumigation of aseptic areas or after major civil modifications. There shall be Standard Operating Procedures for this purpose. Its use for routine purpose shall be discouraged and an equally effective surface cleaning regime shall be followed.

6.7. Cleaning of sterile processing facilities shall be undertaken with air suction devices or with non-linting sponges or clothes.

6.8. Air particulate quality shall be evaluated on a regular basis and record maintained.

7. *Equipment:*

7.1 The special equipment required for manufacturing sterile products includes component washing machines, steam sterilizers, dry heat sterilizers, membrane filter assemblies, manufacturing vessels, blenders, liquid filling machines, powder filling machines, sealing and labelling machines, vacuum testing chambers, inspection machines, lyophilisers, pressure vessels etc. Suitable and fully integrated washing sterilizing filling lines may be provided, depending upon the type and volume of activity.

7.2. Unit-sterilizers shall be double-ended with suitable inter-locking arrangements between the doors. The effectiveness of the sterilization process shall be established initially by biological inactivation studies using microbial spore indicators and then at least once a year by carrying out thermal mapping of the chamber. Various sterilization parameters shall be established based on these studies and documented. For membrane filters used for filtration, appropriate filter integrity tests that ensure sterilization shall be carried out before and after filtration.

7.3. Filling machines shall be challenged initially and then at periodic intervals by simulation trials including sterile media fill. Standard Operating Procedures and acceptance criteria for media fills shall be established, justified and documented. Special simulation trial procedures shall be developed, validt. and documented for special products like ophthalmic ointments.

7.4. The construction material used for the parts which are in direct contact with products and the manufacturing vessels may be stainless steel 316 or Boro-silicate glass (if glass containers) and the tubing shall be capable of being washed and autoclaved.

7.5 On procurement, installation qualification of each of the equipment shall be done by engineers with the support of production and quality assurance personnel. Equipment for critical processes like aseptic filling and sterilizers shall be suitably validt. according to a written program before putting them to use.

7.6. Standard Operating Procedures shall be available for each equipment for its calibration and operation and cleaning. Gauges and other measuring devices attached to equipment shall be calibrated at suitable intervals against a written program. Calibration status of equipment gauges shall be adequately documented and displayed.

1. Subs. by G.S.R. 431(E), dt. 30.6.2005.

8. *Water and Steam Systems:*

8.1. Potable water meeting microbiological specification of not more than 500 cfu/ml and indicating absence of individual pathogenic micro-organisms. *Escherichia coli, Salmonella, Staphylococcus aureus and Pseudomonas aeruginosa* per 100 ml sample shall be used for the preparation of purified water.

8.2 Purified water prepared by de-mineralization shall meet the microbiological specification of not more than 100 cfu per ml and indicate absence of pathogenic micro-

organisms in 100 ml. Purified water shall also meet IP specification for chemical quality. Purified water shall be used for hand washing in change rooms. Containers, closures and machine parts may be washed with potable water followed by suitably filtered purified water. Purified water shall be stored in stainless steel tanks or plastic tanks.

8.3. Water for Injection (hereinafter as WFI) shall be prepared from potable water or purified water meeting the above specifications by distillation. Water for Injection shall meet microbiological specification of not more than 10 cfu per 100 ml. WFI shall also meet IP specification for Water for Injection and shall have an endotoxin level of not more than 0.25 EU/Ml. Bulk solutions of liquid parenterals shall be made in WFI. Final rinse of product containers and machine parts shall be done with WFI. Disinfectant solutions for use in aseptic areas shall be prepared in WFI.

8.4. Water for Injection for the manufacture of liquid injectables shall be freshly collected from the distillation plant or from a storage or circulation loop where the water has been kept at above 70 degree centigrade. At the point of collection, water may be cooled using suitable heat exchanger.

8.5 Water for non-injectable sterile products like eye drops shall meet IP specifications for purified water. In addition, microbiologial specification of not more than 10 cfu per 100 ml and absence of *Pseudomonas aeruginosa* and *Enterobacter coli* in 100 ml shall also be met.

8.6. Water for Injection shall be stored in steam jacketed stainless steel tanks of suitable size and the tanks shall have hydrophobic bacterial retention with 0.22 µ vent filters. The filters shall be suitably sterilized at periodic intervals. The distribution lines for purified water and distilled water shall be of stainless steel 316 construction and shall not shed particles.

8.7. There shall be a written procedure and program for the sanitation of different water systems including storage tanks, distribution lines, pumps and other related equipment. Records of sanitation shall be maintained.

8.8. There shall be written microbiological monitoring program for different types of water. The results shall justify the frequency of sampling and testing. Investigation shall be carried out and corrective action taken in case of deviation from prescribed limits.

[1][8.9 Steam coming in contact with the product, primary containers and other product contact surfaces shall be sterile and pyrogen free.]

9. *Manufacturing Process:*

9.1. Manufacture of sterile products shall be carried out only in areas under defined conditions.

1. Omitted by G.S.R. 431(E), dt. 30.6.2005.

9.2. Bulk raw materials shall be monitored for bio-burden periodically. Bio- burden of bulk solution prior to membrane filtration shall be monitored periodically and a limit of not more than 100 cfu per ml is recommended.

9.3 The time between the start of the preparation of the solution and its sterilization or filtration through a micro-organism retaining filter shall be minimized. There shall be a set maximum permissible time for each product that takes into account its composition and method of storage mentioned in the Master formula record.

9.4. Gases coming in contact with the sterile product shall be filtered through two 0.22 µ hydrophobic filters connected in-series. These filters shall be tested for integrity. Gas cylinders shall not be taken inside aseptic areas.

9.5. Washed containers shall be sterilized immediately before use. Sterilized containers, if not used within an established time, shall be rinsed with distilled or filtered purified water and re-sterilized.

9.6. Each lot of finished product shall be filled in one continuous operation. In each case, where one batch is filled in using more than one operation, each lot shall be tested separately for sterility and held separately till sterility test results are known.

9.7. Special care shall be exercised while filling products in powder form so as not to contaminate the environment during transfer of powder to filling machine-hopper.

10. ***Form-Fill-Seal Technology or Blow, Fill-Seal Technology****:*

10.1 Form-Fill-Seal units are specially built automated machines in which through one continuous operation, containers are formed from thermoplastic granules, filled and then sealed. Blow, fill-seal units are machines in which containers are moulded / blown (pre- formed) in separate clean rooms, by non-continuous operations.

Note:

(i) These shall be installed in at least Grade C environment.

(ii) These shall comply with the limits as recommended in Table at Item 4.2.

10.2. Form-Fill-Seal/Blow, Fill-Seal machines used for the manufacture of products for terminal sterilization shall be installed in at least Grade C environment and the filling zone within the machine shall fulfil Grade A requirements.

10.3. *Terminally sterilized products.–*

10.3.1. Preparation of primary packaging material such as glass bottles, ampoules and rubber stoppers shall be done in at least Grade D environment. Where there is unusual risk to the product from microbial contamination, the above operation shall be done in Grade C environment. All the processes used for component preparation shall be validt..

10.3.2. Filling of products requiring terminal sterilization shall be done under Grade A environment with a Grade C background.

10.4 Preparation of solutions, which are to be sterilized by filtration, shall be done in Grade C environment, and if not to be filtered, the preparation of materials and products shall be in a Grade A environment with Grade B in background.

10.5 *Filtration (Membrane).-*

(i) Solutions for Large Volume Parenterals shall be filtered through a non-fibre releasing, sterilizing grade cartridge/membrane filter of nominal pore size of 0.22 µ for aseptic filling whereas 0.45 µ porosity shall be used for terminally sterilized products.

(ii) A second filtration using another 0.22 µ sterilizing grade cartridge / membrane filter shall be performed immediately prior to filling. Process specifications shall indicate the maximum time during which a filtration system may be used with a view to precluding microbial build-up to levels that may affect the microbiological quality of the Large Volume Parenterals.

(iii) The integrity of the sterilized filter shall be verified and confirmed immediately after use by an appropriate method such as Bubble Point, Diffusive Flow or Pressure Hold Test.

10.6 *Sterilization (Autoclaving).–*

10.6.1. Before any sterilization process is adopted, its suitability for the product and its efficacy in achieving the desired sterilizing conditions in all parts of each type of load pattern to be processed, shall be demonstrated by physical measurements and by biological indicators, where appropriate.

10.6.2 All the sterilization process shall be appropriately validt.. The validity of the process shall be verified at regular intervals, but at least annually. Whenever significant modifications have been made to the equipment and product, records shall be maintained thereof.

10.6.3 The sterilizer shall be double ended to prevent mix-ups.

10.6.4 Periodic bio-burden monitoring of products before terminal sterilization shall be carried out and controlled to limits specified for the product in the Master Formula.

10.6.5 The use of biological indicators shall be considered as an additional method of monitoring the sterilization. These shall be stored and used according to the manufacturer‘s instructions. Their quality shall be checked by positive controls. If biological indicators used, strict precautions shall be taken to avoid transferring microbial contamination from them.

10.6.6 There shall be clear means of differentiating ‗ sterilized‘ and ‗un-sterilized‘ products. Each basket, tray or other carrier of products or components shall be clearly labelled with the name of the material, its batch number, and sterilization status. Indicators shall be used, where appropriate, to indicate whether a batch (or sub-batch) has passed through the sterilization process.

10.6.7 Sterilization records shall be available for each sterilization-run and may also include thermographs and sterilization monitoring strips. They shall be maintained as part of the batch release procedure.

10.7. *Sterilization (By dry heat).–*

10.7.1 Each heat sterilization cycle shall be recorded on a time/temperature chart of a suitable size by appropriate equipment of the required accuracy and precision. The position of temperature probes used for controlling and/or recording shall be determined during the validation and, where applicable, shall also be checked against a second independent temperature probe located in the same position. The chart shall form a part of the

batch record. Container mapping may also be carried out in the case of Large Volume Parenterals.

10.7.2 Chemical or biological indicators may also be used, but shall not take the place of physical validation.

10.7.3. Sufficient time shall be allowed for the load to reach the required temperature before measurement of sterilization time commences. This time shall be separately determined for each type of load to be processed.

10.7.4. After the high temperature phase of a heat sterilization cycle, precautions shall be taken against contamination of sterilized load during cooling. Any cooling fluid or gas in contact with the product shall be sterilized unless it can be shown that any leaking container would not be approved for use. Air inlet and outlets shall be provided with bacterial retaining filters.

10.7.5. The process used for sterilization by dry heat shall include air-circulation within the chamber and the maintenance of a positive pressure to prevent the entry of non- sterile air. Air inlets and outlets should be provided with micro-organism retaining filters. Where this process of sterilization by dry heat is also intended to remove pyrogens, challenge tests using endotoxins would be required as part of the validation process.

10.8. *Sterilization (By Moist Heat).-*

10.8.1 Both the temperature and pressure shall be used to monitor the process. Control instrumentation shall normally be independent of monitoring instrumentation and recording charts. Where automated control and monitoring systems are used for these applications, these shall be validt. to ensure that critical process requirements are met. System and cycle faults shall be registered by the system and observed by the operator. The reading of the independent temperature indicator shall be routinely checked against the chart-recorder during the sterilization period. For sterilizers fitted with a drain at the bottom of the chamber, it may also be necessary to record the temperature at this position throughout the sterilization period. There shall be frequent leak tests done on the chamber during the vacuum phase of the cycle.

10.8.2 The items to be sterilized, other than products in sealed containers, shall be wrapped in a material which allows removal of air and penetration of steam but which prevents re-

contamination after sterilization. All parts of the load shall be in contact with the sterilizing agent at the required temperature for the required time.

10.8.3. No Large Volume Parenteral shall be subjected to steam sterilization cycle until it has been filled and sealed.

10.8.4 Care shall be taken to ensure that the steam used for sterilization is of a suitable quality and does not contain additives at a level which could cause contamination of the product or equipment.

10.9. *Completion/finalisation of sterile products–*

10.9.1. All unit operations and processes in the manufacture of a batch shall have a minimum time specified and the shortest validt. time shall be used from the start of a batch to its ultimate release for distribution.

10.9.2. Containers shall be closed by appropriately validt. methods. Containers closed by fusion e.g. glass or plastic ampoules shall be subjected to 100% integrity testing. Samples of other containers shall be checked for integrity according to appropriate procedures.

10.9.3 Containers sealed under vacuum shall be tested for required vacuum conditions.

10.9.4 Filled containers of parenteral products shall be inspected individually for extraneous contamination or other defects. When inspection is done visually, it shall be done under suitably controlled conditions of illumination and background. Operators doing the inspection shall pass regular eye-sight checks with spectacles, if worn, and be allowed frequent rest from inspection. Where other methods of inspection are used, the process shall be validt. and the performance of the equipment checked at suitable intervals. Results shall be recorded.

11. ***Product Containers and Closures. –***

11.1 All containers and closures intended for use shall comply with the pharmacopoeial and other specified requirements. Suitable samples sizes, specifications, test methods, cleaning procedures and sterilization procedures, shall be used to assure that containers, closures and other component parts of drug packages are suitable and are not reactive, additive, adsorptive or leachable or presents the risk of toxicity to an extent that significantly affects the quality or purity of the drug. No second hand or used containers and closures shall be used.

11.2 Plastic granules shall also comply with the pharmacopoeial requirements including physio-chemical and biological tests.

11.3. All containers and closures shall be rinsed prior to sterilization with Water for Injection according to written procedure.

11.4. The design of closures, containers and stoppers shall be such as to make cleaning, easy and also to make airtight seal when fitted to the bottles.

11.5 It shall be ensured that containers and closures chosen for a particular product are such that when coming into contact they are not absorbed into the product and they do not affect the product adversely. The closures and stoppers should be of such quality substances as not to affect the quality of the product and avoid the risk of toxicity.

11.6. Whenever glass bottles are used, the written schedule of cleaning shall be laid down and followed. Where bottles are not dried after washing, these shall be finally rinsed with distilled water or pyrogen free water, as the case may be, according to written procedure.

11.7. Individual containers of parenteral preparations, ophthalmic preparations shall be examined against black/white background fitted with diffused light after filling so as to ensure freedom from foreign matters.

11.8 *Glass Bottles. –*

11.8.1 Shape and design of the glass bottle shall be rational and standardized. Glass bottles made of USP Type-I and USP Type-II glass shall only be used. Glass bottles shall not be

reused. Before use, USP Type-II bottles shall be validt. for the absence of particulate matter generated over a period of the shelf -life of the product and shall be

regularly monitored after the production, following statistical sampling methods. USP Type- III glass containers may be used for non-parenteral sterile products such as Otic Solutions.

11.9. *Plastic Containers.* –

11.9.1 Pre-formed plastic containers intended to be used for packing of Large Volume Parenteral shall be moulded in-house by one-continuous operation through an automatic machine.

11.9.2. Blowing, filling and sealing (plugging) operation shall be conducted in room(s) conforming to requirements as mentioned in Table III of Item 3.10. Entry to the area where such operations are undertaken, shall be through a series of airlocks. Blowers shall have an air supply which is filtered through 0.22µ filters. Removal of runners and plugging operations shall be conducted under a laminar airflow workstation.

11.10 *Rubber Stoppers.* –

11.10.1 The rubber stoppers used for Large Volume Parenterals shall comply with specifications prescribed in the current edition of the Indian Pharmacopoeia.

12. ***Documentation:***

12.1 The manufacturing records relating to manufacture of sterile products shall indicate the following details:-

(1) Serial number of the Batch Manufacturing Record.
(2) Name of the product
(3) Reference to Master Formula Record.
(4) Batch/Lot number
(5) Batch/Lot size.
(6) Date of commencement of manufacture and date of completion of manufacture. (7) Date of manufacture and assigned date of expiry.
(8) Date of each step in manufacturing.
(9) Names of all ingredients with the grade given by the quality control department. (10) Quality of all ingredients.
(11) Control reference numbers for all ingredients.
(12) Time and duration of blending, mixing, etc. whenever applicable.
(13) pH of solution whenever applicable.
(14) Filter integrity testing records
(15) Temperature and humidity records whenever applicable (16) Records of plate-counts whenever applicable.
(17) Results of pyrogen and/or bacterial endotoxin & toxicity.
(18) Records of weight or volume of drug filled in containers.
(19) Bulk sterility in case of aseptically filled products.
(20) Leak test records.
(21) Inspection records.
(22) Sterilization records including autoclave leakage test records, load details, date, duration, temperature, pressure, etc.
(23) Container washing records.
(24) Total number of containers filled.

(25) Total numbers of containers rejected at each stage

(26) Theoretical yield, permissible yield, actual yield and variation thereof.

(27) Clarification for variation in yield beyond permissible yield.

(28) Reference numbers of relevant analytical reports.

(29) Details of reprocessing, if any.

(30) Name of all operators carrying out different activities.

(31) Environmental monitoring records.

(32) Specimens of printed packaging materials.

(33) Records of destruction of rejected containers and printed packaging materials.

(34) Signature of competent technical staff responsible for manufacture and testing.

***Note*:** (*1) Products shall be released only after complete filling and testing.*

(2) Result of the tests relating to sterility, pyrogens, and Bacterial endotoxins shall be maintained in the analytical records.

(3) Validation details and simulation trial records shall be maintained separately,

(4) Records of environmental monitoring like temperature, humidity, microbilogical data, etc. shall be maintained. Records of periodic servicing of HEPA filters, sterilizers and other periodic maintenance of facilities and equipment carried out also be maintained.

(5) Separate facilities shall be provided for filling-cum-sealing of Small Volume Injectables and Large Volume Parenterals.

(6) It is advisable to provide separate facilities for manufacture of Large Volume Parenterals in glass containers and / or plastic containers.

(7) For manufacture of Large Volume Parenterals in plastic containers, it is advisable to instal automatic (with all operations) Form–Fill-Seal machines having one continuous operation.

PART IB

SPECIFIC REQUIREMENTS FOR MANUFACTURE OF ORAL SOLID DOSAGE FORMS (TABLETS AND CAPSULES)

Note: - *The General Requirements as given in Part 1 of this Schedule relating to requirements of Good Manufacturing Practices for Premises and materials for pharmaceutical products shall be complied with, mutatis mutandis, for the manufacture of oral Solid Dosage Forms (Tablets and Capsules). In addition to these requirements, the following Specific Requirement shall also be followed, namely :-*

1. *General:*

1.1 The processing of dry materials and products creates problems of dust control and cross-contamination. Special attention is therefore, needed in the design, maintenance and use of premises and equipment in order to overcome these problems. Wherever required, enclosed dust control manufacturing systems shall be employed.

1.2. Suitable environmental conditions for the products handled shall be maintained by installation of air-conditioning wherever necessary. Effective air-extraction systems, with discharge points situated to avoid contamination of other products and processes shall be provided. Filters shall be installed to retain dust and protect the factory and local environment.

1.3. Special care shall be taken to protect against subsequent contamination of the product by particles of metal or wood. The use of metal detector is recommended. Wooden equipment should be avoided. Screens, sieves, punches and dies shall be examined for wear and tear or for breakage before and after each use.

1.4. All ingredients for a dry product shall be sifted before use unless the quality of the input material can be assured. Such sifting shall normally be carried out at dedicated areas.

1.5. [1][Where the facilities are designed to provide special environmental conditions of pressure differentials between rooms, these conditions shall be regularly monitored and any deviation shall be brought to the immediate attention of the production and quality assurance departments].

1.6. Care shall be taken to guard against any material lodging and remaining undetected in any processing or packaging equipment. Particular care shall be taken to ensure that any vacuum, compressed air or air-extraction nozzles are kept clean and that there is no evidence of lubricants leaking into the product from any part of the equipments.

2. ***Sifting, Mixing and Granulation:***

2.1. Unless operated as a closed system, mixing, sifting and blending equipments shall be fitted with dust extractors [1][or in a dedicated area for each operation].

2.2. Residues from sieving operations shall be examined periodically for evidence of the presence of unwanted materials.

2.3. Critical operating parameters like time and temperature for each mixing, blending and drying operation shall be specified in a Master Formula, monitored during processing, and recorded in the batch records.

2.4. Filter bags fitted to fluid-bed dryer shall not be used for different products, without being washed in-between use. With certain highly potent or sensitizing products, bags specific to one product only shall be used. Air entering the dryer shall be filtered. Steps shall be taken to prevent contamination of the site and local environment by dust in the air leaving the dryer due to close positioning of the air-inlets and exhaust.

2.5. Granulation and coating solutions shall be made, stored and used in a manner which minimizes the risk of contamination or microbial growth.

3. ***Compressions (Tablets):***

3.1. Each tablet compressing machine shall be provided with effective dust control facilities to avoid cross-contamination. Unless the same product is being made on each machine, or unless the compression machine itself provides its own enclosed air controlled environment, the machine shall be installed in separate cubicles.

3.2. Suitable physical, procedural and labelling arrangements shall be made to prevent mix up of materials, granules and tablets on compression machinery.

3.3. Accurate and calibrated weighing equipment shall be readily available and used for in-process monitoring of tablet weight variation. Procedures used shall be capable of detecting out-of-limits tablets.

1. Ins. by G.S.R. 431(E), dt. 30.6.2005.

3.4. At the commencement of each compression run and in case of multiple compression points in a compression machine, sufficient individual tablets shall be examined at fixed intervals to ensure that a tablet from each compression station or from each compression point has been inspected for suitable pharmacopoeial parameters like _appearance‘, _weight variation‘, _disintegration‘, _hardness‘, _friability‘ and _thickness‘. The results shall be recorded as part of the batch documentation.

3.5. Tablets shall be de-dusted, preferably by automatic device and shall be monitored for the presence of foreign materials besides any other defects.

3.6. Tablets shall be collected into clean, labelled containers.

3.7. Rejected or discarded tablets shall be isolated in identified containers and their quantity recorded in the Batch Manufacturing Record.

3.8 In-process control shall be employed to ensure that the products remain within specification. During compression, samples of tablets shall be taken at regular intervals of not greater than 30 minutes to ensure that they are being produced in compliance with specified in-process specification. The tablets shall also be periodically checked for additional parameters such as _appearance‘, _weight variation‘, _disintegration‘, _hardness‘, _friability‘ and _thickness‘ and contamination by lubricating oil.

4. ***Coating (Tablets):***

4.1. Air supplied to coating pans for drying purposes shall be filtered air and of suitable quality. The area shall be provided with suitable exhaust system and environmental control (temperature, humidity) measures.

4.2 Coating solutions and suspensions shall be made afresh and used in a manner, which shall minimize the risk of microbial growth. Their preparation and use shall be documented and recorded.

5. ***Filling of Hard Gelatin Capsule:***

Empty capsules shells shall be regarded as _drug component‘ and treated accordingly. They shall be stored under conditions which shall ensure their safety from the effects of excessive heat and moisture.

6. ***Printing (Tablets and Capsules)***

6.1. Special care shall be taken to avoid product mix-up during any printing of tablets and capsules. Where different products, or different batches of the same product, are printed simultaneously, the operations shall adequately be segregated. Edible grade colours and suitable printing ink shall be used for such printing.

6.2. After printing, tablets and capsules shall be approved by Quality Control before release for packaging or sale.

7. ***Packaging (Strip and Blister):***

7.1. Care shall be taken when using automatic tablet and capsule counting, strip and blister packaging equipment to ensure that all _rogue‘ tablets, capsules or foils from packaging operation are removed before a new packaging operation is commenced. There shall be an independent recorded check of the equipment before a new batch of tablets or capsules is handled.

7.2. Uncoated tablets shall be packed on equipment designed to minimize the risk of cross-contamination. Such packaging shall be carried out in an isolated area when potent tablets or Beta-Iactum containing tablets are being packed.

1. Ins. by G.S.R. 431(E), dt. 30.6.2005.

7.3. The strips coming out of the machine shall be inspected for defects such as misprint, cuts on the foil, missing tablets and improper sealing.

7.4. Integrity of individual packaging strips and blisters shall be subjected to vacuum test periodically to ensure leak proofness of each pocket strip and blister and records maintained.

PART IC

SPECIFIC REQUIREMENTS FOR MANUFACTURE OF ORAL LIQUIDS (SYRUPS, ELIXIRS, EMULSIONS AND SUSPENSIONS)

Note: *The General Requirements as given in Part I of this Schedule relating to Requirements of Good Manufacturing Practices for Premises and Materials for pharmaceutical products shall be complied with, mutatis mutandis, for the manufacture of (Syrups, Elixirs, Emulsions and*

Suspensions). In addition to these requirements, the following Specific Requirements shall also be followed, namely:-

1. ***Building and Equipment***:.

1.1. The premises and equipment shall be designed, constructed and maintained to suit the manufacturing of Oral Liquids. The layout and design of the manufacturing area shall strive to minimize the risk of cross-contamination and mix-ups.

1.2. Manufacturing area shall have entry through double door airlock facility. It shall be made fly proof by use of ‗fly catcher' and/or ‗air curtain'.

1.3. Drainage shall be of adequate size and have adequate traps, without open channels and the design shall be such as to prevent back flow. Drains shall be shallow to facilitate cleaning and disinfecting.

1.4. The production area shall be cleaned and sanitized at the end of every production process.

1.5. Tanks, containers, pipe work and pumps shall be designed and installed so that they can be easily cleaned and sanitized. Equipment design shall be such as to prevent accumulation of residual microbial growth or cross-contamination.

1.6. Stainless steel or any other appropriate material shall be used for parts of equipments coming in direct contact with the products. The use of glass apparatus shall be minimum.

1.7. Arrangements for cleaning of containers, closures and droppers shall be made with the help of suitable machines/devices equipped with the high pressure air, water and steam jets.

1.8. The furniture used shall be smooth, washable and made of stainless steel [1][or any other appropriate material which is scratch proof, washable and smooth].

2. ***Purified Water***.

2.1. The chemical and microbiological quality of purified water used shall be specified and monitored routinely. The microbiological evaluation shall include testing for absence of pathogens and shall not exceed 100 cfu/ml (as per Appendix 12.5 of IP 1996.)

1. Added by G.S.R. 431(E), dt. 30.6.2005.

2.2. There shall be a written procedure for operation and maintenance of the purified water system. Care shall be taken to avoid the risk of microbial proliferation with appropriate methods like re-circulation, use of UV treatment, treatment with heat and sanitizing agent. After any chemical sanitisation of the water system, a flushing shall be done to ensure that the sanitizing agent has been effectively removed.

3. ***Manufacturing:***

3.1. [1][Manufacturing personnel shall wear wherever required, non-fiber shedding clothing to prevent contamination of the products].

3.2. Materials likely to shed fibre like gunny bags, or wooden pallets shall not be carried into the area where products or cleaned-containers are exposed.

3.3. Care shall be taken to maintain the homogenecity of emulsion by use of appropriate emulsifier and suspensions by use of appropriate stirrer during filling. Mixing and filling processes shall be specified and monitored. Special care shall be taken at the beginning of the filling process, after stoppage due to any interruption and at the end of the process to ensure that the product is uniformly homogenous during the filling process.

3.4. The primary packaging area shall have an air supply which is filtered through 5 micron filters. The temperature of the area shall not exceed 30 degrees centigrade.

3.5. When the bulk product is not immediately packed, the maximum period of storage and storage conditions shall be specified in the Master Formula. The maximum period of storage time of a product in the bulk stage shall be validt..

PART ID

SPECIFIC REQUIREMENTS FOR MANUFACTURE OF TOPICAL PRODUCTS , *i.e.* EXTERNAL PREPARATIONS (CREAMS, OINTMENTS, PASTES, EMULSIONS, LOTIONS, SOLUTIONS, DUSTING POWDERS AND IDENTICAL PRODUCTS)

Note*:* *The General Requirements as given in Part I of this Schedule relating to Requirements of Good Manufacturing Practices for Premises and Materials for pharmaceutical products shall be complied with, mutatis mutandis, for the manufacture of Topical Products i.e. External preparations (Creams, Ointments, Pastes, Emulsions, Lotions, Solutions, Dusting powders and identical products used for external applications). In addition to these requirements, the following Specific Requirements shall also be followed, namely: -*

1. The entrance to the area where topical products are manufactured shall be through a suitable airlock. Outside the airlock, insectocutors shall be installed.

2. The air to this manufacturing area shall be filtered through at least 20µ air filters and shall be air-conditioned. [2] [***].

3. The area shall be fitted with an exhaust system of suitable capacity to effectively remove vapours, fumes, smoke, floating dust particles.

4. The equipment used shall be designed and maintained to prevent the product from being accidentally contaminated with any foreign matter or lubricant.

5. [3][Suitable cleaning equipment and material] shall be used in the process of cleaning or drying the process equipment or accessories used.

1. Subs. by G.S.R. 431(E), dt. 30.6.2005.

2. The words ―The air shall be ventilated.‖ omitted by G.S.R. 431(E), dt. 30.6.2005. 3. Subs. by G.S.R. 431(E), dt. 30.6.2005, for ― no rags or dusters‖.

6. Water used in compounding shall be Purified Water IP.

7. Powders, wherever used, shall be suitably sieved before use.

8. Heating vehicles and a base like petroleum jelly shall be done in separate mixing area in suitable stainless steel vessels, using steam, gas, electricity, solar energy, etc.

9. A separate packing section may be provided for primary packaging of the products.

PART 1E

SPECIFIC REQUIREMENTS FOR MANUFACTURE OF METERED-DOSE-INHALERS (MDI)

Note*:* *The General Requirements as given in Part I of this Schedule relating to Requirements of Good Manufacturing Practices for Premises and Materials for pharmaceutical products shall be complied with, mutatis mutandis, for the manufacture of Metered-Dose-Inhalers (MDI). In addition to these requirements, the following Specific Requirements shall also be followed, namely: -*

1. ***General:***

Manufacture of Metered-Dose-Inhalers shall be done under conditions which shall ensure minimum microbial and particulate contamination. Assurance of the quality of components and

the bulk product is very important. Where medicaments are in suspended state, uniformity of suspension shall be established.

2. *Building and Civil Works:*

2.1. The building shall be located on a solid foundation to reduce risk of cracking walls and floor due to the movement of equipment and machinery.

2.2 All building surfaces shall be impervious, smooth and non-shedding. Flooring shall be continuous and provided with a cove between the floor and the wall as well as the wall to the ceiling. Ceiling shall be solid, continuous and covered to walls. Light fittings and air-grills shall be flush with the ceiling. All service lines requiring maintenance shall be erected in such a manner that these are accessible from outside the production area.

2.3. The manufacturing area shall be segregated into change rooms for personnel, container preparation area, bulk preparation and filling area, quarantine area and spray testing and packing areas.

2.4. Secondary change rooms shall be provided for operators to change from factory clothing to special departmental clothing before entering the manufacturing and filling area.

2.5. Separate area shall be provided for de-cartoning of components before they are air washed.

2.6. The propellants used for manufacture shall be delivered to the manufacturing area distribution system by filtering them through 2μ filters. The bulk containers of propellants shall be stored, suitably identified, away from the manufacturing facilities.

3. *Environmental Conditions:*

3.1. Where products or clean components are exposed, the area shall be supplied with filtered air of Grade C.

3.2. The requirements of temperature and humidity in the manufacturing area shall be decided depending on the type of product and propellants handled in the facility. Other support areas shall have comfort levels of temperature and humidity.

3.3. There shall be a difference in room pressure between the manufacturing area and the support areas and the differential pressure shall be not less than 15 Pascals (0.06 inches or 1.5 mm water gauge).

3.4. There shall be a written schedule for the monitoring of environmental conditions. Temperature and humidity shall be monitored daily.

4. *Garments:*

4.1. Personnel in the manufacturing and filling section shall wear suitable single-piece-garment made out of non-shedding, tight weave material. Personnel in support areas shall wear clean factory uniforms.

4.2. Gloves made of suitable material having no interaction with the propellants shall be used by the operators in the manufacturing and filling areas. Preferably, disposable gloves shall be used.

4.3. Suitable department-specific personnel protective equipment like footwear and safety glasses shall be used wherever hazard exists.

5. *Sanitation:*

5.1. There shall be written procedures for the sanitation of the MDI manufacturing facility. Special care should be taken to handle residues and rinses of propellants.

5.2. Use of water for cleaning shall be restricted and controlled. Routinely used disinfectants are suitable for sanitizing the different areas. Records of sanitation shall be maintained.

6. *Equipment:*

6.1. Manufacturing equipment shall be of closed system. The vessels and supply lines shall be of stainless steel.

6.2. Suitable check weights, spray testing machines and labelling machines shall be provided in the department.

6.3. All the equipment shall be suitably calibrated and their performance validt. on receipt and thereafter periodically.

7. *Manufacture:*

7.1. There shall be an approved Master Formula Records for the manufacture of metered dose inhalers. All propellants, liquids and gases shall be filtered through 2µ filters to remove particles.

7.2. The primary packing material shall be appropriately cleaned by compressed air suitably filtered through 0.2µ filter. The humidity of compressed air shall be controlled as applicable.

7.3. The valves shall be carefully handled and after de-cartoning, these shall be kept in clean, closed containers in the filling room.

7.4. For suspensions, the bulk shall be kept stirred continuously.

7.5. In-process controls shall include periodical checking of weight of bulk formulation filled in the containers. In a two-shot-filling process (liquid filling followed by gaseous filling), it shall be ensured that 100% check on weight is carried out.

7.6. Filled containers shall be quarantined for a suitable period established by the manufacturer to detect leaking containers prior to testing, labelling and packing.

8. *Documentation-*

8.1. In addition to the routine good manufacturing practices documentation, manufacturing records shall show the following additional information:-

(1) Temperature and humidity in the manufacturing area.

(2) Periodic filled weights of the formulation.

(3) Records of rejections during on-line check weighing.

(4) Records of rejection during spray testing.

PART 1F

SPECIFIC REQUIREMENTS OF PREMISES, PLANT AND MATERIALS FOR MANUFACTURE OF ACTIVE PHARMACEUTIAL INGREDIENTS (BULK DRUGS)

Note: *The General Requirements as given in Part I of this Schedule relating to Requirements of Good Manufacturing Practices for premises and Materials for pharmaceutical products shall be complied with, mutatis mutandis, for the manufacture of active pharmaceutical ingredients (Bulk Drugs). In addition to these requirements, the following Specific Requirements shall also be followed, namely: -*

1. *Building and Civil Works:*

1.1. Apart from the building requirements contained in Part I, General ante, the active pharmaceutical ingredients facilities for manufacture of hazardous reactions, Beta- Lactum antibiotics. Steroids and Steroidal Hormones / Cytotoxic substances shall be provided in confined areas to prevent contamination of the other drugs manufactured.

1.2. The final stage of preparation of a drug, like isolation/filtration/drying/ milling / sieving and packing operations shall be provided with air filtration systems including pre-filters and finally with a 5 micron filter. Air handling systems with adequate number of air changes per hour or any other suitable system to control the air borne contamination shall be

provided. Humidity / Temperature shall also be controlled for all the operations wherever required.

1.3. Air filtration systems including pre-filters and particulate matter retention air filters shall be used, where appropriate, for air supplies to production areas. If air is re- circulated to production areas, measures shall be taken to control re-circulation of floating dust particles from production. In areas where air contamination occurs during production, there shall be adequate exhaust system to control contaminants.

1.4. Ancillary area shall be provided for Boiler-house. Utility areas like heat exchangers, chilling workshop, store and supply of gases shall also be provided.

1.5. For specified preparation like manufacture of sterile products and for certain antibiotics, sex hormones, cytotoxic and oncology products, separate enclosed areas shall be designed. The requirements for the sterile active pharmaceutical ingredient shall be in line with the facilities required for formulation to be filled aseptically.

2. *Sterile Products:*

Sterile active pharmaceutical ingredient filled aseptically shall be treated as formulation from the stage wherever the process demands like crystallization, lyophilisation, filtration etc. All conditions applicable to formulations that are required to be filled aseptically shall apply *mutatis mutandis* for the manufacture of sterile active pharmaceutical ingredients involving stages like filtration, crystallization and lyophilisation.

3. *Utilities / Services:*

Equipment like chilling plant, boiler, heat exchangers, vacuum and gas storage vessels shall be serviced, cleaned, sanitized and maintained at appropriate intervals to prevent mal-functions or contamination that may interfere with safety, identity, strength, quality or purity of the drug product.

4. *Equipment Design, Size and Location:*

4.1. Equipment used in the manufacture, processing, packing or holding of an active pharmaceutical ingredient shall be of appropriate design, adequate size and suitably located to facilitate operations for its intended use and for its cleaning and maintenance.

4.2. If equipment is used for different intermediates and active pharmaceutical ingredients, proper cleaning before switching from one product to another becomes particularly important. If cleaning of a specific type of equipment is difficult, the equipment may need to be dedicated to a particular intermediate or active pharmaceutical ingredient.

4.3. The choice of cleaning methods, detergents and levels of cleaning shall be defined and justified. Selection of cleaning agents (e.g. solvents) should depend on :

(a) the suitability of the cleaning agent to remove residues of raw materials; intermediates, precursors, degradation products and isomers, as appropriate.

(b) whether the cleaning agent leaves a residue itself;

(c) compatibility with equipment construction materials like centrifuge/ filtration, dryer/fluid bed dryer, rotocone proton dryer, vacuum dryer, frit mill, multi-mill/jet mills/sewetters cut sizing;

(d) test for absence of intermediate or active pharmaceutical ingredient in the final rinse.

4.4. Written procedures shall be established and followed for cleaning and maintenance of equipment, including utensils used in the manufacture, processing, packing or holding of active pharmaceutical ingredients. These procedures shall include but should not be limited to the following :

(a) assignment of responsibility for cleaning and maintaining equipment;

(b) maintenance and cleaning program schedules, including where appropriate, sanitizing schedules;

(c) a complete description of the methods and materials used to clean and maintain equipment, including instructions for de-assembling and re-assembling each article of equipment to ensure proper cleaning and

maintenance.;

(d) removal or obliteration of previous batch identification;

(e) protection of clean equipment from contamination prior to use;

(f) inspection of equipment for cleanliness immediately before use;

(g) establishing the maximum time that may elapse between completion of processing and equipment cleaning as well as between cleaning and equipment reuse.

4.5. Equipment shall be cleaned between successive batches to prevent contamination and carry-over of degraded material or contaminants unless otherwise established by validation.

4.6. As processing approaches the final purified active pharmaceutical ingredient, it is important to ensure that incidental carry over between batches does not have adverse impact on the established impurity profile. However, this does not generally hold good for any biological, active pharmaceutical ingredient where many of the processing steps are accomplished aseptically and where it is necessary to clean and sterilize equipment between batches.

5. *In-Process Controls:*

5.1. In-process control for chemical reactions may include the following:

(a) reaction time or reaction completion;

(b) reaction mass appearance, clarity, completeness or pH solutions; (c) reaction temperature;

(d) concentration of a reactant;

(e) assay or purity of the product;

(f) process completion check by TLC / any other means.

5.2. In-process control for physical operations may include the following:

(a) appearance and colour;

(b) uniformity of the blend;

(c) temperature of a process;

(d) concentration of a solution;

(e) processing rate or time;

(f) particle size analysis;

(g) bulk/tap density;

(h) pH determination;

(i) moisture content.

6. *Product Containers and Closures:*

6.1. All containers and closures shall comply with the pharmacopoeial or any other requirement, suitable sampling methods, sample sizes, specifications, test methods, cleaning procedures and sterilization procedures, when indicated, shall be used to assure that containers, closures and other component parts of drug packages are suitable and are not reactive, additive, adsorptive or leachable to an extent that significantly affects the quality or purity of the drug.

6.2. The drug product container shall be tested or re-examined as appropriate and approved or rejected and shall be identified and controlled under a quarantine system designed to prevent their use in manufacturing or processing operations for which these are unsuitable.

6.3 Container closure system shall provide adequate protection against foreseeable external factors in storage / transportation and use that may cause deterioration or contamination of the active pharmaceutical ingredient.

6.4. Bulk containers and closures shall be cleaned and, where indicated by the nature of the active pharmaceutical ingredient, sterilized to ensure that they are suitable for their intended use.

6.5. The container shall be conspicuously marked with the name of the product and the following additional information concerning :

(a) quality and standards, if specified;
(b) manufacturing licence number/drug master file number (whichever applicable), batch number;
(c) date of manufacture and date of expiry;
(d) method for container disposal (label shall give the methodology, if required);
(e) storage conditions, if specified and name and address of the manufacturer, if available.

6.6. Areas for different operation of active pharmaceutical ingredients (bulk drugs) section shall have appropriate area which may be suitably partitioned for different operations.

PART II

REQUIREMENTS OF PLANT AND EQUIPMENT

1. ***External Preparations:***

The following equipment is recommended for the manufacture of ‗External preparations' i.e. Ointments, Emulsion, Lotions, Solutions, Pastes, Creams, Dusting powders and such identical products used for external applications, whichever is applicable, namely :-

(1) [1][Mixing and storage tanks preferably of stainless steel or any other appropriate material].
(2) [2][Stainless steel container] (steam, gas or electrically heated). (3) Mixer (electrically operated).
(4) Planetary mixer.
(5) A colloid mill or a suitable emulsifier.
(6) A triple roller mill or an ointment mill.

1. Subs. by G.S.R. 431(E), dt. 30.6.2005; for ―mixing and storage tanks (Stainless steel)‖.
2. Subs. by G.S.R. 431(E), dt. 30.6.2005; for ―Jacketted Kettle‖.

(7) Liquid filling equipment (electrically operated).
(8) Jar or tube filling equipment [1] [***]

Area. - (1) A minmum area of thirty square meters for basic installation and ten square meters for Ancillary area is recommended.

(2) Areas for formulations meant for external use and internal use shall be separately provided to avoid mix-up.

[2][**Note:** The requirement for ancillary area in this part shall not apply to units registered before 1st January, 2002.]

2. ***Oral Liquid Preparations:***

The following equipments are recommended for the manufacture of oral/internal use preparations i.e. Syrups, Elixirs, Emulsions and Suspensions, whichever is applicable, namely: -

(1) [3][Mixing and storage tanks preferably of Stainless steel or any other appropriate material].
(2) Jacketted Kettle / Stainless steel tank (steam, gas or electrically heated).
(3) Portable stirrer (electrically operated).
(4) A colloid mill or suitable emulsifier (electrically operated).
(5) Suitable filtration equipment (electrically operated).
(6) Semi-automatic/automatic bottle filling machine.

(7) Pilfer proof cap sealing machine.
(8) Water distillation unit or deionizer.
(9) Clarity testing inspection units.

Area. - A minimum area of thirty square meters for basic installation and ten square meters for Ancillary area is recommended.

2[**Note:** The requirement for ancillary area in this part shall not apply to units registered before 1st January, 2002.]

3. ***Tablets:***

The Tableting section shall be free from dust and floating particles and may be air-conditioned. For this purpose, each 4[tablet compression machine] shall be isolated into cubicles and connected to a vacuum dust collector or an exhaust system. For effective operations, the tablet production department shall be divided into four distinct and separate sections as follows: -

(a) Mixing, Granulation and Drying section.
(b) Tablet compression section.
(c) Packaging section (strip/blister machine wherever required).
(d) Coating section (wherever required).

3.1. The following electrically operated equipments are recommended for the manufacture of compressed tablets and hypodermic tablets, in each of the above sections, namely: -

(a) Granulation-cum-Drying section:

(1) Disintegrator and sifter.
(2) Powder mixer.
(3) Mass mixer/Planetary mixer/Rapid mixer granulator.

1. The word _electrically operated' Omitted by G.S.R. 431(E), dt. 30.6.2005.
2. Ins by G.S.R. 431(E), dt. 30.6.2005.
3 Subs. by G.S.R. 431(E), dt. 30.6.2005, for —mixing and storage tanks (Stainless steel)‖.
4. Subs. by G.S.R. 431(E), dt. 30.6.2005, for _tablet machine'.

(4) 1[Granulator wherever required].
(5) Thermostatically controlled hot air oven with trays (preferably mounted on a trolley)/Fluid bed dryer.
(6) Weighing machines.

(b) Compression section:

(1) Tablet compression machine, single/multi punch/rotatory.
(2) Punch and dies storage cabinets.
(3) Tablet de-duster
(4) Tablet inspection unit/belt.
(5) 1[Dissolution test apparatus wherever required].
(6) In-process testing equipment like single pan electronic balance, hardness tester, friability and disintegration test apparatus.
(7) Air-conditioning and dehumidification arrangement (wherever necessary)

(c) Packaging section:

(1) Strip/blister packaging machine.
(2) Leak test apparatus (vacuum system).
(3) Tablet counters (wherever applicable).
(4) Air-conditioning and dehumidification arrangement (wherever applicable).

Area. – A minimum area of sixty square meters for basic installation and twenty square meters for Ancillary area is recommended for un-coated tablets.

(d) Coating section:

(1) Jacketted kettle [2][stainless steel container or any other appropriate material] (steam, gas or electrically heated for preparing coating suspension).

(2) Coating pan (Stainless steel).

(3) Polishing pan (where applicable).

(4) Exhaust system (including vacuum dust collector).

(5) Air-conditioning and Dehumidification Arrangement.

(6) Weighing balance.

[2][**Note:** The requirement for ancillary area in this part shall not apply to units registered before 1st January, 2002.]

3.2. The coating section shall be made dust free with suitable exhaust system to remove excess powder and fumes resulting from solvent evaporation. It shall be air-conditioned and dehumidified wherever considered necessary.

Area. – A minimum additional area of thirty square meters for coating section for basic installation and ten square meters for Ancillary area is recommended.

Separate area and equipment for mixing, granulation, drying, tablet compression, coating and packing shall be provided for Penicillin group of drugs on the lines indicated above. In case of operations involving dust and floating particles, care shall be exercised to avoid cross-contamination.

[2][**Note:** The requirement for ancillary area in this part shall not apply to units registered before 1st January, 2002.]

3.3. The manufacture of Hypodermic tablets shall be conducted under aseptic conditions in a separate air-conditioned room, the walls of which shall be smooth and washable. The granulation, tableting and packing shall be done in this room.

1. Subs. by G.S.R. 431(E), dt. 30.6.2005.
2. Ins. by G.S.R. 431(E), dt. 30.6.2005.

3.4. The manufacture of effervescent and soluble [1] [***] tablets shall be carried out in air-conditioned and dehumidified areas.

4. ***Powders:***

The following equipment is recommended for the manufacture of powders, namely:-

(1) Disintegrator.

(2) Mixer (electrically operated).

(3) Sifter.

(4) Stainless steel vessels and scoops of suitable sizes. (5) Filling equipment [1][***].

(6) Weighing balance.

In the case of operation involving floating particles of fine powder, suitable exhaust system shall be provided. Workers should be provided with suitable masks during operation.

Area. – A minimum area of thirty square meters is recommended to allow for the basic installations. Where the actual blending is to be done on the premises, an additional room shall be provided for the purpose.

[2][**Note:** The requirement for additional room in this part shall not apply to units registered before 1st January, 2002.]

5. ***Capsules:***

For the manufacture of capsules, separate enclosed area suitably air-conditioned and dehumidified with an airlock arrangement shall be provided. The following equipment is recommended for filling Hard Gelatin Capsules, namely: -

(1) Mixing and blending equipment (electrically or power driven). (2) Capsules filling units [1][***].

(3) Capsules counters (wherever applicable).
(4) Weighing balance.
(5) Disintegration test apparatus.
(6) Capsule polishing equipment.

Separate equipment and, filling and packaging areas shall be provided in penicillin and non-penicillin sections. In case of operations involving floating particles of fine powder, a suitable exhaust system shall be provided. Manufacture and filling shall be carried out in air- conditioned area. The room shall be dehumidified.

Area. –A minimum area of twenty-five square meters for basic installation and ten square meters for Ancillary area each for penicillin and non-penicillin sections is recommended.

[2][**Note:** The requirement for ancillary area in this part shall not apply to units registered before 1st January, 2002.]

6. ***Surgical Dressing:***

The following equipment is recommended for the manufacture of Surgical Dressings other than Absorbent Cotton Wool, namely:-

(1) Rolling machine.

1. Omitted by G.S.R. 431(E), dt. 30.6.2005.
2. Ins. by G.S.R. 431(E), dt. 30.6.2005.

(2) Trimming machine.
(3) Cutting equipment.
(4) Folding and pressing machine for gauze.
(5) Mixing tanks for processing medicated dressing.
(6) Hot air dry oven.
(7) Steam sterilizer or dry heat sterilizer or other suitable equipment. (8) Work tables/benches for different operations.

Area. – A minimum area of thirty square meters is recommended to allow for the basic installations. In case medicated dressings are to be manufactured, another room with a minimum area of thirty square meters shall be provided.

7. ***Ophthalmic Preparations***:.

For the manufacture of Ophthalmic preparations, separate enclosed areas with airlock arrangement shall be provided. The following equipment is recommended for the manufacture under aseptic conditions of Eye-Ointment, Eye-Lotions and other preparations for external use, namely:-

(1) Thermostatically controlled hot air ovens (preferably double ended).
(2) Jacketted kettle/stainless steel tanks (steam, gas or electrically heated).
(3) Mixing and storage tanks of stainless steel/Planetary mixer.
(4) Colloid mill or ointment mill.
(5) Tube filling and crimping equipment (semi-automatic or automatic filling machines). (6) Tube cleaning equipment (air jet type).
(7) Tube washing and drying equipment, if required.
(8) Automatic vial washing machine.
(9) Vial drying oven.

(10) Rubber bung washing machine.

(11) Sintered glass funnel, Seitz filter and filter candle (preferably cartridge and membrane filters).

(12) Liquid filling equipment (semi-automatic or automatic filling machines).

(13) Autoclave (preferably ventilator autoclave).

(14) Air conditioning and dehumidification arrangement (preferably centrally air-conditioned and dehumidification system).

(15) Laminar airflow units.

Area. – (1) A minimum area of twenty-five square meters for basic installation and ten square meters for Ancillary area is recommended. Manufacture and filling shall be carried out in air-conditioned areas under aseptic conditions. The rooms shall be further dehumidified as considered necessary if preparations containing antibiotics are manufactured.

(2) Areas for formulations meant for external use and internal use shall be separately provided to avoid mix up.

1[**Note:** The requirement for ancillary area in this Part shall not apply to units registered before 1st January, 2002.]

8. ***Pessaries and Suppositories:***

(i) The following equipment is recommended for manufacture of Pessaries and Suppositories, namely: -

(1) Mixing and pouring equipment

(2) Moulding equipment.

(3) Weighing devices.

1. Ins. by G.S.R. 431(E), dt. 30.6.2005.

Area. – A minimum area of twenty square meters is recommended to allow for the basic installation.

(ii) In the case of pessaries manufactured by granulation and compression, the requirements as indicated under ―Item 3 of Tablet‖, shall be provided.

9. ***Inhalers and Vitrallae:***

The following equipment is recommended for manufacture of inhalers and vitrallae, namely: -

(1) Mixing equipment.

(2) Graduated delivery equipment for measurement of the medicament during filling. (3) Sealing equipment.

Area. – An area of minimum twenty square meters is recommended for the basic installations.

10. ***Repacking of drugs and pharmaceutical chemicals:***

The following equipment is recommended for repacking of drugs and pharmaceuticals chemicals, namely:-

(1) Powder disintegrator.

(2) Powder sifter (electrically operated).

(3) Stainless steel scoops and vessels of suitable sizes.

(4) Weighing and measuring equipment.

(5) Filling equipment (semi-automatic / automatic machines).

(6) Electric sealing machine.

Area. – An area of minimum thirty square metres is recommended for the basic installation. In case of operations involving floating particles of fine powder, a suitable exhaust system shall be provided.

11. ***Parenteral Preparations***

The whole operation of manufacture of parenteral preparations (small volume injectables and large volume parenterals) in glass and plastic containers may be divided into the following separate areas/rooms, namely: -

11.1 *Parenteral preparations in glass* containers*:* –

(1) *Water management area*: This includes water treatment and storage.

(2) *Containers and closures preparation area*: This includes washing and drying of ampoules, vials, bottles and closures.

(3) *Solution preparation area*: This includes preparation and filtration of solution. (4) *Filling, capping and sealing area*: This includes filling and sealing of ampoules and/or filling, capping and sealing of vials and bottles.

(5) Sterilization area

(6) Quarantine area

(7) Visual inspection area.

(8) Packaging area

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The following equipment is recommended for different above-mentioned areas, namely: -

(a) Water management area:

(1) De-ionised water treatment unit.

(2) Distillation (multi-column with heat exchangers) unit.

(3) Thermostatically controlled water storage tank.

(4) Transfer pumps.

(5) Stainless steel service lines for carrying water into user areas.

(b) Containers and closures preparation area:

(1) Automatic rotary ampoule/vial/bottle washing machine having separate air, water distilled water jets.

(2) Automatic closures washing machine,

(3) Storage equipment for ampoules, vials, bottles and closures.

(4) Dryer/sterilizer (double ended)

(5) Dust proof storage cabinets.

(6) Stainless steel benches/stools.

(c) Solution preparation area:

(1) Solution preparation and mixing stainless steel tanks and other containers. (2) Portable stirrer.

(3) Filtration equipment with cartridge and membrane filters/bacteriological filters. (4) Transfer pumps.

(5) Stainless steel benches/stools

(d) Filling, capping and sealing area:

(1) Automatic ampoule/vial/bottle filling, sealing and capping machine under laminar air flow workstation.

(2) Gas lines (Nitrogen, Oxygen, Carbon dioxide) wherever required. (3) Stainless steel benches / stools.

(e) Sterilization area:

(1) Steam sterilizer (preferably with computer control for sterilization cycle along with trolley sets for loading/unloading containers before and after sterilization). (2) Hot air sterilizer (preferably double ended).

(3) Pressure leak test apparatus.

(f) Quarantine area. –

(1) Storage cabinets.

(2) Raised platforms/steel racks.

(g) Visual inspection area:

(1) Visual inspection units (preferably conveyor belt type and composite white and black assembly supported with illumination).

(2) Stainless steel benches/stools.

(h) Packaging area. -

(1) Batch coding machine (preferably automatic).

(2) Labelling unit (preferably conveyor belt type).

(3) Benches/stools.

Area. – (1) A minimum area of one hundred and fifty square meters for the basic installation and an Ancillary area of one hundred square meters for Small Volume Injectables is recommended. For Large Volume Parenterals, an area of one hundred and fifty square meters each for the basic installation and for Ancillary area is recommended. These areas shall be partitioned into suitable enclosures with airlock arrangements.

(2) Areas for formulations meant for external use and internal use shall be separately provided to avoid mix up.

(3) Packaging materials for large volume parenteral shall have a minimum area of 100 square meters.

[1][**Note:** The requirement for ancillary area in this part shall not apply to units registered before 1st January, 2002.]

11.2 *Parenteral preparations in plastic containers by Form-Fill-Seal/Blow, Fill-Seal Technology.*-The whole operation of manufacture of large volume parenteral preparations in plastic containers including plastic pouches by automatic (all operations in one station) Form-Fill-Seal machine or by semi-automatic blow moulding, filling-cum-sealing machine may be divided into following separate areas/rooms, namely: -

(1) Water management area.

(2) Solution preparation area.

(3) Containers moulding-cum-filling and sealing area.

(4) Sterilization area.

(5) Quarantine area .

(6) Visual inspection area.

(7) Packaging area.

The following equipment is recommended for different above mentioned areas namely: -

(a) Water management area:

(1) De-ionised water treatment unit.

(2) Distillation unit (multi column with heat exchangers).

(3) Thermostatically controlled water storage tank.

(4) Transfer pumps.

(5) Stainless steel service lines for carrying water into user areas.

(b) Solution preparation area:

(1) Solution preparation and storage tanks.

(2) Transfer pumps.

(3) Cartridge and membrane filters.

(c) Container moulding-cum-filling and sealing area:

(1) Sterile Form-Fill-Seal machine (all operations in one station with built-in laminar air flow workstation having integrated container output conveyor belt through pass box).

(2) Arrangement for feeding plastic granules through feeding-cum-filling tank into the machine.

1. Ins. by 431(E), dt. 30.6.2005.

(d) Sterilization area: Super heated steam sterilizer (with computer control for sterilization cycle along with trolley sets for loading/unloading containers for sterilization).

(e) Quarantine area:- Adequate number of platforms/racks with storage system.

(f) Visual inspection area. - Visual inspection unit (with conveyor belt and composite white and black assembly supported with illumination).

(g) Packaging area:

(1) Pressure leak test apparatus (pressure belt or rotating disc type). (2) Batch coding machine (preferably automatic).

(3) Labelling unit (preferably conveyor belt type).

Area. – (1) A minimum area of two hundred and fifty square meters for the basic installation and an Ancillary area of one hundred and fifty square metres for large volume parenteral preparations in plastic containers by Form-Fill-Seal technology is recommended. These areas shall be partitioned into suitable enclosures with airlock arrangements.

(2) Areas for formulations meant for external use and internal use shall be separately provided to avoid mix up.

(3) Packaging materials for large volume parenteral shall have a minimum area of 100 square meters.]

1[**Note:** The requirement for ancillary area in this part shall not apply to units registered before 1st January, 2002.]

1[**Note I:** There are certain categories of drugs such as chemicals and pharmaceutical aids, gauzes and bandages, medicinal gases, empty gelatin capsules, non- chemical/mechanical contraceptives, diagnostic kits and reagents, medical devices, new dosage forms and their delivery systems, disinfectant fluids, antacids, raw-materials manufactured from sea bittern, veterinary biologicals including poultry vaccines, re-packing of drugs, etc. for which this Schedule does not prescribe specific requirements of space and equipments. The Licensing Authority, as the case may be, in respect of such categories of drugs, have the discretion to modify the requirements of this Schedule, if he is of the opinion that having regard to the nature off the products and extent of manufacturing operations and for reasons to be recorded in writing, it is necessary to relax or alter them in the circumstances of a particular case and direct the manufacturer to carry out necessary modifications in them and the modifications having been made, approve the manufacturer of such categories of the drugs.

Note II: In case of manufacturers licensed to manufacture drugs prior to the 11th December, 2001, the requirements of this Schedule shall also apply to them from 1st July, 2005.]

1. Ins. by G.S.R. 431(E), dt. 30.6.2005.

[1] [SCHEDUE M-I

[*See* Rule 85E (2)]

GOOD MANUFACTURING PRACTICES AND REQUIREMENTS OF PREMISES, PLANT AND EQUIPMENT FOR HOMOEOPATHIC MEDICINES

1.GENERAL REQUIREMENTS:

1.1 Location and Surroundings: - The premises shall be situated at a clean place which shall not be adjacent to open drains, public lavatory or any factory producing pollution of any kind, garbage dump, slaughter house or any other source likely to cause contamination from the external environment. The premises shall be located away from railway lines so that the performance of sensitive electronic equipment is not affected by vibrations. There shall be no open drains inside or outside the manufacturing premises. It shall be so designed that the entry of rodents is checked. The drains shall facilitate easy flow of the effluent and shall be cleared periodically.

1.2 Building: - The premises shall not be used for any purpose other than manufacture of homoeopathic drugs and no part of the manufacturing premises shall be used for any other purpose. Other facilities, if needed, could be provided in separate building(s) in the same campus. Crude raw materials, packing materials, etc. shall be stored and handled in places earmarked for them and shall not be taken inside areas where critical operations of manufacture are done excepting processed raw material. Heating, washing, drying, packing and labelling etc. wherever needed, shall be done in dedicated ancillary areas adjacent to the manufacturing sections concerned. The walls and floorings of manufacturing areas shall be smooth and free from chinks, cracks and crevices and shall be washable. The design of the windows, windowpanes and all fittings shall be such that they will not facilitate accumulation / lodging of dust and other contaminants.

1.Subs. by G.S.R. No. 678(E) , dt. 31-10-2006, for Schedule MI. Earlier Schedule MI was inserted by G.S.R. 507 (E), dt: 12.6.1987. Schedule M1, before substitution, stood as under.:

—SCHEDUE M-I

[*See* Rule 85E (2)]

1. Requirement of factory premises for manufacture of Homeopathic preparations-

(a) *Location and surroundings.* - The factory shall be situated in a place which shall not be adjacent to an open sewage drain, public lavatory or any factory which produces a disagreeable or obnoxious odour or fumes or large quantities of soot, dust or smoke. The factory shall be located in a sanitary place, remove from filthy surroundings.

(b) *Buildings*. - The part of the building used for manufacturing shall not be used for a sleeping place and no sleeping place adjoining to it shall communicate therewith except through open air or through an intervening open space. The walls of the room in which manufacturing operations are carried out shall, upto a height of six feet from the floor, be smooth, waterproof and shall be capable of being kept clean. The flooring shall be smooth, even and washable and shall be such as not to permit retention or accumulation of dust. There shall be no chinks or crevices in the walls or floor.

(c) The building used for the factory shall be constructed so as to permit production under hygienic conditions laid down in the Factories Act, 1948 (63 of 1948).

(d) *Water Supply.* - The water used in manufacture shall be pure and drinkable quality, free from pathogenic microorganisms.

(e) *Disposal of waste*. - There should be adequate arrangement for disposal of waste-water and other residues from the laboratory.

(f) The rooms should be airy and clean and the temperature of the room should be moderately comfortable.

(g) *Health, Clothing and Sanitary requirement of the Staff.* - All workers shall be free from contagious or obnoxious disease. Their clothing shall consist of a white or coloured uniform suitable to the nature of the work and the climate, and shall be clean. Adequate facilities for personal cleanliness, such as clean towels, soap and hand scrubbing brushes, shall be provided separately for each sex. The workers shall be required to wash and change into clean footwear before entering the rooms where the manufacturing operations are carried on. Workers shall be

required to wear either a clean cap or a suitable headgear so as to avoid any possibility of contamination by air or perspiration.

(h) *Medical services.* - The manufacturer shall provide adequate facilities for First Aid, Medical inspection of workers at the time of employment and periodically check-up thereafter at least once a year.

(i) *Working benches.* - Working benches shall be provided for carrying out operations such as filling, labelling, packing etc. Such benches shall be fitted with smooth, impervious tops capable of being washed.

(j) *Container management*. - Where operations involving use of containers such as bottles, phials and jars are conducted, there shall be adequate arrangements separated from potentisation chamber for washing, cleaning and drying such containers, with suitable equipment for the purpose. Wherever these are attended manually adequate precaution of perfection in respect of cleanliness and avoidance of pollutants shall be taken.

2. Requirements of Plant and Equipment:

(a) Mother tinctures. External tinctures and Mother solution section. - The following plant and equipment shall be provided namely: -

(i) Disintegrator.
(ii) Sieved Separator.
(iii) Balances and fluid measures.
(iv) Chopping boards and knives.
(v) Macerators with lids.
(vi) Percolators with lids and regulated discharge.
(vii) Moisture determination apparatus or other suitable arrangement. (viii) Filtering arrangement.
(ix) Mixing vessels and suitable non-metallic storage containers.
(x) Portable stirrers.
(xi) Water still.

Note*:* (1) As far as possible metal contacts may be avoided once the drug is processed. (2) An area of 55 sq. meters is recommended for basic installations.

(3) Adequate separate storage facility should be provided for raw material quarantine, storage and bonded room for alcohol where applicable.

(4) Separate and suitable storage facility should be provided for fresh herbs and odorous raw materials.

(5) Adequate laboratory facility shall be provided for testing of raw materials and finished products,

(b) Potentisation Section. - (1) The following arrangements are recommended for container for closure preparation section namely:

(i) Washing tanks with suitable brushing arrangement manual or mechanical.
(ii) Purified Water rinsing tank
(iii) Closure macerating or washing tanks.
(iv) Drying chambers.

An area of 20 sq. meters is recommended for basic installations.

(2) The following arrangements are recommended for potency preparation section, namely: –
(i) Working tables with washable top.
(ii) Facilities for separate storage of different grades of back potencies.
(iii) Suitable measuring devices for discharge of drug and diluent in potentisation vial, (iv) Potentiser with counter or suitable manual arrangement.

Note*:* - (1) Different droppers shall be used for different drugs potencies.

(2) All measuring devices shall be of metric system and be made of glass and shall be free from metallic contents.

(3) It is desired that glass droppers etc. intended for re-use after cleaning should be sterilized by autoclave or heating in a hot air oven.

(4) Plastics, rubber tubes, bulks etc. coming in contact with tinctures or back potencies should not be re-used for other tincture and potencies.

(5) Method of potentisation will be adopted as specified in Homoeopathic Pharmacopoeia of India Vol. I.

3. Triturating, Tableting and Pill/Globules section -

(3) The following arrangements are recommended: (i)

Triturating machine for suitable device.

(ii) Disintegrator.

(iii) Mass Mixer. (iv)
Granulator. (v)
Oven.

(vi) Tableting punches or machines.

(vii) Kettle (Steam/gas/electrically heated) for preparation solution. (viii) Dryers. (ix) Sieved separator, tablet counters and balances.

Note: Tablet section shall be free from dust and floating particles. An area of 55 sq. meters is recommended for basic installations.

(4) Ointments and lotion section:

The following arrangements are recommended namely: -

(i) Mixing tank
(ii) Kettle (Steam, gas or electrically heated). (iii)
Suitable powder mixer
(iv) Ointment mill
(v) Filling equipment or arrangement.

An area of 20 sq. meters is recommended for basic installations. (5) Syrups and tonics:

The following arrangements are recommended namely:- (i)
Mixing and storage tank.

(ii) Potable mixer.

(iii) Filtering equipment. (iv)
Water still / Deioniser.

(v) Filling and sealing equipment.

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An area of 20 sq. meters is recommended for basic installations. (6)

Ophthalmic Preparations:

The following equipment is recommended for manufacture under aseptic conditions of Eye-Ointments, Eye-Drops, Eye-lotions and other preparations for external use, namely: -

(i) Hot air even electrically heated with thermostatic control. (ii) Colloid mill or ointment mill.

(iii) Kettle (gas or electrically heated) with suitable mixing arrangement. (iv) Tube filling equipment.

(v) Mixing and storage tanks of stainless steel or of other suitable material.

(vi) Sintered glass funnel, Seitz filter or filter candle. (vii)
Liquid filling equipment.

(viii) Autoclaves.

Adequate precaution should be taken to ensure that the finished product is sterile. An area of 20 sq. meters is recommended for basic installations.

(7) Adequate arrangements for space and equipment should be made for labelling and packing.

2.PLANT AND EQUIPMENT:

2.1 General: - The design of the plant shall be suitable for the nature and quantum of the activities involved. Equipment shall be installed in such a manner as to facilitate easy flow of materials and to check criss-cross movement of the personnel. The entry to all manufacturing sections shall be regulated and persons not associated with the activities in the sections shall not have access to them. There shall be arrangements for personal cleanliness of workers and toilets. These shall be separate for men and women workers. There shall be suitable arrangement, separate for men and women, to change from their outside dress and footwear into the factory dress and footwear. Uniforms of suitable colours and fabric which facilitate proper washing and which do not shed fibres other contaminants shall be provided. Suitable head-covers and gloves shall be provided to the workers. The manufacturing premises shall not be used for dining. There shall be

separate area for the personnel to take food or rest. Toilets shall be located in or adjacent to any of the areas concerned with any manufacturing activity. Spitting, smoking, chewing, littering, etc. in the manufacturing or ancillary areas shall not be permitted. Standard operating practices (SOPs) for cleaning and sanitation, personal hygiene of the workers, general and specific upkeep of the plant, equipment and premises and every activity associated with manufacture of drugs including procurement, quarantine, testing and warehousing of material shall be written and adopted. No person with any contagious disease shall be involved in any of the manufacturing activities. There shall be proper arrangements for maintenance of the equipment and systems. The performance of every equipment and system shall be properly validated and their use shall be monitored. Dos and don'ts in the matter of the use of the plant and equipment as may be applicable shall be written and displayed in all places.

There shall be separate dedicated areas for each ancillary activity such as receipt, cleaning, warehousing and issue of raw materials, packaging materials, containers and closures, finished goods etc. Adequate measures shall be taken to prevent entry/presence etc. of insects, rodents, birds, lizards and other animals into the raw material handling areas. Every material shall have proper identification and control numbers and inventory tags and labels displaying status of the quality being used, etc. There shall be proper arrangements and SOPs for preventing mix-up of materials at every stage of handling. There shall be separate arrangements for handling and warehousing of materials of different origins. Materials with odour shall be kept in tightly closed containers and shall be well protected from other materials. Fresh materials and odorous materials shall, preferably be stored in separate dedicated areas. Where bonded manufacturing and / or warehousing facilities are required as per

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Excise laws, the facilities required shall be provided without compromise on the requirements specified above.

A well equipped laboratory for quality control/quality assurance of raw materials and finished products and for carrying out in-process controls shall be provided.

(a) Rooms: - The rooms shall be airy, ventilated, and maintained at temperatures which are moderate and comfortable. Sections which are required to be sterile, air-conditioned and provided with air handling system shall be designed accordingly. All sections shall be free from insects, birds, rodents, worms etc. and suitable measures shall be taken to prevent the same from finding ways to the sections and equipment.

(b) Water: - The water used for manufacture of drugs shall be of the quality as prescribed in the rules or in the Homoeopathic Pharmacopoeia concerned, as the case may be, and shall be prepared from pure drinking quality water, free from pathogenic organisms.

(c) Disposal of waste: - Effluents, organic and inorganic wastes shall be disposed of in such a manner as may be prescribed in the laws pertaining to pollution control and if no such law exists in the place of manufacture, they shall be rendered harmless and shall be disposed of in such a manner that they are not hazardous to health of the public or cattle or plants.

(d) Factories Act: - The provisions of the Factories Act, 1948(Act 63 of 1948), as applicable shall be adhered to.

(e) Medical Services:- All persons concerned with any activity pertaining to manufacture of drugs including handling of raw materials, packing materials, packing and labelling of drugs, etc. shall be medically examined for fitness at the time of employment and subsequently at periodic intervals and records thereof shall be maintained.

(f) Safety measures: - First-aid facilities shall be provided in such a manner that they are easily accessible and staff shall be imparted knowledge and training in first-aid

measures as may be needed. Fire control equipment in suitable numbers shall be provided at easily accessible places near all sections including stores and warehouses.

(g) Workbenches: - Workbenches suitable to the nature and quantum of the work involved shall be provided in all sections. Such work benches in general, shall have smooth, washable and impervious tops and the parts shall not be rough or rusty or damaged otherwise.

(h) Container management: - Proper arrangements shall be made for receiving containers, closures and packing materials in secluded areas and for de-dusting the same, removal of wastes, washing, cleaning and drying. Suitable equipment shall be provided as may be needed, considering the nature of work involved. Where soaps and detergents are used to wash containers and closures used for primary packing, suitable procedure shall be prescribed and adopted for total removal of such materials from the containers and closures. Plastic containers which are likely to absorb active principle or which are likely to contaminate the contents may not be used.

Glass containers used shall be made of neutral glass. The closures and washers used shall be of inert materials which shall not absorb the active principles or contaminate the contents or which may otherwise be likely to cause deterioration of quality. The containers, closures and packing materials shall protect the properties of the medicines, Tablets, if blister-packed, shall have secondary protective packaging to protect the medicines from moisture, odour etc. Neutral glass phials and epoxy-coated closure shall be used for eye-drops. Transparent plastic containers may be used for eye-drops containing only aqueous preparations. Sterile plastic nozzles may be provided to eye-drops separately along with the medicine, whatever needed.

2.2. Personnel.- Manufacture of drugs shall be under the control of approved technical staff that shall possess the qualifications prescribed in rule 85.

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3. REQUIREMENT OF EQUIPMENT AND FACILITIES:

3.1 Mother tinctures and mother solutions:- The following equipment and facilities shall be provided:-

(i) Disintegrator;
(ii) Sieved separator;
(iii) Balances, weights and fluid measures, all in metric system;
(iv) Chopping table/board and knives;
(v) Macerators with lids (all made of stainless steel of grade 304 or neutral glass); (vi) Percolators (all made of stainless steel of grade 304);
(vii) Moisture determination apparatus;
(viii) Filter press/Sparkler filter (all metal parts shall be of stainless steel);
(ix) Mixing and storage vessels (Stainless steel of grade 304);
(x) Portable stirrers (Rod, blades and screws shall be of stainless steel);
(xi) Water still/water purifier;
(xii) Macerators and percolators for preparing mother solutions of materials of chemical origin. These shall be of material, which will not react with the chemicals, used and which do not bleach; and
(xiii) Filling and sealing machine.

The area and facilities for manufacture of mother tinctures and mother solutions shall be separate and shall be 55 square meters for each for basic installations.

3.2 Potentisation section :- The section shall have the following facilities:-

(i) Work benches with washable impervious tops;
(ii) Facilities for orderly storage of different potencies and back-potencies of various drugs;
(iii) Suitable devices for measuring and dispensing of potencies/back-potencies into the

potentisation phials;

(iv) Potentiser with counter.

An area of 20 square meters shall be provided for basic installations.

Note: -

(a) The requirement of potentiser is not mandatory. The process may be done manually also with proper SOPs. Potentiser, if used, shall be properly validated and shall be calibrated every time before commencement of work for proper performance.

(b) The manufactur er sh all use back-poten cies procur ed fr om Licen sed manufacturers and the firm shall maintain proper records of purchase or shall prepare own-back potencies . Every container of potencies and back-potencies shall be kept properly labelled and there shall not be mix-up of different medicines and different potencies.

3.3 Containers and Closures Section: - Separate area for preparation of containers and closures shall be provided adjacent to the potentisation section. This area shall have the following facilities:-

(i) Washing tanks with suitable mechanical or hand operated brushes;

(ii) Rinsing tanks. Purified water shall be used for rinsing;

(iii) Closures washing / macerating tanks;

(iv) Driers;

Note: -

(a) Different droppers shall be used only for each different medicine and different potency.

(b) All measures shall be in metric system. Measures used shall be of neutral glass. Metal droppers and plastic droppers shall not be used.

(c) Glass droppers shall be reused only after proper cleaning and sterilization.

(d) Potentisation shall be done by the method(s) prescribed in the Homoeopathic Pharmacopoeia of India.

3.4 Trituration, Tableting, Pills and Globules making sections:- The following basic equipment and facilities shall be provided:-

(i) Triturating Machine;

(ii) Disintegrator;

(iii) Mass Mixer;

(iv) Granulator;

(v) Electrical Oven;

(vi) Tablets punching Machine;

(vii) Kettle (steam or electrically heated) for preparing solutions;

(viii) Driers for drying granules and tablets;

(ix) Sieved separator (stainless steel);

(x) Tablet counter;

(xi) Balances;

(xii) Coating Pan with spray-gun;

(xiii) Multi-sifter

(xiv) Mill with perforations.

An area of 55 square meters shall be provided for basic installations. The area shall be suitably divided into cubicles to minimize cross contamination, mix-up etc.

Note: - The section shall be free from insects, worms, rodents, dust and other floating particles and moisture.

3.5 Syrups and other oral liquids section:- The following basic equipment and facilities shall be provided:-

(i) Mixing and storage tanks (stainless steel of grade 304);

(ii) Portable stirrer (rod, blades and screws shall be of stainless steel);

(iii) Filter press / Sparkler filter (all metal parts shall be of stainless steel); (iv) Filling

and sealing machine;

(v) pH meter.

An area of 20 square meters shall be provided for basic installations. The section shall be free from dust and other floating particles, cobwebs, flies, ants and other insects, birds, lizards and rodents.

(1) Adequate number of workbenches shall be provided.

(2) Visual inspection table shall be provided. This shall comprise of a colour con trast backgr ound with lamp for providing diffused ligh t, mounted on a suitable table.

3.6 Ointments and lotions section :- The following basic equipments and facilities shall be provided:-

(i) Mixing tanks (Stainless steel)

(ii) Kettle (steam or electrically heated) for preparing solutions

(iii) Suitable powder / planetary Mixer

(iv) Ointment mill / colloidal Mill / Emulsifier

(v) Filling and sealing machine / Crimping machine

(vi) Filtering equipment

(vii) Balance and weights

A minimum area of 20 square meters shall be provided for basic installations. An ancillary area for washing vessels and equipment shall be provided. An ancillary area for heating purposes shall also be provided.

3.7 Ophthalmic preparations section:- The following basic equipment and facilities shall be provided:-

(i) Hot air oven, electrically heated, with thermostatic control;

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(ii) Laminar Air Flow bench;

(iii) Air Handling Unit with HEPA filters to provide filtered air and positive pressure to the section and air-locks;

(iv) Ointment mill / colloidal mill;

(v) Mixing and storage tanks (Stainless steel of grade 304);

(vi) Pressure vessels, as may be needed;

(vii) Sintered glass funnels, Seitz Filter / Filter candle;

(viii) Vacuum pump;

(ix) Filling machines for liquids ointments etc.;

(x) Autoclaves with pressure and temperature gauges; and

(xi) Necessary workbenches, visual inspection bench, etc.

Area: Minimum area of 20 square meters shall be provided for basic installations.

Note: -

1. The section shall have a clean room facility of Class 100 specification.

2. The section shall be air-conditioned and humidity controlled.

3. Entry to the sections shall be regulated through air-locks with differential air pressures with the air-lock adjacent to the section having higher pressure and the first one through which entry is made with the least pressure.

4. Materials shall be passed to the sections through suitable hatches.

5. The personnel shall wear sterile clothing including headgear, which shall not shed fibre.

6. Washing of phials shall be done in separate areas with proper equipment. Proper facilities shall be provided in the area for washing vessels.

7. Separate area shall be provided for packing and labelling.

4. QUALITY CONTROL DIVISION:

4.1 Functions: - A separate quality control division shall be provided in the premises. The section shall be under the control of an approved technical officer, independent of the manufacturing division and directly responsible to the management. The section shall be responsible for ensuring the quality of all raw materials, packing materials and finished goods. The section shall also carry out in-process quality

checks of the products. The section shall be responsible for the stability of the products and for prescribing their shelf life wherever applicable.

The functions of the division shall include:-

(1) To test the identity, quality and purity of the raw materials and to recommend rejection of the material of poor quality and approve materials of the prescribed quality only.

(2) To test the identity, quality and purity of the finished products and to recommend rejection of the material of poor quality and to approve materials of the prescribed quality only.

(3) To prepare and validate the methods of analysis, validate the equipment, monitor their use, take steps for proper maintenance, etc.

(4) To approve or reject container s, closures and packaging materials in accordance with the prescribed norms.

(5) To exercise / carry out in-process control of products.

(6) To prescribe SOPs on all matters concerning quality of materials and products.

(7) To monitor the storage and handling of raw materials, finished products, containers, closures and packaging materials.

(8) To investigate complaints on quantity of products and take / recommend appropriate measures and to examine returned goods and recommend their proper disposal.

4.2 Personnel: - The quality control staff shall be full-time personnel. Analysis and tests of drugs, raw materials, etc. shall be done by qualified and approved technical staff. The technical staff shall have the minimum qualification of degree in Homoeopathic Pharmacy or Science with Chemistry or Botany as the principal subject and experience of not less than

two years in the test and analysis of medicines including handling of instruments.

4.3 Equipment: - The following equipment shall be provided:-

(i) Microscope of suitable magnification and photographic device; (ii) Dissecting microscope;

(iii) TLC apparatus;

(iv) UV lamp viewer; (v) Monopan Digital Electronic Balance;

(vi) Hot air oven;

(vii) Distillation apparatus;

(viii) Water Bath; (ix) Polarimeter;

(x) Refractometer;

(xi) Melting point apparatus;

(xii) pH meter;

(xiii) Magnetic stirrer;

(xiv) Table Centrifuge;

(xv) Muffle furnace / electric Bunsen;

(xvi) Moisture determination apparatus;

(xvii) U.V. Spectrophotometer;

(xviii) Rotary microtome / Section cutting facilities;

(xix) Tablet Disintegration Machine.

5. RAW MATERIALS:

5.1 Raw materials of Plant Origin:-

(a) The raw materials of plant origin used for manufacture of drugs shall be of the following specifications:-

(i) the materials shall be those recently collected and dried and shall be free from moisture so as to eliminate the risk of deterioration and infestation with pests moulds, etc. The materials shall be collected when the atmospheric temperature is suitable where its active constituents are not changed / damaged / destroyed.

(ii) when fresh materials are to be used, the time lapse from the time of collection to use shall be minimized to the extent possible;
(iii) the materials should be taken from healthy plants and shall be free from parasites, moulds, etc.;
(iv) the materials shall be free of inorganic or organic foreign matter;
(v) when dry materials are procured, they shall be from healthy plants and shall be in unprocessed form, free from all extraneous matters such as fungus, insects, moulds, pathogenic organisms, etc. and should not be more than six months old. Plant materi alsof Agaricaceae, which are perishable shall be used within one week of ollection.

(b) To facilitate proper identification and purity of the material and to exercise proper quality control of the material, the following conditions must be satisfied:-
(i) a small twig of the plant with leaves shall be available if the part used is bark of the plant;
(ii) an entire plant or part or aerial twig with leaves and some uncut roots / rhizomes / bulbs shall be available if the part used is a root /rhizome / bulb;
(iii)
if plants with flowers are to be used, a few dry flowers shall also be available with the aerial twig;
(iv) if the material used is a mould or of the plant families Agaricaceae, Polyporaceae/ amanitacaea / Boletaceae / Russulaceae, a whole specimen plant / mould shall be available in properly dried form;
(v) the materials shall be free from insecticides, fungicides, etc;
(vi) the materials shall be in open mesh bags or in suitable material which permits the passage of air inside;
(vii) each consignment of the material shall be accompanied by a statement of the supplier‘s name; name of the plant with description of the part supplied. The

pharmacopoeial reference, place of collection /harvest, date and time of collection and packaging and weight.

5.2 Raw material of Chemical origin: - They shall be of respective pharmacopoeial standards and statements of their specification shall accompany the materials.

5.3 Raw materials of animal origin: - The materials shall be those collected from healthy animals and shall be of pharmacopoeial specifications. The materials shall be those collected, packed and transported under proper hygienic conditions and well protected from all contamination. The materials shall be accompanied by statements as in para _a‘ above. In case of drugs derived from a whole insect, bulk of such drugs along with some uncut whole insect should be provided / maintained for records.

5.4 Sarcodes: - The materials shall be those collected from healthy animals and shall be of pharmacopoeial specification. The materials shall be those collected, packed and transported under proper hygienic conditions and well protected from all contamination. The materials shall be accompanied by statements as in the Para _a‘ above. The materials shall be tested to see that they are free from pathogenic organisms such as E. Coli, Salmonella, etc.

5.5 Nosodes: - These shall be of pharmacopoeial specifications. As these are derived from diseased animals or human beings, they shall be autoclaved immediately after collection and preserved and transported under proper hygienic conditions and well protected from all contamination. Before use, these shall be sterilized by autoclaving and shall comply with the test for sterility as specified in the Homoeopathic Pharmacopoeia.

6. PROCEDURES:

6.1 Manufacture of Mother tinctures: -

(a) Every material shall be identified and checked for its purity. They shall be cleaned and processed by cutting, chopping, etc. for use in macerators / percolators. A specimen of the material shall be preserved till approval of the product for release for sale.

(b) The design and procedures adopted shall ensure reproduction of the product of the same quality every time.

(c) Mother tinctures shall be preserved in tight closed neutral containers at temperatures preferably below 250 C, protected from light.

6.2 Manufacture of Attenuations: -

(a) Attenuations shall be prepared in a clean room environment with filtered air and positive pressure inside suitable for the operations.

(b) The methods used shall be reproducible and shall be validated.

(c) The containers, tubings, etc. of the machines used for manufacture of attenuations shall be thoroughly washed, cleaned and dried after attenuation of a drug. Regular checks shall be carried out on the materials.

(d) The parts of the equipment that come into contact with the attenuation materials shall be of neutral quality and shall not cause any contamination to the material.

(e) Attenuations shall be preserved in properly labeled glass containers.

(f) Alcohol and other vehicles used shall be of Homoeopathic pharmacopoeia specification and shall be free from impurities.

6.3 Trituration: - Trituration technique is used to manufacture drugs from insoluble strains. The procedure / method specified in the Homoeopathic pharmacopoeia shall be adopted. **6.4 Formulations:-** Compound formulations shall preferably be in liquid and solid forms and the potency of the ingredients shall be in detectable quantity preferably be in 3x except in case of highly poisonous material and toxins which should not be below 6x. The ingredients shall be compatible to each other. Complete pharmacopoeial name of each ingredient shall be printed on the label along with composition.

6.5 Medicated Insert Pellets: - (a) Pellets shall be manufactured in clean rooms free from particulate contaminants. The equipment used shall enable prevention of contamination and cross- contamination.

(b) The procedures shall be validated.

7. LABORATORY CONTROLS:

Tests as per the pharmacopoeia and requirements shall be carried out on products and materials. The stability of the products shall be established by proper methods. Sterility tests,

wherever applicable, shall be carried out. Control samples shall be preserved for not less than three years after the last sales.

8. PACKINGAND LABELLING:

A minimum area of 50 square meters shall be provided for packing and labeling section.

9. EXPIRYDATE:

Not exceeding sixty (60) months from the date of manufacture.

10. STANDARD OPERATING PRACTICES:

Standard Operating Practices (SOPs) shall be developed for various activities such as receipt, identification, cleaning, drying, warehousing, issue, handling, sampling etc. of all materials. Labels and packing materials shall be examined for correctness and compliance with rules. Records shall be maintained for their printing, use, destruction etc.

11. RECORDSAND REGISTERS:

Records shall be maintained for all the activities. These shall include records of production, records of raw materials, records of testing, records of sales and other supplies, records of rejection, complaints and actions taken, SOPs and records in respect of compliance thereof, log books of equipment, master formula records, records of medical examination and fitness of personnel etc. All records shall be maintained for a period of one year after the expiry of a batch or for three years whichever is later.

[1][SCHEDULE M-II

[*See* Rule 139]

REQUIREMENTS OF FACTORY PREMISES FOR MANUFACTURE OF COSMETICS

I. *GENERAL REQUIREMENTS*

(A) *Location and surroundings.*–The factory shall be located in a sanitary place and hygienic conditions shall be maintained in the premises. Premises shall not be used for residence or be interconnected with residential area. It shall be well ventilated and clean.

(B) *Buildings.*– The buildings used for the factory shall be constructed so as to permit production under hygienic conditions and not to permit entry of insects, rodents, files, etc.

The walls of the room in which manufacturing operations are carried out, shall be up to a height of six feet from the floor, be smooth, waterproof and capable of being kept clean.

The flooring shall be smooth, even and washable and shall be such as not to permit retention or accumulation of dust.

(C) *Water supply*: - The water used in manufacture shall be of potable quality.

(D) *Disposal of water.* –- Suitable arrangements shall be made for disposal of waste-water.

(E) *Health, clothing and sanitary requirements of the staff.*– All workers shall be free from contagious or infectious diseases. They shall be provided with clean uniforms, masks, headgears, and gloves wherever required. Washing facilities shall also be provided.

(F) *Medical Services.* - Adequate facilities for first aid shall be provided.

(G) Work benches shall be provided for carrying out operations such as filling, labelling, packing, etc. Such benches shall be fitted with smooth, impervious tops capable of being washed.

(H) Adequate facilities shall be provided for washing and drying of glass containers if the same are to be used for packing the product.

II. *REQUIREMENTS OF PLANT AND EQUIPMENT*

The following equipment, area and other requirements are recommended for the manufacture of: −

A. *Powders:*− Face powder, cake make-up, compacts, face packs, masks and rouges, etc.

1. *Equipment:*

(a) Powder mixer of suitable type provided with a dust collector.

(b) Perfume and colour blender.

(c) Sifter with sieves of suitable mesh size.

(d) Ball mill or suitable grinder.

1. Ins. by G.S.R 723(E) , dt. 11-8-1992.

(e) Trays and scoops (stainless steel).

(f) Filling and sealing equipment provided with dust extractor.

(g) For compacts: -

(i) a separate mixer, (ii) compact pressing machine.

(h) Weighing and measuring devices

(i) Storage tanks.

An area of 15 square meters is recommended. The section is to be provided with adequate exhaust fans.

B. Creams, lotions, emulsions, pastes, cleansing milks, shampoos, pomade, brilliantine, shaving creams and hair-oils etc.

(a) Mixing and storage tanks of suitable materials.

(b) Heating kettle – steam, gas or electrically heated.

(c) Suitable agitator.

(d) Colloidal mill or homogeniser (wherever necessary). (e) Triple roller mill (wherever necessary).

(f) Filling and sealing equipment.

(g) Weighing and measuring devices.

An area of 25 square meters is recommended.

C. Nail Polishes and Nail lacquers.

1. Equipment:

(a) A suitable mixer.

(b) Storage tanks.

(c) Filling machine – hand operated or power driven.

(d) Weighing and Measuring devices.

An area of 15 square meters is recommended. The section shall be provided with flameproof exhaust system.

2. ***Premises***:–The following are the special requirements related to Nail Polishes and Nail Lacquers: -

(a) It shall be situated in an industrial area.

(b) It shall be separate from other cosmetic-manufacturing areas by metal/brick partition up to ceiling.

(c) Floors, walls, ceiling and doors shall be fireproof.

(d) Smoking, cooking and dwelling shall not be permitted and no naked flame shall be brought in the premises.

(e) All electrical wiring and connections shall be concealed and main electric switch shall be outside the manufacturing area.

(f) All equipment, furniture and light fittings in the section shall be flameproof.

(g) Fire extinguisher like foam and dry powder and sufficient number of buckets containing sand shall be provided.

(h) All doors of the section shall open outwards.

3. ***Storage:***

All explosive solvents and ingredients shall be stored in metal cupboards or in a separate enclosed area.

4. ***Manufacture:***

(a) Manufacture of lacquer shall not be undertaken unless the above conditions are complied with.

(b) Workers shall be asked to wear shoes with rubber soles in the section.

5. ***Other requirements:***

No objection certificate from the local Fire Brigade Authorities shall be furnished.

D. Lipsticks and Lip-gloss, etc.

1. Equipment

(a) Vertical mixer.

(b) Jacketted kettle – steam, gas or electrically heated. (c) Mixing vessel (stainless steel).

(d) Triple roller mill/Ball mill.

(e) Moulds with refrigeration facility.

(f) Weighing and measuring devices.

An area of 15 square meters is recommended.

E. Depilatories.

1. Equipment:

(a) Mixing tanks.

(b) Mixer

(c) Triple roller mill or homogeniser (where necessary). (d) Filling and sealing equipment.

(e) Weighing and measuring devices.

(f) Moulds (where necessary).

An area of 10 square meters is recommended.

F. ***Preparations used for Eyes***: - Such preparations shall be manufactured under strict hygienic conditions to ensure that these are safe for use.

1. *Eyebrows, Eyelashes, Eyeliners, etc.*

1 *Equipment:*

(a) Mixing tanks.

(b) A suitable mixer.

(c) Homogeniser (where necessary)

(d) Filling and sealing equipment.

(e) Weighing and measuring devices.

An area of 10 square meters is recommended.

2. *Kajal and Surma*

1. *Equipment:*

(a) Base sterilizer.

(b) Powder sterilizer (dry heat oven).

(c) Stainless steel tanks.

(d) A suitable Mixer.

(e) Stainless steel sieves.

(f) Filling and sealing arrangements.

(g) Weighing and measuring devices.

(h) Homogeniser (where necessary).

(i) Pestle and Mortar (for Surma).

An area of 10 square meters with a separate area of 5 square meters for base sterilization is recommended.

Other requirements for 1 and 2:

(a) False ceiling shall be provided wherever required.

(b) Manufacturing area shall be made fly proof. An airlock or an aircurtain shall be provided.

(c) Base used for Kajal shall be sterilized by heating the base at 150 degree C for required time in a separate enclosed area.

(d) The vegetable carbon black powder shall be sterilized in a drying oven at 120 degree C for required time.

(e) All utensils used for manufacture shall be of stainless steel and shall be washed with detergent water, antiseptic liquid and again with distilled water.

(f) Containers employed for _Kajal‘ shall be cleaned properly with bactericidal solution and dried.

(g) Workers shall put on clean overalls and use hand gloves wherever necessary.

G. Aerosol.

1. *Equipment:* -

(a) Air-compressor (wherever necessary).

(b) Mixing tanks.

(c) Suitable propellant filling and crimping equipments. (d) Liquid filling unit.

(e) Leak testing equipment.

(f) Fire extinguisher (wherever necessary)

(g) Suitable filtration equipment.

(h) Weighing and measuring devices.

An area of 15 square meters is recommended.

2. *Other requirements:* - No objection certificate from the Local Fire Brigade Authorities shall be furnished.

H. Alcoholic Fragrance Solutions.

Equipment: -

(a) Mixing tanks with stirrer

(b) Filtering equipment.

(c) Filling and sealing equipment.

(d) Weighing and measuring devices.

An area of 15 square meters is recommended.

I. Hair Dyes.

Equipment:

(a) Stainless steel tanks.

(b) Mixer.

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(c) Filling Unit.

(d) Weighing and measuring devices.

(e) Masks, gloves and goggles.

An area of 15 square meters with proper exhaust is recommended.

J. Tooth powders and toothpastes, etc.:

1. *Tooth-powder in General.*

Equipment:

(a) Weighing and measuring devices.

(b) Dry mixer (powder blender).

(c) Stainless steel sieves.

(d) Powder filling and sealing equipments.

An area of 15 square meters with proper exhaust is recommended.

2. *Toothpastes.*

Equipment:

(a) Weighing and measuring devices.

(b) Kettle – steam, gas or electrically heated (where necessary). (c) Planetary mixer with de-aerator system.

(d) Stainless steel tanks.

(e) Tube filling equipment.
(f) Crimping machine.

An additional area of 15 square meters with proper exhaust is recommended.

3. *Tooth-powder (Black)*

Equipment:

(a) Weighing and measuring devices.
(b) Dry mixer powder blender.
(c) Stainless steel sieves.
(d) Powder filling arrangements.

An area of 15 square meters with proper exhaust is recommended. Areas for manufacturing ―Black‖ and ―White‖ tooth powders should be separate.

K. Toilet Soaps:

Equipment: -

(a) Kettles/pans for saponification.
(b) Boiler or any other suitable heating arrangement. (c) Suitable stirring arrangement.
(d) Storage tanks or trays.
(e) Driers.
(f) Amalgamator/chipping machine.
(g) Mixer.
(h) Triple roller mill.
(i) Granulator.
(j) Plodder.
(k) Cutter.
(l) Pressing, stamping and embossing machine.
(m) Weighing and measuring devices.

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A minimum area of 100 square meters is recommended for the small-scale manufacture of toilet soaps.

The areas recommended above are for basic manufacturing of different categories of cosmetics. In addition to that separate adequate space for storage of raw materials, finished products, packing materials shall be provided in factory premises.[1][***]

Note No. I−The above requirements of the Schedule are made subject to modification at the discretion of the Licensing Authority, if he is of the opinion that having regard to the nature and extent of the manufacturing operations it is necessary to relax or alter them in the circumstances of a particular case.

Note No. II.−The above requirements do not include requirements of machinery, equipments and premises required for preparation of containers and clousers of different categories of cosmetics. The Licensing Authority shall have the discretion to examine the suitability and adequacy of the machinery, equipments and premises for the purpose of taking into consideration of the requirements of the licensee.

Note No. III.−Schedule M-II specifies equipments and space required for certain categories of cosmetics only. There are other cosmetics items, viz. Attars, perfumes, etc., which are not covered in the above categories. The Licensing Authority shall, in respect of such items or categories of cosmetics have the discretion to examine the adequacy of factory premises, space, plant and machinery and other requisites having regard to the nature and extent of the manufacturing operations involved and direct the licensee to carry on necessary modification in them.

1. The words ―A testing laboratory shall also be provided‖ omitted by G.S.R.285 (E) , dt. 16.7.1996.

[1]

[SCHEDULE M-III

[See rules 69, 69A, 75, 75A and 76]

QUALITY MANAGEMENT SYSTEM –FOR NOTIFIED MEDICAL DEVICES AND IN-VITRO DIAGNOSTICS

1. General Requirements:

1.1. This schedule specifies requirements for a quality management system that shall be used by the manufacturer for the design and development, manufacture, packaging, labeling, testing, installation and servicing of medical devices and *in-vitro* diagnostics. If the manufacturer does not carry out design and development activity, the same shall be recorded in the quality management system. The manufacturer shall maintain conformity with this Schedule to reflect the exclusions.

1.2. If any requirement in clause 7(product realisation) of this Schedule is not applicable due to the nature of the medical device and *in-vitro* diagnostics for which the quality management system is applied, the manufacturer does not need to include such a requirement in its quality management system.

1.3. The processes required by this Schedule, which are applicable to the medical device and *in-vitro* diagnostic devices, but which are not performed by the manufacturer are the responsibility of the manufacturer and are accounted for in the manufacturer‘s quality management system.

1.4. If a manufacturer engages in only some operations subject to the requirements of this part, and not in others, that manufacturer need only to comply with those requirements which are applicable to the operations in which it is engaged.

1.5. It is emphasised that the quality management system requirements specified in this Schedule are in addition to complementary to technical requirements for products.

1.6. Manufacturers of components or parts of finished devices and *in-vitro* diagnostics are encouraged to use appropriate provisions of this regulation as guidance.

2. Applicability:

The provisions of this Schedule shall be applicable to manufacturers of finished devices, In-Vitro Diagnostics, mechanical contraceptives (condoms, intrauterine devices, tubal rings), surgical dressings, surgical bandages, surgical staplers, surgical sutures and ligatures, blood and blood components collection bags with or without anticoagulants intended for human or animal use.

1. Subs.by G.S.R. 640 (E) , dt. 29.6.2016. Previously, Ins. by G.S.R. 109 (E) , dt. 22.2.1994.

3. Terms and definitions:

3.1 Active implantable medical device.- Active medical device which is intended to be totally or partially introduced, surgically or medically, into the human or animal body or by medical intervention into a natural orifice and which is intended to remain after the procedure.

3.2 Active medical device.- Medical device relying for its functioning on a source of electrical energy or any source of power other than that directly generated by the human or animal body or gravity.

3.3 Advisory notice.- Notice issued by the manufacturer, subsequent to delivery of the medical device and *in-vitro* diagnostic devices, to provide supplementary information or to advise what action should be taken in or both in:-

a. the use of a medical device and *in-vitro* diagnostic devices;

b. the modification of a medical device and *in-vitro* diagnostic devices;

c. the return of the medical device and *in-vitro* diagnostic devices to the organization that

supplied it; or

d. the destruction of a medical device and *in-vitro* diagnostic devices.

3.4 Customer complaint.- Written, electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness or performance of a medical device and *in-vitro* diagnostic devices that has been placed on the market.

3.5 Implantable medical device.- Medical device intended:-

a. to be totally or partially introduced into the human or animal body or a natural orifice; or

b. to replace an epithelial surface or the surface of the eye;

by surgical intervention, and which is intended to remain after the procedure for at least thirty days, and which can only be removed by medical or surgical intervention.

3.6 Component means any raw material, substance, piece, part, software, firmware, labeling, or assembly which is intended to be included as part of the finished, packaged, and labeled device.

3.7 Design input means the physical and performance requirements of a device that are used as a basis for device design.

3.8 Design output means the results of a design effort at each design phase and at the end of the total design effort. The finished design output is the basis for the device master record. The total

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finished design output consists of the device, its packaging and labeling, and the device master record.

3.9 Design review means a documented, comprehensive, systematic examination of a design to evaluate the adequacy of the design requirements, to evaluate the capability of the design to meet these requirements, and to identify problems.

3.10 Finished device means any device or accessory to any device that is suitable for use or capable of functioning, whether or not it is packaged, labeled or sterilized.

3.11 *In-vitro* Diagnostic means *in-vitro* diagnostics referred in this Schedule including diagnostics kits and reagents that fall under sub-clause (i) of clause (b) of section 3 of Drugs and Cosmetics Act, 1940.

3.12 Management with executive responsibility means those senior employees of a manufacturer who have the authority to establish or make changes to the manufacturer's quality policy and quality system.

3.13 Medical device referred in this Schedule means devices that are notified under clause (iv) of sub-section (b) of section 3 of Drugs and Cosmetics Act, 1940.

3.14 Quality audit means a systematic, independent examination of a manufacturer's quality system that is performed at defined intervals and at sufficient frequency to determine whether both quality system activities and the results of such activities comply with quality system procedures, that these procedures are implemented effectively, and that these procedures are suitable to achieve quality system objectives.

3.15 Quality policy means the overall intention and direction of an organization with respect to quality, as established by management with executive responsibility.

3.16 Quality system means the organisational structure, responsibilities, procedures, processes,

and resources for implementing quality management.

3.17 Rework means action taken on a nonconforming product that will fulfill the specified

Device Master File requirements before it is released for distribution.

3.18 Specification means any requirement with which a product, process, service, or other

activity must conform.

3.19 Validation means confirmation by examination and provision of objective evidence that the particular requirement for a specific intended use can be consistently fulfilled;

3.19.1 Process validation means establishing by objective evidence that a process consistently produces a result or product meeting its predetermined specifications.

3.19.2 Design validation means establishing by objective evidence that device specifications conform with user needs and intended use(s).

3.20 Verification means confirmation by examination and provision of objective evidence that specified requirements have been fulfilled.

4 Quality management system.-

4.1 General:

The manufacturer shall establish, document, implement and maintain a quality management system and maintain its effectiveness in accordance with the requirements of this schedule.

The manufacturer shall;-

(a) identify the processes needed for the quality management system and their application throughout the organization;

(b) determine the sequence and interaction of these processes;

(c) determine criteria and methods needed to ensure that both the operation and control of these processes are effective;

(d) ensure the availability of resources and information necessary to support the operation and monitoring of these processes;

(e) monitor, measure and analyse these processes; and

(f) implement actions necessary to achieve planned results and maintain the effectiveness of these processes.

These processes shall be managed by the manufacturer in accordance with the requirements of this Schedule. Where a manufacturer chooses to outsource any process that affects product conformity with requirements, the manufacturer shall ensure control over such processes. Control of such outsourced processes shall be identified within the quality management system.

NOTE: Processes needed for the quality management system referred to above shall include processes for management activities, provision of resources, product realization and measurement.

4.2 Documentation requirements.-

4.2.1 General

The quality management system documentation shall include;-

(a) documented statements of a quality policy and quality objectives;

(b) a quality manual;

(c) documented procedures required by this schedule;

(d) documents needed by the manufacturer to ensure the effective planning, operation and control of its processes;

(e) records required by this schedule, and

where this schedule specifies that a requirement, procedure, activity or special arrangement be ―documented‖, it shall, in addition, be implemented and maintained.

For each type or model of medical device or *In-vitro* Diagnostics, the manufacturer shall establish and maintain a file either containing or identifying documents defining product specifications and quality management system requirements. These documents shall define the complete manufacturing process and, if applicable, installation.

The manufacture shall prepare documentation for device or *in-vitro* diagnostics in a form of a Device Master File containing specific information as referred to in Annexure-A appended to this Schedule.

Data may be recorded by electronic data processing systems or other reliable means, but documents and record relating to the system in use shall also be available in a hard copy to facilitate checking of the accuracy of the records. Wherever documentation is handled by electronic data processing methods, authorized persons shall enter or modify data in the computer. There shall be record of changes and deletions. Access shall be restricted by _passwords‘ or other means and the result of entry of critical data shall be independently checked. Batch records electronically stored shall be protected by a suitable back-up. During the period of retention, all relevant data shall be readily available.

4.2.2 Quality manual.-

The manufacturer shall establish and maintain a quality manual that includes:-

(a)the scope of the quality management system, including details of and justification for any exclusion or non-application or both;

(b) the documented procedures established for the quality management system, or reference to them; and

(c) a description of the interaction between the processes of the quality management system.

The quality manual shall outline the structure of the documentation used in the quality management system.

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The manufacturer shall prepare documentation in a form of a Plant Master File containing specific information about the facilities, personnel and other details as prescribed in Annexure B appended to this Schedule.

4.2.3 Control of documents.-

Documents required by the quality management system shall be controlled. Records are a special type of document and shall be controlled according to the requirements given in the control of records. Documents shall be approved, signed and dated by the appropriate and the authorised person.

A documented procedure shall be established to define the controls needed.-

(a) to review and approve documents for adequacy prior to issue;

(b) to review and update as necessary and re-approve documents;

(c) to ensure that changes and the current revision status of documents are identified;

(d)

to ensure that relevant versions of applicable documents are available at points of use; (e) to ensure that documents remain legible and readily identifiable;

(f) to ensure that documents of external origin are identified and their distribution controlled; and

(g) to prevent the unintended use of obsolete documents, and to apply suitable identification to them if they are retained for any purpose.

Changes to document shall be reviewed and approved. Change records shall be maintained which will include a description of the change, identification of the affected documents, the signature of the approving individual, the approval date, and when the change becomes effective.

The manufacturer shall ensure that changes to documents are reviewed and approved either by the original approving functionary or another designated functionary which has access to pertinent background information upon which to base its decisions.

The manufacturer shall define the period for which at least one copy of obsolete controlled documents shall be retained. This period shall ensure that documents to which medical devices or *in-vitro* diagnostics have been manufactured and tested are retained for at least one year after the date of expiry of the medical device or *in-vitro* diagnostic as defined by the manufacturer.

4.2.4 Control of records.-

Records shall be established and maintained to provide evidence of conformity to the requirements and of the effective operation of the quality management system. Records shall remain legible, readily identifiable and retrievable. A documented procedure shall be established to define the

controls needed for the identification, storage, protection, retrieval, retention time and disposition of records.

The manufacturer shall retain the records for a period of time at least one year after the date of expiry of the medical device or *in-vitro* diagnostics as defined by the manufacturer, but not less than two years from the date of product release by the manufacturer.

5 Management responsibility.-

5.1 Management commitment:

Top management of the manufacturer shall provide evidence of its commitment to the development and implementation of the quality management system and maintaining its effectiveness by:- (a) communicating to the employees the importance of meeting customer as well as statutory and regulatory requirements;

(b)

establishing the quality policy; (c) ensuring that quality objectives are established;

(d) conducting management reviews; and

(e) ensuring the availability of resources.

5.2 Customer focus:

Top management of the manufacturer shall ensure that customer requirements are determined and are met.

5.3 Quality policy:

Top management of the manufacturer shall ensure that the quality policy:-

(a) is appropriate to the purpose of the manufacturing facility;

(b) includes a commitment to comply with requirements and to maintain the effectiveness of the quality management system;

(c)

provides a framework for establishing and reviewing quality objectives; (d) is communicated and understood within the manufacturer‘s organization; and

(e) is reviewed for continuing suitability.

5.4 Planning.-

5.4.1 Quality objectives:

Top management of the manufacturer shall ensure that quality objectives, including those needed to meet requirements for product, are established at relevant functions and levels within the manufacturing organization. The quality objectives shall be measurable and consistent with the quality policy.

5.4.2 Quality management system planning: 502

Top management of the manufacturer shall ensure that.-

(a) the planning of the quality management system is carried out in order to meet the specified requirements, as well as the quality objectives; and

(b) the integrity of the quality management system is maintained when changes to the quality management system are planned and implemented.

5.5 Responsibility, authority and communication.-

5.5.1 Responsibility and authority:

Top management of the manufacturer shall ensure that responsibilities and authorities are defined, documented and communicated within the manufacturing organisation.

Top management of the manufacturer shall establish the interrelation of all personnel who manage, perform and verify work affecting quality, and shall ensure the independence and authority necessary to perform these tasks.

5.5.2 Management representative:

Top management shall appoint a member of management who, irrespective of other responsibilities, shall have responsibility and authority that includes:-

(a) ensuring that processes needed for the quality management system are established, implemented and maintained;

(b) reporting to top management on the performance of the quality management system and any need for improvement; and

(c) ensuring the promotion of awareness of regulatory and customer requirements throughout the manufacturing organization.

5.5.3 Internal communication:

Top management shall ensure that appropriate communication processes are established within the Manufacturing organization and that communication takes place regarding the effectiveness of the quality management system.

5.6 Management review.-

5.6.1 General:

Top management shall review the organization‘s quality management system, at planned intervals, to ensure its continuing suitability, adequacy and effectiveness. This review shall include assessing opportunities for improvement and the need for changes to the quality management system, including the quality policy and quality objectives. Records from management reviews shall be maintained.

5.6.2 Review input:

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The input to management review shall include information on:-

(a) results of audits,

(b) customer feedback,

(c) process performance and product conformity,

(d) status of preventive and corrective actions,

(e) follow-up actions from previous management reviews,

(f) changes that could affect the quality management system,

(g) recommendations for improvement, and

(h) new or revised regulatory requirements as and when issued.

5.6.3 Review output:

The output from the management review shall include any decisions and actions related to:-

(a) improvements needed to maintain the effectiveness of the quality management system and its processes,

(b) improvement of product related to customer requirements, and

(c) resource needs.

6 Resource management.-

6.1 Provision of resources:

The manufacturing organization shall determine and provide the resources needed

(a) to implement the quality management system and to maintain its effectiveness, and

(b) to meet regulatory and customer requirements.

6.2 Human resources.-

6.2.1 General:

Personnel performing work affecting product quality shall be competent on the basis of appropriate education, training, skills and experience. Number of personnel employed shall be adequate and in direct proportion to the workload. Prior to employment, all personnel, shall undergo medical examination including eye examination, and shall be free from communicable or contagious diseases. Thereafter, they should be medically examined periodically, at least once a year. Records shall be maintained thereof.

6.2.2 Competence, awareness and training:

The manufacturer shall:-

(a) determine the necessary competence for personnel performing work affecting product quality,

(b) provide training or take other actions to satisfy these needs,

(c) evaluate the effectiveness of the actions taken,

(d) ensure that its personnel are aware of the relevance and importance of their activities and how they contribute to the achievement of the quality objectives,

(e) maintain appropriate records of education, training, skills and experience, and

(f) establish documented procedures for identifying training needs and ensure that all personnel are trained to adequately perform their assigned responsibilities.

6.3 Infrastructure:

The organisation shall determine, provide and maintain the infrastructure needed to achieve conformity to product requirements. Infrastructure includes, as applicable:-

(a) buildings, workspace and associated utilities.

(b) process equipment (both hardware and software), and (c) supporting services (such as transport or communication).

The manufacturer shall establish documented requirements for maintenance activities, including their frequency, when such activities or lack thereof can affect product quality. Records of such maintenance shall be maintained.

6.4 Work environment:

The organisation shall determine and manage the work environment needed to achieve conformity to product requirements. The following requirements shall apply, namely:-

(a) the manufacturer shall establish documented requirements for health, cleanliness and clothing of personnel if contact between such personnel and the product or work environment could adversely affect the quality of the product;

(b)

if work environment conditions can have an adverse effect on product quality, the manufacturer shall establish documented requirements as per **Annexure-C** of this schedule for the work environment conditions and documented procedures or work instructions to monitor and control these work environment condition;

(c) the manufacturer shall ensure that all personnel who are required to work temporarily under special environmental conditions within the work environment are appropriately trained and supervised by a trained person;

(d) if appropriate, special arrangements shall be established and documented for the control of contaminated or potentially contaminated product in order to prevent contamination of other product, the work environment or personnel.

(e) all personnel shall bear clean body covering appropriate to their duties. Smoking, eating, drinking, chewing or keeping food and drink shall not be permitted in production, laboratory and storage areas.

7 Product realisation.-

7.1 Planning of product realization:

The manufacturer shall plan and develop the processes needed for product realization. Planning of product realization shall be consistent with the requirements of the other processes of the quality management system.

In planning product realisation, the manufacturer shall determine the following, as appropriate:-
(a) quality objectives and requirements for the product;
(b) the need to establish processes, documents, and provide resources specific to the product;

(c) required verification, validation, monitoring, inspection and test activities specific to the product and the criteria for product acceptance;
(d) records needed to provide evidence that the realisation processes and resulting product meet requirements.

The output of this planning shall be in a form suitable for the manufacturer‘s method of operations.

The manufacturer organisation shall establish documented requirements for risk management (as per the IS or ISO 14971) throughout product realisation. Records arising from risk management shall be maintained.

7.2 Customer-related processes.-

7.2.1 Determination of requirements related to the product:

The manufacturer shall determine:-
(a) requirements specified by the customer, including the requirements for delivery and post-delivery activities,
(b) requirements not stated by the customer but necessary for specified or intended use, where known;
(c) statutory requirements related to the product, and
(d) any additional requirements determined by the manufacturer.

7.2.2 Review of requirements related to the product:

The manufacturer shall review the requirements related to the product. This review shall be conducted prior to the manufacturer's commitment to supply a product to the customer and shall ensure that:-

(a) product requirements are defined and documented;
(b) contract or order requirements differing from those previously expressed are resolved; and (c) the manufacturer has the ability to meet the defined requirements.

Records of the results of the review and actions arising from the review shall be maintained.

Where the customer provides no documented statement of requirement, the customer requirements shall be confirmed by the manufacturer before acceptance.

Where product requirements are changed, the manufacturer shall ensure that relevant documents are amended and that relevant personnel are made aware of the changed requirements.

7.2.3 Customer communication:

The manufacturer shall determine and implement effective arrangements for communicating with customers in relation to:-

(a) product information;
(b) enquiries, contracts or order handling, including amendments;
(c) customer feedback, including customer complaints; and (d) advisory notices.

7.3 Design and development.-

7.3.1 Design and development planning:

The manufacturer shall establish documented procedures for design and development. The manufacturer shall plan and control the design and development of product. During the design and development planning, the manufacturer shall determine :-

(a) the design and development stages;

(b) the review, verification, validation and design transfer activities that are appropriate at each design and development stage; and

(c) the responsibilities and authorities for design and development.

The manufacturer shall manage the interfaces between different groups involved in design and development to ensure effective communication and clear assignment of responsibility.

Planning output shall be documented, and updated as appropriate, as the design and development progresses.

NOTE: Design transfer activities during the design and development process ensure that design and development outputs are verified as suitable for manufacturing before becoming final production specifications.

7.3.2 Design and development inputs:

Inputs relating to product requirements shall be determined and records maintained. The design requirements relating to a device are appropriate and address the intended use of the device, including the needs of the user and patients.

These inputs shall include:-

(a) functional, performance and safety requirements, according to the intended use;

(b) applicable statutory and regulatory requirements;

(c) where applicable, information derived from previous similar designs;

(d) other requirements essential for design and development; and

(e) output(s) of risk management.

These inputs shall be reviewed for adequacy and approved by designated individual.
Requirements shall be complete, unambiguous and not in conflict with each other.

7.3.3 Design and development outputs:

The outputs of design and development shall be provided in a form that enables verification against the design and development input and shall be documented, reviewed, and approved prior to release.

Design and development outputs shall:-

(a) meet the input requirements for design and development;

(b) provide appropriate information for purchasing, production and for service provision; (c) contain or reference product acceptance criteria; and

(d) specify the characteristics of the product that are essential for its safe and proper use.

Records of the design and development outputs shall be maintained.

Records of design and development outputs can include specifications, manufacturing procedures, engineering drawings, and engineering or research logbooks.

7.3.4 Design and development review:

At suitable stages, systematic reviews of design and development shall be performed in accordance with planned arrangements:-

(a) to evaluate the ability of the results of design and development to meet requirements; and (b) to identify any problems and propose necessary actions.

Participants in such reviews shall include representatives of functions concerned with the design and development stage being reviewed, as well as other specialist personnel.

Records of the results of the reviews and any necessary actions shall be maintained

7.3.5 Design and development verification:

Verification shall be performed in accordance with planned arrangements to ensure that the design and development outputs have met the design and development input requirements. Records of the results of the verification and any necessary actions shall be maintained.

7.3.6 Design and development validation:

Design and development validation shall be performed in accordance with planned arrangements to

ensure that the resulting product is capable of meeting the requirements for the specified application or intended use.

Design validation shall be performed under defined operating conditions on initial production units, lots, or batches or their equivalence. Design validation shall include software validation and risk analysis, where appropriate validation shall be completed prior to the delivery or implementation of the product.

Records of the results of validation and any necessary actions shall be maintained.

As part of design and development validation, the manufacturer shall perform clinical evaluations and/or evaluation of performance of the medical device or *In-vitro* Diagnostics.

NOTE 1.- If a medical device or *In-vitro* Diagnostic can only be validated following assembly and installation at point of use, delivery is not considered to be complete until the product has been formally transferred to the customer.

NOTE 2.- Provision of the medical device for purposes of clinical evaluations and/or evaluation of performance is not considered to be delivery.

7.3.7 Control of design and development changes:

Design and development changes shall be identified and records maintained. The changes shall be reviewed, verified and validated, as appropriate, and approved before implementation. The review of design and development changes shall include evaluation of the effect of the changes on constituent parts and product already delivered. Records of the results of the review of changes and any necessary actions shall be maintained.

Note.-Each manufacturer shall establish and maintain a Design History File for each type of device. The Design History File shall contain or reference the records necessary to demonstrate that the design was developed in accordance with the approved design plan and the requirements of design and development.

7.4 Purchasing.-

7.4.1 Purchasing process:

The manufacturer organisation shall establish documented procedures to ensure that purchased product conforms to specified purchase requirements. The type and extent of control applied to the supplier and the purchased product shall be dependent upon the effect of the purchased product on subsequent product realisation or the final product.

The manufacturer shall evaluate and select suppliers based on their ability to supply product in accordance with the manufacturer‘s requirements. Criteria for selection, evaluation and re-evaluation shall be established.

Records of the results of evaluations and any necessary actions arising from the evaluation shall be maintained.

7.4.2 Purchasing information:

Purchasing information shall describe the product to be purchased, including where appropriate:- (a) requirements for approval of product, procedures, processes and equipment;

(b) requirements for qualification of personnel; and

(c) quality management system requirements.

The manufacturer shall ensure the adequacy of specified purchase requirements prior to their communication to the supplier.

To the extent required for traceability, the manufacturer shall maintain documents and records of relevant purchasing information.

7.4.3 Verification of purchased product:

The manufacturer shall establish and implement the inspection or other activities necessary for ensuring that purchased product meets specified purchase requirements. Where the manufacturer intends to perform verification at the supplier‘s premises, the manufacturer shall state the intended verification

arrangements and method of product release in the purchasing information. Records of the verification shall be maintained.

7.5 Production and service provision.-

7.5.1 Control of production and service provision:

7.5.1.1 General requirements:

The manufacturer shall plan and carry out production and service provision under controlled conditions. Controlled conditions shall include, as applicable:-

(a) the availability of information that describes the characteristics of the product,

(b) the availability of documented procedures, documented requirements, work instructions; and reference materials and reference measurement procedures as necessary;

(c) the use of suitable equipment;

(d) the availability and use of monitoring and measuring devices;

(e) the implementation of monitoring and measurement; (f) the implementation of release, delivery and post-delivery activities; and

(g) the implementation of defined operations for labeling and packaging.

The manufacturer shall establish and maintain a record for each batch of medical device or *In-vitro* Diagnostic devices that provides traceability and identifies the amount manufactured and amount approved for distribution. The batch record shall be verified and approved.

7.5.1.2 Control of production and service provision — Specific requirements

7.5.1.2.1 Cleanliness of product and contamination control:

The manufacturer shall establish documented requirements for cleanliness of product if:-

(a) product is cleaned by the manufacturer prior to sterilisation or its use; or

(b) product is supplied non-sterile to be subjected to a cleaning process prior to sterilisation or its use; or

(c) product is supplied to be used non-sterile and its cleanliness is of significance in use; or (d) process agents are to be removed from product during manufacture.

If the product is cleaned in accordance with (a) or (b) above, the requirements content in clause 6.4 (a) and (b) do not apply prior to the cleaning process

7.5.1.2.2 Installation activities:

If appropriate, the manufacturer shall establish documented requirements which contain acceptance criteria for installing and verifying the installation of the medical device or *In-vitro* Diagnostic device.

If the agreed customer requirements allow installation to be performed other than by manufacturer or its authorised agent, the manufacturer shall provide documented requirements for installation and verification. Records of installation and verification performed by the manufacturer or its authorized agent shall be maintained.

7.5.1.3 Particular requirements for sterile medical devices:

The manufacturer shall maintain records of the process parameters for the sterilisation process which was used for each sterilisation batch. Sterilisation records shall be traceable to each production batch of medical device.

7.5.2 Validation of processes for production and service provision.-

7.5.2.1 General:

The manufacturer shall validate any processes for production and service provision where the resulting output cannot be verified by subsequent monitoring or measurement. This includes any processes where deficiencies become apparent only after the product is in use. Validation shall demonstrate the ability of these processes to achieve planned results.

The manufacturer shall establish arrangements for these processes including, as applicable:- (a) defined criteria for review and approval of the processes;

(b) approval of equipment and qualification of personnel

(c) use of specific methods and procedures,;
(d) requirements for records; and
(e) revalidation.

The manufacturer shall establish documented procedures for the validation of the application of computer software (and its changes to such software or its application) for production and service provision that affect the ability of the product conform to specified requirements. Such software applications shall be validated prior to initial use.

Records of validation shall be maintained.

7.5.2.2 Particular requirements for sterile medical devices:

The manufacturer shall establish documented procedures for the validation of sterilization processes. Sterilisation processes shall be validated prior to initial use. The records of validation of each sterilisation process shall be maintained.

7.5.3 Identification and traceability.-

7.5.3.1 Identification:

The manufacturer shall identify the product by suitable means throughout product realization, and shall establish documented procedures for such product identification. The manufacturer shall establish documented procedures to ensure that medical devices and *In-vitro* Diagnostics returned to the manufacturer are identified and distinguished from conforming product.

7.5.3.2 Traceability.-

7.5.3.2.1 General:

The manufacturer shall establish documented procedures for traceability. Such procedures shall define the extent of product traceability and the records required.

Where traceability is a requirement, the manufacturer shall control and record the unique identification of the product.

NOTE.- Configuration management is a means by which identification and traceability can be maintained.

7.5.3.2.2 Particular requirements for active implantable medical devices and implantable medical devices:

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In defining the records required for traceability, the manufacturer shall include records of all components, materials and work environment conditions, if these could cause the medical device not to satisfy its specified requirements.

The manufacturer shall require that its agents or distributors maintain records of the distribution of active implantable medical devices and implantable medical devices to allow traceability and that such records are available for inspection. Records of the name and address of the shipping package consignee shall be maintained.

7.5.3.3 Status identification:

The manufacturer shall identify the product status with respect to monitoring and measurement requirements. The identification of product status shall be maintained throughout production, storage, implant, usage and installation of the product to ensure that only product that has passed the required inspections and tests (or released under an authorized concession) is dispatched, used or installed.

7.5.4 Customer property:

The manufacturer shall exercise care with customer property while it is under the manufacturer‘s control or being used by the manufacturer. The manufacturer shall identify, verify, protect and safeguard customer property provided for use or incorporation into the product. If any customer property is lost, damaged or otherwise found to be unsuitable for use, this shall be reported to the customer and records maintained.

NOTE.- Customer property can include intellectual property or confidential health information.

7.5.5 Preservation of product:

The manufacturer shall establish documented procedures or documented work instructions for

preserving the conformity of product during internal processing and delivery to the intended destination. This preservation shall include identification, handling, packaging, storage and protection. Preservation shall also apply to the constituent parts of a product.

The manufacturer shall establish documented procedures or documented work instructions for the control of product with a limited shelf-life or requiring special storage conditions. Such special storage conditions shall be controlled and recorded.

7.6 Control of monitoring and measuring devices:

The manufacturer shall determine the monitoring and measurement to be undertaken and the monitoring and measuring devices needed to provide evidence of conformity of product to determined requirements.

The manufacturer shall establish documented procedures to ensure that monitoring and measurement can be carried out and are carried out in a manner that is consistent with the monitoring and measurement requirements.

Where necessary to ensure valid results, measuring equipment shall be:-

(a) calibrated or verified at specified intervals, or prior to use, against measurement standards traceable to Bureau of Indian Standards wherever available ; where no such standards exist, the basis used for calibration or verification shall be recorded;

(b) adjusted or re-adjusted as necessary;

(c) identified to enable the calibration status to be determined; (d) safeguarded from adjustments that would invalidate the measurement result;

(e) protected from damage and deterioration during handling, maintenance and storage.

In addition, the manufacturer shall assess and record the validity of the previous measuring results when the equipment is found not to conform to requirements. The manufacturer shall take appropriate action on the equipment and any product affected. Records of the results of calibration and verification shall be maintained.

When used in the monitoring and measurement of specified requirements, the ability of computer software to satisfy the intended application shall be confirmed. This shall be undertaken prior to initial use and reconfirmed as necessary.

8 Measurement, analysis and improvement.-

8.1 General:

The manufacturer shall plan and implement the monitoring, measurement, analysis and improvement processes needed:-

(a) to demonstrate conformity of the product;

(b) to ensure conformity of the quality management system; and

(c) to maintain the effectiveness of the quality management system.

This shall include determination of applicable methods, including statistical techniques, and the extent of their use.

Note.- If relevant Indian standards are not available, International standards are applicable. In case no Indian or International standards are available, validated testing process of the manufacturer is applicable.

8.2 Monitoring and measurement.-

8.2.1 Feedback:

As one of the measurements of the performance of the quality management system, the manufacturer shall monitor information relating to whether the manufacturer has met customer or regulatory requirements. The methods for obtaining and using this information shall be determined.

The manufacturer shall establish a documented procedure for a feedback system to provide early warning of quality problems and for input into the corrective and preventive action processes.

8.2.2 Internal audit:

The manufacturer shall conduct internal audits at planned intervals to determine whether the quality management system:-

a) conforms to the planned arrangements, to the requirements of this schedule and to the quality management system requirements established by the manufacturer, and

b) is effectively implemented and maintained.

An audit programme shall be planned, taking into consideration the status and importance of the processes and areas to be audited, as well as the results of previous audits. The audit criteria, scope, frequency and methods shall be defined. Selection of auditors and conduct of audits shall ensure objectivity and impartiality of the audit process. Auditors shall not audit their own work.

The responsibilities and requirements for planning and conducting audits, and for reporting results and maintaining records shall be defined in a documented procedure. The management responsible for the area being audited shall ensure that actions are taken without undue delay to eliminate detected nonconformities and their causes. Follow-up activities shall include the verification of the actions taken and the reporting of verification results.

8.2.3 Monitoring and measurement of processes:

The manufacturer shall apply suitable methods for monitoring and, where applicable, measurement of the quality management system processes. These methods shall demonstrate the ability of the processes to achieve planned results. When planned results are not achieved, correction and corrective action shall be taken, as appropriate, to ensure conformity of the product.

8.2.4 Monitoring and measurement of product.-

8.2.4.1 General requirements:

The manufacturer shall monitor and measure the characteristics of the product to verify that product requirements have been met. This shall be carried out at appropriate stages of the product realisation process in accordance with the planned arrangements and documented procedures.

Evidence of conformity with the acceptance criteria shall be maintained. Records shall indicate the person(s) authorizing release of product. Product release shall not proceed until the planned arrangements have been satisfactorily completed.

8.2.4.2 Particular requirement for active implantable medical devices and implantable medical Devices wherever applicable:

The manufacturer shall record the identity of personnel performing any inspection or testing.

8.3 Control of nonconforming product

The manufacturer shall ensure that product which does not conform to product requirements is identified and controlled to prevent its unintended use or delivery. The controls and related responsibilities and authorities for dealing with nonconforming product shall be defined in a documented procedure.

The manufacturer shall deal with nonconforming product by one or more of the following ways:

(a) by taking action to eliminate the detected nonconformity;

(b) by authorizing its use, release or acceptance under concession;

(c) by taking action to preclude its original intended use or application.

The manufacturer shall ensure that nonconforming product is accepted by concession only if regulatory requirements are met. Records of the identity of the person authorisng the concession shall be maintained.

Records of the nature of nonconformities and any subsequent actions taken, including concessions obtained, shall be maintained.

When nonconforming product is corrected it shall be subject to re-verification to demonstrate conformity to the requirements. When nonconforming product is detected after delivery or use has started, the manufacturer shall take action appropriate to the effects, or potential effects, of the non-conformity.

If product needs to be reworked (one or more times), the manufacturer shall document the rework process in a work instruction that has undergone the same authorisation and approval procedure as the original work instruction. Prior to authorisation and approval of the work instruction, a determination of any adverse effect of the rework upon product shall be made and documented.

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8.4 Analysis of data:

The manufacturer shall establish documented procedures to determine, collect and analyze appropriate data to demonstrate the suitability and effectiveness of the quality management system and to evaluate whether improvement of the effectiveness of the quality management system can be made.

This shall include data generated as a result of monitoring and measurement and from other relevant sources.

The analysis of data shall provide information relating to:-

(a) feedback
(b) conformity to product requirements;
(c) characteristics and trends of processes and products including opportunities for preventive action; and
(d) suppliers.

Records of the results of the analysis of data shall be maintained.

8.5 Improvement.-

8.5.1 General:

The manufacturer shall identify and implement any changes necessary to ensure and maintain the continued suitability and effectiveness of the quality management system through the use of the quality policy, quality objectives, audit results, analysis of data, corrective and preventive actions and management review.

The manufacturer shall establish documented procedures for the issue and implementation of advisory notices. These procedures shall be capable of being implemented at any time. Records of all customer complaint investigations shall be maintained. If investigation determine that the activities outside the manufacturer‘s organisation contributed to the customer complaint, relevant information shall be exchanged between the organisations involved.

If any customer complaint is not followed by corrective or preventive action, the reason shall be recorded and approved. Manufacturer shall notify the adverse event to the regulatory authority and establish documented procedures for the same.

8.5.2 Corrective action:

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The manufacturer shall take action to eliminate the cause of nonconformities in order to prevent recurrence. Corrective actions shall be appropriate to the effects of the nonconformities encountered.

A documented procedure shall be established to define requirements for:-

(a) reviewing nonconformities (including customer complaints);
(b) determining the causes of nonconformities;
(c) evaluating the need for action to ensure that nonconformities do not recur
(d) determining and implementing action needed, including, if appropriate, updating documentation;
(e) recording of the results of any investigation and of action taken; and
(f) reviewing the corrective action taken and its effectiveness.

8.5.3 Preventive action:

The manufacturer shall determine action to eliminate the causes of potential nonconformities in order to prevent their occurrence. Preventive actions shall be appropriate to the effects of the potential problems. A documented procedure shall be established to define requirements for

(a) determining potential nonconformities and their causes,
(b) evaluating the need for action to prevent occurrence of nonconformities, (c)

determining and implementing action needed,

(d) recording of the results of any investigations and of action taken, and (e) reviewing preventive action taken and its effectiveness.

Annexure ‗A'

(refer para 4.2.1)

The manufacturer shall prepare a succinct document in the form of Device Master File containing specific information about the device manufacturing in the premises.

1.0Executive Summary:

An executive summary shall be provided by the manufacturer and shall contain:

Introductory descriptive information on the medical device or *In-vitro* Diagnostics, the intended use and indication for use, Class of Device, novel features of the device (if any), shelf life of the device and a synopsis on the content of the dossier information regarding sterilisation of the device (whether it is sterile or non-sterile; if sterile, mode of sterilisation)

2.0Device Description And Product Specification, Including Variants And Accessories:

2.1 Device Description

2.2 Product Specification

2.3 Reference to predicate and/or previous generations of the device

3.0 Labelling

4.0 Design And Manufacturing Information:

4.1 Device Design

4.2 Manufacturing Processes

5.0 Essential Principles (EP) Checklist

6.0 Risk Analysis And Control Summary

7.0 Product Verification And Validation:

7.1 Biocompatibility

7.2 Medicinal Substances

7.3 Biological Safety

7.4 Sterilisation

7.5 Software Verification and Validation

7.6 Animal Studies

7.7 Shelf Life/Stability Data

7.8 Clinical Evidence

7.9 Post Marketing Surveillance Data (Vigilance Reporting)

8. Additional information in case of the diagnostic kits:

Product dossier showing the:

8.1 The details of source antigen or antibody as the case may be and characterization of the same.

Process control of coating of antigen or antibody on the base material like Nitrocellulose

paper, strips or cards or enzyme-linked immunosorbent assay (ELISA) wells etc.

Detailed composition of the kit and manufacturing flow chart process of the kit showing the specific flow diagram of individual components or source of the individual components.

8.2 Test protocol of the kit showing the specifications and method of testing. In house evaluation report of sensitivity, specificity and stability studies.

8.3 The detailed test report of all the components used/packed in the finished kit.

8.4 Pack size and labelling.

8.5 Product inserts.

Specific evaluation report, if done by any laboratory in India, showing the sensitivity and specificity of the kit.

Specific processing like safe handling, material control, area control, process control, and stability studies, storage at quarantine stage and finished stage, packaging should be highlighted in the product dossier.

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Annexure `B`

(refer para 4.2.2)

The manufacturer shall prepare a succinct document in the form of Plant Master File containing specific information about the production and/or control of device manufacturing carried out at the premises. It shall contain the following information:

1.General Information:

(i) brief information on the site (including name and address), relation to other sites; (ii) manufacturing activities;

(iii) any other operations carried out on the site

(iv)

name and exact address of the site, including telephone, fax numbers, web site URL and e-mail address;

(v) type of medical devices handled on the site and information about specifically toxic or hazardous substances handled, mentioning the way they are handled and precautions taken;

(vi) short description of the site (size, location and immediate environment and other activities on the site);

(vii) number of employees engaged in Production, Quality Control, warehousing, and distribution;

(viii) use of outside scientific, analytical or other technical assistance in relation to the design, manufacture and testing;

(ix)

short description of the quality management system of the company; (x) devices details registered with foreign countries;

2. Personnel:

(i) organisation chart showing the arrangements for key personne;l

(ii) qualifications, experience and responsibilities of key personnel;

(iii) outline of arrangements for basic and in-service training and how records are maintained;

(iv)

health requirements for personnel engaged in production (v) personnel hygiene requirements, including clothing.

3. Premises and Facilities:

(i) layout of premises with indication of scale;

(ii) nature of construction, finishes/fixtures and fittings;

(iii)brief description of ventilation systems. More details should be given for critical areas with potential risks of airborne contamination (including schematic drawings of the systems). Classification

of the rooms used for the manufacture of sterile products should be mentioned;

(iv) special areas for the handling of highly toxic, hazardous and sensitizing materials;

(v) brief description of water systems (schematic drawings of the systems are desirable) including sanitation;

(vi) maintenance (description of planned preventive maintenance programmes for premises and recording system);

4. Equipment:

(i) Brief description of major production and quality control laboratories equipment (a list of the equipment is required);

(ii) maintenance (description of planned preventive maintenance programmes and recording system);

(iii)qualification and calibration, including the recording system. Arrangements for computerized systems validation.

5. Sanitation:

Availability of written specifications and procedures for cleaning the manufacturing areas and equipments.

6. Production:

(i) Brief description of production operations using, wherever possible, flow sheets and charts specifying important parameters ;

(ii) arrangements for the handling of starting materials, packaging materials, bulk and finished products, including sampling, quarantine, release and storage;

(iii)arrangements for reprocessing or rework;

(iv) arrangements for the handling of rejected materials and products;

(v) brief description of general policy for process validation.

7. Quality Assurance:

Description of the Quality Assurance system and of the activities of the Quality Assurance Department. Procedures for the release of finished products.

8. Storage:

Policy on the storage of medical device.

9. Documentation:

Arrangements for the preparation, revision and distribution of necessary documentation, including storage of master documents.

10. Medical Device Complaints and Field Safety Corrective Action:

(i) Arrangements for the handling of complaints ;

(ii) Arrangements for the handling of field safety corrective action

11. Internal Audit:

Short Description of the internal audit system.

12. Contract Activities:

Description of the way in which the compliance of the contract acceptor is assessed.

Annexure _C'

Environmental requirement for Notified medical devices and *in-vitro* diagnostics

Name of Device	**Type of Operation**	**ISO Class (At rest)**
Cardiac stent/Drug Eluting Stent	Primary Packing and Crimping	5
	Washing, Ultrasonic cleaning &Drug coating	7
	Assembly, Wrapping & Packaging	8
	Laser cutting, Descaling, Annealing & Electro polishing	9
Heart Valves	Valve Packing	5
	Ultrasonic Cleaning & Visual Inspection	7
	Frame & Disc Assembly	7
Intra Ocular Lenses	Packing & Sealing	5
	Final Inspection	7
	Power Checking& Final Cleaning	8
	Tumble Polishing & Lathe Cutting	9
Bone Cements	Final Product Filling	5
	Sieving & Calcinations	7
	Powder Preparation, Granulation &Drying	8
Internal Prosthetic Replacement	Packing	5
	Product Preparation	7
	Component Preparation	8
Orthopedic Implants	Polishing &Cleaning & packaging (to be sterilized in factory premises)	7
	Polishing , cleaning & packaging (Non Sterile- to be sterilized in Hospital)	8
	Cutting, lathing	9
Catheters /Ablation Device / I V Cannulae / Scalp Vein Set/ Hypodermic Syringes/ Hypodermic Needles /	Assembly, Coating, Wrapping & Packing	7
	Component Preparation & Cleaning	8
	Moulding	9
Condom	Compounding	Well ventilated area with minimum 5 micron filter
	Moulding	Well ventilated area with minimum 5 micron filter
	Vulcanising	Normal air
	Packing	Air conditioned
Intra Uterine Devices	Moulding	Well ventilated area with minimum 5 micron filter
	Assembling	7
	Packaging	7
Tubal ring	Extrusion	7
	Cutting and Assembly	7
	Packaging	7
Blood bags	Moulding/Extrusion of components	8
	Assembly	7
	Filing	5
Suture	Extrusion	9
	Assembly	8
	Packing	8
Staplers	Staple formation	9
	Staple assembly 523	8

	Staple final pack	8
Ligatures	Extrusion	9
	Cutting and assembly	8
	Final Pack	8
Surgical dressings	Weaving	9
	Assembly and Gauzing	9
	Final pack	9
In-vitro diagnostics Kit/Reagents	Dry, Liquid Reagent Preparation	Well Lighted and Ventilated controlled temperature & humidity as per process or product
	Coating of sheets etc.	
	Assembly and primary packing	
	Filling	Well Lighted and Ventilated controlled temperature and humidity as per process or product requirement. Provision of Laminar hood if required, Clean Room class 8 or class 9 as per product/process
	Secondary Packing	Well Lighted and Ventilated controlled temperature if required
	Storage	As per recommended storage condition of the product]

[1][SCHEDULE N

[*See* Rule 64(1)]

LIST OF MINIMUM EQUIPMENT FOR THE EFFICIENT RUNNING OF A PHARMACY

1. *Entrance.* - The front of a pharmacy shall bear an inscription ―Pharmacy‖ in front.

2. *Premises.* - The premises of a pharmacy shall be separated from rooms for private use. The premises shall be well built, dry, well lit and ventilated and, of sufficient dimensions to allow the goods in stock, especially medicaments and poisons to be kept in a clearly visible and appropriate manner. The areas of the section to be used as dispensing department shall be not less than 6 square meters for one pharmacist working therein with additional 2 square meters for each additional pharmacist. The height of the premises shall be at least 2.5 meters.

The floor of the pharmacy shall be smooth and washable. The walls shall be plastered or tiled or oil painted so as to maintain smooth, durable and washable surface devoid of holes, cracks and crevices.

A pharmacy shall be provided with ample supply of good quality water.

The dispensing department shall be separated by a barrier to prevent the admission of the public.

3. *Furniture and apparatus.* - The furniture and apparatus of a pharmacy shall be adopted to the uses for which they are intended and correspond to the size and requirements of the establishment.

Drugs, chemicals, and medicaments shall be kept in a room appropriate to their properties and in such special containers as will prevent any deterioration of the contents or of contents of containers kept near them. Drawers, glasses and other containers used for keeping medicaments shall be of suitable size and capable of being closed tightly to prevent the entry of dust.

Every container shall bear a label of appropriate size, easily readable with names of medicaments as given in the Pharmacopoeias.

A pharmacy shall be provided with a dispensing bench, the top of which shall be covered with washable and impervious material like stainless steel, laminated or plastic, etc.

A pharmacy shall be provided with a cupboard with lock and key for the storage of poisons and shall be clearly marked with the work _POISON' in red letters on a white background.

Containers of all concentrated solution shall bear special label or marked with the words —To be diluted‖.

A Pharmacy shall be provided with the following minimum apparatus and books necessary for making of official preparations and prescriptions:-

1.Subs. by S.O.2139 , dt. 12.8.1972.

Apparatus: -

Balance, dispensing, sensitivity 30 mg.

Balance, counter, capacity 3 Kgm., sensitivity 1 gm.

Beakers, lipped, assorted sizes.

Bottles, prescription, ungraduated assorted sizes.

Corks assorted sizes and tapers.

Cork, extracter.

Evaporating dishes, porcelain.

Filter paper.

Funnels, glass.

Litmas paper, blue and red.

Measure glasses cylindrical 10 ml, 25 ml, 100 ml and 500 ml.

Mortars and pestles, glass.

Mortars and pestles, wedgwood.

Ointment pots with bakelite or suitable caps.

Ointment slab, porcelain

Pipette graduated, 2 ml, 5 ml and 10 ml.

Ring, stand (retort) iron, complete with rings.

Rubber stamps and pad

Scissors

Spatulas, rubber or vulcanite

Spatulas, stainless steel.

Spirit lamp

Glass stirring rods.

Thermometer, 0°C to 200°C.

Tripod stand.

Watch glasses.

Water bath.

Water distillation still in case Eye drops and Eye lotions are prepared.

Weights, Metric, 1 mg. to 100 gm.

Wire Gauze.

*Pill finisher, boxwood.

* Pill Machine.

* Pill Boxes.

* Suppository mould.

Books :

The Indian Pharmacopoeia (Current Edition).
National Formulary of Indian (Current Edition). The
Drugs and Cosmetics Act, 1940.

The Drugs and Cosmetics Rules, 1945.

The Pharmacy Act, 1948.

The Dangerous Drugs Act, 1930.

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4. *General provisions.* - A pharmacy shall be conducted under the continuous personal supervision of a Registered Pharmacist whose name shall be displayed conspicuously in the premises.

The Pharmacist shall always put on clean white overalls.

The premises and fittings of the pharmacy shall be properly kept and everything shall be in good order and clean.

All records and registers shall be maintained in accordance with the laws in force.

Any container taken from the poison cupboard shall be replaced therein immediately after use and the cupboard locked. The keys of the poison cupboard shall be kept in the personal custody of the responsible person.

Medicaments when supplied shall have labels conforming to the provisions of laws in force.

Note*:* - The above requirements are subject to modifications at the discretion of the licensing authority, if he is of opinion that having regard to the nature of drugs dispensed, compounded or prepared by the licensee. It is necessary to relax the above requirements or to impose additional requirements in the circumstances of a particular case. The decision of the licensing authority in that regard shall be final.

* *These items are to be provided only by those who intend to dispense pills or suppositories, as the case may be.*]

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[1][SCHEDULE O

[*See* Rule 126]

STANDARD FOR DISINFECTANT FLUIDS

[2][PART I

PROVISION APPLICABLE TO BLACK FLUIDS AND WHITE FLUIDS

The standards for disinfectants shall conform to the Indian Standards specification (IS 1061:1997) laid down from time to time by the Bureau of Indian Standards.]

1. Subs. by G.S.R. 1243, dared 19-09-1979, for Schedule O (w.e.f. 6-10-979). EARLIER Schedule O was added y Notification No. F.1-20/60-D, dated 24-01-1964.
2. Subs. by G.S.R. 735(E), dated 21-12-2005, for

—PART I

Provision applicable to Black Fluids and White Fluids

1.*Classification* - The disinfectants shall be classified as follows: -

(a) Black fluids

(b) White fluids

(A) *Black fluids*.– These shall be homogeneous dark brown solution of coal tar acid or similar acids derived from petroleum with or without hydrocarbon, and/or other phenolic compounds, and their derivatives and a suitable emulsifier.

(B) *White fluids*.– These shall be finely dispersed homogeneous white to off- white emulsion consisting of coal tar acids or similar acids derived from petroleum, with or without hydrocarbons, and/or other phenolic compounds, and their derivatives.

2.*Gradation* – Each of the above classes of disinfectant fluids shall be graded on the basis of the minimum requirements in respect of:

Rideal Walker (RW) Coefficient as follows: -

Grade	Rideal Walker (RW) Coefficient (Minimum)
1.	18
2.	10
3.	5

3.*Type*- Each of the above grades of disinfectant fluids shall be stable in the range of temperature indicated against each type. -

Type	Stable in the range of
(I) Normal	15° C to 45° C. (II) Winter 5 ° C to 30 ° C

4.*Requirements* - All classes and grades of disinfectant fluids shall comply with the following requirements, namely: -

(1) *Stability after dilution* - When tested by the method described hereinafter the disinfectant fluid shall be miscible with artificial hard water (for Black fluids) or with artificial sea water (for White fluids) in all proportion from 1 per cent to 5 per cent by volume, to give

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emulsion which shall not break or show more than traces of separation of either top or bottom oil when kept for 6 hours at 15° C to 45° C for Type (I) (Normal) and 5° C to 30° C for Type (II) (Winter).

(2) *Germicidal Value.*– Rideal Walker Coefficient – Black fluids and White fluids shall be tested for determination of Rideal Walker Coefficient (R.W.Coefficient) by the method described hereinafter.

(3) *Storage.*– Disinfectant fluids of all classes shall be stored in mild steel, tinned mild steel or other suitable containers. These shall not be stored in containers made of galvanized iron.

(4) *Labelling.* -Subject to the other provisions in these rules, the label on the container shall state-

(i) the name of the product,

(ii) the name and full address of the manufacturer,

(iii) grade, type, R.W. Coefficient of product,

(iv) date of manufacture,

(v) quantity present in the container,

(vi) indications and mode of use, and

(vii) date up to which the product can be used.

5.*Method of testing* - (1) *Preparation of sample* - The sample of disinfectant fluid to be tested should be mixed thoroughly taking care that no air is beaten into the fluid immediately before withdrawing any portion for testing. The rest portion should be withdrawn from the middle of the sample.

(2) *Method of resting stability after dilution.* - (a) Preparation of Artificial Hard Water: 40 ml of I N Hydrochloric Acid (Analytical Reagent Quality) is neutralized with a slight excess of Calcium Carbonate and filtered. The filtrate is diluted to 1000 ml with distilled water, 10 parts of this solution is further diluted to 100 parts with distilled water.

(b) Preparation of Artificial Sea Water: 27G of Sodium Chloride (Analytical Reagent Quality) and 5 G of Magnesium Sulphate (Analytical Reagent Quality) are dissolved in distilled water and diluted to 1000 ml. The solution is filtered before use.

(c) Procedure: Take 1 ml and 5 ml portions of the sample in duplicate in 100 ml stoppered measuring cylinder (IS: 878 – 1956) by means of pipettes. Dilute the sample with artificial Hard water or Artificial Sea water (as the case may be) upto 10 ml mark. Mix thoroughly by inverting the cylinders

5 times. Keep the cylinders containing the diluted fluids for 6 hours at the extremes of the temperature range specified for the particular type. The sample complies with the test if the solution shows not more than a trace of separation at its top and bottom.

(3) Method of determination of Rideal Walker Coefficient (R.W.C)-

Apparatus – A loop, 4 mm in internal diameter is made at the end of 28 swg (0.376 mm) wire of platinum or platinum iridium alloy, 38 mm long from the loop to the holder. The loop is bent at such an angle to the length of the wire as will facilitate in removal vertically from the surface of the liquid while keeping the place of the loop horizontal.

Incubator – Set and maintained at 37° C ± 1° C

Pipettes – Standard graduated pipettes of capacity 10 ml; 5 ml and 1 ml

Dropping Pipette – Made of delivery 0.2 ml

Medication tubes – 5 sterile plugged rimless test tubes 125 mm x 22 mm (5 inch x ¾ inch) made of hard neutral glass.

Both tubes – About 2 dozens of the same description as medication tubes.

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Standard measuring cylinders stopped and graduated—500 ml graduated in 10 ml–;one 100 ml graduated 1 ml– five. All apparatus must be scrupulously clean and sterile; immediately before use.

Reagents– (a) Broth.– Prepare a mixture of the following ingredients:
Meat extract (Microbiological grade) 20 g Peptone (Micro biological grade) 20g. Sodium Chloride (Regent Quality) 10 g Distilled Water- 1000 ml.

Dissolve the solids in distilled water. Add sufficient sodium hydroxide to neutralize the solution; then boil it to bring down phosphates and filter while hot. The broth thus prepared is then adjusted to pH 7.6 with normal Hydrochloric acid. The broth is then sterilized by autoclaving at 15 lbs pressure for 20 minutes. It is then filtered and placed in 5 ml quantities in sterilized broth tubes. The tubes of media thus prepared are sterilized by autoclaving at 15 lbs pressure for 10 minutes. The final pH of the medium should lie between 7.3 and 7.5. Further resterilization in bulk or in tubes is not permissible.

(b) Test Organism- Test organism used is Salmonella typhi (NCTC 786) of which suitable culture shall be obtained from the Director, Central Drugs Laboratory, Calcutta. This culture is maintained by weekly sub-culture on a nutrient agar slope (made by dissolving 2.5 per cent Agar Agar (Bacteriological grade) in broth prepared as above), incubating the sub- culture for 24 hours at 37° C and then storing in refrigerator at a temperature below 22° C. For the purpose of the test a little of the growth from the most recent sub-culture in nutrient agar slope is placed in tube of R.W. broth and incubated for 23 hours at 38° C. A standard loopful is then transferred to a second tube and incubated as before. This is done at least three times before a test is carried out. Sub-culturing in broth is limited to 14 days.

(c) Standard phenol: 5 per cent W/V solution in sterile distilled water of chemically pure phenol having a crystallizing point of not less than 40.5°C is prepared. Test dilutions are prepared from this stock solution containing 1 g of phenol in each 95, 100, 105, 115 ml of the solution made. These dilutions shall be used within a week of preparation.

(d) Test dilutions of Disinfectant (sample)- The sample is prepared as described under ―Preparation of samples‖. A test portion of 5 ml is withdrawn and discharged into about 480 ml of sterile distilled water in a 500 ml glass stoppered sterile measuring cylinder and the pipette is rinsed three times or more in the clear liquid. The whole is then made up to 500 ml with sterile distilled water, the cylinder is stoppered and the contents thoroughly mixed by inverting the cylinder several times. Suitable test dilutions in sterile distilled water are then immediately prepared from this stock solution.

Procedure: 5 ml of 4 chosen dilutions of the disinfectant are placed in 4 medication tubes which are then placed in a rack provided with water bath maintained at a constant temperature between 17° C and 19° C, with the strongest dilution on the left. The fifth medication tube containing 5 ml of the particular phenol dilution is placed on the right. When the content on the medication tubes and broth

culture of the test organism have reached the temperature of the water bath, starting at Zero time, 0.2 ml of the culture is added to the left hand medication tube and the tube is shaken gently. After 30 seconds the next tube is inoculated similarly and the process is repeated with each successive tube at intervals of 30 seconds until the phenol control has been inoculated. Thirty seconds after this last addition (that is 2-1/2 minutes from zero) a loopful of the well-shaken content of the tube at the extreme left is withdrawn and placed in tube containing 5 ml of the broth medium. Thirty seconds after this similar operation is performed on the second medication tube. The procedure is repeated at an interval of 30 seconds with each of the 5 medication tubes working from left to right until 4 sets of cultures have been made i.e. at 2-1/2, 5, 7-1/2 and 10 minutes respectively after exposure. In each withdrawal care should

be taken to ensure that the loop is removed vertically from the surface of the liquid with its plane horizontally and without touching the side of the test tubes. The loop shall be sterilized by flaming between each operation, care being taken that the loop is cooled before being again used. The inoculated broth tubes are incubated for not less than 48 hours and not more than 72 hours at 37° C when the tubes showing growth of the test organisms will be recognized by turbidity of the broth.

Calculation of Coefficient –The R.W. Coefficient is obtained by dividing that dilution of the disinfectant which shows life of test organism in 2-1/2 and 5 minutes but no life thereafter by that dilution of the phenol which gives the same response.A typical set of sample is given below:

Sample disinfectant	*Time of exposures in minutes*				
Dilutions	2½	5	7½	10	
1:1000	−	−	−	−	
1:1100	+	−	−	−	R.W. Coefficient
1:1200	+	+−	−	=1200/100	=12
1:1300	+	+	+	−	
1:100 Pheno control	+	+−	−		

(+ = growth − = No growth)

PART II

Provisions applicable to other disinfectant fluids:

Disinfectant fluids which are made with chemicals other than those specified under Part I of this

Schedule shall conform to the formula or list of ingredients shown on the label.

Labelling : Subject to the provisions of rules on labelling, the label of container shall state:

(i) the name of the product;

(ii) the name and full address of the manufacturer;

(iii) the full formula or list of ingredients of the preparation;

(iv) date of manufacture;

(v) date up to which the product can be used;

(vi) quantity present in the container; and

(vii) indications and mode of use.

Cautionary note:

Mercury compounds shall be strictly excluded from all grades.]

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1[SCHEDULE P

[*See* Rule 96]

LIFE PERIOD OF DRUGS

Sl. No.	*Name of thedrug*	*Period in months (unless otherwise specified) between date of manufacture and date of expiry which the labelled potency period of the drug shall not exceed under the conditions of storage specified in Column No.4*	*Condition of storage*
1	2	3	4
ANTIBIOTICS			
1.	Adramycin	30	In a cool place
2.	Ampicillin	36	In a cool place
3.	Ampicillin Capsules	24	
4.	Ampicillin Dry Syrup	24	
5.	Ampicillin Injection	24	
6.	Ampicillin Sodium	36	In a cool place
7.	Ampicillin Trihydrate	30	In a cool place
8.	Amoxycillin Trihydrate	36	In a cool place
9	Amoxycillin Trihydrate Capsules	24	
10.	Amoxycillin Trihydrate Dry Syrup	18	
11.	Bacitracin	18	In a cool place
12.	Bacitracin or Zinc Bacitracin Tablets	12	
13.	Bacitracin Lozenges	12	
14.	Carbenicillin Sodium Injection	24	At temperature not Exceeding 5°C
15.	Carbenicillin Sodium Powder	24	At temperature not Exceeding 5°C
16.	Cephalexin	24	In a cool place
17.	Chloramphenicol	60	In a cool place
18.	Chloramphenicol Capsules & Tablets	48	
19.	Chloramphenicol Palmitate	48	
20.	Chloramphenicol Palmitate Oral Suspension	36	
21.	Chloramphenicol Eye drops	24	
22.	Chloramphenicol Sodium Succinate Powder	48	In a cool palace
23.	Chloramphenicol Sodium Succinate Injection	36	In a cool place
24	Chlortetracycline Hydrochloride	60	In a cool place
25.	Chlortetracycline Hydrochloride Capsules	60	

26.	Chlortetracycline Hydrochloride Tablets	24	
27.	Chlortetracycline Hydrochloride Ointment	24	
28.	Cloxacillin (Oral)	36	In a cool place
29.	Cloxacillin Sodium (Injection Grade)	36	In a cool place

1. Subs. by G.S.R. 17(E) , dt. 7.1.1986 (w.e.f. 7.1.1986).

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1	2	3	4
30.	Colistin Sulphate	60	Protected from light
31.	D-Cycloserine	48	In a cool place
32.	Dimethyl Chlortetracycline Hydrochloride	48	
33.	Dimethyl Chlortetracycline Hydrochloride Capsules	36	
34.	Daunoblastin Injection.	36	
35.	Doxycycline Hydrochloride	48	In a cool place
36.	Doxcycline Monohydrate	36	In a cool place
37.	Doxycyline Monohydrate for Oral Suspension.	24	
38.	Doxycycline Monohydrate Capsules.	36	
39.	Erythromycin Estolate	36	In a cool place
40.	Erythromycin Ethylsuccinate	60	In a cool place
41.	Erythromycin Oral Suspension	36	
42.	Erythromycin Estolate for Oral Suspension	36	
43.	Erythromycin Ethyl Succinate Tablet	24	
44.	Erythromycin Estolate Tablets	24	
45.	Erythromycin Stearate	36	In a cool place
46.	Framycetin Sulphate	48	In a well closed container with temperature not exceeding 30°C
47.	Framycetin Sulphate Eye drops	24	In a well closed container with temperature not exceeding 30°C
48.	Framycetin Sulphate Ointment	24	In a well closed container with temperature not exceeding 30°C
49.	Gentamycin Sulphate	60	In a cool place.
50.	Gentamycin Sulphate Injection	36	
51.	Gramicidin	60	In a cool place
52.	Griseofulvin	48	In a cool place
53.	Griseofulvin Tablets	36	
54.	Kanamycin Sulphate Injection.	24	
55.	Kanamycin Acid Sulphate Powder	48	In a cool place
56.	Mitomycin C	48	In a cool place
57.	Neomycin Sulphate.	48	In a cool place
58.	Nystatin	36	At temperature not exceeding 5°C
59.	Oleandomycin Phosphate sterile	24	In a cool place
60.	Oleandomycin Phosphate non sterile	36	In a cool place
61.	Oxytetracline Hydrochloride	36	In a cool place
62.	Oxytetracycline Hydrochloride Capsules.	36	
63.	Oxytetracycline Hydrochloride Tablets	24	
64.	Oxytetracycline Hydrochloride Injection	24	
65.	Oxytetracycline Hydrochloride Ointment	36	
66.	Penicillin Crystalline	36	In a cool place
67.	Penicillin Tablets	18	In a cool place
68.	68. Procaine Penicillin G	36	In a cool place

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1 2 3 4

69.	Benzathin Penicillin G	48	
70.	Potassium Phenoxy Methyl Penicillin	48	In a cool place
71.	Potassium Phenoxy Methyl PenicillinTablets	24	
72.	Polymixin B Sulphate	48	In a cool place
73.	Polymixin B Sulphate Ointment or Powder	24	In a cool place
74.	Rifampicin	36	In a cool place
[1][75	Rifampicin Capsules	36]	
76.	Spramycin Base	24	In a cool place
77.	Strepromycin Injection.	36	
78.	Streptomycin Ointment	24	
79.	Streptomycin Tablets	24	
80.	Streptomycin Sulphate	48	At temperature not exceeding 20oC
81.	Tetracycline Base	24	In a cool place
82.	Tetracycline Hydrochloride	36	In a cool place
83.	Tetracycline Hydrochloride Capsules	36	
84.	Tetracycline Tablets	24	
85.	Tyrothricin	60	In a cool place.

VITAMINS

1.	Vitamin A Injection	24	
2.	Vitamin B1 Injection	24	
3.	Thiamine Mononitrate Tablets	36	
4.	Thiamine Hydrochloride	48	In a well closed container, protected from light, in a cool place.
5.	Thiamine Mononitrate	48	In a well closed container, protected from light, in a cool place.
6.	Riboflavin	60	In a well closed container, protected from light, in a cool place.
7.	Riboflavin-5-Phosphate	24	In a well closed container, protected from light, in a cool place.
8.	Riboflavin Tablets	36	
9.	Vitamin B2 Injection	24	
10.	Vitamin B6	60	In a well closed container, protected from light, in a cool place.
11.	Vitamin B6 tablets	36	
12.	Cyanacobalamin	48	In a well closed container, protected from light, in a cool place.
13.	Hydroxycobalamin	48	In a well closed container, protected from light, in a cool place.
14.	Vitamin B12 Injection	36	
15.	Calcium Pantothenate	36	In a well closed container, protected from light, in a cool place.
16.	Vitamin C Injection	24	
17.	Calcium Pantothenate Tablets	36	
[2]18.	Vitamin C	48	In a well closed container, protected from light, in a cool place.

1. Subs. by G.S.R. 250(E), dt. 4.4.2002

2. Subs. by G.S.R. 626(E), dt. 14.10.1991

1	2	3	4
19.	Vitamin D_2 D_3	36	In a well closed container, protected from light, in a cool place.
20.	Vitamin E or E-Acetate	60	In a well closed container, protected from light, in a cool place.

21.	Folic Acid	60	In a well closed container, protected from light, in a cool place.
22.	Folic Acid Tablets	36	
23.	Vitamin K	60	In a well closed container, protected from light, in a cool place.
24.	Vitamin K Injection	36	
25.	Niacinamide	60	In a well closed container, protected from light, in a cool place.
26.	Niacinamide Tablets	36	
27.	D-Panthenol	60	In a well closed container, protected from light, in a cool place.
INSULIN PREPARATIONS			
1.	Globuline Zinc Insulin Injection	24	At temperature between 2°C and 8°C, must not be allowed to freeze.
2.	Insulin Injection	24	At temperature between 2°C and 8°C, must not be allowed to freeze.
3.	Insulin Zinc Suspension	24	At temperature between 2°C and 8°C, must not be allowed to freeze.
4.	Isophane Insulin Injection.	24	At temperature between 2°C and 8°C, must not be allowed to freeze.
[1][5.	Human Insulin Injection	30	At temperature between 2°C and 8°C, must not be allowed to freeze.

NORMAL HUMAN PLASMA

1. Anti-Haemophillic Human Globulin	12	In a cool place
2. Dried Plasma	60	At a temperature not exceeding 25°C
3. Dried Normal Human Serum Albumin	60	At a temperature not exceeding 25°C
4. Frozen Plasma	60	In deep freeze
5. Liquid Plasma	24	In cold place
6. Liquid Normal Human Serum Albumin.	60	In cold place.
[2][7. Whole Human Blood-		
(a) Collected in ACD solution	21days	At temperature between 4°C and 6°C
(b) Collection in CPDA solution.	35days	At temperature between 4°C and 6°C]

1. Subs. by G.S.R. 626(E) , dt. 14.10.1991.

2. Subs. by G.S.R. 626(E) , dt. 14.10.1991.

SERA TOXIN AND TOXOID

1.	Alum Precipitated Diphtheria Toxoid	24	In cold place.
2.	Alum Precipitated Diphtheria and Tetanus toxoid and Pertusis vaccine combined	18	In cold place
3.	Alum Precipitated Tetanus Toxoid	24	In a cold place
4.	Aluminium Hydroxide Absorbed Diphtheria Toxoid	24	In a cold place.
5.	Aluminium Hydroxide Absorbed Diphtheria Tetanus Toxoid and Pertussis Vaccine combined.	18	In a cold place
6.	Aluminium Phosphate Absorbed Diphtheria Toxoid.		

7.	Aluminium Phosphate absorbed Diphtheria and Tetanus Toxoid		
8.	Aluminium phosphate absorbed diphtheria Toxoid Tetanus Toxoid and Pertussis vaccine combined.	24	In a cold place.
9.	Diagnostic Diphtheira Toxin (Schick Test)	12	In cold place
10.	Cobra venom in solution	3	Between 2°C and 5°C protected from light.
11.	Diphtheria Toxoid	24	In cold place
12.	Inactivted Diagnostic Diphtheria Toxin.	12	In cold place
13.	Liquid serum	12	Between 2°C and 10 °C preferable at the lower limit.
14.	Lyophilised anti-snake venom serum	60	
15.	Lyophilised Schick test Toxin and control	60	
16	Old Tuberculin	60	In cold place
17.	Thrombin (Bovine origin)	36	In cold place.
1[18.	Tetanus Toxoid	36	In cold place]
19.	uberculin PPD	60	In cold place

OTHER VACCINES

1.	Alum precipitatd pertussis Vaccine.	18	In cold place
2[2.	BCG Vaccine	24	In cold place]
3.	Cholera Vaccine	18	In cold place
4.	DHL Vaccine (for dog)	12	In cold place
5.	Measles Vaccine	24	In cold place
6.	Plague Vaccine	36	In cold place
7.	Polio Vaccine	24	When stored at minus 20°C
		6	When stored at Zero °C
		3	When stored at 4 °C
8.	Rabies vaccine	6	In cold place
9.	Typhoid vaccine	18	In cold place
10.	Typhoid and Para Typhoid Vaccine.	18	In cold place
11.	Typhoid Para Typhoid A and B vaccine.	18	In cold place

1. Subs. by G.S.R. 26(E) , dt. 19.01.2006.
2. Subs. by G.S.R. 174(E) , dt. 16.03.2005.

1	2	3	4
12.	Typhoid Para Typhoid A,B & C Vaccine	18	In cold place
13.	Typhoid Para Typhoid A, B & C and Tetanus Vaccine.	18	In cold place
14.	Typhus vaccine	12	In cold place
15.	Yellow Fever Vaccine	12	In cold place
1 [16.	Anti-Rabies Vaccine (Cell Culture)	24	In cold place.]

ANTITOXIN

(For serum extracted preparations)

20% Excess potency	12	In cold place
30% Excess potency	24	In cold place
40% Excess potency	36	In cold place
50% Excess potency (for enzyme preparations)	48	In cold place
5% Excess potency	12	In cold place
10% Excess potency	24	In cold place
15% Excess potency	36	In cold place
20% Excess Potency	48	In cold place

MISCELLANEOUS DRUGS

[2][1. Andrenaline for Injection	12	[As prescribed in Indian Pharmacopoeia]
2. Chorionic Gonadotrophin for Injection (Lyophilised)	36	At temperature not exceeding 20°C
3. Corticotrophin	24	In cold place
4. Corticotrophin Lyophilised	36	In cold place
5. Heparin Injection	36	In a cool place.
6. Liquid Extract of Ergot	12	In cold place
7. Liver Extract Crude Injection	24	In a cool place
8. Oxytocin Injection	24	In cold place
9. Paraldehyde Injection	6	In cool place protected from light.
10. Pituitary Injection	24	In cold place.
11. Vasopressin Injection	24	In cold place.

Note : (1) The term ―cool place‖ means place having a temperature between 10°C and 25°C.

(2) The term ―cold place‖ means a place having a temperature not exceeding 8 °C.

(3) Capsules should be kept in a well-closed container at temperature not exceeding 30 ° C.

(4) Wherever condition of storage is not specified in Column 4, it may be stored under normal room temperature.]

1. Ins. by G.S.R. 215(E) , dt. 19. 3. 1999.

2. Subs. by G.S.R. 174(E) , dt. 16. 3.2005.

[1][SCHEDULE P1

[*See* Rule 109]

PACK SIZES OF DRUGS

Name of the Drug	Dosage form	Pack size
1	2	3
Albendazole	Suspension	10ml
Atenolol	Tablets	14
Anti-Haemmorhoidal Topicals	Rectal Capsules	20
Aspirin (Low-dose)	Tablets	14
Cholecalciferol or Ergocalciferol	Granules	1 gm. Sachet
Ciclopiroxolamine	Vaginal Cream	30 gms.
Catalin	Ophthalmic drops	15 ml
Famotidine	Tablets	14
Glyceryl Trinitrate	Spansules (Long Acting)	25

Isosorbide Dinitrate	Spansules (Long Acting)	25
Isoniazide	Syrup	200 ml
Ipecacuanha	Syrup	10 ml
Oral Rehydration Salt (ORS)	Powder	Pouches to be reconstituted to one litre in one pack or in 5 unit dose sachets in one pack.
Piperazine	Granules	5 gm.
	Syrup	30 ml
Pyrantel Pamoate	Syrup	8 ml or 10 ml
Potassium Chloride.	Syrup	60 ml and 200 ml.
Progestogen Qestrogen (Combinations for Oral Contraception)	Tablets	21 or 22 with or without placebo.
Roxatidine Acetate Hydrochloride	Tablets	14
Vitamin A Oral Drops	Drops	7.5 ml.]
[2][Co-trimoxazole	Suspension	50 ml.
Haloperidol	Oral Solution	15 ml.
Loxapine	Oral Liquid Concentrate	15 ml.]

1. Ins. by G.S.R. 796(E) , dt. 1.10.1992 (w. e. f. 1.1.1993).

2. Ins. by G.S.R. 753(E), dt. 4.11.1999.

Drugs and Cosmetics Rules 1945

[1] [SCHEDULE Q

(See rules 134 and 144)

[2][PART I]

[3][LIST OF DYES, COLOURS AND PIGMENTS PERMITTED TO BE USED IN COSMETICS AND SOAPS AS GIVEN UNDER IS : 4707 (PART I)-1988

(AS AMENDED BY THE BUREAU OF INDIAN STANDARDS)

Common name of the Colour	*colour Index Number*	*Chemical name of the colour*
1	2	3
Guinea Green B	42085	Monosodium salt of 4-(N-ethyl-p-sulfobenzylamino)–diphenylmethylone-(1-(N-ethyl-N-p-sulfoniumbenzyl)Δ 2,5-cyclohexadienimine).
Light Green SF Yellowish	42095	Disodium salt of 4-[4-(N-ethyl-p-sulfobenzylamine)-phenyl)-4-sulphoniumphenyl) methylene]-2(-(N-ethyl-N-sulfobenzyl) Δ 2,5-Cyclohexadienimine.
Tartrazine	19140	Trisodium salt of 3-carboxy-5-hydroxy-1-p-sulfophenyl-4-p-sulfophenylazo-pyrazole.
Sunset yellow FCF	15985	Disodium salt of 1-p-sulfophenylazo-2- naphthol-6-sulfonic acid.
Ponceau 3R	16155	Disodium salts of a mixture of 1-alkyl- phenylazo-2-napthol 3,

		6-disulfonic acids.
Amarnath.	16185	Trisodium salt of 1-(4-sulfo-1- napthylazo) 2-naphthol 3, 6-disulfonic acid.
Erythrosine.	45430	Disodium salt of 9-0-carboxyphenyl-6- hydroxy 2,4,5, 7-tetraiodo-3- isoxanthone.
Ponceau SX.	14700	Disodium salt of 2-(5 sulfo-2, 4-xylyl- azo)-1-naphthol-4-sulfonic acid.
Brilliant Blue FCF	42090	Disodium salt of 4-(9-4-(N-ethyl-p-sulfobenzylamino)-phenyl)-2-sulfonium phenyl)- methylene)-(1-(N-ethyl-N-p-sulfobenzyl)-Δ 2, 5-cyclohexadienimine).
Indigocarmine.	73015	Disodium salt of 5,5‘-indigotindisulfonic acid.
Wool Violet 5 BN	42640	Monosodium salt of 4-(N-ethyl-p-sulfobenzylamino)-phenyl)-(4-
(Acid- violet 6B)		(N-ethyl-p-(sulfonium-benzylamine)-phenyl) methylene)-(N, N-dimethyl-Δ 2,5-cyclohexadienimine)
Light Green SF	42095	Calcium salt of 4-(4-(N-ethyl-p-sulfobenzyl) (minophenyl)
Yellowish		(4- sulfonium-phenyl)methylene), (1-(N-ethyl-N-p-sulfobenzyl)-Δ2,5-cyclohexadienimine).

1. Inserted by Notification F.-1-36/64 D, dated 17.8.1964.
2. Renumbered as Part I by G.S.R. 11(E) , dated 7.1.1991.
3. Substituted by G.S.R. 811(E) , dated 14.11.1994.

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1	2	3
Alizarin Cyanine Green F	61570	Disodium salt of 1,4-bis (O-sulfo-p-toluino) anthraquinone
Quinazarine Green SS	61565	1,4-bis-(p-Toluino)-anthraquinone
Fast Green FCF	42053	Disodium salt of 4-(4-(ethyl-p-sulfobenzylamino)-phenyl) (4-hydroxy-2 sulphoniumphenyl) methylene)-(1-N-ethyl-N-p-sulfobenzyl) Δ 2, 5, cyclohexadienimine).
Acid Fast Green	42100	Monosodium salt of 4-(4-N-ethyl-p-sulfobenzylomino) phenyl)-(o-chlorophenyl)-methylene)- 1-(N-ethyl-N- p-sulfonium-benzyl- Δ 2,5, cyclohexadienimine).
Pyranine Concentrated	59040	Trisodium salt of acid.
Quinoline Yellow WS	47005	Disodium salt of disulfonic acid of 2-(2-Quinolyl)-1, 3-indandione.
Quinoline Yellow SS	47000	2-(2-quinolyl)-1, 3 indandiene.
Poneceau 2 R	16150	Disodium salt of 1-xylylazo-2-naphthol-3, 6-disulfonic acid.
Lithol Rubin B. naphthoic	15850	Monosodium salt of 4-(o-sulfo-p-tolylazo)3 hydroxy-2- acid.
Lithol Rubin BCA naphthoic	15850	Calcium salt of 4-(o-sulfo-p-tolylazo)-3-hydroxy-2- acid
Lake Red D.	15500	Monosodium salt of 1-0-carboxyphenylazo-2-naphthol.
Lake Red DBA	15500	Barium salt of 1-o-carboxyphenylazo-2-naphthol.
Lake Red DCA.	15500	Calcium salt of 1-o-carboxyphenylazo-2-naphthol.
Toney Red.	26100	I-p-phenylazophenylazo-2-naphthol.
Oil Red OS.	26125	I-Xylylazoxylylazo-2-napththol

Tetrabromofluorescein	45380	2,4,5,7-Tetrabromo-3, 6-flurandiol.
Eosin TS	45380	Disodium salt of 2,4,5,7-tetrabromo-9-0 carboxyphenyl-6-hyroxy-3-isoxanthone.
Eosin YSK. .	45380	Dipotassium salt of 2,4,5,7-tetrabromo-9-0 carboxyphenyl-6-hyroxy-3-isoxanthone
Tetrachlorofluorescein NA	45366	2,4,5,7- tetrachloro-S, 6-Fluorandiol
Tetrachlorofluorescein K.	45366	Disodium salt of 9-0-carboxyphenyl-2,4,5,7-tetrachloro-6-hydroxy-3-isoxanthone.
Tetrachloro Tetrabromo fluorescein	45410	2,4,5,7-Tetrabromo-12,13,14,15-tetrachloro-3, 6-fluorandiol.
Phloxine B	45410	Disodium salt of 2,4,5,7-tetrabromo-9 (3,4,5,6-tetra chloro-o-carboxyphenyl)-6-hydroxy-3-isoxanthone
Bluish Orange T.R.	45457	1,4,5,8, 15-Pentabromo-2, 7-dicarboxy-3, 6-fluoran diol.
Helindone Pink CN.	73360	5, 5-Dichloro-3, 3‘ dimethyl-thioindigo

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1	2	3
Deep Maroon (Fanchon Maroon)	15880	Calcium salt of 4-(I-sulfo-2-naphthylazo 3- hydroxy-2-naphthoic acid.
Toluidine Red. .	12120	1-(o-Nitro-p-tolylazo)-2-naphthol.
Flaming Red.	12085	I- (o-Chloro-p-nitrophenylazo)-2-naphthol
Deep Red (Maroon).	12350	3-Hydroxy-N- (m-nitrophenyl)-4-(o-nitro-p-tolylazo)-2-naphthamide.
Alba Red.	13058	o-(p,β,β-Dihydroxy-diethylamino)- phenylazo)-benzoic acid.
Orange G.	16230	Disodium salt of 1-phenylazo-2-naphthol-6-8-disulfonic acid.
Orange II	15510	Monosodium salt of 1-p-sulfophenylazo-2-naphthol.
Dichlorofluorescein	45365	4,5-Dichloro-3, 6-fluorandiol.
Dichlorofluorescein. NA	45365	Disodium salt of 9-o-carboxyphenyl-1-4,5- dichloro-6-hydroxy-3-isoxanthone
Diiodofluorescein.	45425	4,5 –Diiodo-3, 6-fluorandiol
Erythrosine Yellowish NA.	45425	Disodium salt of 9-o-carboxyphenyl-6- hydroxy-4, 5-diiodo-3-isoxanthone.
Erythrosine Yellowish K.	45425	Dipotassium salt of 9-o-carboxyphenyl-6-hydroxy-4, 5-diiodo-3-isoxanthone.
Erythrosine Yellowish NH	45425	Dipotassium salt of 9-o-carboxyphenyl-6-hydroxy-4, 5-diiodo-3-isoxanthone
Orange TR	45456	4,5, 15-Tribromo 2, 7-dicarboxy-3, 6- fluorandiol.
Alizarin.	58000	1,2- Anthraquinonediol.
Dibromodiiodofluorescein.	45371	4 ,5- Dibromo-2, 7-diiodo-3, 6-fluorandiol.
[1][***]		
Alphazurine FG.	42090	Diammonium salt of 4-(N-ethyl-p- sulfobenzyl amino)-phenyl)-(2-sulfoniumphenyl)-Methytlene)-(-(1 (N-ethyl-N-p-sulfobenzyl) Δ 2 ,5-cyclohexadienimine).

Allarin Astrol B. toluino)-	61530	Monosodium salt of 1-methylamino-4-(o-sulfo-p- anthroquinone.
Indigo.	73000	Indigotin.
Patent Blue NA. .	42052	Monosodium salt of 4-(4- (N-ethyl- benzyl-amino)-phenyl – (5-hydroxy-4-sulfo-2-sulfoniumphenyl-methylene)(N-ethyl-Benzyl- Δ 2, 5-cyclohexadienimine).
Patent Blue CA.	42052	Calcium salt of 4-(4- (N-ethyl- benzyl-amino)-phenyl)-(5 hydroxy-4-sulfo-2-sulfoniumphenyl, methylene)- (N-ethyl-N-benzyl- Δ 2- 5-cyclohexadienimine).
Carbrantherene Blue	69825	3, 3- Dichloroindanthrene.

1.Omitted by G.S.R. 203(E), dated 18-03-2015.

1	2	3
Napthol Blue Black	20470	Disodium salt of 8-amino-7-p- nitrophenylazo 3-phenylazo-1- naphthol-3, 6-disulfonic acid
Alizurol purple SS	60725	I-hydroxy-4-p-toluino-anthraquinone.
Acid Red 89	23910	----
Acid Red 97	22890	----
Acid Blue 1	42045	----
Food Blue 3	42045	----
Natural Orange	75480	----
Solvent Blues 4	44045	----
Solvent Yellow 18	12740	----
Food Yellow 12.	12740	----
[1][***]		----
Solvent Yellow 32.	48045	----
Fanchon Yellow (Hansa Yellow G).	11680	(α) -(O-Nitro-p-tolylazo) accetoacetanilide

[2][Part II

LIST OF COLOURS PERMITTED TO BE USED IN SOAPS.

Common name of the Colour	*Colour Index No.*	*Chemical name of the colour*
Phthalocyanine Blue	74160	(phthalocyninate (2--) copper.
Iragalite Red CVPB Paste or Pigment Orange 5	12075	1-(2,4-dinithro phenylazo)-2-Naphthalenol.
Citrus Red No.2.	12156	1-2(2,5-dimethoxy phenylazo) 2-naphthol.
Rhodamine B 500	45170	3-ethochloride of 9-0 carboxy-ethenyl-6-diethylamino-3-ethylamine-3-isoxanthene.
Aqueous Green Paste	74260	Polychloro copper Phthalocyanine.
Pigment Yellow 3	11710	2-(4-Chloro-2-nitrophenyl)-azo-N-(-2-Chloro-phenyl)-3- Oxobutamide.
Irgalite Carmine F-P Powder or Pigments Red 5.	12490	N-(5-Chloro-2, 4-dimethoxy-phenyl)-4-(CS-diathylamine) Sulfonyl-2-methoxyphenyl)azo-3-hydroxy-2-naphthalene carboxamide.

Monolite Red 4R HV Paste or Pigment Red 7.	12420	N-(4-Chloro-2-methylphenyl-4-(-4-Chloro-2-methylphenyl) Azo 3-hydroxy-2-naphthalenol Carboxamide.
Oil Red No.1 or Solvent Red 24 or Oil Red 3R.	26105	4-0-Tolylazo-Toluidine azo 2-naphthalenol.]

*This list of colour for use in soaps is in addition to those colours already given in Schedule Q and are used for soaps.]

1. Omitted by G.S.R. 203(E) dated 18-03-2015

2. Ins. by G.S.R. 11(E) , dt. 7.1.1991.

Drugs and Cosmetics Rules 1945

1[SCHEDULE R

[*See* Rule 125]

STANDARDS FOR CONDOMS MADE OF RUBBER LATEX INTENDED FOR SINGLE USE AND OTHER MECHANICAL CONTRACEPTIVES

I-Condoms

1. ***Description*** - Condoms consist of cylindrical rubber sheaths with one end open. The open end shall terminate with an integral rim. The closed end may have a receptacle. They may be supplied rolled and shall be free from tackiness and shall be capable of being unrolled readily.

2. ***Materials*** - (1) Condoms shall be manufactured from good quality rubber latex and shall be free from embedded grit and shall be opaque or translucent prior to the application of dusting materials or lubricants.

(2) The rubber latex, colours used and any dusting materials or lubricants applied to the condoms shall neither contain nor liberate substances which are known to have toxic or other harmful effects under normal conditions of use. Any dusting material or lubricant or colour used shall not have deleterious effect on the condoms or be harmful to the users.

3. ***Procedure for sampling during production*** − *(*1) Specimens constituting the test samples shall be taken at random successively from each quantum of production that is, from the quantity produced from the same finished rubber latex and under the same processing and finishing conditions of manufacture and samples from each quantum shall be tested separately to ascertain conformity of quantum with the specified requirements in accordance with the tests described in this Schedule.

(2) (*a*) The number of samples drawn from each quantum shall be not less than 0.5 per cent of the number.

(*b)* The number of samples drawn from each quantum shall be tested for Burst Volume and Pressure Test and Water Leakage Test in accordance with the method prescribed in paras 9 and 10 of this Schedule. 75 per cent of the samples drawn will be tested for Water Leakage Test and 25 per cent will be tested for Burst Volume and Pressure Test.

(c) The number of test samples ‗N' and the number of rejected samples ‗R' from a sequence of production quanta shall be recorded in a register. The cumulative total of test samples ‗N' and the cumulative total of rejects ‗R' from the test shall be recorded and the condoms shall be deemed to comply with the requirements if the cumulative total of rejects ‗R' is not more than 2[0.0025N+3 x √0.0025N] for Water Leakage Test, and 2[0.015N+3 x √0.015N] for Burst Volume and Pressure Test.

(3) Each unit of 100 test samples shall be distributed for the various tests as follows: -

25 for Burst Volume Pressure Test, and;

75 for Water Leakage Test.

1 Subs. by G.S.R. 495(E) , dt. 9.6.1995.
2. Subs. by G.S.R. 353(E), dt. 26.4.2000.

(4) Where the number of test samples is a multiple of 100 the distribution scale mentioned above shall be prorated.

(5) If the cumulative total sample rejected exceeds the number of allowables at any point in the sequence of quanta, the quantum at which this occurs shall be liable to rejection. The assessment of quality of further production quanta shall include all previous test results starting from quantum number 1 and approval of production shall be in suspense until the condition required by the scheme is again fulfilled.

(6) At least one sample shall be taken at random from each production quantum not exceeding 10,000 condoms and shall satisfy all requirements regarding dimensions as specified in paragraph 8 of this Schedule.

4. Procedure for sampling and testing of finished products by a manufacturer –

A. *Water Leakage Test.*- (1) Statistical sampling for quality control assessment of the finished product in respect of Water Leakage Test shall be done in accordance with the plan set out in Annexure 1 to this Schedule.

(2) A test sample failing in the above test is to be considered as defective. If the cumulative total of rejects _R' is found to be equal to or greater than the number shown against _R' in Annexure-I, the batch or lot shall be declared as not of standard quality.

B. *Bursting Volume and Pressure Test.*- (1) Sample condoms shall be tested for Bursting Volume and Pressure Test. Statistical sampling for this test shall be done in accordance with the plan set out in Annexure III to this Schedule.

Condoms shall not leak or burst at a volume of less than that specified or at a pressure less than 1.0 kpa (gauge), when tested as per paragraph 9, both before and after oven conditioning as specified in Annexure V. Bursting Volume minimum limit in litres shall be equal to $\frac{[\text{mean condom width (mm)}2]}{151.8}$ rounded to the nearest 0.5 litre.

(2) A test sample failing in the above test is to be considered defective. If the cumulative total of rejects _R' is found to be equal or greater than the number shown against _R' in Annexure III, the batch or lot shall be declared as not of standard quality.

C. *Dimensions.* - At least 2 samples drawn from the lot or batch shall satisfy the requirements regarding dimensions as specified in paragraph 8 of this Schedule.

5. Procedure for sampling and testing of condoms by a purchaser -

A. *Water Leakage Test*- (1) Statistical sampling of condoms by a purchaser for Water Leakage Test shall be done in accordance with the plan set out in Annexure II to this Schedule;

(2) A test sample failing in the above test is to be considered as defective. If the cumulative total of rejects _R' is found to be equal to or greater than the number shown against _R' in the Annexure-II, the batch or lot shall be declared as not of standard quality.

B. *Bursting Volume and Pressure Test* - Sample condoms shall be tested for Bursting Volume and Pressure Test. Statistical sampling for this test shall be done in accordance with the plan set out in Annexure III to this Schedule. If the cumulative total of rejects _R' is found

to be equal to or greater that the number shown against _R' in Annexure III, the batch or lot shall be declared as not of standard quality.

Condom shall not leak or burst at a volume of less than that specified or at a pressure less than 1.0 kpa (gauge), when tested as specified in paragraph 9, both before and after oven conditioning as per specified in Annexure V. Bursting volume minimum limit in litres shall be equal to

$$\frac{[\text{mean condom width (mm)}2]}{151.8}$$ rounded to the nearest 0.5 litre.

C. *Dimensions.* - At least two samples from the lot or batch shall satisfy the requirements regarding dimensions as specified in paragraph 8 of this Schedule.

6. ***Sampling plan for a Drugs Inspector*** - (1) Where an Inspector under the Act desires to take test samples from the premises of manufacturer or a distribution depot; twenty containers from each batch of production may be selected by him on a random basis and from each of the containers, five samples shall be taken. The hundred samples so selected shall be distributed for various tests as specified in paragraph 7 of this Schedule. In case the number of container is less than twenty, the number of samples to be taken from each container shall be proportionately increased.

(2) Where an Inspector under the Act desires to take samples from a sales premises, he shall take hundred samples from each batch of production in accordance with the procedure as specified in sub- paragraph (1).

7. Sampled condoms drawn under sub-paragraph.- (1) shall be distributed for various tests as follows: - Two samples for thickness, length and width;

Forty-five samples for Water Leakage Test;
Forty-five samples for Bursting Volume and Pressure Test; and
Eight samples as reserve.

The samples shall be declared as not of standard quality, if, - (i) the number of condoms found defective in the Water Leakage Test exceeds one; (ii) the number of condoms found defective in Bursting Volume and Pressure Test exceeds two; (iii) samples fail to conform to the requirements of dimensions as specified in paragraph 8 of this Schedule.

8. ***Dimensions*** - (1) The length when unrolled (excluding test) shall be not less than -

(i) 170 mm.

(ii) 180 mm.

(2) The width of a condom which laid flat and measured at any point within 85 mm from the open end shall be,–

(i) 49 ± 2 mm for 170 mm length.

(ii) 53 ± 2 mm for 180 mm length.

(3) The single-wall thickness of a condom when measured at three points, one at 30 ± 2mm from the open end, 30 ± 5mm from the close end excluding the reservoir tip and at the mid distance between these two point shall be from 0.045 mm to 0.075 mm.

NOTE 1. - The single-wall thickness shall be determined with a suitable micrometer dial gauge graduated in intervals of 0.01 mm.

NOTE 2. - Condoms shall, prior to the measurement of thickness, have the dusting powder or the lubricant or both removed by means of water or Isopropanol.

9. ***Bursting Volume and Pressure Test*** **-**Determination of Bursting Volume and Pressure Test shall be done as specified in Annexure IV.

10. ***Water Leakage Test*** **-**Unroll the condom and fit the open end on a suitable mount, the condom thus being suspended open end upwards. Fill it with 300 ml water at room temperature

and inspect it after a period of at least 1 minute for leakage up to 25.mm from the open end. If, because of distension of the condom the water does not extend to 25 mm from the open end, raise the closed end until the water level reaches this distance. After at least 1 minute, inspect the newly-wetted part of the condom for leakage. The condom shall be deemed to be defective if it bursts during test or shows any evidence of leakage or seepage of micro-droplets or does not hold 300 ml water.

11. ***Quantity of Lubricant*** - (1) The condoms shall be dressed with silicone lubricant. The quantity required on each individual condom should not be less than 200 mg and minimum viscosity shall be 200 centistokes.

(2) Lubricated condoms in individual foil packages shall be weighed on an Analytical Balance. Each condom shall be removed from its foil package and both condom and its foil package shall be washed in denatured ethanol or isopropanol, dried and then weighed again. All weights shall be recorded to the nearest milligram (mg.). Compliance with the requirement shall be determined by subtracting the weight of the washed and dried condom and its foil package from the weight of sample condom in individual foil package prior to the removal of lubricant. Washing and drying may be required upto a total of four times if the lubricant quantity is less than the required minimum.

(3) At least thirteen samples shall be drawn from the lot or batch and the samples shall satisfy the requirements regarding the quantity of lubricant.

12. ***Colour Fastness***- Not less than ten samples taken at random from each batch of coloured condoms shall pass the following test for colour fastness, namely :-

Thoroughly wet inside and outside of the condom with distilled water. Make no attempt to remove any dusting material or lubricant. Wrap the wet condom in white absorbent paper so that the largest possible surface area of the condom is in contact with the paper and seal the whole in a suitable container to prevent loss of moisture. Allow the container and its contents to stand for 16 hours to 24 hours at room temperature. After removing the absorbent paper from the container, examine it visually in the natural daylight for any indication of staining. No part of the absorbent paper shall be stained. If there is any indication of staining of the absorbent paper by any colouring agent present in any of the condoms or any dusting material or lubricant, the entire batch shall be declared to be not of standard quality.

13. ***Labelling, packing and storage*** **-**(1) The condoms shall be individually wrapped and sealed in laminates containing at least eight microns of aluminium foil. The individual condom shall be packed in square (non-squeeze condition) / rectangular aluminium foil. The packing shall protect the condoms from contamination and mechanical damage. The smallest packing offered to the consumer shall bear a clear permanent marking with the following particulars, namely: -

(i) Manufacturer‘s name and address and the trade name of the condoms, if any;

(ii) Batch number;

(iii) Date of manufacture (Month and year only);

(iv) Date of expiry (Month and year only) which shall not be more than thirty-six months from the date of manufacture;

(v) The words ―For single use only‖

(2) The condoms shall be stored in a cool dry place away from heat and direct sunlight.

14. ***Integrity of individual package seals*** **-**Sample condoms in individual packages shall be placed in a sealed, transparent container (such as a laboratory Bell jar) and subjected to vacuum of 50± 10 kpa (gauge) for a period of one minute.

Condom packages that do not inflate or remain inflated for the period of the test shall be deemed non- compliers. In doubtful cases, the test may be repeated, and both the inflation and deflation of packages may be observed on application and removal of vacuum. An AQL of 2.5 per cent will be applied in assessing the results of this test. Thirty-two samples of condoms for a batch size less than 5 lakhs and fifty samples of condoms for batch size more than 5 lakhs shall be tested for integrity test of individual package seals and compliance limit or acceptance number shall be not more than two or three condoms respectively.

II- Other Mechanical Contraceptive

15. ***Standards for other mechanical contraceptive*** - Standards for _Copper T‘ and _Tubal Ring‘shall be as laid down in Annexure VI.

[1]
[ANNEXUR
E I

[*See* Paragraph 4-A]

SAMPLING PLAN FOR QUALITY CONTROL OF CONDOMS AT MANUFACTURER’S LEVEL.

BATCH SIZE: 35,001 TO 1.5

LAKH Single Sampling Plan

Sample Size 200: AQL - 0.25

AC - 1

R - 2

1. Subs. by. G.S.R. 353(E) , for ― Annexures I to III‖ dt. 26-4-2000.

BATCH SIZE: 150001 TO 5 LAKHS

Single Sampling Plan

Sample Size 315 : AQL - 0.25

AC - 2

R - 3

BATCH SIZE: OVER 5 LAKHS

Single Sampling Plan.

Sample Size 500: AQL - 0.25

AC - 3

R - 4

Note : AQL denotes Acceptance Quality Level;

AC denotes Acceptance Number i.e. the maximum allowable number of defectives for acceptance of the Batch; and

R denotes Rejection Number i.e., the minimum number of defectives for rejection of the Batch.

ANNEDURE II

[*See* Paragraph 5A]

SAMPLING PLAN FOR QUALITY CONTROL OF CONDOMS AT PURCHASER'S LEVEL.

BATCH SIZE: 35,001 TO 1.5 LAKHS

Single Sampling Plan

Sample Size 200: AQL - 0.25
AC - 1
R - 2

BATCH SIZE : 15,001 TO 5 LAKHS

Single Sampling Plan.

Sample Size 315: AQL - 0.25
AC - 2
R - 3

BATCH SIZE : OVER 5 LAKHS

Single Sampling Plan

Sample Size 500: AQL - 0.25
AC - 3
R - 4

Note: AQL denotes Acceptance Quality Level;

AC denotes Acceptance Number i.e. the maximum allowable number of defectives for acceptance of the Batch; and

R denotes Rejection Number i.e., the minimum number of defectives for rejection of the Batch.

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ANNEXURE III

[*See* Paragraph 4-B and 5-B]

SAMPLING PLAN FOR BURSTING VOLUME AND PRESSURE TEST.

BATCH SIZE: 35,001 TO 1.5

LAKH. Single Sampling Plan.

Sample Size 200: AQL -
1.5 AC - 7
R - 8

BATCH SIZE: 150001 LAKHS TO 5 LAKHS

Single Sampling Plan.

Sample Size 315: AQL -
1.5 AC -
10 R -
11

BATCH SIZE: OVER 5 LAKHS

Single Sampling Plan.

Sample Size 500: AQL -
1.5 AC -
14 R - 15

Note : AQL denotes Acceptance Quality Level;

AC denotes Acceptance Number i.e. the maximum allowable number of defectives for acceptance of the Batch; and

R denotes Rejection Number i.e., the minimum number of defectives for rejection of the Batch.]

ANNEXURE IV

(See Paragraph 9)

DETERMINATION OF BURSTING VOLUME AND PRESSURE

1. Principle - Inflation of constant length of the condom with air and recording the volume and pressure at the moment of bursting.

2.Apparatus - (1) Apparatus suitable for inflating the condom with clean air at a specified rate and provided with equipment for measuring volume and pressure.

(2) Suitable mount for fitting the condoms to the apparatus as shown in the figure annexed. (3) Rod, 140 mm in length having a smooth sphere 20 mm in diameter at its top (see the figure) for hanging the unrolled condom when fixed to the apparatus.

3. Procedure - (1) Unroll the condom, hang it on the rod (2.3), affix to the mount (2.2) and inflate with air at a rate of 0.4 to 0.5 litre/sec. (24 to 30 litres/min.)

(2) Measure and note the bursting volume, in litres rounded to the nearest 0.5 litre and the bursting pressure, in kilopascals rounded to the nearest 0.1 kpa.

4. Test report - The test report shall include the following particulars:

(a) the identification of the sample;

(b) the bursting volume and bursting pressure of each tested condom; *(c)* the date of testing.

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ANNEXURE V

[See Paragraphs 4(B) and 5 (B)

OVEN CONDITIONING

1. Principle of the Method - The test consists in subjecting test samples to controlled deterioration by air at an elevated temperature and at atmospheric pressure after which burst volume and pressure limits are measured.

2. Apparatus - The air oven shall be of such a size that the total volume of the test samples does not exceed 10 per cent of the free air space of the oven. Provision shall be made for slow circulation of air in the oven of not less than three changes and not more than ten changes per hour. The temperature of the oven shall be thermostatically controlled so that the test samples are kept within ± 2o C of the specified ageing temperature. A thermometer shall be placed near the centre of the ageing test samples to record the actual ageing temperature.

Note: - Copper or copper alloys shall not be used for the material of construction of the oven prescribed.

3. Test sample - The foil laminations of individual packages should remain intact throughout all laboratory handling including over conditioning.

4. Temperature of the oven – Maintain the oven at 70 ± 2o C.

5. Duration of test - 96 hours.

6. Procedure - Condition the requisite number of unopened packages of rubber condoms in the oven at 70 ± 2o C for 96 hours. After heating, keep the packages at 23 ± 5o C for at least 12 hours but not more than 96 hours. Open the packages and examine conditioned condoms for tackiness, brittleness, or other signs of deterioration. Within 96 hours but not sooner than 12 hours after conditioning, do the bursting volume and pressure Test as described in this Schedule.

ANNEXURE VI

(*See* Paragraph 15)

1. Standards for Copper T (200B) (IS-12418) (part 4)-1991-UDC 615.477.87) - Contraceptive Device Copper T (200 B) shall conform to the Indian Standards laid down from time to time by the Bureau of Indian Standards.

2. Standards for Contraceptive Tubal Ring (IS 13009 : 1990-UDC 615.472.6 : 611.656) - Contraceptive Device Tubal Ring shall conform to the Indian Standards laid down from time to time by the Bureau of Indian Standards.]

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[1][**SCHEDULE R1**

(*See* Rules 109A, 109, 109C and 125A)

The medical devices shall conform to the Indian Standards laid down from time to time by the Bureau of Indian Standards. If there are no Bureau of Indian Standards then it shall conform to the International Standards, like International Organisation for Standardisation, or other International Pharmacopeia Standards and such other standards as may be specified for this purpose. In case national or international standards are not available, the device shall conform to the manufacturer‘s validated standards.]

[2][**SCHEDULE S**

[*See* Rule 150-A]

STANDARDS FOR COSMETICS

Standards for cosmetics in finished form − The following cosmetics in finished form shall conform to the Indian Standards specifications laid down from time to time by the [3] [Bureau of Indian Standards (BIS)].

1. Skin Powders.
2. Skin Powder for infants.
3. Tooth Powder.
4. Toothpaste.
5. Skin Creams.
6. Hair Oils.
7. Shampoo, Soap-based.
8. Shampoo, Synthetic-Detergent based.
9. Hair Creams.
10. Oxidation hair dyes, Liquid.
11. Cologne.]

[4]

[12. Nail Polish (Nail Enamel).

13. After Shave Lotion.
14. Pomades and Brilliantines.
15. Depliatories Chemical.
16 Shaving Creams.
17. Cosmetic Pencils.
18. Lipstick.]

[5]

[19. Toilet Soap.

20. Liquid Toilet Soap.

21. Baby Toilet Soap.

22. Shaving Soap.

23. Transparent Toilet Soap.]

1. Subs. by G.S.R. 690(E), dt. 25.9.2014.
2. Ins. by G.S.R. 510(E) , dt. 26.07.1982.
3. Subs. by G.S.R. 673(E), dt. 27.10.1993.
4. Ins. By G.S.R. 731(E) dated 23-08-1990
5. Ins. By G.S.R. 673(E) dated 27-10-1993

1[24. Lipsalve IS:10284.

25. Powder Hair Dye IS: 10350.

26. Bindi (Liquid) IS: 10998.

27. Kum Kum Powder IS: 10999.

28. Henna Powder IS: 11142.]

2[29. Bathing Bars IS: 13498: 1997

3[30. Sindoor IS: 14649: 1999

4[31. Liquid Foundation makeup IS 14318

4[32. Cold Wax Hair remover IS 15152

4[33. Face pack IS 15153

4[34. Kajal IS 15154

4[35. Oxidation Hair Dyes (Emulson Type) IS 15205

4[36. Cream Bleach IS 15608

1. Ins. by G.S.R. 553(E), dt. 20.7.1995.
2. Ins. by G.S.R. 592(E), dt.13.8.2008.
3. Ins. by G.S.R. 724(E), dt. 07.11.2013.
4. Ins. by G.S.R. 203(E), dt.18.03.2015.

5[SCHEDULE T

(*See* rule 157)

GOOD MANUFACTURING PRACTICES FOR AYURVEDIC, SIDDHA AND UNANI MEDICINES

The Good Manufacturing Practices (GMP) are prescribed as follows in Part I and Part II to ensure that:

(i) Raw materials used in the manufacture of drugs are authentic, of prescribed quality and are free from contamination.

(ii) The manufacturing process is as has been prescribed to maintain the standards. (iii) Adequate quality control measures are adopted.

(iv) The manufactured drug which is released for sale is of acceptable quality. (v) To achieve the objectives listed above, each licensee shall evolve methodology and procedures for following the prescribed process of manufacture of drugs which should be documented as a manual and kept for reference and inspection. However, under IMCC Act 1970 registered Vaidyas, Siddhas and Hakeems who prepare medicines on their own to dispense to their patients and not selling such drugs in the market are exempted from the purview of G.M.P.

5. Subs. by G.S.R. 560(E), dt. 07.3.2003.

PART I

GOOD MANUFACTURING PRACTICES

1.1 Factory Premises:

The manufacturing plant should have adequate space for: -

(i)Receiving and storing raw material.
(ii)Manufacturing process areas.
(iii)Quality control section.
(iv)Finished goods store.
(v)Office.
(vi)Rejected goods/drugs store.

1.1 General Requirements:

1.1(A) *Location and surroundings* - The factory building for manufacture of Ayurveda, Siddha and Unani medicines shall be so situated and shall have such construction as to avoid contamination from open sewerage, drain, public lavatory for any factory which produces disagreeable or obnoxious odour or fumes or excessive soot, dust and smoke.

1.1(B) *Buildings* - The buildings used for factory shall be such as to permit production of drugs under hygienic conditions and should be free from cobwebs and insects/rodents. It should have adequate provision of light and ventilation. The floor and the walls should not be damp or moist. The premises used for manufacturing, processing, packaging and labelling will be in conformity with the provisions of the Factory Act. It shall be located so as to be:

(I) Compatible with other manufacturing operations that may be carried out in the same or adjacent premises.

(II) Adequately provided with working space to allow orderly and logical placement of equipment and materials to avoid the risk of mix-up between different drugs or components thereof and control the possibility of cross contamination by other drugs or substances and avoid the risk of omission of any manufacturing or control step.

(III) Designed, constructed and maintained to prevent entry of insects and rodents.

Interior surface (walls, floors and ceilings) shall be smooth and free from cracks and permit easy cleaning and disinfection. The walls of the room in which the manufacturing operations are carried out shall be impervious to and be capable of being kept clean. The flooring shall be smooth and even and shall be such as not to permit retention or accumulation of dust or waste products.

(IV) Provided with proper drainage system in the processing area. The sanitary fittings and electrical fixtures in the manufacturing area shall be proper and safe.

(V) Furnace/Bhatti section could be covered with tin roof and proper ventilation, but sufficient care should be taken to prevent flies and dust.

(VI) There should be fire safety measures and proper exits should be there.

(VII) Drying Space: -There should be separate space for drying of raw material, in process medicine or medicines which require drying before packing. This space will be protected from flies/ insects/dust etc., by proper flooring, wire-mash window, glass panels or other material.

1.1(C) *Water Supply* - The water used in manufacture shall be pure and of potable quality. Adequate provision of water for washing the premises shall be made.

1.1(D) *Disposable of Waste* - From the manufacturing section and laboratories the waste water and the residues which might be prejudicial to the workers or public health shall be disposed off.

1.1(E) *Container's Cleaning* - In factories where operations involving the use of containers such as glass bottles, vials and jars are conducted, there shall be adequate arrangements separated from the manufacturing operations for washing, cleaning and drying of such containers.

1.1(F) *Stores* - Storage should have proper ventilation and shall be free from dampness. It should provide independent adequate space for storage of different types of material, such as raw material, packaging material and finished products.

1.1. (F)(A) *Raw Materials* - All raw materials procured for manufacturing will be stored in the raw materials store. The manufacture based on the experience and the characteristics of the particular raw material used in Ayurveda, Siddha and Unani system shall decide the use of appropriate containers which would protect the quality of raw materials as well as prevent it from damage due to dampness, microbiological contamination or rodent and insect infestation, etc. If certain raw materials require such controlled environmental conditions, the raw materials stores may be sub-divided with proper enclosures to provide such conditions by suitable cabinization. While designing such containers, cupboard or areas in the raw materials store, care may be taken to handle the following different categories of raw materials:-

1. Raw material of metallic origin.
2. Raw material of mineral origin.
3. Raw material from animal source.
4. Fresh herbs.
5. Dry herbs or plant parts
6. Excipients etc.
7. Volatile oils/perfumes and flavours
8. Plant concentrates/ extracts and exudates/resins.

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Each container used for raw material storage shall be properly identified with the label which indicates name of the raw material, source of supply and will also clearly state the status of raw material such as _UNDER TEST' or _APPROVED' or _REJECTED'. The labels shall further indicate the identity of the particular supply in the form of Batch No. or Lot No. and the date of receipt of the consignment.

All the raw materials shall be sampled and got tested either by the in-house Ayurvedic, Siddha and Unani experts (Quality control technical person) or by the laboratories approved by the Government and shall be used only on approval after verifying. The rejected raw material should be removed from other raw material store and should be kept in separate room. Procedure of _First in first out' should be adopted for raw materials wherever necessary. Records of the receipt, testing and approval or rejection and use of raw material shall be maintained.

1.1. (F)(B) *Packaging Materials*. - All packaging materials such as bottles, jars, capsules etc. shall be stored properly. All containers and closure shall be adequately cleaned and dried before packing the products.

1.1. (F)(C) Finished *Goods Stores*. - The finished goods transferred from the production area after proper packaging shall be stored in the finished goods stores within an

area marked ―Quarantine‖. After the quality control laboratory and the experts have checked the correctness of finished goods with reference to its packing/labelling as well as the finished product quality as prescribed, then it will be moved to ―Approved Finished Goods Stock‖ area. Only approved finished goods shall be dispatched as per marketing requirements. Distribution records shall be maintained as required.

If any Ayurvedic, Siddha and Unani drug needs special storage conditions, finished goods store shall provide necessary environmental requirements.

1.1(G) *Working space*. - The manufacturing area shall provide adequate space (manufacture and quality control) for orderly placement of equipment and material used in any of the operations for which these employed so as to facilitate easy and safe working and to minimize or to eliminate any risk of mix-up between different drugs, raw materials and to prevent the possibility of cross contamination of one drug by another drug that is manufactured, stored or handled in the same premises.

1.1(H) *Health Clothing, Sanitation and Hygiene of Workers*.- All workers employed in the Factory shall be free from contagious diseases. The clothing of the workers shall consist of proper uniform suitable to the nature of work and the climate and shall be clean. The uniform shall also include cloth or synthetic covering for hands, feet and head wherever required. Adequate facilities for personal cleanliness such as clean towels, soap and scrubbing brushes shall be provided. Separate provision shall be made for lavatories to be used by men and women, and such lavatories shall be located at places separated from the processing rooms. Workers will also be provided facilities for changing their clothes and to keep their personal belongings.

1.1. (I) *Medical Services*: The manufacturer shall also provide:-

(*a*) adequate facilities for first aid;

(*b)* medical examination of workers at the time of employment and periodical check up thereafter by a physician once a year, with particular attention being devoted to freedom from infections. Records thereof shall be maintained.

1.1(J) *Machinery and Equipments* - For carrying out manufacturing depending on the size of operation and the nature of product manufactured, suitable equipment either manually operated or operated semi-automatically (Electrical or steam based) or fully automatic machinery shall be made available. These may include machines for use in the process of manufacture such as crushing, grinding, powdering, boiling, mashing, burning, roasting, filtering, drying, filling, labelling and packing etc. to ensure ease in movement of workers and orderliness in operations a suitably adequate space will be ensured between two machines or rows of machines. These equipments have to be properly installed and maintained with proper cleaning. List of equipments and machinery recommended is indicated in Part II-A.

Proper Standard Operational Procedures (SOPs) for cleaning, maintaining and performance of every machine should be laid down.

1.1(K) Batch *Manufacturing Records* - The licensee shall maintain batch manufacturing record of each batch of Ayurvedic, Siddha and Unani drugs manufactured irrespective of the type of product manufactured (classical preparation or patent and proprietary medicines). Manufacturing records are required to provide an account of the list of raw materials and their quantities obtained from the store, tests conducted during the various stages of manufacture like taste, colour, physical characteristics and chemical tests as may be necessary or indicated in the approved books of Ayurveda, Siddha and Unani mentioned in the First Schedule of the Drugs and Cosmetics Act, 1940 (23 of 1940). These tests may include any in-house or pharmacopoeial test adopted by the manufacturer in the raw material or in the process material

and in the finished product. These records shall be duly signed by Production and Quality Control Personnel respectively. Details of transfer of manufactured drug to the finished products store including dates and quantity of drugs transferred along with record of testing of the finished product, if any, and packaging, records shall be maintained. Only after the manufactured drugs have been verified and accepted quality shall be allowed to be cleared for sale.

It should be essential to maintain the record of date, manpower, machine and equipments used and to keep in process record of various shodhana, bhavana, burning and fire and specific grindings in terms of internal use.

1.1(L) *Distribution Records* - Records of sale and distribution of each batch of Ayurveda, Siddha and Unani Drugs shall be maintained in order to facilitate prompt and complete recall of the batch, if necessary.The duration of record keeping should be the date of expiry of the batch. Certain category of Ayurvedic, Siddha and Unani medicines like Bhasma, Rasa, Kupi-pakva, Parpati, Sindura, Karpu/Uppu/Puram, Kushta, Asava-arishta etc. do not have expiry date in contrast their efficacy increases with the passage of time. Hence, records need be maintained upto five years of the exhausting of stock.

1.1(M) Record *of Market Complaints* - Manufacturers shall maintain a register to record all reports of market complaints received regarding the products sold in the market. The manufacturer shall enter all data received on such market complaints, investigations carried out by the manufacturers regarding the complaint as well as any corrective action initiated to prevent recurrence of such market complaints shall also be recorded. Once in a period of six months the manufacturer shall submit the record of such complaints to the licensing authority. The Register shall also be available for inspection during any inspection of the premises.

Reports of any adverse reaction resulting from the use of Ayurvedic, Siddha and Unani drugs shall also be maintained in a separate register by each manufacturer. The manufacturer shall investigate any of the adverse reaction to find if the same is due to any defect in the product, and whether such reactions are already reported in the literature or it is a new observation.

1.1(N) *Quality Control*. - Every licensee is required to provide facility for quality control section in his own premises or through Government approved testing laboratory. The test shall be as per the Auurveda, Siddha and Unani pharmacopoeial standard. Where the tests are not available, the test should be performed according to the manufacturers‘ specification or other information available. The quality control section shall verify all the raw materials, monitor in-process quality checks and control the quality of finished product being released to finished goods store/warehouse. Preferably for such quality control there will be a separate expert. The quality control section shall have the following facilities:–

(1) There should be 150 sq. feet area for quality control section.

(2) For identification of raw drugs, reference books and reference samples should be maintained.

(3) Manufacturing record should be maintained for the various processes. (4) To verify the finished products, controlled samples of finished products of each batch will be kept till the expiry date of product for 3 years.

(5) To supervise and monitor adequacy of conditions under which raw materials, semi- finished products and finished products are stored.

(6) Keep record in establishing shelf life and storage requirements for the drugs.

(7) Manufacturers who are manufacturing patent and proprietary Ayurveda, Siddha, and Unani medicines shall provide their own specification and control references in respect of such formulated drugs.

(8) The record of specific method and procedure of preparation, that is, ―Bhavana‖, ―Mardana‖ and ―Puta‖ and the record of every process carried out by the manufacturer shall be maintained.

(9) The standards for identity, purity and strength as given in respective pharmacopoeias of Ayurveda, Siddha and Unani systems of medicines published by Government of India shall be complied with.

(10) All raw materials will be monitored for fungal, bacterial contamination with a view to minimize such contamination.

(11) Quality control section will have a minimum of: –

[1][(i) (a) Expert in Ayurveda or Sidha or Unani medicine who possesses a degree qualification recognized under Schedule II of Indian Medicine Central Council Act 1970;

(b) Chemist, who shall possess at least Bachelor Degree in Science or Pharmacy or Pharmacy (Ayurveda), awarded by a recognized University; and (c) Botanist (Pharmacognosist), who shall possess at least Bachelor Degree in Science (Medical) or Pharmacy or Pharmacy (Ayurveda) awarded by a recognized University.]

(ii) The manufacturing unit shall have a quality control section as explained under Section 35 (ii). Alternatively, these quality control provisions will be met by getting testing etc., from a recognised laboratory for Ayurveda, Siddha and Unani drugs; under Rule 160-A of the Drugs and Cosmetics Act. The manufacturing company will maintain all the record of various tests got done from outside recognised laboratory.

(iii) List of equipments recommended is indicated in Part II C.

1.2. Requirement for Sterile Product:

(A) *Manufacturing Areas*: – For the manufacture of sterile Ayurvedic, Unani and Siddha drugs, separate enclosed areas specifically designed for the purpose shall be provided. These areas shall be provided with air locks for entry and shall be essentially dust free and ventilated with an air supply. For all areas where aseptic manufacture has to be carried out, air supply shall be filtered through bacteria retaining filters (HEPA Filters) and shall be at a pressure higher than in the adjacent areas. The filters shall be checked for performance on installation and periodically thereafter the record of checks shall be maintained. All the surfaces in sterile manufacturing areas shall be designed to facilitate cleaning and disinfection. For sterile manufacturing routine microbial counts of all Ayurvedic, Siddha and Unani drug manufacturing areas shall be carried out during operations. Results of such count shall be checked against established in-house standards and record maintained.

1. Subs. by G.S.R. 463(E) dated 08-07-2005.

Access to manufacturing areas shall be restricted to minimum number of authorized personnel. Special procedure to be followed for entering and leaving the manufacturing areas shall be written down and displayed.

For the manufacturing of Ayurvedic, Siddha and Unani drug that can be sterilized in their final containers, the design of the areas shall preclude the possibility of the products intended for sterilization being mixed with or taken to be products already sterilized. In case of

terminally sterilized products, the design of the areas shall preclude the possibility of mix-up between non-sterile products.

(B) *Precautions against contamination and mix*:

(a) Carrying out manufacturing operations in a separate block of adequately isolated building or operating in an isolated enclosure within the building, (b) Using appropriate pressure differential in the process area.

(c) Providing a suitable exhaust system.

(d) Designing laminar flow sterile air system for sterile products.

(e) The germicidal efficiency of UV lamps shall be checked and recorded indicating the burning hours or checked using intensity.

(f) Individual containers of liquids and ophthalmic solutions shall be examined against black-white background fitted with diffused light after filling to ensure freedom from contamination with foreign suspended matter.

(g) Expert technical staff approved by the Licensing Authority shall check and compare actual yield against theoretical yield before final distribution of the batch.

All process controls as required under master formula including room temperature, relative humidity, volume filled, leakage and clarity shall be checked and recorded.

PART II

A. LIST OF RECOMMENDED MACHINERY, EQUIPMENT AND MINIMUM MANUFACTURING PREMISES REQUIRED FOR THE MANUFACTURE OF VARIOUS CATEGORIES OF AYURVEDIC, SIDDHA SYSTEM OF MEDICINES

One machine indicated for one category of medicine could be used for the manufacturing of other category of medicine also. Similarly some of the manufacturing areas like powdering, furnace, packing of liquids and Avaleha, Paks, could also be shared for these items.

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Sl.No.	Category of Medicine	Minimum manufacturing space required	Machinery/equipment recommended
(1)	(2)	(3)	(4)
		1200 Square feet covered area with separate cabins or partitions for each activity. If Unani medicines are manufactured in same premises an additional area of 400 sq. feet will be required.	
1.	Anjana/Pisti	100 sq. feet.	Karel/mechanized/motorized, karel. End runner/Ball-Mill Sieves/Shifter.
2.	Churna / Nasya/ Manjan/Lepa/ Kwath Churn	200 sq feet	Grinder/disintegrator/Pulveriser/ Powder mixer/sieves/shifter.
3.	Pills/Vati /Gutika	Matirai and tablets	

	100 sq. feet		Ball Mill, Mass mixer/powder mixer, Granulator, drier, tablet compressing machine, pill/vati cutting machine, stainless steel trays/container for storage and sugar coating, polishing pan in case of sugar-coated tablets,mechanised chattoo (for mixing guggulu) where required.
4.	Kupi pakava/Ksara/ Parpati/LavanaBhasma Satva/Sindura Karpu/ Uppu / Param	150 sq. feet	Bhatti, Karahi/Stainless steel Vessels/Patila Flask, Multani Matti/Plaster of Paris, Copper Rod, Earthern container, Gaj Put Bhatti, Mufflefurnace(Electrically operated) End/EdgeRunner, Exhaust Fan, Wooden/S.S.Spatula.
5.	Kajal	100 sq. feet	Earthern lamps for collection of Kajal, Triple Roller Mill, End Runner, Sieves, S.S.Patila, Filling/ packing and manufacturing room should be provided with exhaust fan and ultra violet lamps.
6.	Capsules	100 sq. feet	Air Conditioner, De-humidifier, hygrometer, thermometer, Capsule filling machine and chemical balance.
7.	Ointment/Marham Pasai	100sq. feet	Tube filling machine, Crimping Machine/Ointment Mixer, End Runner/ Mill (Where required) S.S. Storage Container S.S.Patila.

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Sl.No.	Category of Medicine	Minimum manufacturing space required	Machinery/equipment recommended (1)
(2)	(3)	(4)	
8.	Pak/Avaleh/Khand/ Modak/Lakayam	100 sq. feet	Bhatti section fitted with exhaust fan and should be fly proof, Iron Kadahi/S.S. Patila and S.S. Storage container.
9.	Panak, Syrup / Pravahi Kwath Manapaku	150 sq, feet	Tincture press, exhaust fan fitted and fly proof, Bhatti section, Bottle washing machine, filter press / Gravity filter, liquid filling machine P.P. Capping Machine
10.	Asava / Arishta	200 sq. ft	Same as mentioned above. Fermentation tanks, containers and distillation plant where necessary, Filter Press.
11.	Sura	100 sq. ft	Same as mentioned above plus Distillation plant and Transfer pump.
12.	Ark Tinir	100 sq. ft	Maceration tank, Distillation plant, Liquid filling tank with tap / Gravity filter/Filter press, Visual inspection box.
13.	Tail/Ghrit Ney	100 sq. ft	Bhatti, Kadahi/S.S. Patila S.S.Storage Containers, Filtration equipment, filling tank with

		tap/Liquid filling machine.
14. Aschyotan / Netra Malham Panir/Karn Bindu/Nasa-bindu	100 sq. ft	Hot air oven electrically heated with thermostatic control, kettle gas or electrically heated with suitable mixing arrangements, collation mill, or ointment mill, tube filling equipment, mixing and storage tanks of stainless steel or of other suitable material sintered glass funnel, seitz filter or filter candle, liquid filling equipment, autoclave.
15. Each manufacturing unit will have a separate area for Bhatti, furnace boilers, puta, etc. This will have proper ventilation, removal of smoke, prevention of flies, insets, dust etc. The furnace section could have tin roof.	200 sq. ft	

B. LIST OF MACHINERY, EQUIPMENT AND MINIMUM MANUFACTURING PREMISES REQUIRED FOR THE MANUFACTURE OF VARIOUS CATEGORIES OF UNANI SYSTEM OF MEDICINES

One machine indicated for one category of medicine could be used for the manufacturing of other category of medicine also. Similarly some of the manufacturing areas like powdering, furnace, packing of liquids could also be shared for these items.

Sl.No.	Category of Medicine required	Minimum manufacturing space	Machinery/equipment recommended
(1)	(2)	(3)	(4)
		1200 square feet covered area with separate cabins, partitions for each activity. If Ayurveda / Siddha medicines are also manufactured in same premises an additional area of 400 square feet will be required.	
1.	Itrifal Tirya/majoon/ Laooq/Jawarish Khamiras	100 sq. feet	Grinder/ Pulveriser, Sieves, powder mixer (if required), S.S. Patilas, Bhatti and other accessories, plant mixer for Khamiras.
2.	Arq.	100 sq. feet	Distillation Plant (garembic) S.S. storage tank, Boiling Vessel, Gravity filter, Bottle filling machine, Bottle washing machine, Bottle

			drier.
	3. Habb (Pills) and tablets.	100 sq. feet	Ball Mill, Mass Mixer/Powder mixer, Granulator drier, tablet compressing machine, pill/vati cutting machine, stainless steal trays/ container for storage and sugar coating, polishing pan in case of sugar-coated tablets, mechanized chattoo, (for mixing guggul) where required.
		Drugs and Cosmetics Rules 1945	
	4. Sufoof (Powder)	200 sq. feet	Grinder / pulveriser, Sieves, Trays, Scoops, Powder mixer (where required).
	5. Raughan (oils) (Crushing and boiling)	100 sq. feet	Oil Expeller, S.S. Patilas Oil filter bottle, Filling machine, Bottle drier, Bhatti.
	6. Shiyaf, Surma, Kajal	100 sq. feet	End runner, mixing S.S. Vessel..
7.	Marham, Zimad (Ointment)	100 sq. feet	Kharal, Bhatti, End runner, Grinder, Pulveriser, Triple Roller Mill (if required).
8.	Qurs (Tab.)	100 sq. feet	Grinder/Pulveriser, mixer (where needed), Granulator, Sieves, Powder Drier, Tablet Compressing Machine, Die punches Trays, O.T. Apparatus, Balance with weights, Scoops, Sugar Coating Pan, polishing pan, Heater.
9.	Kushta	100 sq. feet	Bhatti, Kharal, Sil Batta, Earthen pots.
10.	Murabba	100 sq. feet.	Aluminium Vessels 50-100kgs. Capacity, Gendna, Bhatti.
11.	Capsule	100 sq. feet	Pulveriser, Powder mixer (where needed), capsule filling machine, Air conditioner, De-humidifier, Balance with weights, storage containers, glass.
12.	Sharbat and Joshanda	100 sq. feet	Tinctum Press, exhaust fan fitted, Bhatti section, Bottle washing machine, Filter Press Gravity filter, Liquid filling tank with tap/liquid filling machine, hot air oven electrically heated with thermostatic control, kettle.
13.	Qutoor-e- Chashm and Marham(Eye drops, eye ointment)	100 sq. feet	Hot air oven electrically heated with thermostatic control, kettle
14.	Each manufacturing	200 sq. feet	

	unit will have a separate area for Bhatti, furnaces, boilers, putta,etc. This will have proper ventilation,removal of smoke, prevention of flies, insects, dust, etc.

C. LIST OF EQUIPMENT RECOMMENDED FOR IN-HOUSE QUALITY CONTROL SECTION

(Alternatively, unit can get testing done from the Government approved laboratory).

(A)	CHEMISTRY SECTION	(B)	PHARMACOGNOSY SECTION
1.	Alcohol Determination Apparatus (complete set)	1.	Microscope Binoculor.
2.	Volatile Oil Determination Apparatus.	2.	Dissecting Microscope.
3.	Boiling Point Determination Apparatus.	3.	Microtome.
4.	Melting Point Determination Apparatus.	4.	Physical Balance.
5.	Refractometer.	5.	Aluminium Slide Trays.
6.	Polarimeter.	6.	Stage Micrometer.
7.	Viscometer.	7.	Camera Lucida (Prism and Mirror Type).
8.	Tablet Disintegration Apparatus.	8.	Chemicals, Glassware etc.
9.	Moisture Meter.		
10.	Muffle Furnace.		
11.	Electronic Balance.		
12.	Magnetic Stirrer.		
13.	Hot Air Oven.		
14.	Refrigerator.		
15.	Glass/Steel Distillation Apparatus.		
16.	LPG Gas Cylinders with Burners.		
17	Water Bath (Temperature controlled.)		
18	Heating Mantles/ Hot Plates.		
19.	TLC Apparatus with all accessories (Manual)		
20	Paper Chromatography apparatus with accessories.		
21.	Sieve size 10 to120 with Sieve shaker.		
22			
23.			
24			
25.			

[1][D. SUPPLEMENTARY GUIDELINES FOR MANUFACTURING OF RASAUSHADHIES OR RASAMARUNTHUKAL AND KUSHTAJAT (HERBO-MINERAL-METALLIC COMPOUNDS) OF AYURVEDA, SIDDHA AND UNANI MEDICINES

These guidelines are intended to complement those provided above and should be read in conjunction with the parent guidelines. The supplementary guidelines are to provide general and minimum technical requirements for quality assurance and control in manufacturing Rasaushadhis or Rasamarunthukal and Kushtajat (Herbo-mineral-metallic

formulations). These supplementary guidelines deal with Bhasmas, Sindura, Pishti, Kajjali, Khalviya Ras, Kupipakwa, Rasayan, Parpati, Potali Rasa, Satwa (of Metals and Minerals origin) Druti Parpam, Karpu, and Kushta etc. used in Ayurvedic, Siddha and Unani Systems of medicine.

The supplementary GMP guidelines for Rasaushadhi or Rasamarunthukal and Kushtajat are needed to establish the authenticity of raw drug, minerals and metals, in-process validation and quality control parameters to ensure that these formulations are processed and prepared in accordance with classical texts and for which safety measures are complied. Only those manufacturing units which have Good Manufacturing Practices for ASU drugs and supplementary certificate for Rasaushadhi or Rasamarunthukal and Kushtajat formulations shall be allowed to manufacture th e same. Supplementary Good Manufactur ing Pr actices Certificate for Rasaushadhies shall be issued by the State Licensing Authority only after thorough inspection by an expert team including Rasashastra experts nominated by the Department of AYUSH.

2. Manufacturing Process Areas :-

For the manufacture of Bhasma and Kupipakawa and Rasaushadhi preparations made from metals and minerals the following specific areas shall be provided, which should be completely segregated from the production area used for preparation of plants and animal by product based formulation to avoid cross contamination. The following exclusive areas the required for Rasaushadhies or Rasamarunthukal and Kushtajat:-

2.2 (a) Bhatti or Heating Device Section for Bhasma and Rasaushadhies :- 100 sq. feet for heating, burning, putta and any heat related work with proper ventilation, exhaust and chimney. This could be tin shed also.

1. Ins. By G.S.R. 157(E), dated 04-03-2009

(b) Grinding, Drying and Processing Section for Bhasma and Rasaushadhies:- 100 Sq. feet (Manual or Mechanical, oven etc.). Drying [1][Shall be] done in a space which is covered by glass or other transparent material to allow entry of sunrays on the material to keep for the purpose. If drying is being done in oven the temperature of the same may be selected specific temperature.

(c) Rashaushadi Related Store :-100 Sq. feet.

The size and dimensions of each Bhatti Section would be so designed to suit the batch size or quantity of materials to be processed, keeping in mind the processing is done as per the conditions of Drug and Cosmetics Act mentioned under Schedule I official books.

In addition to the fuels prescribed in the schedule books namely coal, fire wood, cow dung cakes etc., use of other heating devices e.g. electrical heating, oil or gas fired furnaces and others Shall be] employed so as to provide the required temperature as per the nature of material and object of heating. Depending on the formulation being manufactured, manufacturers may adopt aerobic or anaerobic process. Properly baked and clean earthen pots of other crucibles and glass containers of appropriate design shall be used.

The manufacturing area should be designed with special attention to process the products that generate toxic fumes like SO2, arsenic and mercury vapor, etc. When heating and boiling of the materials is necessary, suitable ventilation and air exhaust flow mechanism should be provided to prevent accumulation of unintended fumes and vapors. Such areas may be provided with properly designed chimneys or ducts fitted with exhaust system and suitable scrubbing system to remove fumes and smoke, so that safety of personnel and environment is taken care of.

Since processing of Rasaushadhis may introduce heavy metal contamination and cross contamination etc., therefore, cleaning of equipment is particularly important after every process by using appropriate cleaning agent which should not react with material of equipment and must be free from unwanted properties e.g. corrosiveness.

2.3 Records shall be maintained specially for temperatures attained during the entire process of Bhasmikaran, while employing different kinds of classical puta, furnaces using oil, gas or electricity. Appropriate temperature measuring instrument should be employed such as pyrometer and, pyrograph for manual reading or recording by heat sensors, connected to computer as the case may be.

In order to handle large quantities, appropriate technology like use of hand operated extruders for making chakrikas or pellets may be adopeted. However, such equipments made of aluminium or its alloys should not be used.

1. Subs. by G.S.R.Subs. by G.S.R.338(E), dated 15-04-2010.

Access to manufacturing areas shall be restricted to minimum number of authorized personnel only.

3. Quality Control :-

A. Inprocess Quality Control :-

The registers as indicated below should exclusively be maintained for ready reference :-

(a) Shodhan Register with following details :-

1. Sl No.
2. Batch No. and Size
3. Date, time and duration
4. Name of the Raw-material with Quality reference and quantity
5. Quantity of Shodhana Dravya
6. Book Reference followed
7. Methodology

(b) Bhavana and Putta Register with following details :-

1. Sl No.
2. Batch No.
3. Date, time
4. Name of the material and quantity of starting materials
5. Quantity of Nirvapya Dravya
6. Quantity of Bhavana Dravya
7. Date and time of Starting and completion of Bhavana or Mardana and duration
8. Type and Number of Puttas
9. Time and Date of completion of Puttas
10. Color and texture of the product or standards
11. Inprocess tests followed (Bhasma Pariksha and any other tests)
12. In case heating at a particular temperature is required, record of attainment of that temperature.

(c) Grinding Record Register:- (Finished Product / Intermediate procedure)

1. Sl. No.
2. Batch No.
3. Date and time
4. Name of the material and quantity
5. Name of the equipment (SS/granite)
6. Duration of grinding
7. Repeat the grinding if required (Number of repetition)

(d) Packing details:-

1. Name of Rasaushadhi
2. Type of Dosage Form (eg. Powder, pill, tablet etc)
3. Weight of Rasaushadhi in each unit

B. Product Quality Control:-

The specifications for finished Rasaushadhi are primarily intended to define the quality rather than to establish full characterization, and should focus on those characteristics found to be useful in ensuring the quality. Consistent quality for Rasaushadhi can only be assured if the starting material-metals and minerals are used of pharmacopoeial standards. In some cases more detailed information may be needed on aspects of their process. The manufacturer will ensure in-house standards for the uniform quality of product.

Quality testing will be carried out as per official Pharmaceutica or Schedule books for texts namely, color, taste, varitaratwa, Rekhapurnatwa, Laghutva, Nirdhumatwa, Dntagre Kachakacha, Niruttha, Apunarbhava and Nischandratwa.

The Particle size of the product should be tested by adopting microscope fitted with micrometer or particle size analyzer or any appropriate other techniques. Required physio-chemical characterization of the product should be undertaken by appropriate analytical equipment. The Standard Manufacturing Process of the product should be evolved/follow up. The disintegration time of pills-vati and tablets should also be recorded.

4. Product recalls:- Literature inserted inside the product package should indicate the name, address of the manufacturing unit [1][and] telephone number for reporting of any adverse drug reaction by physicians or patients. On receipt of such Adverse Drug Reaction report, it will be the responsibility of the manufacturer to ensure the recall of the product from the market.

Standard Operating Procedures (SOP) should be included for storage of recalled Rasaushadhies in a secure segregated area, complying with the requirements specified for storage till their final disposal.

5. Medical examination of the Employees:- Employees engaged in manufacturing should be medially examined periodically at least once a year for any adverse effect of the drug during manufacturing process for which necessary investigations [1][Shall be] carried out for ensuring that there is no effect of material on the vital organs of the employees. Annual examination reports of the employees shall be made available to statutory inspectors during Good Manufacturing Practices inspections.

6. Self-Inspection:- The release of Rasaushadhis should be under the control of a person who has been trained in the specific features of the processing and quality assurance of Rasaushadhis. Personnel dealing with the production and quality assurance of Rasaushadhis manufacturing section should have an adequate training in the specific subject of Rasaushadhis manufacturing. He will be at least a degree holder in Ayurvedic, Siddha / Unani medicines or B.Pharma degree holder in Ayurvedic / Siddha / Unani medicines.

1. Subs. by G.S.R. 338(E) dated 15-04-2010.

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7. Dosage form of Rasaushadhis:- The Rasaushadhis may be made into an acceptable dosage forms such as churna, vati, guti, tablet or capsules etc. after adding suitable permissible fillers or binding agents as permissible under the Ayurvedic Pharmacopoeia of India or Indian pharmacopoeia as updated from time to time. In such cases the label must indicate the quantity of Ayurveda, Siddha and Unani medicines in one Tablet or Pill or Capsule in addition to the filler. The crystalline product may be grinded before packing in the individual dispensing size. All the Rasaushadhis or Rasamaruthukal or Kushtajat shall be packed in a dosage form which is ready for use for the consumer. Grinding and weighing of individual dose of potentially poisonous products will not be permissible in patient consumer pack. This arrangement may reduce the Adverse Drug Reaction of Rasaushadhi which takes place due to dose variation. However, for hospital bulk pack, it will not be applicable and label will clearly indicate the ―Hospital pack.‖

8. Area Specifications/ requirement for an applicant companies only to have GMP of Rasaushadhis or Rasamarunthukal and Kushtajat (Herbomineral/metallic compounds) of Ayurveda, Siddha and Unani medicines:-

1. Subs. by G.S.R. 338(E) dated 15-04-2010

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Sr. No.	Category of Medicine / Manufacturing area	Minimum Manufacturing space required (1500 sq. ft.)	Machinery equipme recommended
1.	Pisti / grinding area for Bhasma, Pishti, Kushtajat	100 sq. ft.	Kharal/mechanized/motorized Kharal, End runner / Ball-Mill Sieves / Sifter.
2.	Powdering area for raw drugs of plant origin giving in Rasaushadhis (Herbo-metalic formulations)	200 sq. ft.	Grinder / Distintegrator /Pulverisor / Powder mixer / Sieves / Sifter
3.	Pills / Vati/ Gutika Matrica and tablets / Habb making area	100 sq. ft.	Ball Mills, Mass Mixer/Powder mixer, Granulator, drier, tablet compressing machine, pill/ vati cutting machine, stainless steel trays / container for storage and sugar coating, polishing pan in case of sugar coated tablets, mechanized chatoo, (for mixing of guggulu) where required.
4.	Kupi pakva / Ksara / Parpati / Lavana Bhasma Satva / Sindura Kapu / Uppa / Param / Qushta / Jawhar	150 sq. ft.	Bhatti, Karahi / stainless steel vessels /patila flask, Multani Matti / Plaster of Paris, Copper Rod, Earthen container, Gaj Put Bhatti, Muffle furnace (electrically operated) End / Edge Runner, Exhaust Fan, Wooden, S.S. Spatula.
5.	Receiving and storing raw material	200 sq. ft.	
6.	Quality Control Section	150 sq. ft.	
7.	Quarantine / observation	50 sq. ft.	
8.	Finished goods store	150 sq. ft.	
9.	Rejected goods store	50 sq. ft.	
10.	Bhatti-putta area	200 sq. ft.	
11.	Area for water and washing etc.	50 sq. ft.	
12.	Office	100 sq. ft.	
	TOTAL	**1500 sq. ft**	

Note : The above requirements of machinery, equipments, space are made subject to the modification at the discretion of the Licensing Authority; if he is of the opinion that having regard to the nature and extent of the manufacturing operations it is necessary to relax or alter them in the circumstances in a particular case, 1[he may do so after recording reasons in writing]].

1. Added by G.S.R.463(E), dated 08-07-2005

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1[Schedule TA

(See rule 157 A)

FORM FOR RECORD OF UTILIZATION OF RAW MATERIAL BY AYURVEDA OR SIDDHA OR UNANI LICENSED MANUFACTURING UNITS DURING THE FINANCIAL YEAR

Identification Particulars:

Manufacturing License No .....
Issued
by.....

Name: .....

Address: .....

State: ..... Pin Code: .....

Telephone:..... Fax: .....

Email: .....

1. Quantity of Medicinal Plants/Extracts/Essential Oils/Metals/Animal By-Products Minerals Used During 1st April, to 31st March of the preceeding year (For Productions at the identified facility)

(a) Herbs Used

Common Name as in AFI/API*	Plant's Botanical Name	Quantity Used/per annum (in Kgs.)	Sources of Supply					Part Used			
			Traders/ Manufacturers	Forest Collectors	Cultivators	Imported	Total	Whole plans	Root	Leaf	Others

*Ayurvedic Formulary of India/Ayurvedic Pharmacopoeia of India

(b) Extracts Used

Name of Extracts		Quantity Used/per annum (in Kgs.)	Sources of Supply			
Common Name as in AFI/API*	Botanical Name		In-House	Export Suppliers	Imported	Total

* Ayurvedic Formulary of India/Ayurvedic Pharmacopoeia of India

(c) Metals/Minerals Used

Name of Mineral		Quantity Used/per annum (in Kgs.)	Sources of Supply		
Common Name	Chemical Name		Manufacturers Traders (Domestic)	Importers	Total

1. Ins. By G.S.R. 512 (E), dated 09-07-2008

(d) Animal By-Products Used

Name of By-Product		Quantity Used/per annum (in Kgs.)	Sources of Supply			
Common Name	Biological/Chemical Name (if any)		Manufacturers Traders (Domestic)		Importers	Total

2. Shortage of raw material(s)/inputs during the preceeding year.

Y

N

If yes, please indicate name(s) of such raw material(s) by level of importance starting from most important to least important, reason for shortage [availability, quality or any other (please specify)]

Name of Raw Materials		Appro. Qty of shortage (in Kgs.)	Reason
Name of the drug and part used as mentioned in official formulary / Pharmacopoeial/ Schedue I books	**Biological/ Chemical Name (if any)**		

[1][SCHEDULE U

(*See* rules 74, 74A, 74B, 78 and 78A)

I. PARTICULARS TO BE SHOWN IN MANUFACTURING RECORDS

A.SUBSTANCES, OTHER THAN PARENTERAL PREPARATIONS IN GENERAL.

1. Serial number
2. Name of the product
3. Reference of Master Formula Records.
4. Lot/Batch Size.
5. Lot/Batch Number.
6. Date of commencement of manufacture and date of completion of manufacture and assigned date of expiry.
7. Name of all ingredients, specifications quantities required for the lot/Batch size and quantities actually used. All weighings and measurements shall be carried out by a responsible person and initialled by him and shall be counter-checked and signed by the competent technical staff under whose personal supervision the ingredients are used for manufacture.
8. Control Numbers of raw materials used in the formulation.
9. Date, time and duration of mixing.
10. Details of environmental controls like room temperature, relative humidity.
11. Date of granulation, wherever applicable.
12. Theoretical weight and actual weight of granules/powder blend.
13. Records of in-processes controls (Periodically whenever necessary): (a) Uniformity of mixing.
    (b) Moisture content of granules/powder in case of Tablet/Capsules.
    (c) pH of solution in case of liquid.
    (d) Weight variation.
    (e) Disintegration time.

1. Subs. by G.S.R. 735(E) dated 24-06-1988

(h) Leak test in case of strip packing.

(i) Filled volume of liquids.

(j) Quantity of tablets/capsules in the final container.

(k) Content of ointment in the filled containers.

14. Date of compression in case of Tablets/date of filling in case of capsules.

15. Date of sealing/coating /polishing in case of capsules/tablets wherever applicable.

16. Reference to analytical Report number stating the result of test and analysis.

17. Separate records of the disposal of the rejected batches and of batches withdrawn from the market.

18.The theoretical yield and actual productions yield and packing particulars indicating the size and quantity of finished packings.

19. Specimen of label/strip, carton with batch coding information like Batch Number, date of manufacture, date of expiry, retail price as applicable stamped thereon and inserts used in the finished packings.

20. Signature with date of competent technical staff responsible for the manufacture.

21. Counter-signature of the head of the testing units or other approved person-in-charge of testing for having verified the batch records and for having released and batch for sale and distribution, the quantity released and date of release.

22. Date of release of finished packings and quantity released for sale and distribution.

23. Quantity transferred to warehouse.

24. For Hypodermic tablets and ophthalmic preparations, which are required to be manufactured under aseptic conditions, records shall be maintained indicating the precautions taken during the process of manufacture to ensure that aseptic conditions are maintained.

B. PARENTERAL PREPARATIONS.

1. Serial number.
2. Name of the product.
3. Reference of the master formula record.
4. Batch /Lot size.
5. Batch No. and/or Lot No.
6. Date of commencement of manufacture and date of completion.
7. Names of all ingredients, specifications and quantity required for the Lot/Batch size and quantity actually used. All weighings and measurements shall be carried out by a responsible person and initialled by him and shall be countersigned by the technical staff under whose personal supervision the stock are issued and by another competent technical staff under whose supervision the ingredients are used for manufacture.
8. Control numbers of raw materials used in the formulation.
9. Date, time and duration of mixing.
10. Details of environmental controls like temperature, humidity, microbial count in the sterile working areas.
11. pH of the solution, wherever applicable.
12. Date and method of filtration.
13. Sterility test, reference on bulk batch wherever applicable.
14. Record of check on volume filled.
15. Date of filling.
16. Records of tests employed: -

(a) To ensure that sealed ampoules are leak

proof (b) To check the presence of foreign particles.

(c) Pyrogen test, wherever applicable

(d) Toxicity test, wherever applicable.

17. Records of checking of instruments and apparatus of sterilization (indicators).

18. Records of cleaning and sterilization of containers and closures, if necessary.

19. Records of sterilization in case of parenteral preparations which are heat sterilized including particulars of time, temperature and pressure employed. Such records should be marked to relate to the batch sterilized.

20. Number and size of containers filled and quantity rejected.

21. The theoretical yield and actual yield and the percentage yield thereof.

22. Reference to Analytical report numbers stating whether of standard quality or otherwise.

23. Specimen of labels, cartons, etc. with Batch coding information like batch number, date of manufacture, date of expiry, as applicable, stamped thereon, and inserts used in the finished packings.

24. Signature with date of the component technical staff responsible for manufacture.

25. Particulars regarding the precautions taken during the manufacture to ensure that aseptic conditions are maintained.

26. Countersignature of head of the testing unit or person in charge of testing for having verified the documents and for having released the product for sale and distribution, the quantity released and date of release.

27. Records for having transferred to warehouse giving packings and quantities.

28. Separate records of the disposal of the rejected batches and of all batches withdrawn from the market.

29. Records of reprocessing if any and particulars of reprocessing.

II. RECORDS OF RAW MATERIALS

Records in respect of each raw material shall be maintained indicating the date of receipt, invoice number, name and address of the manufacturer/supplier, batch number, quantity received, pack size, date of manufacture, date of expiry, if any, date of analysis and release/rejection by quality control, analytical report number with special remarks, if any, quantity issued, date of issue and the particulars of the name and batch numbers of products for the manufacture of which issued and the proper disposal of the stocks.

III. PARTICULARS TO BE RECORDED IN THE ANALYTICAL RECORDS

A. TABLETS AND CAPSULES.

1. Analytical report number.
2. Name of the sample.
3. Date of receipt of sample.
4. Batch/Lot number.
5. Protocols of tests applied.

(a) Description.

(b) Identification.

(c) Uniformity of weight.

(d) Uniformity of diameter (if applicable).

(e) Disintegration test (time in minutes).

(f) Any other tests.

(g) Results of Assay.

Note: Records regarding various tests applied (including readings and calculations) should be

maintained and necessary reference to these records should be entered in Col. 5 above whenever necessary.

6. Signature of the Analyst.
7. Opinion and signature of the approved Analyst.

B.PARENTERAL PREPARATIONS.

1. Analytical report number.
2. Name of the sample.
3. Batch number.
4. Date of receipt of samples.
5. Number of containers filled.
6. Number of containers received.
7. Protocols of tests applied.

(a) Clarity.
(b) pH wherever applicable.
(c) Identification.
(d) Volume in container.
(e) Sterility –
(i) Bulk sample wherever applicable
(ii) container sample.
(f) Pyrogen test, wherever applicable.
(g) Toxicity test, wherever applicable.
(h) Any other tests.
(i) Results of Assay.

Note: Records regarding various tests applied (including readings and calculations) should be maintained and necessary reference to these records should be entered in Col. 7 above, wherever necessary.

8. Signature of the Analyst.
9. Opinion and signature of the approved Analyst.

PYROGEN TEST:

1. Test Report Number.
2. Name of the sample.
3. Batch Number.
4. Number of rabbits used.
5. Weight of each rabbit.
6. Normal temperature of each rabbit.
7. Mean initial temperature of each rabbit.
8. Dose and volume of solution injected into each rabbit and time of injection.
9. Temperature of each rabbit noted at suitable intervals.
10. Maximum temperature.
11. Response.
12. Summed response.
13. Signature of the Analyst.
14. Opinion and signature of the approved Analyst.

TOXICITY TEST

1. Test Report Number.
2. Name of the sample.

4. Number of mice used and weight of each mouse.
5. Strength and volume of the drugs injected.
6. Date of injection.
7. Results and remarks.
8. Signature of Analyst.
9. Opinion and signature of the approved Analyst.

C. FOR OTHER DRUGS

1. Analytical report number.
2. Name of the sample.
3. Batch/Lot number.
4. Date of receipt of sample.
5. Protocol of tests applied.
   (a) Description.
   (b) Identification.
   (c) Any other tests.
   (d) Results of Assay.

Note:Particulars regarding various tests applied (including readings and calculations) shall be maintained and necessary reference to these records shall be entered in Column 5 above, wherever necessary.

6. Signature of Analyst.
7. Opinion and signature of the approved Analyst.

D. RAW MATERIALS

1. Serial number.
2. Name of the materials.
3. Name of the manufacturer/supplier.
4. Quantity received.
5. Invoice/Challan number and date.
6. Protocols of tests applied.

Note: Particulars regarding various tests applied (including readings and calculations) shall be maintained and necessary reference to these records shall be entered in Column 6 above, wherever necessary.

E. CONTAINER, PACKING MATERIALS ETC.

1. Serial number.
2. Name of the item.
3. Name of the manufacturer/supplier.
4. Quantity received.
5. Invoice/Challan number and date
6. Results of tests applied.

Note: Particulars regarding various tests applied shall be maintained and necessary reference to these records shall be entered in Column 6 above, wherever necessary

7. Remarks.
8. Signature of the examiner.

Notes: 1. The foregoing provisions represent the minimum requirements to be complied with by the licensee. The Licensing Authority may, however, direct the nature of records to be maintained by the licensee for such products as are not covered by the categories described above.

2. The Licensing Authority may permit the licensee to maintain records in such manner as are considered satisfactory, provided the basic requirements laid down above are complied with.

3. The Licensing Authority may at its discretion direct the licensee to maintain records for such additional particulars as it may consider necessary in the circumstances of a particular case.]

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[1][SCHEDULE U(I)

(See rules 142 and 142B)

I. PARTICULARS TO BE SHOWN IN THE MANUFACTURING RECORDS:

1. Serial number.
2. Name of the product.
3. Lot/Batch size.
4. Lot/Batch number.
5. Date of commencement of manufacture and date when manufacture was completed. 6. Names of all ingredients, quantities required for the lot/batch size, quantities actually used.
7. Control reference numbers in respect of raw materials used in formulation.
8. Reference to analytical report numbers.
9. Actual production and packing particulars indicating the size and quantity of finished packings.
10. Date of release of finished packing for distribution or sale.
11. Signature of the expert staff responsible for the manufacture.

II. RECORDS OF RAW MATERIALS:

Records in respect of each raw material shall be maintained indicating the quantity received, control reference number, the quantity issued from time to time, the names and batch numbers of the products for the manufacture of which the said quantity of raw material has been issued and the particulars relating to the proper disposal of the stocks.

Notes: (1) The Licensing Authority may permit the licensee to maintain records in such manner as is considered satisfactory, provided the basic requirements laid down above are complied with.

(2) The Licensing Authority may direct the licensee to maintain records for such additional particulars, as it may consider necessary in the circumstances of a particular case.]

[2][SCHEDULE V

(See rule 124B)

STANDARDS FOR PATENT OR PROPRIETARY MEDICINES [3] [***]

[4][2. Standards for patent or proprietary medicines, containing vitamins: Patent or proprietary medicines containing vitamins for prophylactic, therapeutic or paediatric use shall contain the vitamins in quantities not less than and not more than those specified below in single or in two divided daily doses, namely: - [see table below].

[3] [***]

[5][**4.** *General Standards for Different Categories of Patent or Proprietary Medicines.* - In the case of pharmaceutical products containing several active ingredients, the selection shall be such that the ingredients do not interact with one another and do not affect the safety and therapeutic efficacy of the product. The combination shall not also lead to analytical difficulties for the purpose of assaying the content of such ingredient separately. The substances added as additives shall be innocuous, shall not affect the safety or therapeutic efficacy of the active ingredients, and shall not affect the assays and identity tests in the amount present.]

1. Added by G.S.R. 1594, dt. 28-10-1976.

2. Added by G.S.R. 665, dt. 06-05-1977.

3. Omitted. G.S.R. 56(E) ,dt. 22.1.1992.

4. Added by G.S.R. No. 930 ,dt. 13-7-1978.

5. Ins. by. G.S.R. 792(E) ,dt. 17.9.1987.

Subject to the provisions of these rules, patent or proprietary medicines shall comply with the following standards, namely: -

1. Patent or proprietary medicines shall comply with the general requirements of the dosage form under which it falls as given in the Indian Pharmacopoeia. If the dosage

form is not included in the Indian Pharmacopoeia, but is included in any other pharmacopoeia, prescribed for the purpose of the Second Schedule to the Act, it shall comply with the general requirements of the dosage of such pharmacopoeia. Without prejudice to the generality of the foregoing requirements, general requirements shall include compliance with colour consistency, clarity, stability, freedom from contamination with foreign matter or fungal growth, defects like chipping and capping of tablets, cracking of the coating, mottled appearance and other characteristic defects that can be perceived by visual inspection.

2. Without prejudice to the generality of the following paras, dosage forms of patent or proprietary medicines shall comply with the following requirements, namely:-

(a) Tablets: Medicines shall comply with requirements for tablets as laid down in the Indian Pharmacopoeia. The nature of coating shall be indicated on the label. Permitted colours may, however, be added and declared on the label. Nature of tablets, such as uncoated, sugar coated or film coated, shall be declared on the label.

[1][***]

(b) Capsules : Medicines shall comply with the requirements for capsules laid down in the Indian Pharmacopoeia. However, the capsules shall be free from distortion or shape, dis-colouration and other physical defects like leakage of powder from joints, pinholes or cracks in the capsules;

(c) Liquid oral dosage forms: Emulsions and suspensions shall disperse uniformly on shaking. Homogeneous solutions shall contain no sediments. The volume of the product (net content) in the container shall be not less than the labelled volume. The limit for ethanol content of pharmaceutical products shall be not less than 90 per cent and not more than 110 per cent of the labelled contents.

(d) Injections: Medicines shall comply with the requirements for injections as laid down in the Indian Pharmacopoeia.

(e) Ointments: Medicines shall comply with the requirements for injections as laid down in the Indian Pharmacopoeia.

3. The content of active ingredients, other than vitamins, enzymes and antibiotics, in patent or proprietary medicines shall be not less than 90 per cent and not more than 110 per cent of the labelled content; however, for enzymes and vitamins, only for lower limit of 90 per cent shall apply. In all dry formulations containing antibiotics, the limit shall be 90 to 130 per cent of the labelled contents and in case of liquid antibiotic formulations, the limit shall be 90 to 140 per cent of labelled contents.

Fiducial limits for error for microbiological assay of antibiotics may be estimated depending upon the design of assay procedure. Methods, used for assaying active ingredients shall employ the same basic principles and shall use same organisms as given in the latest edition of the Indian Pharmacopoeia or shall follow any other methods as approved by the authority competent to grant licence to manufacture.

1. Omitted. by G.S.R. 59(E) ,dt. 22.1.1992.

4. All patent or proprietary medicines containing aspirin shall be subjected to ―Free Salicylic Acid Test‖ and the limit of such acid shall be 0.75 per cent. Except in case of soluble type aspirin in which case the limit of such acid shall be 3 per cent.

5. Patent or proprietary medicine to be tested under the provisions of rule 121-A for pyrogen shall be tested by injecting into rabbits not less than the human dose of the medicine based on body weight of a 60 kg. human being. Methodology and limits shall be based on the method recorded in the Indian Pharmacopoeia. Dose selected shall be indicated in the protocol but the dose shall be not greater than 5 times the human dose based on body weight of 60 kg for man.

6. In injectable patent or proprietary medicines, the test for freedom from toxicity, shall be performed as described in the Indian Pharmacopoeia. Dose selected shall be indicated in the protocol but the dose shall not be less than five times the human dose based on body weight of 60 kg. human being.]

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Vitamin	Unit	Patent or proprietary Medicines containing for paediatric use. Vitamins for prophylactic Use.	Patent or proprietary medicines containing vitamins for therapeutic	Patent or proprietary vitamins
(in single dose or in two divided doses) per daily dose				
		For adults	**For infants less than one year.**	**For children above one year up to adults**
1	2	3	4	5 6
Vitamin A.	I.U	Not less than 1600 and not more than 2,500	Not less than 5000 and not more than 10,000	Not less than 750 and not more than 3,000
Vitamin D.	I.U	Not less than 100 and not more than 200.	Not less than 400 and not more than 1,000	Not less than 200 and not more than 400
Vitamin B1	mg.	Not less than 1 and not more than 2	Not less than 4.5 and not more than 10	Not less than 0.5 and not more than 1
Vitamin B2	mg	Not less than 1 and not more than 3	Not less than 5 and not more than 10	Not less than 0.5 and not more than 1.5
Vitamin B6	mg	Not less than 0.5 and not more than 1.5	Not less than 1.5 and not more than 3	Not less than 0.5 and not more than 1.5
Niacinamide	mg	Not less than 15 and not more than 26	Not less than 45 and not more than 100	Not less than 5 and not more than 15
d-Pantothenic acid or its salts and panthenol.	mg	Not less than 1 and not more than 5	Not less than 5 and not more than 50	Not less than 1 and not more than 3
Folic acid	mg.	Not less than 50 and not more than 300	Not less than 1000 and not more than 1500	Not less than 25 and not more than 100

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1	2	3	4	5 6
Vitamin B12	mcg	Not less than 0.5 and not more than 1	Not less than 5 and not more than 10	Not less than 1 and not more than 2

		than 1 than 15	than 3	than 5
Vitamin C and not	mg	Not less than 25 and not more than 50	Not less than 75 and not more Not less than 30 and not more than 150	Not less than 20 more than 40 than 80
Vitamin E and not	I.U	Not less than 5 and not more than 10	Not less than 15 and not more Not less than 5 and not more than 25	Not less than 2.5 more than 10 than 20.

Notes: (1) Patent or proprietary medicines containing vitamins intended for prophylactic, therapeutic or paediatric use shall bear on the label the words ―For Prophylactic Use‖ ― For Therapeutic Use,‖ or ―For Paediatric Use‖ as the case may be. In the case of paediatric preparations the age of the infant or the child for whose use it is intended, shall be given in addition to the particulars required to be given under these rules.

(2)The above standards shall not apply to any preparation containing a single vitamin only and also to any preparation containing vitamins intended for parenteral use.

Provided, however, that in the case of patent or proprietary medicines containing vitamins which are intended for the treatment of certain specific conditions or diseases, the Licensing Authority specified in clause (b) of rule 21, may permit the addition of vitamins therein in relaxation of the limits specified above, if satisfactory evidence is produced in justification of such relaxation.

1. Subs. by G.S.R. dated 22-12-2009

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[1][***]

[2]SCHEDULE X

[*See* Rules 23, 61, 75, 97 and 105A]

Amobarbital
Glutethimide
Pentobarbital
[3][Ketamine hydrochloride]
Amphetamine
Meprobamate
Phencyclidine
Barbital
Methamphetamine
Phenometrazine
Cyclobarbital
[4][***]
[5][***]
Dexamphetamine
Methylphenidate
Secobarbital
Ethclorvynol
Methylphenobarbital

Note*:* 1**.** Any stereoisometric form of the substance specified in this Schedule, any salt of the substance and preparation containing such substances are also covered by this Schedule.

2. Preparations containing the above substances are also covered by this Schedule.

Provided, however, preparations containing Meprobamate [5][***] in combination

with other drugs may be exempted by the Licensing Authority specified in clause (b) of rule 21, from the provisions of this Schedule, if satisfactory evidence is adduced that these preparations are not liable to be misused.]

1.Omitted by. G.S.R. 94(E) ,dt. 8.5. 2000
2 Ins. by G.S.R. 462(E) ,dt. 22.6.1982
3. Ins. by G.S.R. 724(E) ,dt. 07.11.2013
4. Omitted by G.S.R. 647(E) ,dt. 28.10.1998.
5.Omitted by. G.S.R. 673(E) ,dt. 27.10.1993.

[1][SCHEDULE Y

(See rules 122A, 122B, 122D, 122DA, 122DAA and 122E)

REQUIREMENTS AND GUIDELINES FOR PERMISSION TO IMPORT AND / OR MANUFACTURE OF NEW DRUGS FOR SALE OR TO UNDERTAKE CLINICAL TRIALS

1. Application for permission.- (1) Application for permission to import or manufacture new drugs for sale or to undertake clinical trials shall be made in Form 44 accompanied with following data in accordance with the appendices, namely:-

(i) chemical and pharmaceutical information as prescribed in item 2 of Appendix I; (ii) animal pharmacology data as prescribed in item 3 of Appendix I and Appendix IV; (a) specific pharmacological actions as prescribed in item 3.2 of Appendix I, and demonstrating, therapeutic potential for humans shall be described according to the animal models and species used. Wherever possible, dose-response relationships and ED_{50s} shall be submitted. Special studies conducted to elucidate mode of action shall also be described (Appendix IV);

(b) general pharmacological actions as prescribed in item 3.3 of Appendix I and item 1.2 of Appendix IV;

(c) pharmacokinetic data related to the absorption, distribution, metabolism and excretion of the test substance as prescribed in item 3.5 of Appendix I. Wherever possible, the drug effects shall be corelated to the plasma drug concentrations;

(iii) animal toxicology data as prescribed in item 4 of Appendix I and Appendix III; (iv) human Clinical Pharmacology Data as prescribed in items 5, 6 and 7 of Appendix I and as stated below:-

(a) for new drug substances discovered in India, clinical trials are required to be carried out in India right from Phase I and data should be submitted as required under items 1, 2, 3, 4, 5 (data, if any, from other countries), and 9 of Appendix I;

(b) for new drug substances discovered in countries other than India, Phase I data as required under items 1, 2, 3, 4, 5 (data from other countries) and 9 of Appendix I should be submitted along with the application. After submission of Phase I data generated outside India to the Licensing Authority, permission may be granted to repeat Phase I trials and/or to conduct Phase II trials and subsequently Phase III trials concurrently with other global trials for that drug. Phase III trials are required to be conducted in India before permission to market the drug in India is granted; (c) the data required will depend upon the purpose of the new drug application . The number of study subjects and sites to be involved in the conduct of clinical trial will depend upon the nature and objective of the study. Permission to carry out these trials shall generally be given in stages, considering the data emerging from earlier Phase(s);

(d) application for permission to initiate specific phase of clinical trial should also accompany Investigator‘s brochure, proposed protocol (Appendix X), case record form, study subject‘s informed consent document(s) (Appendix V), investigator‘s undertaking (Appendix VII) and ethics committee clearance, if available (Appendix VIII);

1. Subs. G.S.R. 32(E), dt. 20.1.2005.

(e) reports of clinical studies submitted under items 5-8 of Appendix I should be in consonance with the format prescribed in Appendix II of this Schedule. The study report shall be certified by the Principal Investigator or, if no Principal Investigator is designated, then by each of the Investigators participating in the study. The certification should acknowledge the contents of the report, the accurate presentation of the study as undertaken, and express agreement with the conclusions. Each page should be numbered;

(v) regulatory status in other countries as prescribed in item 9.2 of Appendix I, including Information in respect of restrictions imposed, if any, on the use of the drug in other countries, e.g. dosage limits, exclusion of certain age groups, warning about adverse drug reactions,.etc. (item 9.2 of Appendix I). Likewise, if the drug has been withdrawn in any country by the manufacturer or by regulatory authorities, such information should also be furnished along with the reasons and their relevance, if any, to India. This information must continue to be submitted by the sponsor to the Licensing Authority during the course of marketing of the drug in India; (vi) the full prescribing information should be submitted as part of the new drug application for marketing as prescribed in item 10 of Appendix I. The prescribing information (package insert) shall comprise the following sections: generic name; composition; dosage form/s, indications; dose and method of administration; use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.); contra-indications; warnings; precautions; drug interactions; undesirable effects; overdose; pharmacodynamic and pharmacokinetic properties; incompatibilities; shelf-life; packaging information; storage and handling instructions. All package inserts, promotional literature and patient education material subsequently produced are required to be consistent with the contents of the approved full prescribing information. The drafts of label and carton texts should comply with provisions of rules 96 and 97. After submission and approval by the Licensing Authority, no changes in the package insert shall be effected without such changes being approved by the Licensing Authority; and

(vii) complete testing protocol/s for quality control testing together with a complete impurity profile and release specifications for the product as prescribed in item 11 of Appendix I should be submitted as part of new drug application for marketing. Samples of the pure drug substance and finished product are to be submitted when desired by the regulatory authority.

(2) If the study drug is intended to be imported for the purposes of examination, test or analysis, the application for import of small quantities of drugs for such purpose should also be made in

Form 12.

(3) For drugs indicated in life threatening / serious diseases or diseases of special relevance to the Indian health scenario, the toxicological and clinical data requirements may be abbreviated, deferred or omitted, as deemed appropriate by the Licensing Authority.

2. Clinical Trial:

(1) *Approval for clinical trial*

(i) Clinical trial on a new drug shall be initiated only after the permission has been granted by the Licensing Authority under rule 21 (b), and the approval obtained from the respective ethics committee (s). The Licensing Authority as defined shall be informed of the approval of the respective institutional ethics committee(s) as prescribed in Appendix VIII, and the trial initiated at each respective site only after obtaining such an approval for that site. The trial site(s) may accept the approval granted to the protocol by the ethics committee of another trial site or the approval granted by an independent ethics committee (constituted as per Appendix VIII), provided that the approving ethics committee(s) is/are willing to accept their responsibilities for the study at such trial site(s) and the trial site(s) is/are willing to accept such an arrangement and that the protocol version is same at all trial sites.

(ii) All trial Investigator(s) should possess appropriate qualifications, training and experience and should have access to such investigational and treatment facilities as are relevant

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to the proposed trial protocol. A qualified physician (or dentist, when appropriate) who is an investigator or a sub-investigator for the trial, should be responsible for all trial-related medical (or dental) decisions. Laboratories used for generating data for clinical trials should be compliant with Good Laboratory Practices. If services of a laboratory or a facilities outside the country are to be availed, its/their name(s), address(s) and specific services to be used should be stated in the protocol to avail Licensing Authority‘s permission to send clinical trial related samples to such laboratory(ies) and/or facility(ies). In all cases, information about laboratory(ies) / facilities to be used for the trial, if other than those at the investigation site(s), should be furnished to the Licensing Authority prior to initiation of trial at such site(s).

(iii) Protocol amendments if become necessary before initiation or during the course of a clinical trial, all such amendments should be notified to the Licensing Authority in writing along with the approval by the ethics committee which has granted the approval for the study. No deviations from or changes to the protocol should be implemented without prior written approval of the ethics committee and the Licensing Authority except when it is necessary to eliminate immediate hazards to the trial Subject(s) or when change(s) involve(s) only logistic or administrative aspects of the trial. All such exceptions must be immediately notified to the ethics committee as well as to the Licensing Authority. Administrative and/or logistic changes in the protocol should be notified to the Licensing Authority within 30 days.

(2) *Responsibilities of Sponsor:*

(i) The clinical trial Sponsor is responsible for implementing and maintaining quality assurance systems to ensure that the clinical trial is conducted and data generated, documented and reported in compliance with the protocol and Good Clinical Practice (GCP) Guidelines issued by the Central Drugs Standard Control Organization, Directorate General of Health Services, Government of India as well as with all applicable statutory provisions. Standard operating procedures should be documented to ensure compliance with GCP and applicable regulations.

(ii) Sponsors are required to submit a status report on the clinical trial to the Licensing Authority at the prescribed periodicity.

(iii) In case of studies prematurely discontinued for any reason including lack of commercial interest in pursuing the new drug application, a summary report should be submitted within 3 months. The summary report should provide a brief description of the study, the number of patients exposed to the drug, dose and duration of exposure, details of adverse drug reactions (Appendix XI), if any, and the reason for discontinuation of the study or non-pursuit of the new drug application;

[1][(iv) Any report of the serious adverse event, after due analysis shall be forwarded by the sponsor to the Licensing Authority as referred to in clause (b) of rule 21, the Chairman of the Ethics Committee and the head of the institution where the trial has been conducted, within fourteen days of the occurrence of the serious adverse event.]

[2][(v) in case of injury or death occurring to the clinical trial subject, the Sponsor (whether a pharmaceutical company or an Institution) or his representative, whosoever, had obtained permission from the Licensing Authority for conduct of the clinical trial, shall make payment for medical management of the subject and also provide financial compensation for the clinical trial related injury or death in the manner as prescribed in Appendix XII;

[2][(vi) the Sponsor (whether a pharmaceutical company or an Institution) or his representative, whosoever had obtained permission from the Licensing Authority for conduct of the clinical trial, shall submit details of compensation provided or paid for clinical trial related injury or death, to the Licensing Authority within thirty days of the receipt of the order of the Licensing Authority.]

1. Subs. by G.S.R. 889(E) dated 12-12-2014

2. Ins. By G.S.R. 53(E) dated 30-1-2013

[1][(3)(i)] *Responsibilities of the Investigator(s)*:

The Investigator(s) shall be responsible for the conduct of the trial according to the protocol and the GCP Guidelines and also for compliance as per the undertaking given in Appendix VII. Standard operating procedures are required to be documented by the investigators for the tasks performed by them. During and following a subject's participation in a trial, the investigator should ensure that adequate medical care is provided to the participant for any adverse events. Investigator(s) shall report all serious and unexpected adverse events to the [2][Licensing Authority defined under clause (b) of rule 21, the Sponsor or his repeesentative, whosoever had obtained permission from the Licensing Authority for conduct of the clinical trial, and the Ethics Committee that accorded approval to the study protocol, within twenty four hours of their occurance. [3][In case, the Investigator fails to report any serious adverse event within the stipulated period, he shall have to furnish the reason for the delay to the satisfaction of the Licensing Authority along with the report of the serious adverse event. The report of the serious adverse event, after due analysis, shall be forwarded by the Investigator to the Licensing Authority as referred to in clause (b) of rule 21, the Chairman of the Ethics Committee and the Head of the institution where the trial has been conducted within fourteen days of the occurrence of the serious adverse event.]].

[4][(ii)The Investigator shall provide information to the clinical trial subject through informed consent process as provided in Appendix V about the essential elements of the clinical trial and the subject's right to claim compensation in case of trial related injury or death. He shall also inform the subject or his/her nominees(s) of their rights to contact the Sponsor or his representative whosoever had obtained permission from the Licensing Authority for conduct of the clinical trial for the purpose of making claims in the case of trial related injury or death.]

(4) *Informed Consent*:

(i) In all trials, a freely given, informed, written consent is required to be obtained from each study subject. The Investigator must provide information about the study verbally as well as using a patient information sheet, in a language that is non-technical and understandable by the study subject. The Subject's consent must be obtained in writing using an _Informed Consent Form'. Both the patient information sheet as well as the Informed Consent Form should have been approved by the ethics committee and furnished to the Licensing Authority. Any changes in the informed consent documents should be approved by the ethics committee and submitted to the Licensing Authority before such changes are implemented.

(ii) Where a subject is not able to give informed consent (e.g. an unconscious person or a minor or those suffering from severe mental illness or disability), the same may be obtained from a legally acceptable representative (a legally acceptable representative is a person who is able to give consent for or authorize an intervention in the patient as provided by the law(s) of India). If the Subject or his/her legally acceptable representative is unable to read/write – an impartial

witness should be present during the entire informed consent process who must append his/her signatures to the consent form.

(iii) A checklist of essential elements to be included in the study subject‘s informed consent document as well as a format for the Informed Consent Form for study Subjects is given in Appendix V.

1. Sub-para (3) renumbered as sub-para, (3)(i) thereof by G.S.R 53(E), dated 30-01-2013.

2. Subs. by G.S.R. 53(E), dated 30-01-2013.

3. Subs. by G.S.R. 889(E), dated 12-12-2014.

4. Ins. by G.S.R. 53(E), dated 30-01-2013.

(5) *Responsibilities of the Ethics Committee*:

(i) It is the responsibility of the ethics committee that reviews and accords its approval to a trial protocol to safeguard the rights, safety and well being of all trial subjects. The ethics committee should exercise particular care to protect the rights, safety and well being of all vulnerable subjects participating in the study, e.g., members of a group with hierarchical structure (e.g. prisoners, armed forces personnel, staff and students of medical, nursing and pharmacy academic institutions), patients with incurable diseases, umemployed or impoverished persons, patients in emergency situation, ethnic minority groups, homeless persons, nomads, refugees, minors or others incapable of personally giving consent. Ethics committee(s) should get document ‗standard operating procedures‘ and should maintain a record of its proceedings.

(ii) Ethics Committee(s) should make, at appropriate intervals, an ongoing review of the trials for which they review the protocol(s). Such a review may be based on the periodic study progress reports furnished by the investigators and/or monitoring and internal audit reports furnished by the Sponsor and/or by visiting the study sites.

(iii) In case an ethics committee revokes its approval accorded to a trial protocol, it must record the reasons for doing so and at once communicate such a decision to the Investigator as well as to the Licensing Authority.

[1][(iv) In case of serious adverse event occurring to the clinical trial subject, the Ethics Committee shall forward its report on the serious adverse event, after due analysis, along with its opinion on the financial compensation, if any, to be paid by the Sponsor or his representative, whosoever had obtained permission from the Licensing Authority as referred to in clause (b) of rule 21 for conducting the clinical trial, to the Licensing Authority within thirty days of the occurrence of the serious adverse event.

[2][5(A). *Serious Adverse Events*:

(1) A serious adverse event is an untoward medical occurrence during clinical trial that is associated with death, in patient hospitalization (in case the study was being conducted on out-patient), prolongation of hospitalization (in case the study was being conducted on in-patient), persistent or significant disability or incapacity, a congenital anomaly or birth defect or is otherwise life threatening.

(2) The Investigator shall report all serious [3][***] adverse events to the Licensing Authority as defined under clause (b) of Rule 21, the Sponsor or his representative, whosoever had obtained permission from the Licensing Authority for conduct of the clinical trial and the Ethics Committee that accorded approval to the study protocol, within twenty four hours of their occurrence as per Appendix XI and the said Licensing Authority shall determine the cause of injury or death as per the procedure prescribed under Appendix XII and pass orders as deemed necessary. [4][In case, the Investigator fails to report any serious adverse event within the stipulated period, he shall have to furnish the reason for the delay to the satisfaction of the Licensing Authority along with the report of the serious adverse event.

1. Subs. by G.S.R. 889(E) dated 12-12-2014.

2. Ins. by G.S.R. 53(E) dated 30-01-2013.

3. The words ―and unexpected‖ omitted by G.S.R. 889(E) dated 12-12-2014.

4. Ins. by G.S.R. 889 (E) dated 12-12-2014.

(6) *Human Pharmacology (Phase I)*:

(i) The objective of studies in this Phase is the estimation of safety and tolerability with the initial administration of an investigational new drug into human(s). Studies in this Phase of development usually have non-therapeutic objectives and may be conducted in healthy volunteers subjects or certain types of patients. Drugs with significant potential toxicity e.g. cytotoxic drugs are usually studied in patients**.** Phase I trials should preferably be carried out by Investigators trained in clinical pharmacology with access to the necessary facilities to closely observe and monitor the Subjects.

(ii) Studies conducted in Phase I, usually intended to involve one or a combination of the following objectives:-

(a) Maximum tolerated dose: To determine the tolerability of the dose range expected to be needed for later clinical studies and to determine the nature of adverse reactions that can be expected. These studies include both single and multiple dose administration.

(b) Pharmacokinetics, i.e., characterization of a drug's absorption, distribution, metabolism and excretion. Although these studies continue throughout the development plan, they should be performed to support formulation development and determine pharmacokinetic parameters in different age groups to support dosing recommendations.

(c) Pharmacodynamics:Depending on the drug and the endpoints studied, pharmacodynamic studies and studies relating to drug blood levels (pharmacokinetic/ pharmacodynamic studies) may be conducted in healthy volunteer Subjects or in patients with the target disease. If there are appropriate validated indicators of activity and potential efficacy, pharmacodynamic data obtained from patients may guide the dosage and dose regimen to be applied in later studies.

(d) Early Measurement of Drug Activity: Preliminary studies of activity or potential therapeutic benefit may be conducted in Phase I as a secondary objective. Such studies are generally performed in later Phases but may be appropriate when drug activity is readily measurable with a short duration of drug exposure in patients at this early stage.

(7) *Therapeutic exploratory trials (Phase II)*:

(i) The primary objective of Phase II trials is to evaluate the effectiveness of a drug for a particular indication or indications in patients with the condition under study and to determine the common short-term side-effects and risks associated with the drug. Studies in Phase II should be conducted in a group of patients who are selected by relatively narrow criteria leading to a relatively homogeneous population. These studies should be closely monitored. An important goal for this Phase is to determine the dose(s) and regimen for Phase III trials. Doses used in Phase II are usually (but not always) less than the highest doses used in Phase I.

(ii) Additional objectives of Phase II studies can include evaluation of potential study endpoints, therapeutic regimens (including concomitant medications) and target populations (e.g. mild versus severe disease) for further studies in Phase II or III. These objectives may be served by exploratory analyses, examining subsets of data and by including multiple endpoints in trials.

(iii) If the application is for conduct of clinical trials as a part of multi-national clinical development of the drug, the number of sites and the patients as well as the justification for undertaking such trials in India shall be provided to the Licensing Authority.

(8) *Therapeutic confirmatory trials (Phase III)*:

(i) Phase III studies have primary objective of demonstration or confirmation of therapeutic benefit(s). Studies in Phase III are designed to confirm the preliminary evidence accumulated in Phase II that a drug is safe and effective for use in the intended indication and recipient population. These studies should be intended to provide an adequate basis for marketing approval. Studies in Phase III may also further explore the dose-response relationships (relationships among dose, drug

concentration in blood and clinical response), use of the drug in wider populations, in different stages of disease, or the safety and efficacy of the drug in combination with other drug(s).

(ii) For drugs intended to be administered for long periods, trials involving extended exposure to the drug are ordinarily conducted in Phase III, although they may be initiated in Phase II. These studies carried out in Phase III complete the information needed to support adequate instructions for use of the drug (prescribing information).

(iii) For new drugs approved outside India, Phase III studies need to be carried out primarily to generate evidence of efficacy and safety of the drug in Indian patients when used as recommended in the prescribing information. Prior to conduct of Phase III studies in Indian subjects, Licensing Authority may require pharmacokinetic studies to be undertaken to verify that the data generated in Indian population is in conformity with the data already generated abroad.

(iv) If the application is for the conduct of clinical trials as a part of multi-national clinical development of the drug, the number of sites and patients as well as the justification for undertaking such trials in India should be provided to the Licensing Authority along with the application.

(9) *Post Marketing Trials (Phase IV)*:

Post Marketing trials are studies (other than routine surveillance) performed after drug approval and related to the approved indication(s). These trials go beyond the prior demonstration of the drug‘s safety, efficacy and dose definition. These trials may not be considered necessary at the time of new drug approval but may be required by the Licensing Authority for optimizing the drug's use. They may be of any type but should have valid scientific objectives. Phase IV trials include additional drug-drug interaction(s), dose-response or safety studies and trials designed to support use under the approved indication(s), e.g. mortality/morbidity studies, epidemiological studies etc.

3. Studies in special populations:

Information supporting the use of the drug in children, pregnant women, nursing women, elderly patients, patients with renal or other organ systems failure, and those on specific concomitant medication is required to be submitted if relevant to the clinical profile of the drug and its anticipated usage pattern. Any claim sought to be made for the drug product that is not based on data submitted under preceding items of this Schedule should be supported by studies included under this item of the Schedule (Appendix I, item 8.3).

(1) *Geriatrics*:

Geriatric patients should be included in Phase III clinical trials (and in Phase II trials, at the Sponsor's option) in meaningful numbers, if-

(a) the disease intended to be treated is characteristically a disease of aging; or

(b) the population to be treated is known to include substantial numbers of geriatric patients; or

(c) when there is specific reason to expect that conditions common in the elderly are likely to be encountered; or

(d) when the new drug is likely to alter the geriatric patient's response (with regard to safety or efficacy) compared with that of the non-geriatric patient.

(2) *Paediatrics*:

(i) The timing of paediatric studies in the new drug development program will depend on the medicinal product, the type of disease being treated, safety considerations, and the efficacy and safety of available treatments. For a drug expected to be used in children, evaluations should be made in the appropriate age group. When clinical development is to include studies in children, it is usually appropriate to begin with older children before extending the trial to younger children and then infants.

(ii) If the new drug is for diseases predominantly or exclusively affecting paediatric patients, clinical trial data should be generated in the paediatric population except for initial safety

and tolerability data, which will usually be obtained in adults unless such initial safety studies in adults would yield little useful information or expose them to inappropriate risk.

(iii) If the new drug is intended to treat serious or life-threatening diseases, occurring in both adults and paediatric patients, for which there are currently no or limited therapeutic options, paediatric population should be included in the clinical trials early, following assessment of initial safety data and reasonable evidence of potential benefit. In circumstances where this is not possible, lack of data should be justified in detail.

(iv) If the new drug has a potential for use in paediatric patients – Paediatric studies should be conducted. These studies may be initiated at various phases of clinical development or after post marketing surveillance in adults if a safety concern exists. In cases where there is limited paediatric data at the time of submission of application – more data in paediatric patients would be expected after marketing authorisation for use in children is granted.

(v) The paediatric studies should include –

(a) clinical trials,

(b) relative bioequivalence comparisons of the paediatric formulation with the adult formulation performed in adults, and

(c) definitive pharmacokinetic studies for dose selection across the age ranges of paediatric patients in whom the drug is likely to be used. These studies should be conducted in the paediatric patient population with the disease under study.

(vi) If the new drug is a major therapeutic advance for the paediatric population – the studies should begin early in the drug development , and this data should be submitted with the new drug application.

(vii) Paediatric Subjects are legally unable to provide written informed consent, and are dependent on their parent(s)/ legal guardian to assume responsibility for their participation in clinical studies. Written informed consent should be obtained from the parent/ legal guardian. However, all paediatric participants should be informed to the fullest extent possible about the study in a language and in terms that they are able to understand. Where appropriate, paediatric participants should additionally assent to enrol in the study. Mature minors and adolescents should personally sign and date a separately designed written assent form. Although a participant‘s wish to withdraw from a study must be respected, there may be circumstances in therapeutic studies for serious or life-threatening diseases in which, in the opinion of the Investigator and parent(s)/ legal guardian, the welfare of a pediatric patient would

be jeopardized by his or her failing to participate in the study. In this situation, continued parental/ legal guardian consent should be sufficient to allow participation in the study.

(viii) For clinical trials conducted in the paediatric population, the reviewing ethics committee should include members who are knowledgeable about pediatric, ethical, clinical and psychosocial issues.

(3) *Pregnant or nursing women*:

(i) Pregnant or nursing women should be included in clinical trials only when the drug is intended for use by pregnant/nursing women or foetuses/nursing infants and where the data generated from women who are not pregnant or nursing, is not suitable.

(ii) For new drugs intended for use during pregnancy, follow-up data (pertaining to a period appropriate for that drug) on the pregnancy, foetus and child will be required. Where applicable, excretion of the drug or its metabolites into human milk should be examined and the infant should be monitored for predicted pharmacological effects of the drug.

[1][(4) *Post Marketing Surveillance*:

(i) The applicant shall have a pharmacovigilance system in place for collecting, processing and forwarding the report to the licensing authority for information on adverse drug reactions emerging from the use of the drug manufactured or marketed by the applicant in the country.

(ia) The system shall be managed by qualified and trained personnel and the officer in-charge of collection and processing of data shall be a medical officer or a pharmacist trained in collection and analysis of adverse drug reaction reports.

(ib) Subsequent to approval of the product, new drug shall be closely monitored for its clinical safety once it is marketed.

(ic) The applicant shall furnish Periodic Safety Update Reports (PSURs) in order to- (a) report all the relevant new information from appropriate sources;
(b) relate these data to patient exposure ;
(c) summarize the market authorization status in different countries and any significant variations related to safety; and
(d) indicate whether changes should be made to product information in order to optimize the use of the product.

(ii) Ordinarily all dosage forms and formulations as well as indications for new drugs should be covered in one PSUR. Within the single PSUR separate presentations of data for different dosage forms, indications or separate population need to be given.

(iii) All relevant clinical and non-clinical safety data should cover only the period of the report (interval data). The PSURs shall be submitted every six months for the first two years after approval of the drug is granted to the applicant. For subsequent two years – the PSURs need to be submitted annually. Licensing authority may extend the total duration of submission of PSURs if it is considered necessary in the interest of public health. PSURs due for a period must be submitted within 30 calendar days of the last day of the reporting period.

However, all cases involving serious unexpected adverse reactions must be reported to the licensing authority within 15 days of initial receipt of the information by the applicant. If marketing of the new drug is delayed by the applicant after obtaining approval to market, such data will have to be provided on the deferred basis beginning from the time the new drug is marketed.

(iv) New studies specifically planned or conducted to examine a safety issue should be described in the PSURs.

1. Subs. by G.S.R. 287(E) dated 08-03-2016.

(v) A PSUR should be structured as follows:

(a) A title page stating: Periodic safety update report for the product, applicant‘s name, period covered by the report, date of approval of new drug, date of marketing of new drug and date of reporting;
(b) Introduction,
(c) Current worldwide market authorization status,
(d) Update of actions taken for safety reasons,
(e) Changes to reference safety information,
(f) Estimated patient exposure,
(g) Presentation of individual case histories,
(h) Studies,
(i) Other information,
(j) Overall safety evaluation,
(k) Conclusion,
(l) Appendix providing material relating to indications, dosing, pharmacology and other related information.

(5) *Special studies: Bioavailability / Bioequivalence Studies*:

(i) For drugs approved elsewhere in the world and absorbed systemically, bioequivalence with the reference formulation should be carried out wherever applicable. These studies should be conducted under the labelled conditions of administration. Data on the extent of systemic absorption may be required for formulations other than those designed for systemic absorption.

(ii) Evaluation of the effect of food on absorption following oral administration should be carried out. Data from dissolution studies should also be submitted for all solid oral dosage forms.

(iii) Dissolution and bioavailability data submitted with the new drug application must provide information that assures bioequivalence or establishes bioavailability and dosage correlations between the formulation(s) sought to be marketed and those used for clinical trials during clinical development of the product. (See items 8.1, 8.2 and 8.3 of Appendix I).

(iv) All bioavailability and bioequivalence studies should be conducted according to the Guidelines for Bioavailability and Bioequivalence studies as prescribed.

Note.- The data requirements stated in this Schedule are expected to provide adequate information to evaluate the efficacy, safety and therapeutic rationale of new drugs (as defined under rule 122-E) prior to the permission for sale. Depending upon the nature of new drugs and disease(s), additional information may be required by the Licensing Authority. The applicant shall certify the authencity of the data and documents submitted in support of an application for new drug. The Licensing Authority reserves the right to reject any data or any document(s) if such data or contents of such documents are found to be of doubtful integrity.

APPENDIX I

DATA TO BE SUBMITTED ALONG WITH THE APPLICATION TO CONDUCT CLINICAL TRIALS/IMPORT/MANUFACTURE OF NEW DRUGS FOR MARKETING IN THE COUNTRY

1. Introduction

A brief description of the drug and the therapeutic class to which it belongs.

2. Chemical and pharmaceutical information

2.1. Information on active ingredients

Drug information (Generic Name, Chemical Name or INN)

2.2. Physicochemical Data

(a) Chemical name and Structure

Empirical formula

Molecular weight

(b) Physical properties

Description

Solubility

Rotation

Partition coefficient

Dissociation constant

2.3. Analytical Data

Elemental analysis

Mass spectrum

NMR spectra

IR spectra

UV spectra

Polymorphic identification

2.4. Complete monograph specification including

Identification

Identity/quantification of impurities

Enantiomeric purity

Assay

2.5. Validations

Assay method

Impurity estimation method

Residual solvent/other volatile impurities (OVI) estimation method

2.6. Stability Studies (for details refer Appendix IX)

Final release specification

Reference standard characterization

Material safety data sheet

2.7. Data on Formulation

Dosage

form
Composition
Master manufacturing formula
Details of the formulation (including inactive ingredients)
In process quality control check
Finished product specification
Excipient compatibility study
Validation of the analytical method
Comparative evaluation with international brand(s) or approved Indian brands, if applicable
Pack presentation
Dissolution
Assay
Impurities

Content uniformity
pH
Force degradation study
Stability evaluation in market intended pack at proposed storage conditions
Packing specifications
Process validation

When the application is for clinical trials only, the international non-proprietary name (INN) or generic name, drug category, dosage form and data supporting stability in the intended container-closure system for the duration of the clinical trial (information covered in item nos. 2.1, 2.3, 2.6, 2.7) are required.

3. Animal Pharmacology (for details refer Appendix IV)

3.1. Summary
3.2. Specific pharmacological actions
3.3. General pharmacological actions
3.4. Follow-up and Supplemental Safety Pharmacology Studies
3.5. Pharmacokinetics: absorption, distribution; metabolism; excretion

4. Animal Toxicology (for details refer Appendix III)

4.1. General Aspects
4.2. Systemic Toxicity Studies
4.3. Male Fertility Study
4.4. Female Reproduction and Developmental Toxicity Studies
4.5. Local toxicity
4.6. Allergenicity/Hypersensitivity
4.7. Genotoxicity
4.8. Carcinogenicity

[1][**Note.-** Where the data on animal toxicity as per the specifications of Appendix III has been submitted and the same has been considered by the regulatory authority of the country which had earlier approved the drug, the animal toxicity studies shall not be required to be conducted in India except in cases where there are specific concerns recorded in writing.]

5. Human / Clinical pharmacology (Phase I)

5.1. Summary
5.2. Specific Pharmacological effects
5.3. General Pharmacological effects
5.4. Pharmacokinetics, absorption, distribution, metabolism, excretion
5.5. Pharmacodynamics / early measurement of drug activity

6. Therapeutic exploratory trials (Phase II)

6.1. Summary

6.2. Study report(s) as given in Appendix II

7. Therapeutic confirmatory trials (Phase III)

7.1. Summary

7.2. Individual study reports with listing of sites and Investigators.

8. Special studies

8.1. Summary

8.2. Bio-availability / Bio-equivalence.

8.3. Other studies e.g. geriatrics, paediatrics, pregnant or nursing women

1. Subs. by G.S.R. 313(E) dated 16-03-2016.

Regulatory status in other countries

9.1. Countries where the drug is

a. Marketed

b. Approved

c. Approved as IND

d. Withdrawn, if any, with reasons

9.2. Restrictions on use, if any, in countries where marketed /approved 9.3. Free sale certificate or certificate of analysis, as appropriate.

10. Prescribing information

10.1. Proposed full prescribing information

11. Samples and Testing Protocol/s

11.1. Samples of pure drug substance and finished product (an equivalent of 50 clinical doses, or more number of clinical doses if prescribed by the Licensing Authority), with testing protocol/s, full impurity profile and release specifications.

1[12. New Chemical Entity and Global Clinical Trial:

12.1 Assessment of risk versus benefit to the patients

12.2 Innovation vis-à-vis existing therapeutic option

12.3 Unmet medical need in the country.]

NOTES:

(1) All items may not be applicable to all drugs. For explanation, refer text of Schedule Y.

(2) For requirements of data to be submitted with application for clinical trials refer text of this Schedule.

APPENDIX IA

DATA REQUIRED TO BE SUBMITTED BY AN APPLICANT FOR GRANT OF PERMISSION TO IMPORT AND / OR MANUFACTURE A NEW DRUG ALREADY APPROVED IN THE COUNTRY

1. Introduction

A brief description of the drug and the therapeutic class

2. Chemical and pharmaceutical information

2.1. Chemical name, code name or number, if any; non-proprietary or generic name, if any, structure; physico-chemical properties

2.2. Dosage form and its composition

2.3. Test specifications

(a) active ingredients

(b) inactive ingredients

2.4 Tests for identification of the active ingredients and method of its assay

2.5 Outline of the method of manufacture of active ingredients

2.6 Stability data

1. Ins. by G.S.R. 826 (E), dt. 30-10-2015.

3. Marketing information

3.1 Proposed package insert / promotional literature

3.2 Draft specimen of the label and carton

4. Special studies conducted with approval of Licensing Authority

4.1 Bioavailability / Bioequivalence and comparative dissolution studies for oral dosage forms

4.2 Sub-acute animal toxicity studies for intravenous infusions and injectables.

[1][APPENDIX I B

DATA TO BE SUBMITTED ALONG WITH APPLICATION TO CONDUCT CLINICAL TRIAL OR IMPORT OR MANUFACTURE OF A PHYTOPHARMACEUTICAL DRUG IN THE COUNTRY

PART - I

1. Data to be submitted by the applicant:

1.1. A brief description or summary of the phytopharmaceutical drug giving the botanical name of the plant (including vernacular or scriptural name, wherever applicable), formulation and route of administration, dosages, therapeutic class for which it is indicated and the claims to be made for the phytopharmaceutical product.

1.2. Published literature including information on plant or product or phytopharmaceutical drug, as a traditional medicine or as an ethno medicine and provide reference to books and other documents, regarding composition, process prescribed, dose or method of usage, proportion of the active ingredients in such traditional preparations per dose or per day‘s consumption and uses.

1.3. Information on any contraindications, side effects mentioned in traditional medicine or ethno medicine literature or reports on current usage of the formulation.

1.4. Published scientific reports in respect of safety and pharmacological studies relevant for the phytopharmaceutical drug intended to be marketed,-

(a) where the process and usages are similar or same to the product known in traditional medicine or ethno medicine; and

(b) where process or usage is different from that known in traditional medicine or ethno medicine.

1.5. Information on any contraindications, side effects mentioned or reported in any of the studies, information on side effects and adverse reactions reported during current usage of the phytopharmaceutical in the last three years, wherever applicable.

1.6. Present usage of the phytopharmaceutical drug, – to establish history of usages, provide details of the product, manufacturer, quantum sold, extent of exposure on human population and number of years for which the product is being sold.

2. Human or clinical pharmacology information:

2.1. Published scientific reports in respect of pharmacological studies including human studies or clinical studies or epidemiological studies, relevant for the phytopharmaceutical drug intended to be marketed,-

(a) where the process and usages are similar or same to the product known in traditional medicine or ethno medicine; and

(b) where process or usage is different from that known in traditional medicine or ethno medicine.

2.2. Pharmacodynamic information (if available).

2.3. Monographs, if any, published on the plant or product or extract or phytopharmaceutical. (Copies of all publications, along with english translation to be attached.)

1. Ins. by G.S.R. 918 (E), dt. 30-11-2015.

PART – II

Data generated by applicant

3. Identification, authentication and source of plant used for extraction and fractionation: 3.1. Taxonomical identity of the plant used as a source of the phytopharmaceutical drug giving botanical name of genus, species and family, followed by the authority citation (taxonomist‘s name who named the species), the variety or the cultivar (if any) needs to be mentioned.

3.2 Morphological and anatomical description giving diagnostic features and a photograph of the plant or plant part for further confirmation of identity and authenticity. (Furnish certificate of confirmation of botanical identity by a qualified taxonomist).

3.3 Natural habitat and geographical distribution of the plant and also mention whether the part of the plant used is renewable or destructive and the source whether cultivated or wild.

3.4 Season or time of collection.

3.5 Source of the plant including its geographical location and season or time of collection.

3.6 A statement indicating whether the species is any of the following, namely:-
(a) determined to be endangered or threatened under the Endangered Species Act or the Convention on International Trade in Endangered species (CITES) of wild Fauna and Flora;
(b) entitled to special protection under the Biological Diversity Act, 2002 (18 of 2003); (c) any known genotypic, chemotypic and ecotypic variability of species.

3.7. A list of grower or supplier (including names and addresses) and information on the following items for each grower or supplier, if available or identified already, including information of primary processing, namely:-
(a) harvest location;
(b) growth conditions;
(c) stage of plant growth at harvest;
(d) harvesting time;
(e) collection, washing, drying and storage conditions;
(f) handling, garbling and transportation;
(g) grinding, pulverising of the plant material; and
(h) sieving for getting uniform particle size of powdered plant material.

3.8. Quality specifications, namely:-
(a) foreign matter;
(b) total ash;
(c) acid insoluble ash;
(d) pesticide residue;
(e) heavy metal contamination;
(f) microbial load;
(g) chromatographic finger print profile with phytochemical reference marker;
(h) assay for bio-active or phytochemical compounds; and
(i) chromatographic fingerprint of a sample as per test method given under quality control of the phytopharmaceutical drug (photo documentation).

3.9 . An undertaking to supply specimen sample of plant duly labeled and photocopy of the certificate of identity confirmation issued by a qualified taxonomist along with drawings or photographs of the

diagnostic morphological and histological features of the botanical raw material used for the confirmation of authenticity.

4. Process for extraction and subsequent fractionation and purification:

4.1. Quality specifications and test methods for starting material.

4.2. Steps involved in processing.

(a) details of solvent used, extractive values, solvent residue tests or limits, physico-chemical tests, microbial loads, heavy metal contaminants, chromatographic finger print profile with phytochemical reference markers, assay for active constituents or characteristic markers, if active constituents are not known;

(b) characterisation of final purified fraction;

(c) data on bio-active constituent of final purified fraction;

(d) information on any excipients or diluents or stabiliser or preservative used, if any.

4.3. Details of packaging of the purified and characterised final product, storage conditions and labeling.

5. Formulation of phytopharmaceutical drug applied for:

5.1. Details of the composition, proportion of the final purified fraction with defined markers of phytopharmaceutical drug per unit dose, name and proportions of all excipients, stabilisers and any other agent used and packaging materials.

5.2. Test for identification for the phytopharmaceutical drug.

5.3. Quality specifications for active and inactive phytopharmaceutical chromatographic finger print profile with phytochemical reference marker and assay of active constituent or characteristic chemical marker.

6. Manufacturing process of formulation:

6.1. The outline of the method of manufacture of the dosage form, along with environmental controls, in-process quality control tests and limits for acceptance.

6.2. Details of all packaging materials used, packing steps and description of the final packs.

6.3. Finished product‘s quality specifications, including tests specific for the dosage form, quality and chromatographic finger print profile with phytochemical reference marker and assay for active constituent or characteristic marker, if active constituents are not known.

7. Stability data:

7.1. Stability data of the phytopharmaceutical drug described at 4 above, stored at room temperature at 40 +/- 2 deg. C and humidity at 75%RH +/- 5%RH for 0, 1, 2, 3 and 6 months.

7.2 Stability data of the phytopharmaceutical drug in dosage form or formulation stored at room temperature at 40 +/- 2 deg. C and humidity at 75%RH +/- 5%RH for 0, 1, 2, 3 and 6 months, in the pack intended for marketing.

8. Safety and pharmacological information:

8.1. Data on safety and pharmacological studies to be provided.

8.2. Animal toxicity and safety data:

(a) 28 to 90 days repeat dose oral toxicity on two species of animals;

(b) In-vitro genotoxicity data (Ame‘s test and Chromosomal aberration test as per Schedule Y);

(c) dermal toxicity tests for topical use products;

(d) teratogenicity study (only if phytopharmaceutical drug is intended for use during pregnancy).

9. Human studies:

9.1. Clinical trials for phytopharmaceutical drugs to be conducted as per applicable rules and guidelines for new drugs.

9.2. For all phytopharmaceutical drugs data from phase I (to determine maximum tolerated dose and associated toxicities) and the protocols shall be submitted prior to performing the studies.

9.3. Data of results of dose finding studies performed and the protocols shall be submitted prior to performing the studies: Provided that in the case of phytopharmaceutical drug already marketed for more than five years or where there is adequate published evidence regarding the safety of the phytopharmaceutical drug, the studies may be abbreviated, modified or relaxed.

10. Confirmatory clinical trials:

10.1. Submit protocols for approval for any specific or special safety and efficacy study proposed specific to the phytopharmaceutical drug.

10.2. Submit proposed protocol for approval for human clinical studies appropriate to generate or validate safety and efficacy data for the phytopharmaceutical dosage form or product as per applicable rules and guidelines.

10.3. Submit information on how the quality of the formulation would be maintained during the above studies.

11. Regulatory status:

11.1. Status of the phytopharmaceutical drug marketed in any country under any category like functional food or dietary supplement or as traditional medicine or as an approved drug.

12. Marketing information:

12.1. Details of package insert or patient information sheet of the phytopharmaceutical drug to be marketed.

12.2. Draft of the text for label and carton.

13. Post marketing surveillance (PMS):

13.1. The applicant shall furnish periodic safety update reports every six months for the first two years after approval the drug is granted.

13.2. For subsequent two years the periodic safety update reports need to be submitted annually.

14. Any other relevant information:

Any other relevant information which the applicant considers that it will help in scientific evaluation of the application.]

APPENDIX II

STRUCTURE, CONTENTS AND FORMAT FOR CLINICAL STUDY REPORTS

1. Title Page:

This page should contain information about the title of the study, the protocol code, name of the investigational product tested, development Phase, indication studied, a brief description of the trial design, the start and end date of patient accrual and the names of the Sponsor and the participating Institutes (Investigators).

2. Study Synopsis (1 to 2 pages):

A brief overview of the study from the protocol development to the trial closure should be given here. This section will only summarize the important conclusions derived from the study.

3. Statement of compliance with the _Guidelines for Clinical Trials on Pharmaceutical Products in India :

GCP Guidelines' issued by the Central Drugs Standard Control Organization, Ministry of Health, Government of India.

4. List of Abbreviations and Definitions

5. Table of contents

6. Ethics Committee:

This section should document that the study was conducted in accordance with the ethical principles of Declaration of Helsinki. A detailed description of the Ethics Committee constitution and date(s) of approvals of trial documents for each of the participating sites should be provided. A declaration should state that EC notifications as per Good Clinical Practice Guidelines issued by Central Drugs Standard Control Organization and Ethical Guidelines for Biomedical Research on Human Subjects, issued by Indian Council of Medical Research have been followed.

7. Study Team:

Briefly describe the administrative structure of the study (Investigators, site staff, Sponsor/ designates, Central laboratory etc).

8. Introduction:

A brief description of the product development rationale should be given here.

9. Study Objective:

A statement describing the overall purpose of the study and the primary and secondary objectives to be achieved should be mentioned here.

10. Investigational Plan:

This section should describe the overall trial design, the Subject selection criteria, the treatment procedures, blinding / randomization techniques if any, allowed/ disallowed concomitant treatment, the efficacy and safety criteria assessed, the data quality assurance procedures and the statistical methods planned for the analysis of the data obtained.

11. Trial Subjects:

A clear accounting of all trial Subjects who entered the study will be given here. Mention should also be made of all cases that were dropouts or protocol deviations. Enumerate the patients screened, randomised, and prematurely discontinued. State reasons for premature discontinuation of therapy in each applicable case.

12. Efficacy evaluation

The results of evaluation of all the efficacy variables will be described in this section with appropriate tabular and graphical representation. A brief description of the demographic characteristics of the trial patients should also be provided along with a listing of patients and observations excluded from efficacy analysis.

13. Safety Evaluation:

This section should include the complete list

13.1 All serious adverse events, whether expected or unexpected and

13.2 unexpected advese events whether serious or not (compiled from data received as per Appendix XI).

The comparison of adverse events across study groups may be presented in a tabular or graphical form. This section should also give a brief narrative of all important events considered related to the investigational product.

14. Discussion and overall Conclusion:

Discussion of the important conclusions derived from the trial and scope for further development.

15. List of References:

16. Appendices:

List of Appendices to the Clinical Trial Report

(a) Protocol and amendments
(b) Specimen of Case Record Form
(c) Investigators‘ name(s) with contact addresses, phone, e-mail etc. (d) Patient data listings (e) List of trial participants treated with investigational product
(f) Discontinued participants
(g) Protocol deviations
(h) CRFs of cases involving death and life threatening adverse event cases
(i) Publications from the trial
(j) Important publications referenced in the study
(k) Audit certificate, if available
(l) Investigator‘s certificate that he/she has read the report and that the report accurately describes the conduct and the results of the study.

APPENDIX III

ANIMAL TOXICOLOGY (NON-CLINICAL TOXICITY STUDIES)

1. General Principles:

Toxicity studies should comply with the norms of Good Laboratory Practice (GLP). Briefly, these studies should be performed by suitably trained and qualified staff employing properly calibrated and standardized equipment of adequate size and capacity. Studies should be done as per written protocols with modifications (if any) verifiable retrospectively. Standard operating procedures (SOPs) should be followed for all managerial and laboratory tasks related to these studies. Test substances and test systems (in-vitro or in-vivo) should be properly characterized and standardized. All documents belonging to each study, including its approved protocol, raw data, draft report, final report, and histology slides and paraffin tissue blocks should be preserved for a minimum of 5 years after marketing of the drug.

Toxicokinetic studies (generation of pharmacokinetic data either as an integral component of the conduct of non-clinical toxicity studies or in specially designed studies) should be conducted to assess the systemic exposure achieved in animals and its relationship to dose level and the time course of the toxicity study. Other objectives of toxicokinetic studies include obtaining data to relate the exposure achieved in toxicity studies to toxicological findings and contribute to the assessment of the relevance of these findings to clinical safety, to support the choice of species and

treatment regimen in nonclinical toxicity studies and to provide information which, in conjunction with the toxicity findings, contributes to the design of subsequent non-clinical toxicity studies.

1.1 *Systemic Toxicity Studies*

1.1.1 Single-dose Toxicity Studies: These studies (see Appendix I item 4.2) should be carried out in 2 rodent species (mice and rats) using the same route as intended for humans. In addition, unless the intended route of administration in humans is only intravenous, at least one more

route should be used in one of the species to ensure systemic absorption of the drug. This route should depend on the nature of the drug. A limit of 2g/kg (or 10 times the normal dose that is intended in humans, whichever is higher) is recommended for oral dosing. Animals should be observed for 14 days after the drug administration, and minimum lethal dose (MLD) and maximum tolerated dose (MTD) should be established. If possible, the target organ of toxicity should also be determined. Mortality should be observed for up to 7 days after parenteral administration and up to 14 days after oral administration. Symptoms, signs and mode of death should be reported, with appropriate macroscopic and microscopic findings where necessary. LD10 and LD50 should be reported preferably with 95 percent confidence limits. If LD50s cannot be determined, reasons for the same should be stated.

The dose causing severe toxic manifestations or death should be defined in the case of cytotoxic anticancer agents, and the post-dosing observation period should be up to 14 days. Mice should first be used for determination of MTD. Findings should then be confirmed in rat for establishing linear relationship between toxicity and body surface area. In case of nonlinearity, data of the more sensitive species should be used to determine the Phase I starting dose. Where rodents are known to be poor predictors of human toxicity (e.g., antifolates), or where the cytotoxic drug acts by a novel mechanism of action, MTD should be established in non-rodent species.

1.1.2 Repeated-dose Systemic Toxicity Studies: These studies (see Appendix I, item 4.2) should be carried out in at least two mammalian species, of which one should be a non- rodent. Dose ranging studies should precede the 14-, 28-, 90- or 180- day toxicity studies. Duration of the final systematic toxicity study will depend on the duration, therapeutic indication and scale of the proposed clinical trial (see item 1.8). If a species is known to metabolize the drug in the same way as humans, it should be preferred for toxicity studies.

In repeated-dose toxicity studies the drug should be administered 7 days a week by the route intended for clinical use. The number of animals required for these studies, i.e. the minimum number of animals on which data should be available, is shown in Item 1.9.

Wherever applicable, a control group of animals given the vehicle alone should be included, and three other groups should be given graded doses of the drug. The highest dose should produce observable toxicity; the lowest dose should not cause observable toxicity, but should be comparable to the intended therapeutic dose in humans or a multiple of it . To make allowance for the sensitivity of the species the intermediate dose should cause some symptoms, but not gross toxicity or death, and should be placed logarithmically between the other two doses.

The parameters to be monitored and recorded in long-term toxicity studies should include behavioral, physiological, biochemical and microscopic observations. In case of parenteral drug administration, the sites of injection should be subjected to gross and microscopic examination. Initial and final electrocardiogram and fundus examination should be carried out in the non-rodent species.

In the case of cytotoxic anticancer agents dosing and study design should be in accordance with the proposed clinical schedule in terms of days of exposure and number of cycles. Two rodent species may be tested for initiating Phase I trials. A non-rodent species should be added if the drug has a novel mechanism of action, or if permission for Phase II, III or marketing is being sought.

Drugs and Cosmetics Rules 1945

For most compounds, it is expected that single dose tissue distribution studies with sufficient sensitivity and specificity will provide an adequate assessment of tissue distribution and the potential for accumulation. Thus, repeated dose tissue distribution studies should not be required uniformly for all compounds and should only be conducted when appropriate data cannot be derived from other sources. Repeated dose studies may be appropriate under certain circumstances based on the data from single dose tissue distribution studies, toxicity and toxicokinetic studies. The studies may be most appropriate for compounds which have an apparently long half life, incomplete elimination or unanticipated organ toxicity.

Notes:

(i) *Single Dose Toxicity Study*: Each group should contain at least 5 animals of either sex. At least four graded doses should be given. Animals should be exposed to the test substance in a single bolus or by continuous infusion or several doses within 24 hours. Animals should be observed for 14 days. Signs of intoxication, effect on body weight, gross pathological changes should be reported. It is desirable to include histo-pathology of grossly affected organs, if any.

(ii) *Dose-ranging Study*: Objectives of this study include the identification of target organ of toxicity and establishment of MTD for subsequent studies.

(a) *Rodents:* Study should be performed in one rodent species (preferably rat) by the proposed clinical route of administration. At least four graded doses including control should be given, and each dose group as well as the vehicle control should consist of a minimum of 5 animals of each sex. Animals should be exposed to the test substance daily for 10 consecutive days. Highest dose should be the maximum tolerated dose of single-dose study. Animals should be observed daily for signs of intoxication (general appearance, activity and behaviour etc), and periodically for the body weight and laboratory parameters. Gross examination of viscera and microscopic examination of affected organs should be done.

(b) *Non-rodents*: One male and one female are to be taken for ascending Phase MTD study.

Dosing should start after initial recording of cage-side and laboratory parameters.

Starting dose may be 3 to 5 times the extrapolated effective dose or MTD (whichever is less), and dose escalation in suitable steps should be done every third day after drawing the samples for laboratory parameters. Dose should be lowered appropriately when clinical or laboratory evidence of toxicity are observed. Administration of test substance should then

continue for 10 days at the well-tolerated dose level following which, samples for laboratory parameters should be taken. Sacrifice, autopsy and microscopic examination of affected tissues should be performed as in the case of rodents.

(iii) 14-28 Day repeated-dose toxicity studies: One rodent (6-10/sex/group) and one non-rodent (2-3/sex/group) species are needed. Daily dosing by proposed clinical route at three dose levels should be done with highest dose having observable toxicity, mid- dose between high and low dose, and low dose. The doses should preferably be multiples of the effective dose and free from toxicity. Observation parameters should include cage- side observations, body weight changes, food/water intake, blood biochemistry, haematology, and gross and microscopic studies of all viscera and tissues.

(iv) 90-Day repeated-dose toxicity studies: One rodent (15-30/sex/group) and one non- rodent (4-6/sex/group) species are needed. Daily dosing by proposed clinical route at three graded dose levels should be done. In addition to the control a ―high-dose-reversal‖ 604

group and its control group should be also included. Parameters should include signs of intoxication (general appearance, activity and behaviour etc), body weight, food intake, blood biochemical parameters, haematological values, urine analysis, organ weights, gross and microscopic study of viscera and tissues. Half the animals in ―reversal‖ groups (treated and control) should be sacrificed after 14 days of stopping the treatment. The remaining animals should be sacrificed after 28 days of stopping the treatment or after the recovery of signs and/or clinical pathological changes – whichever comes later, and evaluated for the parameters used for the main study.

(v) 180-Day repeated-dose toxicity studies: One rodent (15-30/sex/group) and one non-rodent (4-6/sex/group) species are needed. At least 4 groups, including control, should be taken. Daily dosing by proposed clinical route at three graded dose levels should be done. Parameters should include signs of intoxication, body weight, food intake, blood biochemistry, hematology, urine analysis, organ weights, gross and microscopic examination of organs and tissues.

1.2 *Male Fertility Study*

One rodent species (preferably rat) should be used. Dose selection should be done from the results of the previous 14 or 28-day toxicity study in rat. Three dose groups, the highest one showing minimal toxicity in systemic studies, and a control group should be taken. Each group should consist of 6 adult male animals. Animals should be treated with the test substance by the intended route of clinical use for minimum 28 days and maximum 70 days before they are paired with female animals of proven fertility in a ratio of 1:2 for mating. Drug treatment of the male animals should continue during pairing. Pairing should be continued till the detection of vaginal plug or 10 days, whichever is earlier. Females getting thus pregnant should be examined for their fertility index after day 13 of gestation. All the male animals should be sacrificed at the end of the study. Weights of each testis and epididymis should be separately recorded. Sperms from one epididymis should be examined for their motility and morphology. The other epididymis and both testes should be examined for their histology.

1.3 Female Reproduction and Developmental Toxicity Studies

These studies (see Appendix I, item 4.4) need to be carried out for all drugs proposed to be studied or used in women of child bearing age. Segment I, II and III studies (see below) are to be performed in albino mice or rats, and segment II study should include albino rabbits also as a second test species.

On the occasion, when the test article is not compatible with the rabbit (e.g. antibiotics which are effective against gram positive, anaerobic organisms and protozoas) the Segment II data in the mouse may be substituted.

1.3.1 *Female Fertility Study (Segment I):* The study should be done in one rodent species (rat preferred). The drug should be administered to both males and females, beginning a sufficient

number of days (28 days in males and 14 days in females) before mating. Drug treatment should continue during mating and, subsequently, during the gestation period.

Three graded doses should be used, the highest dose (usually the MTD obtained from previous systemic toxicity studies) should not affect general health of the parent animals. At least 15 males and 15 females should be used per dose group. Control and the treated groups should be of similar size. The route of administration should be the same as intended for therapeutic use

Dams should be allowed to litter and their medication should be continued till the weaning of pups. Observations on body weight, food intake, clinical signs of intoxication, mating behaviour, progress of gestation/ parturition periods, length of gestation, parturition, post-partum health and gross pathology (and histopathology of affected organs) of dams should be recorded. The pups from both treated and control groups should be observed for general signs of intoxication, sex-wise distribution in different treatment groups, body weight, growth parameters, survival, gross examination, and autopsy. Histopathology of affected organs should be done.

1.3.2 *Teratogenicity Study (Segment II):*

One rodent (preferably rat) and one non-rodent (rabbit) species are to be used. The drug should be administered throughout the period of organogenesis, using three dose levels as described for segment I. The highest dose should cause minimum maternal toxicity and the lowest one should be proportional to the proposed dose for clinical use in humans or a multiple of it. The route of administration should be the same as intended for human therapeutic use.

The control and the treated groups should consist of at least 20 pregnant rats (or mice) and 12 rabbits, on each dose level. All foetuses should be subjected to gross examination, one of the foetuses should be examined for skeletal abnormalities and the other half for visceral abnormalities. Observation parameters should include: (Dams) signs of intoxication, effect on body weight, effect on food intake, examination of uterus, ovaries and uterine contents, number of corpora lutea, implantation sites, resorptions (if any); and for the foetuses, the total number, gender, body length, weight and gross/ visceral/ skeletal abnormalities, if any.

1.3.3 *Perinatal Study (Segment III):*

This study is specially recommended if the drug is to be given to pregnant or nursing mothers for long periods or where there are indications of possible adverse effects on foetal development. One rodent species (preferably rat) is needed. Dosing at levels comparable to multiples of human dose should be done by the intended clinical route. At least 4 groups (including control), each consisting of 15 dams should be used. The drug should be administered throughout the last trimester of pregnancy (from day 15 of gestation) and then the dose that causes low foetal loss should be continued throughout lactation and weaning. Dams should then be sacrificed and examined as described below.

One male and one female from each litter of F_1 generation (total 15 males and 15 females in each group) should be selected at weaning and treated with vehicle or test substance (at the dose levels described above) throughout their periods of growth to sexual maturity, pairing, gestation, parturition and lactation. Mating performance and fertility of F_1 generation should thus be evaluated to obtain the F_2 generation whose growth parameters should be monitored till weaning. The criteria of evaluation should be the same as described earlier (3.4.1).

Animals should be sacrificed at the end of the study and the observation parameters should include (Dams) body weight, food intake, general signs of intoxication, progress of gestation/ parturition periods and gross pathology (if any); and for pups, the clinical signs,

sex-wise distribution in dose groups, body weight, growth parameters, gross examination, survival and autopsy (if needed) and where necessary, histopathology.

1.4 *Local toxicity*

These studies (see Appendix I, item 4.5) are required when the new drug is proposed to be used

by some special route (other than oral) in humans. The drug should be applied to an appropriate site (e.g., skin or vaginal mucous membrane) to determine local effects in a suitable species. Typical study designs for these studies should include three dose levels and untreated and/ or vehicle control, preferably use of 2 species, and increasing group size with increase in duration of treatment. Where dosing is restricted due to anatomical or humane reasons, or the drug concentration cannot be increased beyond a certain level due to the problems of solubility, pH or tonicity, a clear statement to this effect should be given. If the drug is absorbed from the site of application, appropriate systemic toxicity studies will also be required.

Notes:

(i) Dermal toxicity study: The study should be done in rabbit and rat. Daily topical (dermal) application of test substance in its clinical dosage form should be done. Test material should be applied on shaved skin covering not less than 10% of the total body surface area. Porous gauze dressing should be used to hold liquid material in place. Formulations with different concentrations (at least 3) of test substance, several fold higher than the clinical dosage form should be used. Period of application may vary from 7 to 90 days depending on the clinical duration of use. Where skin irritation is grossly visible in the initial studies, a recovery group should be included in the subsequent repeated-dose study. Local signs (erythema, oedema and eschar formation) as well as histological examination of sites of application should be used for evaluation of results.

(ii) Photo-allergy or dermal photo-toxicity: It should be tested by Armstrong/ Harber Test in guinea pig. This test should be done if the drug or a metabolite is related to an agent causing photosensitivity or the nature of action suggests such a potential (e.g., drugs to be used in treatment of leucoderma). Pretest in 8 animals should screen 4 concentrations (patch application for 2 hours ±15 min.) with and without UV exposure (10 J/cm2). Observations recorded at 24 and 48 hours should be used to ascertain highest nonirritant dose. Main test should be performed with 10 test animals and 5 controls. Induction with the dose selected from pretest should use 0.3 ml/patch for 2 hour ±15 min. followed by 10 J/cm2 of UV exposure. This should be repeated on day 0, 2,4,7,9 and 11 of the test. Animals should be challenged with the same concentration of test substance between day 20 to 24 of the test with a similar 2-hour application followed by exposure to 10 J/cm2 of UV light. Examination and grading of erythema and oedema formation at the challenge sites should be done 24 and 48 hours after the challenge. A positive control like musk ambrett or psoralin should be used.

(iii) Vaginal Toxicity Test: Study is to be done in rabbit or dog. Test substance should be applied topically (vaginal mucosa) in the form of pessary, cream or ointment. Six to ten animals per dose group should be taken. Higher concentrations or several daily applications of test substance should be done to achieve multiples of daily human dose. The minimum duration of drug treatment is 7 days (more according to clinical use), subject to a maximum of 30 days. Observation parameters should include swelling, closure of introitus and histopathology of vaginal wall.

(iv) Rectal Tolerance Test: For all preparations meant for rectal administration this test may be performed in rabbits or dogs. Six to ten animals per dose group should be taken. Formulation in volume comparable to human dose (or the maximum possible volume) should be applied once or several times daily, per rectally, to achieve administration of multiples of daily human dose. The minimum duration of application is 7 days (more according to clinical use), subject to a maximum of 30 days. Size of suppositories may be smaller, but the drug content should be several fold higher than the proposed human dose. Observation parameters should include clinical signs (sliding on backside), signs of pain, blood and/or mucus in faeces, condition of anal region/sphincter, gross and (if required) histological examination of rectal mucosa.

(v) Parenteral Drugs: For products meant for intravenous or intramuscular or subcutaneous or intradermal injection the sites of injection in systemic toxicity studies should be specially

examined grossly and microscopically. If needed, reversibility of adverse effects may be determined on a case to case basis.

(vi) Ocular toxicity studies (for products meant for ocular instillation): These studies should be carried out in two species, one of which should be the albino rabbit which has a sufficiently large conjunctival sac. Direct delivery of drug onto the cornea in case of animals having small conjunctival sacs should be ensured. Liquids, ointments, gels or soft contact lenses (saturated with drug) should be used. Initial single dose application should be done to decide the exposure concentrations for repeated-dose studies and the need to include a recovery group. Duration of the final study will depend on the proposed length of human exposure subject to a maximum of 90 days. At least two different concentrations exceeding the human dose should be used for demonstrating the margin of safety. In acute studies, one eye should be used for drug administration and the other kept as control. A separate control group should be included in repeated-dose studies.

Slit-lamp examination should be done to detect the changes in cornea, iris and aqueous humor. Fluorescent dyes (sodium fluorescein, 0.25 to 1.0%) should be used for detecting the defects in surface epithelium of cornea and conjunctiva. Changes in intra-ocular tension should be monitored by a tonometer. Histological examination of eyes should be done at the end of the study after fixation in Davidson‘s or Zenker‘s fluid.

(vii) Inhalation toxicity studies: The studies are to be undertaken in one rodent and one non-rodent species using the formulation that is to be eventually proposed to be marketed. Acute, subacute and chronic toxicity studies should be performed according to the intended duration of human exposure. Standard systemic toxicity study designs (described above) should be used. Gases and vapours should be given in whole body exposure chambers; aerosols are to be given by nose-only method. Exposure time and concentrations of test substance (limit dose of 5mg/l) should be adjusted to ensure exposure at levels comparable to multiples of intended human exposure. Three dose groups and a control (plus vehicle control, if needed) are required. Duration of exposure may vary subject to a maximum of 6 hours per day and five days a week. Food and water should be withdrawn during the period of exposure to test substance.

Temperature, humidity and flow rate of exposure chamber should be recorded and reported. Evidence of exposure with test substance of particle size of 4 micron (especially for aerosols) with not less that 25% being 1 micron should be provided. Effects on respiratory rate, findings of bronchial lavage fluid examination, histological examination of

respiratory passages and lung tissue should be included along with the regular parameters of systemic toxicity studies or assessment of margin of safety.

1.5 *Allergenicity/ Hypersensitivity*:

Standard tests include guinea pig maximization test (GPMT) and local lymph node assay (LLNA) in mouse. Any one of the two may be done.

Notes:

(i) *Guinea Pig Maximization Test*: The test is to be performed in two steps; first, determination of maximum nonirritant and minimum irritant doses, and second, the main test. The initial study will also have two components. To determine the intradermal induction dose, 4 dose levels should be tested by the same route in a batch of 4 male and 4 female animals (2 of each sex should be given Freund‘s adjuvant). The minimum irritant dose should be used for induction. Similarly, a topical minimum irritant dose should be determined for challenge. This should be established in 2 males and 2 females. A minimum of 6 male and 6 female animals per group should be used in the main study. One test and one control group should be used. It is preferable to have one more positive control group. Intradermal induction (day 1) coupled with topical challenge (day 21) should be done. If there is no response, re-challenge

should be done 7-30 days after the primary challenge. Erythema and oedema (individual animal scores as well as maximization grading) should be used as evaluation criteria.

(ii) *Local Lymph Node Assay*: Mice used in this test should be of the same sex, either only males or only females. Drug treatment is to be given on ear skin. Three graded doses, the highest being maximum nonirritant dose plus vehicle control should be used. A minimum of 6 mice per group should be used. Test material should be applied on ear skin on three consecutive days and on day 5, the draining auricular lymph nodes should be dissected out 5 hours after i.v. H-thymidine or bromo-deoxy-uridine (BrdU). Increase in H-thymidine or BrdU incorporation should be used as the criterion for evaluation of results.

1.6 *Genotoxicity*

Genotoxic compounds, in the absence of other data, shall be presumed to be trans- species carcinogens, implying a hazard to humans. Such compounds need not be subjected to long-term carcinogenicity studies. However, if such a drug is intended to be administered for chronic illnesses or otherwise over a long period of time - a chronic toxicity study (up to one year) may be necessary to detect early tumorigenic effects.

Genotoxicity tests are *in vitro* and *in vivo* tests conducted to detect compounds which induce genetic damage directly or indirectly. These tests should enable a hazard identification with respect to damage to DNA and its fixation.

The following standard test battery is generally expected to be conducted:

(i) A test for gene mutation in bacteria.
(ii) An *in vitro* test with cytogenetic evaluation of chromosomal damage with mammalian cells or an *in vitro* mouse lymphoma tic assay.
(iii) An *in vivo* test for chromosomal damage using rodent haematopoietic cells. Other genotoxicity tests e.g. tests for measurement of DNA adducts, DNA strand breaks, DNA repair or recombination serve as options in addition to the standard battery for further investigation of genotoxicity test results obtained in the standard battery. Only under extreme conditions in which one or more tests comprising the standard battery cannot

be employed for technical reasons, alternative validated tests can serve as substitutes provided sufficient scientific justification should be provided to support the argument that a given standard battery test is not appropriate.

Both in-vitro and in-vivo studies should be done. In-vitro studies should include Ames' Salmonella assay and chromosomal aberrations (CA) in cultured cells. In-vivo studies should include micronucleus assay (MNA) or CA in rodent bone marrow. Data analysis of CA should include analysis of _gaps.'

Cytotoxic anticancer agents: Genotoxicity data are not required before Phase I and II trials. But these studies should be completed before applying for Phase III trials.

Notes:

Ames' Test (Reverse mutation assay in Salmonella): S. typhimurium tester strains such as TA98, TA100, TA102, TA1535, TA97 or *Escherichia coli* WP2 *uvrA* or *Escherichia coli* WP2 *uvrA* (pKM101) should be used.

(i) In-vitro exposure (with and without metabolic activation, S9 mix) should be done at a minimum of 5 log dose levels. ―Solvent‖ and ―positive‖ control should be used. Positive control may include 9-amino-acridine, 2-nitrofluorine, sodium azide and mitomycin C, respectively, in the tester strains mentioned above. Each set should consist of at least three replicates. A 2.5 fold (or more) increase in number of revertants in comparison to spontaneous revertants would be considered positive.

(ii) *In-vitro cytogenetic assay* : The desired level of toxicity for *in vitro* cytogenetic tests using cell lines should be greater than 50% reduction in cell number or culture confluency. For lymphocyte cultures, an inhibition of mitotic index by greater than 50% is considered sufficient. It should be performed in CHO cells or on human lymphocyte in culture. In-vitro

exposure (with and without metabolic activation, S9 mix) should be done using a minimum of 3 log doses. ―Solvent‖ and ―positive‖ control should be included. A positive control like Cyclophosphamide with metabolic activation and Mitomycin C for without metabolic activation should be used to give a reproducible and detectable increase clastogenic effect over the background which demonstrates the sensitivity of the test system. Each set should consist of at least three replicates. Increased number of aberrations in metaphase chromosomes should be used as the criteria for evaluation.

(iii) *In-vivo micronucleus assay:* One rodent species (preferably mouse) is needed. Route of administration of test substance should be the same as intended for humans. Five animals per sex per dose groups should be used. At least three dose levels, plus ―solvent‖ and ―positive‖ control should be tested. A positive control like mitomycin C or cyclophosphamide should be used. Dosing should be done on day 1 and 2 of study followed by sacrifice of animals 6 hours after the last injection. Bone marrow from both the femora should be taken out, flushed with fetal bovine serum (20 min.), pelletted and smeared on glass slides. Giemsa-MayGruenwald staining should be done and increased number of micronuclei in polychromatic erythrocytes (minimum 1000) should be used as the evaluation criteria.

(iv) In-vivo cytogenetic assay: One rodent species (preferably rat) is to be used. Route of administration of test substance should be the same as intended for humans. Five animals/sex/dose groups should be used. At least three dose levels, plus ―solvent‖ and ―positive‖ control should be tested. Positive control may include cyclophosphamide.

Dosing should be done on day 1 followed by intra-peritoneal colchicine administration at 22 hours. Animals should be sacrificed 2 hours after colchicine administration. Bone marrow from both the femora should be taken out, flushed with hypotonic saline (20 min.),

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pelletted and resuspended in Carnoy‘s fluid. Once again the cells should be pelletted and

dropped on clean glass slides with a Pasteur pipette. Giemsa staining should be done and increased number of aberrations in metaphase chromosomes (minimum 100) should be used as the evaluation criteria.

1.7 *Carcinogenicity (see Appendix I, item 4.8)*

Carcinogenicity studies should be performed for all drugs that are expected to be clinically used for more than 6 months as well as for drugs used frequently in an intermittent manner in the treatment of chronic or recurrent conditions. Carcinogenicity studies are also to be performed for drugs if there is concern about their carcinogenic potential emanating from previous demonstration of carcinogenic potential in the product class that is considered relevant to humans or where structure-activity relationship suggests carcinogenic risk or when there is evidence of preneoplastic lesions in repeated dose toxicity studies or when long-term tissue retention of parent compound or metabolite(s) results in local tissue reactions or other pathophysiological responses. For pharmaceuticals developed to treat certain serious diseases, Licensing Authority may allow carcinogenicity testing to be conducted after marketing permission has been granted.

In instances where the life-expectancy in the indicated population is short (i.e., less than 2-3 years)- no long-term carcinogenicity studies may be required. In cases where the therapeutic agent for cancer is generally successful and life is significantly prolonged there may be later concerns regarding secondary cancers. When such drugs are intended for adjuvant therapy in tumour free patients or for prolonged use in non-cancer indications, carcinogenicity studies may be / are needed. Completed rodent carcinogenicity studies are not needed in advance of the conduct of large scale clinical trials, unless there is special concern for the patient population.

Carcinogenicity studies should be done in a rodent species (preferably rat). Mouse may be employed only with proper scientific justification. The selected strain of animals should not have a very high or very low incidence of spontaneous tumors.

At least three dose levels should be used. The highest dose should be sub-lethal, and it should not reduce the life span of animals by more than 10% of expected normal. The lowest dose should be comparable to the intended human therapeutic dose or a multiple of it, e.g.
2.5x; to make allowance for the sensitivity of the species. The intermediate dose to be placed logarithmically between the other two doses. An untreated control and (if indicated) a vehicle control group should be included. The drug should be administered 7 days a week for a fraction of the life span comparable to the fraction of human life span over which the drug is likely to be used therapeutically. Generally, the period of dosing should be 24 months for rats and 18 months for mice.

Observations should include macroscopic changes observed at autopsy and detailed histopathology of organs and tissues. Additional tests for carcinogenicity (short-term bioassays, neonatal mouse assay or tests employing transgenic animals) may also be done depending on their applicability on a case to case basis.

Note:

Each dose group and concurrent control group not intended to be sacrificed early should contain atleast 50 animals of each sex. A high dose sattelite group for evaluation of pathology other than neoplasia should contain 20 animals of each sex while the sattelite control group should contain 10
animals of each sex. Observation parameters should include signs of intoxication, effect on body
weight, food intake, clinical chemistry parameters, hematology parameters, urine analysis, organ weights, gross pathology and detailed histopathology. Comprehensive descriptions of benign and

malignant tumour development, time of their detection, site, dimensions, histological typing etc. should be given.

1.8 *Animal toxicity requirements for clinical trials and marketing of a new drug.*

Systemic Toxicity Studies

Route of administration	Duration of proposed human administration	Human Phase(s) for which study is proposed to be conducted	Long term toxicity requirements
[1][Oral or Parenteral or Transdermal	Single dose or several doses in one day, Upto 1wk	I,II,III	2sp,2wks
	> 1 wk but upto 2wks	I,II,III	2sp;4wks
	Upto 2 wks	Marketing permission	2sp;4wks
	> 2 wk but upto 4wks	I,II,III	2 sp; equal to duration of human exposure
		Marketing permission	2 sp; 12 wks
	> 4 wks but upto 12 wks	I,II,III	2 sp; equal to duration of human exposure
		Marketing permission	2sp;24wks
	> 12 wks but upto 24 wks	I,II,III	2 sp; equal to duration of human exposure
		Marketing permission	2 sp; Rodent 24 wks, non-rodent 36 wks

	> 24 wks	I,II,III	2 sp; Rodent 24 wks, non-rodent 36 wks
		Marketing permission	2 sp; Rodent 24 wks, non-rodent 36 wks]
Inhalation (general anaesthetics, aerosols)	Upto 2 wk	I,II,III	2sp;1mo; (Exposure time 3h/d,
	Upto 4wk	I,II,III	5d/wk) 2sp;12wk, (Exposure time
	> 1 4wk	I,II,III	2sp;24wk, (Exposure time 6h/d, 5d/wk)
Local Toxicity Studies Dermal	Upto 2 wk	I,II,	1sp;4wk
		III	2sp;4wk
	> 2 wk	I,II,III	2sp;12wk
Ocular or Otic or Nasal	Upto 2 wk	I,II	1sp;4wk
		III	2sp;4wk
	> 2 wk	I,II,III	2sp;12wk
Vaginal or Rectal	Upto 2 wk	I,II	1sp;4wk
		III	2sp;4wk
	> 2 wk	I,II,III	2sp;12wk

1.Subs. by G.S.R. 287(E), dt. 08.3.2016.

Special Toxicity Studies

Male Fertility Study:

- [1][Phase III in male volunteers/patients]

Female Reproduction and Developmental Toxicity Studies:

- Segment II studies in 2 species; Phase II, III involving female patients of child- bearing age.
- Segment I study; Phase III involving female patients of child-bearing age.
- Segment III study; Phase III for drugs to be given to pregnant or nursing mothers for long periods or where there are indications of possible adverse effects on foetal development.

Allergenicity/Hypersensitivity: Phase I, II, III - when there is a cause of concern or for parenteral drugs (including derrmal application).

Photo-allergy or dermal photo-toxicity:

- Phase I, II, III - if the drug or a metabolite is related to an agent causing photosensitivity or the nature of action suggests such a potential.

Genotoxicity:

- In-vitro studies - Phase I
- Both in-vitro and in-vivo - Phase II, III

Arcinogenicity:

- Phase III - when there is a cause for concern, or when the drug is to be used for more than 6 months.

Abbreviations: sp-species; mo-month; wk-week; d -day; h-hour; I, II, III - Phases of clinical trial;

Note:

1. Animal toxicity data generated in other countries may be accepted and may not be asked to be repeated/duplicated in India on a case to case basis depending upon the quality of data and the credentials of the laboratory(ies) where such data has been generated.

2. Requirements for fixed dose combinations are given in Appendix VI.

1.9 *Number of animals required for repeated-dose toxicity studies*

	14-28 days				84-182 days			
Group	Rodent (Rat)		Non-rodent (Dog or Monkey)		Rodent (Rat)		Non-rodent (Dog or Monkey)	
	M	F	M	F	M	F	M	F
Control	6-10	6-10	2-3	2-3	15-30	15-30	4-6	4-6
Low dose	6-10	6-10	2-3	2-3	15-30	15-30	4-6	4-6
Intermediate dose	6-10	6-10	2-3	2-3	15-30	15-30	4-6	4-6
High dose	6-10	6-10	2-3	2-3	15-30	15-30	4-6	4-6

1. Subs. by G.S.R. 287(E), dt. 08.3.2016.

2.0 *Laboratory parameters to be included in toxicity studies*.

Haematological parameters

- Haemoglobin
- Total RBC Count
- Haematocrit
- Reticulocyte Count
- Total WBC Count
- Differential WBC Count
- Platelet Count
- Terminal Bone Marrow Examination
- ESR (Non-immature rodents only)
- General Blood Picture: A special mention of abnormal and immature cells should be made.
- Coagulation Parameters (Non-rodents only): Bleeding Time, Coagulation Time, Prothrombin Time, Activated Partial Thromboplastin Time

Urinalysis Parameters:

- Colour
- Appearance
- Specific Gravity
- 24-hour urinary output
- Reaction (pH)
- Albumin
- Sugar
- Acetone
- Bile pigments
- Urobilinogen
- Occult Blood
- Microscopic examination of urinary sediment.

Blood Biochemical Parameters

- Glucose
- Cholesterol
- Triglycerides
- HDL Cholesterol (Non-rodents only)

• LDL Cholesterol (Non-rodents only)	• Bilirubin	• SGPT (ALT)	• SGOT (AST)
• Alkaline Phosphatase (ALP)	• GGT (Non-rodents only)	• Blood Urea Nitrogen	• Ceatinine
• Globulin (Calculated values)	• Total Proteins	• Albumin	
• Potassium	• Sodium	• Calcium	
• Phosphorus			

Gross and Microscopic Pathology

• Brain*: Cerebrum, cerebellum, Midbrain	• (Spinal Cord)	• Eye	• (Middle Ear)
•Thyroid •Parathyroid) •Spleen •Thymus			
•Adrenal* •(Pancreas) •(Trachea) •Lung*			
•Heart* •Aorta •Oesophagus •Stomach			
• Duodenum	• Jejunum	• Terminal ileum	• Colon
•(Rectum) •Liver* •Kidney* •Urinary bladder			
•Epididymis •Testis* •Ovary •Uterus*			
• Skin	• Mammary gland lymph node	•Mesenteric	• Skeletal muscle

* Organs marked with an asterisk should be weighed.

() Organs listed in parenthesis should be examined if indicated by the nature of the drug or observed effects.

Non-clinical toxicity testing and safety evaluation data of an IND needed for the conduct of different phases of clinical trials.

Note: Refer Appendix III (Points 1.1 through 1.7 and tables 1.8 and 1.9) for essential features of study designs of the non-clinical toxicity studies listed below.

For Phase I Clinical Trials

Systemic Toxicity studies

(i) Single dose toxicity studies

(ii) Dose Ranging Studies

(iii) Repeat-dose systemic toxicity studies of appropriate duration to support the duration of proposed human exposure.

Male fertility study

In-vitro genotoxicity tests

Relevant local toxicity studies with proposed route of clinical application (duration depending on proposed length of clinical exposure)

Allergenicity/Hypersensitivity tests (when there is a cause for concern or for parenteral drugs, including dermal application)

Photo-allergy or dermal photo-toxicity test (if the drug or a metabolite is related to an agent causing photosensitivity or the nature of action suggests such a potential)

For Phase II Clinical Trials

Provide a summary of all the non-clinical safety data (listed above) already submitted while obtaining the permissions for Phase I trial, with appropriate references.

In case of an application for directly starting a Phase II trial - complete details of the non- clinical safety data needed for obtaining the permission for Phase I trial, as per the list provided above must be submitted.

Repeat-dose systemic toxicity studies of appropriate duration to support the duration of proposed human exposure

In-vivo genotoxicity tests-

Segment II reproductive/developmental toxicity study (if female patients of child bearing age are going to be involved)

For Phase III Clinical Trials

Provide a summary of all the non-clinical safety data (listed above) already submitted while obtaining the permissions for Phase I and II trials, with appropriate references.

In case of an application for directly initiating a Phase III trial - complete details of the non-clinical safety data needed for obtaining the permissions for Phase I and II trials, as per the list provided above must be provided.

Repeat-dose systemic toxicity studies of appropriate duration to support the duration of proposed human exposure

Reproductive/developmental toxicity studies

Segment I (if female patients of child bearing age are going to be involved), and

Segment III (for drugs to be given to pregnant or nursing mothers or where there are indications of possible adverse effects on foetal development).

Carcinogenicity studies (when there is a cause for concern or when the drug is to be used for more than 6 months).

For Phase IV Clinical Trials

Provide a summary of all the non-clinical safety data (listed above) already submitted while obtaining the permissions for Phase I, II and III trials, with appropriate references.

In case an application is made for initiating the Phase IV trial, complete details of the non-clinical safety data needed for obtaining the permissions for Phase I, II and III trials, as per the list provided above must be submitted.

Application Of Good Laboratory Practices (GLP)

The animal studies be conducted in an accredited laboratory. Where the safety pharmacology studies are part of toxicology studies, these studies should also be conducted in an accredited laboratory.

APPENDIX IV

ANIMAL PHARMACOLOGY

1. General Principles

Specific and general pharmacological studies should be conducted to support use of therapeutics in humans. In the early stages of drug development enough information may not be available to rationally select study design for safety assessment. In such a situation, a general approach to safety pharmacology studies can be applied. Safety pharmacology studies are studies that investigate potential undesirable pharmacodynamic effects of a substance on physiological functions in relation to exposure within the therapeutic range or above.

1.1 *Specific Pharmacological Actions*

Specific pharmacological actions are those which demonstrate the therapeutic potential for humans.

The specific studies that should be conducted and their design will be different based on the individual properties and intended uses of investigational drug. Scientifically validated methods should be used. The use of new technologies and methodologies in accordance with sound scientific principles should be preferred.

1.2 *General Pharmacological Actions*

1.2.1 Essential Safety Pharmacology

Safety pharmacology studies need to be conducted to investigate the potential undesirable pharmacodynamic effects of a substance on physiological functions in relation to exposure within the therapeutic range and above. These studies should be designed to identify undesirable pharmacodynamic properties of a substance that may have relevance to its human safety; to evaluate adverse pharmacodynamic and/or pathophysiological effects observed in toxicology and/or clinical studies; and to investigate the mechanism of the adverse pharmacodynamic effects observed and/or suspected.

The aim of the essential safety pharmacology is to study the effects of the test drug on vital functions. Vital organ systems such as cardiovascular, respiratory and central nervous systems should be studied. Essential safety pharmacology studies may be excluded or supplemented based on scientific rationale. Also, the exclusion of certain

test(s) or exploration(s) of certain organs, systems or functions should be scientifically justified.

1.2.1.1 Cardiovascular System

Effects of the investigational drug should be studied on blood pressure, heart rate, and the electrocardiogram. If possible i*n vitro, in vivo* and/or *ex vivo* methods including electrophysiology should also be considered.

1.2.1.2 Central Nervous System

Effects of the investigational drug should be studied on motor activity, behavioral changes, coordination, sensory and motor reflex responses and body temperature.

1.2.1.3 Respiratory System

Effects of the investigational drug on respiratory rate and other functions such as tidal volume and hemoglobin oxygen saturation should be studied.

1.3 Follow-up and Supplemental Safety Pharmacology Studies

In addition to the essential safety pharmacological studies, additional supplemental and follow-up safety pharmacology studies may need to be conducted as appropriate. These depend on the pharmacological properties or chemical class of the test substance, and the data generated from safety pharmacology studies, clinical trials, pharmacovigilance, experimental *in vitro* or *in vivo* studies, or from literature reports.

1.3.1 Follow-up Studies For Essential Safety Pharmacology

Follow-up studies provide additional information or a better understanding than that provided by the essential safety pharmacology.

1.3.1.1 Cardiovascular System

These include ventricular contractility, vascular resistance and the effects of chemical mediators, their agonists and antagonists on the cardiovascular system.

1.3.1.2 Central Nervous System

These include behavioral studies , learning and memory, electrophysiology studies , neurochemistry and ligand binding studies.

1.3.1.3 Respiratory System

These include airway resistance, compliance, pulmonary arterial pressure, blood gases and blood pH.

1.3.2 Supplemental Safety Pharmacology Studies

These studies are required to investigate the possible adverse pharmacological effects that are not assessed in the essential safety pharmacological studies and are a cause for concern.

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1.3.2.1 Urinary System

These include urine volume, specific gravity, osmolality, pH, proteins, cytology and blood urea nitrogen, creatinine and plasma proteins estimation.

1.3.2.2 Autonomic Nervous System

These include binding to receptors relevant for the autonomic nervous system, and functional response to agonist or antagonist responses *in vivo* or *in vitro,* and effects of direct stimulation of autonomic nerves and their effects on cardiovascular responses.

1.3.2.3 Gastrointestinal System

These include studies on gastric secretion, gastric pH measurement, gastric mucosal examination, bile secretion, gastric emptying time *in vivo* and ileocaecal contraction *in vitro.*

1.3.2.4 Other Organ Systems

Effects of the investigational drug on organ systems not investigated elsewhere should be assessed when there is a cause for concern. For example dependency potential, skeletal muscle, immune and endocrine functions may be investigated.

1.4 *Conditions Under Which Safety Pharmacology Studies Are Not Necessary*

Safety pharmacology studies are usually not required for locally applied agents e.g. dermal or ocular, in cases when the pharmacology of the investigational drug is well known, and/or when systemic absorption from the site of application is low. Safety pharmacology testing is also not necessary, in the case of a new derivative having similar pharmacokinetics and pharmacodynamics.

1.5 Timing Of Safety Pharmacology Studies In Relation To Clinical Development

1.5.1 Prior To First Administration In Humans

The effects of an investigational drug on the vital functions listed in the essential safety pharmacology should be studied prior to first administration in humans. Any follow-up or supplemental studies identified, should be conducted if necessary, based on a cause for concern.

1.5.2 During Clinical Development

Additional investigations may be warranted to clarify observed or suspected adverse effects in animals and humans during clinical development

1.5.3 Before applying for marketing Approval

Follow-up and supplemental safety pharmacology studies should be assessed prior to approval unless not required, in which case this should be justified. Available information from toxicology studies addressing safety pharmacology endpoints or information from clinical studies can replace such studies.

1.6 Application Of Good Laboratory Practices (GLP)

The animal studies be conducted in an accredited laboratory. Where the safety pharmacology studies are part of toxicology studies, these studies should also be conducted in an accredited laboratory.

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APPENDIX V

INFORMED CONSENT

1.Checklist for study Subject‘s informed consent documents

1.1 Essential Elements:

1.Statement that the study involves research and explanation of the purpose of the research

2.Expected duration of the Subject's participation.

3.Description of the procedures to be followed, including all invasive procedures and

4.Description of any reasonably foreseeable risks or discomforts to the Subject

5.Description of any benefits to the Subject or others reasonably expected from research. If no benefit is expected Subject should be made aware of this.

6.Disclosure of specific appropriate alternative procedures or therapies available to the Subject.

7.Statement describing the extent to which confidentiality of records identifying the Subject will be maintained and who will have access to Subject‘s medical records

8.Trial treatment schedule(s) and the probability for random assignment to each treatment (for randomized trials)

9. [1][Statement describing the financial compensation and medical management as under: [2][(a) In case of any injury occurring to the subject during the clinical trial, free medical management shall be given as long as required or till such time it is established that the injury is not related to the clinical trial, whichever is earlier.]

(b) In the event of a trial related injury or death, the Sponsor or his representative, whosoever has obtained permission from the Licensing Authority for conduct of the clinical trial, shall provide financial compensation for the injury or death].

10.An explanation about whom to contact for trial related queries, rights of Subjects and in the event of any injury

11.The anticipated prorated payment, if any, to the Subject for participating in the trial

12.Subject's responsibilities on participation in the trial

13.Statement that participation is voluntary, that the subject can withdraw from the study at any time and that refusal to participate will not involve any penalty or loss of benefits to which the Subject is otherwise entitled.

3[14. Statement that there is a possibility of failure of investigational product to provide intended therapeutic effect.

15. Statement that in the case of placebo controlled trial, the placebo administered to the subjects shall not have any therapeutic effect.

16.Any other pertinent information.]

1.2 Additional elements, which may be required

(a) Statement of foreseeable circumstances under which the Subject's participation may be terminated by the Investigator without the Subject's consent.

(b) Additional costs to the Subject that may result from participation in the study.

(c) The consequences of a Subject‘s decision to withdraw from the research and procedures for orderly termination of participation by Subject.

(d) Statement that the Subject or Subject's representative will be notified in a timely manner if significant new findings develop during the course of the research which may affect the Subject's willingness to continue participation will be provided.

(e) A statement that the particular treatment or procedure may involve risks to the Subject (or to the embryo or fetus, if the Subject is or may become pregnant), which are currently unforeseeable

(f) Approximate number of Subjects enrolled in the study.

1. Subs. by G.S.R. 53(E), dt. 30-01-2013. 3. G.S.R. 611(E), dt. 31-7-2015. 2. Subs. by G.S.R. 889(E), dt. 12-12-2014.

2.Format of informed consent form for Subjects participating in a clinical trial

Informed Consent form to participate in a clinical trial

Study Title:

Study Number:

Subject‘s Initials: _____

Date of Birth / Age: _____

1[Address of the Subject_____ Qualification _____

Subject‘s Name: _____

Occupation: Student/Self-Employed/ Service/Housewife/Others (Please tick as appropriate)

Annual Income of the subject _____

Name and address of the nominee(s) and his relation to the subject _____ (for the purpose of compensation in case of trial related death).]

		Please initial box (Subject)
(i)	I confirm that I have read and understood the information sheet dated ___ for the above study and have had the opportunity to ask questions.	[ ]
(ii)	I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	[ ]
(iii)	I understand that the Sponsor of the clinical trial, others working on the Sponsor‘s behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published.	[ ]
(iv)	I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s)	[ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative:_____

Date: _____/_/

Signatory'sName:

Signatureof the Investigator:_____

Date:StudyInvestigator'sName:

Signatureof the Witness

Date:_____/_____/

NameoftheWitness:

1[Copy of the Patient Information Sheet and duly filled Informed Consent Form shall be handled over to the subject or his/her attendant.]

1. Ins. by G.S.R 53(E), dt. 30-01-2013

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APPENDIX VI

FIXED DOSE COMBINATIONS (FDCs)

Fixed Dose Combinations refer to products containing one or more active ingredients used for a particular indication(s). FDCs can be divided into the following groups and data required for approval for marketing is described below:

(a) The first group of FDCs includes those in which one or more of the active ingredients is a new drug. For such FDCs to be approved for marketing data to be submitted will be similar to data required for any new drug (including clinical trials) [see rule 122E, item (a)].

(b)(i) The second group FDCs includes those in which active ingredients already approved/marketed individually are combined for the first time, for a particular claim and where the ingredients are likely to have significant interaction of a pharmacodynamic or pharmacokinetic nature [see rule 122E, item (c)]. If clinical trials have been carried out with the FDC in other countries, reports of such trials should be submitted. If the FDC is marketed abroad, the regulatory status in other countries should be stated. (see Appendix I, item 9).

(ii) For marketing permission, appropriate chemical and pharmaceutical data will be submitted. In case such a combination is not marketed anywhere in the world but these drugs are already in use concomitantly (not as an FDC but individually) for the said claim, marketing permission may be granted based on chemical and pharmaceutical data. Data showing the stability of the proposed dosage form will also have to be submitted.

(iii) For any other such FDCs, clinical trials may be required. For obtaining permission to carry out clinical trials with such FDCs a summary of available pharmacological, toxicological and clinical data on the individual ingredients should be submitted, along with the rationale for combining them in the proposed ratio. In addition, acute toxicity data (LD 50) and pharmacological data should be submitted on the individual ingredients as well as their combination in the proposed ratio.

(c) The third group of FDCs includes those which are already marketed, but in which it is proposed either to change the ratio of active ingredients or to make a new therapeutic claim. For such FDCs, the appropriate rationale including published reports (if any) should be submitted to obtain marketing permission. Permission will be granted depending upon the nature of the claim and data submitted.

(d) The fourth group of FDC includes those whose individual active ingredients (or drugs from the same class) have been widely used in a particular indication(s) for years, their concomitant use is often necessary and no claim is proposed to be made other than convenience. It will have to be demonstrated that the proposed dosage

form is stable and the ingredients are unlikely to have significant interaction of a pharmacodynamic or pharmacokinetic nature.

No additional animal or human data are generally required for these FDCs, and marketing permission may be granted if the FDC has an acceptable rationale.

APPENDIX VII

UNDERTAKING BY THEINVESTIGATOR

1. Full name, address and title of the Principal Investigator (or Investigator(s) when there is no Principal Investigator)

2. Name and address of the medical college, hospital or other facility where the clinical trial will be conducted: Education, training & experience that qualify the Investigator for the clinical trial (Attach details including Medical Council registration number, and / or any other statement(s) of qualification(s))

3. Name and address of all clinical laboratory facilities to be used in the study.

4. Name and address of the Ethics Committee that is responsible for approval and continuing review of the study.

5. Names of the other members of the research team (Co- or sub-Investigators) who will be assisting the Investigator in the conduct of the investigation (s).

6. Protocol Title and Study number (if any) of the clinical trial to be conducted by the Investigator.

7. Commitments:

(i) I have reviewed the clinical protocol and agree that it contains all the necessary information to conduct the study. I will not begin the study until all necessary Ethics Committee and regulatory approvals have been obtained.
(ii) I agree to conduct the study in accordance with the current protocol. I will not implement any deviation from or changes of the protocol without agreement by the Sponsor and prior review and documented approval / favorable opinion from the Ethics Committee of the amendment, except where necessary to eliminate an immediate hazard(s) to the trial Subjects or when the change(s) involved are only logistical or administrative in nature. (iii) I agree to personally conduct and/or supervise the clinical trial at my site.
(iv) I agree to inform all Subjects, that the drugs are being used for investigational purposes and I will ensure that the requirements relating to obtaining informed consent and ethics committee review and approval specified in the GCP guidelines are met.
(v) I agree to report to the Sponsor all adverse experiences that occur in the course of the investigation(s) in accordance with the regulatory and GCP guidelines.

(vi) I have read and understood the information in the Investigator's brochure, including the potential risks and side effects of the drug.

(vii) I agree to ensure that all associates, colleagues and employees assisting in the conduct of the study are suitably qualified and experienced and they have been informed about their obligations in meeting their commitments in the trial.

(viii) I agree to maintain adequate and accurate records and to make those records available for audit / inspection by the Sponsor, Ethics Committee, Licensing Authority or their authorized representatives, in accordance with regulatory and GCP provisions. I will fully cooperate with any study related audit conducted by regulatory officials or authorized representatives of the Sponsor.

(ix) I agree to promptly report to the Ethics Committee all changes in the clinical trial activities and all unanticipated problems involving risks to human Subjects or others.

(x) I agree to inform all unexpected serious adverse events to the Sponsor as well as the Ethics Committee within seven days of their occurence.

(xi) I will maintain confidentiality of the identification of all participating study patients and assure security and confidentiality of study data.

(xii) I agree to comply with all other requirements, guidelines and statutory obligations as applicable to clinical Investigators participating in clinical trials

8. Signature of Investigator with Date

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APPENDIX VIII

ETHICS COMMITTEE

[1][I. Requirements and guidelines for registration of Ethics Committee

1. Scope:

Ethics Committee shall review every clinical trial proposal and evaluate the possible risks to the subjects, expected benefits and adequacy of documentation for ensuring privacy, confidentiality and justice. In the case of any serious adverse event occurring to the clinical trial subjects during the clinical trial, the Ethics Committee shall analyze and forward its opinion as per procedures specified in APPENDIX XII of Schedule Y.

2. Composition of Ethics Committee:

(a) Ethics Committee shall consist of not less than seven members and one among its members, who is from outside the institute, shall be appointed as Chairman; one member as a Member Secretary and rest of the members shall be from Medical, Scientific, Non-medical and Non-scientific fields including lay public.

(b) The committee shall include at least one member whose primary area of interest or specialization is Non-scientific and at least one member who is independent of the institution. Besides, there should be appropriate gender representation on the Ethics Committee.

(c) The Ethics Committee can have as its members, individuals from other Institutions or Communities, if required.

(d) Members should be conversant with the provisions of clinical trials under this Schedule, Good Clinical Practice Guidelines for clinical trials in India and other regulatory requirements to safeguard the rights, safety and well- being of the trial subjects.

(e) For review of each protocol the quorum of Ethics Committee shall be at least five members with the following representations:

(i) Basic medical scientist (preferably one pharmacologist)

(ii) Clinician;

(iii) Legal expert;

(iv) Social scientist or representative of non-governmental voluntary agency or philosopher or ethicist or theologian or a similar person;

(v) Lay person from community.

(f) The members representing medical scientists and clinicians should have post graduate qualification and adequate experience in their respective fields and aware of their role and responsibilities as committee members.

(g) As far as possible, based on the requirement of research area such as HIV, Genetic disorder etc., specific patient group may also be represented in the Ethics Committee.

(h) There should be no conflict of interest. The members shall voluntarily withdraw from the Ethics Committee meeting while making a decision on an application which evokes a conflict of interest which may be indicated in writing to the Chairman prior to the review and be recorded so in the minutes. All members shall sign a declaration on conflict of interest.

(i) Subject experts or other experts may be invited to the meetings for their advice. But no such expert shall have voting rights.

3. Information required to be submitted by the applicant for registration of Ethics Committee:

(a) Name of the Ethics Committee

(b) Authority under which the Ethics Committee has been constituted, membership

requirements, the term of reference, conditions of appointment and the quorum required.

1. Subs. by G.S.R. 72(E), dt. 8-2-2013.

(c) The procedure for resignation, replacement or removal of members.

(d) Address of the office of the Ethics Committee.

(e) Name, address, qualification, organizational title, telephone number, fax number, email, mailing address and brief profile of the Chairman.

(f) Names, qualifications, organizational title, telephone number, fax number, e-mail and mailing address of the members of the Ethics Committee. The information shall also in clude member ‘s specialty (pr imary, scientific or non -scientific), member ‘s affiliation with institutions and patient group representation, if any.

(g) Details of the supporting staff.

(h) In the case of Ethics Committees existing before the publication of the Drugs and Cosmetics (Third Amendment) Rules, 2013,-

(i) Type of clinical research reviewed by the committee (e.g. pharmaceuticals, devices, epidemiological, retrospective, herbals, etc.)

(ii) Documents reviewed for every clinical trial protocol including Informed Consent documents.

(iii) In for mation in respect of number of meetings of the committee and documentation of the minutes of meetings of these committees concerning clinical trials.

(iv) Information regarding review of serious adverse events reported during the conduct of the trial.

(i) The Standard Operating Procedures to be followed by the committee in general.

(j) Standard Operating Procedures to be followed by the committee for vulnerable population.

(k) Policy regarding training for new and existing committee members along with Standard Operating Procedures.

(l) Policy to monitor or prevent the conflict of interest along with Standard Operating Procedures.

(m) If the committee has been audited or inspected before, give details.

4. Maintenance of record:

All documentation and communication of an Ethics Committee are to be dated, filed and preserved according to the Standard Operating Procedures. Strict confidentiality shall be maintained during access and retrieval procedures. Records should be maintained for the following, namely:-

(a) The constitution and composition of the Ethics Committee; (b) The curriculum vitae of all the committee members;

(c) Standard Operating Procedures followed by the committee; (d) National and international guidelines;

(e) Copies of the protocol, data collection formats, Case Report Forms, Investigator‘s brochures, etc, submitted for review;

(f) All correspondence with committee members and Investigators regarding application, decision and follow up;

(g) Agenda of all Ethics Committee meetings;

(h) Minutes of all Ethics Committee meetings with signature of the Chairman; (i) Copies of decisions communicated to the applicants;

(j) Record of all notification issued for premature termination of a study with a summary of the reasons;

(k) Final report of the study including microfilms, compact disks or video-recordings.

All records shall be safely maintained after the completion or termination of the study for not less than five years from the date of completion or termination of the trial (Both in hard and soft copies).

5. The Ethics Committee shall be open to inspection by the officers authorized by the Central Drugs Standard Control Organization, who may include an officer of the State Drug Control Authority concerned, to verify compliance to the requirements of Schedule Y, Good Clinical 625 *Drugs and Cosmetics Rules, 1945*

Practice guidelines and other applicable regulation for safeguarding the rights, safety and well-being of the trial subjects.]

III. Format for According Approval to clinical trial protocol by the Ethics Committee.]

To

Dr.

DearDr.

The Institutional Ethics Committee / Independent Ethics Committee (state name of the committee, as appropriate) reviewed and discussed your application to conduct the clinical trial entitled ―……‖ on …….(date).

The following documents were reviewed:

(a) Trial Protocol (including protocol amendments), dated_____ Version no (s).

(b) Patient Information Sheet and Informed Consent Form (including updates if any) in English and/or vernacular language.

(c) Investigator‘s Brochure,dated_,Versionno.

(d) Proposed methods for patient accrual including advertisement (s) etc. proposed to be used for the purpose.

(e) Principal Investigator‘s current CV.

(f) Insurance Policy / Compensation for participation and for serious adverse events occurring during the study participation.

(g) Investigator‘s Agreement with the Sponsor.

(h) Investigator‘s Undertaking (Appendix VII).

The following members of the ethics committee were present at the meeting held on (date, time, place).

Chairman of the Ethics Committee

Member secretary of the Ethics Committee

Name of each member with designation

We approve the trial to be conducted in its presented form.

The Institutional Ethics Committee / Independent Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

Yours sincerely,

Member Secretary, Ethics Committee.

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APPENDIX IX

STABILITY TESTING OF NEW DRUGS

Stability testing is to be performed to provide evidence on how the quality of a drug substance or formulation varies with time under the influence of various environmental factors such as temperature, humidity and light, and to establish shelf life for the formulation and recommended storage conditions.

Stability studies should include testing of those attributes of the drug substance that are susceptible to change during storage and are likely to influence quality, safety, and/or efficacy. In case of formulations the testing should cover, as appropriate, the physical, chemical, biological, and microbiological attributes, preservative content (e.g., antioxidant, antimicrobial preservative), and functionality tests (e.g., for a dose delivery system).

Validated stability-indicating analytical procedures should be applied. For long term studies, frequency of testing should be sufficient to establish the stability profile of the drug substance.

In general, a drug substance should be evaluated under storage conditions that test its thermal stability and, if applicable, its sensitivity to moisture. The storage conditions and the length of studies chosen should be sufficient to cover storage, shipment and subsequent use.

Stress testing of the drug substance should be conducted to identify the likely degradation products, which in turn establish the degradation pathways, evaluate the intrinsic stability of the molecule and validate the stability indicating power of the analytical procedures used. The nature of the stress testing will depend on the individual drug substance and the type of formulation involved.

Stress testing may generally be carried out on a single batch of the drug substance. It should include the effect of temperatures), humidity where appropriate, oxidation, and photolysis on the drug substance.

Data should be provided for (a) Photostability on at least one primary batch of the drug substance as well as the formulation, as the case may be and (b) the susceptibility of the drug substance to hydrolysis across a wide range of pH values when in solution or suspension.

Long-term testing should cover a minimum of 12 months‘ duration on at least three primary batches of the drug substance or the formulation at the time of submission and should be continued for a period of time sufficient to cover the proposed shelf life. Accelerated testing should cover a minimum of 6 months duration at the time of submission.

In case of drug substances, the batches should be manufactured to a minimum of pilot scale by the same synthetic route and using a method of manufacture that simulates the final process to be used for production batches. In case of formulations, two of the three batches should be at least pilot scale and the third one may be smaller. The manufacturing process(es) used for primary batches should simulate that to be applied to production batches and should provide products of the same quality and meeting the same specifications as that intended for marketing.

The stability studies for drug substances should be conducted either in the same container - closure system as proposed for storage and distribution or in a container - closure system that simulates the proposed final packaging. In case of formulations, the stability studies should be conducted in the final container - closure system proposed for marketing.

Stability Testing of new drug substances and formulations:

(i) Study conditions for drug substances and formulations intended to be stored under general conditions

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Study	Study conditions	Duration of study
Long term	30°C ± 2°C/65% RH ± 5% RH	12 months
Accelerated	40°C ± 2°C/75% RH ± 5% RH	6 months

If at any time during 6 months‘ testing under the accelerated storage condition, such changes occur that

cause the product to fail in complying with the prescribed standards, additional testing under an intermediate storage condition should be conducted and evaluated against significant change criteria.

(ii) Study conditions for drug substances and formulations intended to be stored in a refrigerator

Study	Study conditions	Duration of study
Long term	5°C ± 3°C	12 months
Accelerated	25°C ± 2°C/60% RH ± 5% RH	6 months

(iii) Study conditions for drug substances and formulations intended to be stored in a freezer

Study	Study conditions	Duration of study
Long term	- 20°C ± 5°C	12 months

(iv) Drug substances intended for storage below -20°C shall be treated on a case-by-case basis.

(v) Stability testing of the formulation after constitution or dilution, if applicable, should be conducted to provide information for the labelling on the preparation, storage condition, and in-use period of the constituted or diluted product. This testing should be performed on the constituted or diluted product through the proposed in-use period.

APPENDIX X

CONTENTS OF THE PROPOSED PROTOCOL FOR CONDUCTING CLINICAL TRIALS

1. Title Page

(a) Full title of the clinical study,

(b) Protocol / Study number, and protocol version number with date

(c) The IND name/number of the investigational drug

(d) Complete name and address of the Sponsor and contract research organization if any

(e) List of the Investigators who are conducting the study, their respective institutional affiliations and site locations

(f) Name(s) of clinical laboratories and other departments and/or facilities participating in the study.

2. Table of Contents

A complete Table of Contents including a list of all Appendices.

1. *Background and Introduction*

(a) Preclinical experience.

(b) Clinical experience.

Previous clinical work with the new drug should be reviewed here and a description of how the current protocol extends existing data should be provided. If this is an entirely new indication, how this drug was considered for this should be discussed. Relevant information regarding pharmacological, toxicological and other biological properties of the drug/biologic/medical device, and previous efficacy and safety experience should be described.

2. ***Study Rationale***

This section should describe a brief summary of the background information relevant to the study design and protocol methodology. The reasons for performing this study in the particular population included by the protocol should be provided.

3. Study Objective(s) (primary as well as secondray) and their logical relation to the study design.

4. Study Design

(a) Overview of the Study Design: Including a description of the type of study (i.e., double-blind, multicentre, placebo controlled, etc.), a detail of the specific treatment groups and number of study Subjects in each group and investigative site, Subject number assignment, and the type, sequence and duration of study periods.

(b) Flow chart of the study

(c) A brief description of the methods and procedures to be used during the study.

(d) Discussion of Study Design: This discussion details the rationale for the design chosen for this study.

5. Study Population: the number of Subjects required to be enrolled in the study at the investigative site and by all sites along with a brief description of the nature of the Subject population required is also mentioned.

6. Subject Eligibility

(a) Inclusion Criteria

(b) Exclusion Criteria

7. Study Assessments – plan, procedures and methods to be described in detail

8. Study Conduct stating the types of study activities that would be included in this section would be: medical history, type of physical examination, blood or urine testing, electrocardiogram (ECG),

diagnostic testing such as pulmonary function tests, symptom measurement, dispensation and retrieval of medication, Subject cohort assignment, adverse event review, etc.
Each visit should be described separately as Visit 1, Visit 2, etc.

Discontinued Subjects: Describes the circumstances for Subject withdrawal, dropouts, or other reasons for discontinuation of Subjects . State how dropouts would be managed and if they would be replaced, describe the method of handling of protocol waivers, if any. The person(s) who approves all such waivers should be identified and the criteria used for specific waivers should be provided.

Describes how protocol violations will be treated, including conditions where the study will be terminated for non-compliance with the protocol.

9. Study Treatment

(a) *Dosing schedule (dose, frequency, and duration of the experimental treatment*) Describe the administration of placebos and/or dummy medications if they are part of the treatment plan. If applicable, concomitant drug(s), their doses, frequency, and duration of concomitant treatment should be stated.

(b) Study drug supplies and administration: A statement about who is going to provide the study medication and that the investigational drug formulation has been manufactured following all regulations Details of the product stability, storage requirements and dispensing requirements should be provided.

(c) *Dose modification for study drug toxicity*: Rules for changing the dose or stopping the study drug should be provided.

(d) *Possible drug interactions.*

(e) *Concomitant therapy*: The drugs that are permitted during the study and the conditions under which they may be used are detailed here. Describe the drugs that a Subject is not allowed to use during

parts of or the entire study. If any washout periods for prohibited medications are needed prior to enrolment, these should be described here.

(f) *Blinding procedures*: A detailed description of the blinding procedure if the study employs a blind on the Investigator and/or the Subject.

(g) *Unblinding procedures*: If the study is blinded, the circumstances in which unblinding may be done and the mechanism to be used for unblinding should be given.

10. Adverse Events (See Appendix XI): Description of expected adverse events should be given.

Procedures used to evaluate an adverse event should be described.

11. Ethical Considerations: Give the summary of:

(a) Risk/benefit assessment:

(b) Ethics Committee review and communications.

(c) Informed consent process.

(d) Statement of Subject confidentiality including ownership of data and coding procedures.

12. Study Monitoring and Supervision: A description of study monitoring policies and procedures should be provided along with the proposed frequency of site monitoring visits, and who is expected to perform monitoring.

Case Record Form (CRF) completion requirements, including who gets which copies of the forms and any specifics required in filling out the forms CRF correction requirements, including who is authorized to make corrections on the CRF and how queries about study data are handled and how errors, if any, are to be corrected should be stated.

Investigator study files, including what needs to be stored following study completion should be described.

13. Investigational Product Management

(a) Give Investigational product description and packaging (stating all Ingredients and the formulation of the investigational drug and any placebos used in the study)

(b) The precise dosing required during the study.

(c) Method of packaging, labelling, and blinding of study substances.

(d) Method of assigning treatments to Subjects and the Subject identification code numbering system.

(e) Storage conditions for study substances.

(f) Investigational product accountability: Describe instructions for the receipt, storage, dispensation, and return of the investigational products to ensure a complete accounting of all investigational products received, dispensed, and returned/destroyed.

(g.) Describe policy and procedure for handling unused investigational products.

14. Data Analysis:

Provide details of the statistical approach to be followed including sample size, how the sample size was determined, including assumptions made in making this determination, efficacy endpoints (primary as well as secondary) and safety endpoints.

Statistical analysis: Give complete details of how the results will be analyzed and reported along with the description of statistical tests to be used to analyze the primary and secondary endpoints defined above. Describe the level of significance, statistical tests to be used, and the methods used for missing data; method of evaluation of the data for treatment failures, non-compliance, and Subject withdrawals; rationale and conditions for any interim analysis if planned.

Describe statistical considerations for Pharmacokinetic (PK) analysis, if applicable.

15. Undertaking by the Investigator (see Appendix VII).

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16. Appendices: Provide a study synopsis, copies of the informed consent documents (patient information sheet, informed consent form etc.); CRF and other data collection forms; a summary of relevant pre-clinical safety information and any other documents referenced in the clinical protocol.

APPENDIX XI

Data Elements for reporting serious adverse events occuring in a clinical trial

1. Patient Details

Initials & other relevant identifier (hospital/OPD record number etc.)*
Gender Age and/or date of birth

Weight

Height

2. Suspected Drug(s)

Generic name of the drug*.

Indication(s) for which suspect drug was prescribed or tested. Dosage form and strength.

Daily dose and regimen (specify units - e.g., mg, ml, mg/kg).

Route of administration.

Starting date and time of day.

Stopping date and time, or duration of treatment

3. Other Treatment(s)

Provide the same information for concomitant drugs (including non prescription/OTC drugs) and non-drug therapies, as for the suspected drug(s).

4. Details of Suspected Adverse Drug Reaction(s)

Full description of reaction(s) including body site and severity, as well as the criterion (or criteria) for regarding the report as serious. In addition to a description of the reported signs and symptoms, whenever possible, describe a specific diagnosis for the reaction.*

Start date (and time) of onset of reaction.

Stop date (and time) or duration of reaction.

Dechallenge and rechallenge information.

Setting (e.g., hospital, out-patient clinic, home, nursing home).

5. Outcome

Information on recovery and any sequelae; results of specific tests and/or treatment that may have been conducted.

For a fatal outcome, cause of death and a comment on its possible relationship to the suspected reaction; any post-mortem findings.

Other information: anything relevant to facilitate assessment of the case, such as medical history including allergy, drug or alcohol abuse; family history; findings from special investigations etc.

6. Details about the Investigator*

Name

Address

Telephone number

Profession (speciality)

Date of reporting the event to Licensing Authority:

Date of reporting the event to Ethics Committee overseeing the site:

Signature of the Investigator

Note: Information marked * must be provided.‖]

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[1][APPENDIX XII

Compensation in case of injury or death during clinical trial

[2][(1) In case of an injury occurring to the subject during the clinical trial, free medical management shall be given as long as required or till such time it is established that the injury is not related to the clinical trial, whichever is earlier.]

(2) In case the injury occurring to the trial subject is related to the clinical trial, such subject shall also be entitled for financial compensation as per order of the Licensing Authority defined under clause (b) of Rule 21 and the financial compensation will be over and above any expenses incurred on the medical management of the subject. [3][In case, there is no permanent injury, the quantum of compensation shall be commensurate with the nature of the non-permanent injury and loss of wages.]

(3) In the case of clinical trial related death of the subject, his/her nominee(s) would be entitled for financial compensation as per the order of the Licensing Authority defined under clause (b) of Rule 21, and the financial compensation will be over and above any expenses incurred on the medical management of the subject.

(4) The financial compensation for clinical trial related injury or death could be in the form of:-

(a) Payment for medical management;

(b) Financial compensation for trail related injury;

(c) Financial compensation to nominee(s) of the trial subject in case of death; (d) Financial compensation for the child injured in–utero because of the participation of parent in clinical trial.

(5) The Sponsor or his representative, whosoever had obtained permission from the Licensing Authority for conduct of the clinical trial shall provide financial compensation, if the injury or death has occurred because of any or the following reasons, namely:-

(a) Adverse effect of investigational product(s);

(b) Any clinical trial procedures involved in the study;

(c) Violation of the approved protocol, scientific misconduct or negligence by the Sponsor or his representative or the Investigator;

(d) Failure of investigational product to provide intended therapeutic effect; where, the standard care, though available, was not provided to the subject as per the clinical trial protocol.

(e) Use of placebo in a placebo-controlled trial, where, the standard care, though available, was not provided to the subject as per the clinical trial protocol;

1. Ins. by G.S.R. 53(E), dt. 30.1.2013.
2. Subs. by G.S.R. 889(E), dt. 12.12.2014.
3. Ins. by G.S.R. 889(E), dt. 12.12.2014.

(f) Adverse effects due to concomitant medication excluding standard care, necessitated as part of approved protocol;

(g) Injury to the child in-utero because of the participation of parent in clinical trial.

(6) Procedure for payment of financial compensation.

(a) The Investigator shall report all serious [1][***] adverse events to the Licensing Authority as defined under clause (b) of Rule 21, the Sponsor or his representative whosoever had obtained permission from the Licensing Authority for conduct of the clinical trial and the Ethics Committee that accorded approval to the study protocol, within twenty four hours of their occurrence as per Appendix XI. [2][In case, the Investigator fails to report any serious adverse event within the stipulated period, he shall have to furnish the reason for the delay to the satisfaction of the Licensing Authority along with the report of the serious adverse event.]

(b) (i) The cases of serious adverse events of death shall be examined as under: (A) An independent Expert Committee shall be constituted by the Licensing Authority as defined under Rule 21(b) to examine the cases and recommend to the Licensing Authority for the purpose of arriving at the cause of death and quantum of compensation in case of clinical trial related death.

(B)The Sponsor or his representative, whosoever had obtained permission from the Licensing Authority for conducting the clinical trial and the Investigator shall forward their reports on serious adverse event of death after due analysis to [3][***] the Licensing Authority as defined under Rule 21(b) and the head of the Institution where the trial has been conducted within [4][fourteen days] of occurrence of the serious adverse event of death.

(C) The Ethics Committee shall forward its report on serious adverse event of death after due analysis along with its opinion on the financial compensation, if any, to be paid by the Sponsor or his representative, whosoever had obtained permission from the Licensing Authority as defined under Rule 21(b) for conducting the clinical trial, [5][***] to the Licensing Authority within [6][thirty days] of the occurrence of the serious adverse event of death.

[2][(CA) The Licensing Authority shall forward the report of the Investigator, Sponsor or his representative whosoever had obtained permission from the Licensing Authority for conducting clinical trial and the Ethics Committee to the Chairman of the Expert Committee.]

1. The word ―and unexpected‖ omitted by G.S.R. 889(E), dt. 12.12.2014.

2. Ins. by G.S.R. 889(E), dt. 12.12.2014.

3. The word ―Chairman of the Expert Committee with a copy of the report to‖ omitted by G.S.R. 889(E), dt. 12.12.2014.

4. Subs. by G.S.R. 889(E), dt. 12.12.2014.

5. The word ―to the Chairman of the Expert Committee with a copy of the report‖ omitted by G.S.R. 889(E), dt. 12.12.2014.

6. Subs. by G.S.R. 889(E), dt. 12.12.2014.

(D) The Expert Committee shall examine the report of serious adverse event of death and give its recommendations to the Licensing Authority for the purpose of arriving at the cause of the adverse event with in [1][one hundred and five days of the occurrence of the adverse event,] and the expert committee while examining the event, may take into consideration, the reports of the Investigator, Sponsor or his representative whosoever had obtained permission from the Licensing Authority for conducting the clinical trial and the Ethics Committee.

(E) In the case of clinical trial related death, the Expert Committee shall also recommend the quantum of compensation to be paid by the Sponsor or his representative, whosoever had obtained permission from the Licensing Authority as defined under Rule 21(b) for conducting the clinical trial.

(F) The Licensing Authority shall consider the recommendations of the Expert Committee and shall determine the cause of death and pass orders as deemed necessary.

(G) In case of clinical trial related death, the Licensing Authority, after considering the recommendations of the Expert Committee, shall decide the quantum of compensation to be paid by the Sponsor or his representative, whosoever had obtained permission from the Licensing Authority for conducting the clinical trial and shall pass orders as deemed necessary within [1][one hundred and fifty days of the occurrence of the adverse event].

(ii) Cases of serious adverse events, other than deaths, shall be examined as under:

(A)The Sponsor or his representative, whosoever had obtained permission from

the Licensing Authority for conducting the clinical trial, and the Investigator shall forward their reports on serious adverse event, after due analysis, to the Licensing Authority as defined under Rule 21(b), Chairman of the Ethics Committee and the head of the Institution where the trial has been conducted within [1][fourteen days] of occurrence of the serious adverse event.

(B)The Ethics Committee shall forward its report on the serious adverse event, after due analysis along with its opinion regarding the financial compensation, if any, to be paid by the Sponsor or his representative, whosoever had obtained permission from the Licensing Authority as defined under Rule 21(b) for conducting the clinical trial, to the Licensing Authority within [1][thirty days] of occurrence of the serious adverse event.

(C)The Licensing Authority shall determine the cause of injury and pass order as deemed necessary. The Licensing Authority shall have the option to constitute an independent Expert Committee, wherever considered necessary, to examine such serious adverse events of injury, which will recommend to the Licensing Authority for arriving at the

1. Subs. by G.S.R. 889(E), dt. 12.12.2014.

cause considered necessary, to examine such serious adverse events of injury, which will recommend to the Licensing Authority for arriving at the cause of the injury and also the quantum of compensation in case of clinical trial related injury, to be paid by the Sponsor or his representative whosoever had obtained permission from the Licensing Authority as defined under Rule 21(b) for conducting the clinical trial.

(D) In case of clinical trial related injury, the Licensing Authority, shall decide the quantum of compensation to be paid by the Sponsor or his representative whosoever had obtained permission from the Licensing Authority for conducting the clinical trial and shall pass orders as deemed necessary within [1][one hundred and fifty days of the occurrence of the adverse event].

(c) The sponsor or his representative, whosoever had obtained permission from the Licensing Authority for conducting the clinical trial shall pay the compensation in case of clinical trial related injury or death as per the order of the Licensing Authority as defined under Rule 21(b) within thirty days of the receipt of such order.]

1. Subs. by G.S.R. 889(E), dt. 12.12.2014.