

REGULATORY REQUIREMENTS OF BLOOD AND/OR ITS COMPONENTS INCLUDING BLOOD PRODUCTS

INTRODUCTION

Blood Transfusion Service is a vital part of the National Health Service and there is no substitute for Human Blood and its components. Increasing advancement in the field of Transfusion Technology has necessitated to enforce stricter control over the quality of Blood and its products. In most of the developed countries, the blood banking system has advanced in all facets of donor management, storage of blood, grouping and cross matching, testing of transmissible diseases, rationale use of blood and distribution. The Govt. has the full responsibility for the blood programme even though, in some countries, the management of blood transfusion services are delegated fully or partly to an appropriate non-governmental organization (NGOs) working on a non-profit basis, e.g. Red Cross Society. When a NGO is assigned this responsibility, the Govt. should formally recognize it and give a clear mandate formulating the national blood policy, it is important to consider policy decisions enforcing appropriate regulations or necessary functions of health service to ensure high quality service and safe blood.

In order to improve the standards of Blood and its components, the Central Govt. through Drugs Controller General of India, has formulated a comprehensive legislation to ensure better quality control system on collection, storage, testing and distribution of blood and its components. Central Govt. amended from time to time the existing requirements of Blood Banks in the Drugs & Cosmetics Act, 1940 and Rules thereunder to meet the latest standards. Consequent to a public litigation case recently, Supreme Court of India directed Central Govt. to enact a comprehensive legislation on Blood Banks in collection, storage, testing and distribution of blood and its components. In this context, the office of Drugs Controller General of India made draft rules to further amend the existing law in the Drugs & Cosmetics Act, 1940 and Rules thereunder to meet the direction of Hon'ble Supreme Court in order to improve the blood banking system in the country.

NATIONAL BLOOD POLICY

Government of India published in the year 2002 the National Blood Policy. The objective of the policy is to provide safe, adequate quantity of blood, blood components and products. The main aim of the policy is to procure non remunerated regular blood donors by the blood banks. The policy also addresses various issues with regard to technical personnel, research , development and to eliminate profiteering by the blood banks by selling blood. The policy also envisages

that fresh licences to stand alone blood banks in private sector shall not be granted and renewal of such blood banks shall be subjected to thorough scrutiny.

SCENARIO OF LEGAL FRAMEWORK

Human blood is covered under the definition of 'Drug' under Sec. 3(b) of Drugs & Cosmetics Act. Hence, it is imperative that Blood Banks need to be regulated under the Drugs & Cosmetics Act and rules thereunder.

In the year 1967, Central Govt. (Ministry of Health) enacted a separate provision in Schedule F Part XII B of Drugs & Cosmetics Rules. Various requirements such as Accommodation, Technical staff, equipments etc. for operation of blood bank were included in this Part. State Drugs Controllers were authorized to issue the licences for blood banks. The standards for 'Whole Human Blood' was prescribed in Indian Pharmacopoeia.

Due to prevalence of AIDS virus, the Ministry of Health & Family Welfare (Govt. of India) issued a notification in the year 1989 under the Drugs and Cosmetics Rules and made the test HIV 1&2 antibodies of Whole Human Blood as mandatory requirement before transfusion. It is imperative that each unit of blood and blood products were regulated in the year 1990 and 3 laboratories viz. NICD Delhi, NIV Pune and CMC, Vellore were notified to function as laboratory under 3A of Drugs and Cosmetics Rules to test HIV antibodies in respect of human blood and human blood products.

As trained technicians were not available in the Blood Banks to carry out the test for HIV 1&2 antibodies, the Ministry of Health & Family Welfare notified 112 Surveillance Centres to act as a testing lab for the blood banks for carrying out the above test (ZBTC). The list of 112 Surveillance Centres is annexed.

Following M/s. Ferguson's Report (which brought out various deficiencies with regard to quality control of blood and blood products etc. in the year 1990 and based on concern expressed in different fora and in Parliament, the D&C Rules were again amended (Rules 68A, Part XB and Part XIIB of Schedule F) in the year 1992-93 and Drugs Controller General (India) was vested with the power of Central Licence Approving Authority (CLAA) to approve the licence of notified drugs viz. Blood and Blood Products, I.V. Fluids and Vaccines and Sera.

The requirement of a blood bank is inserted in Part X-B of the Drugs and Cosmetics Rules, 1945. The Rules from 122F to 122P explain the various procedure of making applications by a blood bank, fees to be paid for grant/renewal of licence

by the applicant and conditions of licence to be followed by the applicant after grant/renewal and conditions of licence to be followed by the applicant after grant/renewal of licence.

In accordance with the Supreme Court order, blood bank legislation has been extensively revised on 5.4.1999 to include Good Manufacturing Practices, Standard Operating Procedure and validation of equipments etc. The brief requirements for grant/renewal of blood bank licences are as follows:

PART X-B

REQUIREMENTS FOR THE COLLECTION, STORAGE, PROCESSING AND DISTRIBUTION OF WHOLE HUMAN BLOOD, HUMAN BLOOD COMPONENTS BY BLOOD BANKS AND MANUFACTURE OF BLOOD PRODUCTS

122-EA. Definitions.- (1) In this Part and in the Forms contained in Schedule A and in Part XII B and Part XIIC of schedule F, unless there is anything repugnant in the subject or context,-

- (a) 'apheresis' means for the process by which blood drawn from a donor, after separating plasma or platelets or leucocytes, is retransfused – 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 or blood by fractionation, drawn from donors;
- (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 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 or 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 separated, 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.

122-F. Form of application for licence for operation of Blood Bank/processing of whole human blood for components/manufacture or Blood Products for sale or distribution – (1) Application for the grant and/or renewal of licence for the operation of Blood Bank/processing of Human Blood for components/manufacture of Blood Products shall be made to the Licensing Authority appointed under Part VII in Form 27-C or Form 27-E as the case may be and shall be accompanied by licence fees of rupees six thousand and an inspection fees 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 the expiry but within six months of such expiry the fee payable for the renewal of the licence shall be rupees six thousand and inspection fees of rupees one thousand and five hundred plus an additional fees at the rate of rupees one thousand per month or a part thereof in addition to the inspection fee.

Provided further that a licensee holding a licence in Form 28-C or Form 28-E as the case may be for operation of blood bank/processing of whole human blood for components/manufacture of blood products shall apply for grant of licence under sub-rule (1) before the expiry of the said licence on Form 27-C or Form 27-E as the case may be and he shall continue to operate the same till the orders on his application are communicated to him.

1. {EXPLANATION.- For the purpose of this rule, 'Blood Bank' means a place or organizational unit or an institution, or other arrangement made by such organizational unit or institution for carrying out all or any of the operations of manufacture of human blood components or blood products or whole human blood for its collection, storage, processing, distribution from selected human donors.}
2. A fee of rupees one thousand shall be paid for a duplicate copy of licence issued under this rule, if the original is defaced, damaged or lost.
3. Application by licensee to manufacture additional drugs listed in the application shall be accompanied by a fee of 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 provisions of rules 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 position to fulfill the requirements laid down in the rules, he shall prepare a report to that effect and forward it 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 fulfill the requirements laid down in these rules, he may, by order, for reason to be recorded in writing, refuse to grant or renew the licence, as the case may be.
6. If, on receipt of application and the report of the Licensing Authority referred to in Sub-rule 5 and after taking such measures including inspection of the premises, by the inspector, appointed by the Central Govt. under Section 21 of the Act, and/or along with expert in the field concerned if deemed necessary, the Central Licence Approving Authority, is satisfied that the applicant is in a position to fulfill the requirement laid down in this rule. 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 fulfill the requirements laid down in these rules he may, notwithstanding the report of the Licensing Authority, by order, for reason to be recorded in the 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.

122-G. Form of licence for the operation of a Blood Bank/Processing of Whole Human Blood for components and manufacture of Blood products and the conditions for the grant or renewal of such licence.- A licence for the operation of a Blood Bank or for processing whole Human Blood for components and manufacture of blood products shall be issued in Form 28-C or Form-28-E or Form 26-G or Form 26-I as the case may be. Before a licence in Form 28-C or Form-28-E or Form 26-G or Form 26-I, as the case may be, is granted or renewed the following conditions shall be complied with by the applicant.-

- (i) The operation of the Blood Bank and/or processing of whole human blood for components/manufacture of blood product shall be carried out under the active direction and personal supervision of component technical staff consisting of at least one person who is whole time employee and who is a Medical Officer, and possessing-
 - a) Post Graduate 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 & 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 operations is given in Schedule 'F', Part XII-B and / or XII-C.
- (iii) The applicant shall provide and maintain adequate technical staff as specified in Schedule 'F', Part XII-B and/or XII-C.
- (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.

122-H. Duration of Licence.- An original licence in Form 28-C or Form 28 –E or a renewed licence in Form 26-G or Form 26-I unless sooner suspended or cancelled shall valid for a period of five years and from the date on which the year in 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 Form 28-C or Form 28 –E is granted or a renewal of licence in Form 26-G or Form 26-I is made ,as the case may be, the Licensing Authority or 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 component 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.

122-J. Report by Inspector.- The Inspector or Inspectors shall forward a detailed descriptive report giving his finding 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.

122-K. Further application after rejection.- If within a period of six months from the rejection of application for a licence the applicant informs the licensing Authority that the conditions laid down have been satisfied and deposits an inspection fee of rupees two hundred and fifty the Licensing Authority, if after causing further inspection to be made is satisfied that the conditions for the grant of a licence have been complied with, shall grant or renew a licence in Form 28-C or Form 28 –E;

Provided that in case of 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.

122-L. Delegation of powers by the Central Licensing Approving Authority.- The Central Licensing Approving Authority may, with the approval of the Central Government, by notification delegate his power 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.

122-M. 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.

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, 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 by 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, [or direct the licensee to stop collection, storage, processing, manufacture and distribution of the said substances and [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 provision of the Act or Rules thereunder.

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

122-P. Conditions of licence- A licence in Form 28-C, Form 28-E, Form 26-G or Form 26-I shall be subject to the special conditions set out in Schedule F, Part XII-B and Part XII-C, 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 equipments 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, Part XII-B and Part XII-C. The records and registers 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 adequate quantity to conduct all the prescribed tests. The licensee shall supply to the Inspector the reference sample for the purpose of testing.

- (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 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 the Central Licence Approving 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 subparagraph 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 so, 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 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 impressions and defects noticed.
- (xi) The licensee shall destroy the stocks 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.

(xii) All bio-medical waste shall be treated, disposed off 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.

Form 26-G
(See Rule 122-F)

**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 number _____ granted on _____ to M/s _____ for the operation of a Blood Bank for processing of whole 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.
- 4.
- 5.
- 6.

Dated _____

Signature _____

Name and Designation _____
Licensing Authority

Central Licence Approving Authority

* delete, whichever is not applicable.”;

(b) after Form 26-H, the following Form shall be inserted, namely :-

“Form 26-I
(See rule 122-I)

**CERTIFICATE OF RENEWAL OF LICENCE FOR
MANUFACTURE OF BLOOD PRODUCTS**

Certified that licence number _____ granted on
_____ to M/s _____ for 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. Names of competent Technical Staff :

(a) responsible for manufacturing
testing

(b) responsible for

- 1.
- 2.
- 3.
- 4.

- 1.
- 2.
- 3.
- 4.

Signature _____

Name and Designation _____
Licensing Authority

Central Licence Approving
Authority”.;

(c) for Form 27-C, the following form shall be substituted, namely:-

“Form 27-C
(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.

Note 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 concerned Zonal/Sub- Zonal Officers of the Central Drugs Standard Control Organization.”;

(d) after Form 27-D, the following Form shall be inserted, namely :-

“Form 27-E
(See rule 122-F)

**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 item(s) :

- 1.
- 2.
- 3.
- 4.

3. The name(s), qualification and experience of competent Technical Staff as under :

(a) responsible for manufacturing testing

- 1.
- 2.
- 3.

(b) responsible for

- 1.
- 2.
- 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),

Dated _____

signature _____

Name & Designation

* delete, whichever is not applicable.

NOTE 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 concerned Zonal / Sub Zonal Officers of the Central Drugs Standard Control Organisation.”;

(e) for Form 28-C, the following Form shall be substituted, namely :-

“Form 28-C
(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.
 - 3.
4. Name(s) of competent Technical Staff :
 - 1.
 - 2.
 - 3.
 - 4.
 - 5.
 - 6.
5. The licence authorizes 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 the
Drugs and Cosmetics Act, 1940.

Dated _____

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 nor 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 place, 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.”;
- (f) after Form 28-D, the following Form shall be inserted, namely :-

“Form 28-E
(See rule 122-G)

LICENCE TO MANUFACTURE AND STORE BLOOD PRODUCTS FOR SALE OR DISTRIBUTION

1. Number of licence _____ date of issue _____
_____at
the premises situated at _____
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.
 - 5.
4. Name(s) of competent Technical Staff :

(a) responsible for manufacturing	(b) responsible for testing
1.	1.
2.	2.
3.	3.
5. The licence authorizes 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 the Drugs and Cosmetics Act, 1940.

Dated _____ Signature _____

Name and Designation

Licensing Authority

Central Licence Approving

Authority

*delete, whichever is not applicable

CONDITIONS OF LICENCE

1. The licensee shall not manufacture blood products from any professional donor or paid donor.
2. This 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 place, 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.;

**“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. ACCOMODATION 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);
- (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 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 (MLT) with one year's experience in the testing of blood and/or its components, the degree or diploma being from a University/Institution recognised 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 recognised by the Central Government or State Government.

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 or 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, labeling 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.

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, standardised 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, standardised 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 cyanamethemoglobin standard	Each day of use	---
7.	Refractometer or Urinometer	Standardize against distilled water .	---ditto ---	---
8.	Blood container weighing device	standardize against container of known weight	---ditto --	As often as necessary,
9.	Water Bath	Observe Temperature	---ditto --	----ditto----
10.	Rh view box(wherever necessary)	--ditto --	--ditto--	----ditto----
11.	Autoclave	--ditto --	Each time of use	-- ditto --
12.	serologic rotators	Observe controls for correct results	Each day of use	speed as often as necessary

13.	Laboratory thermometers	--	--	Before initial use
14.	Electronic thermometers	--	Monthly	--
15.	Blood agitator	Observe weight of the first container of blood filled for correct results	Each day of use	standardize with container of known mass or volume 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 and 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 solution 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 quantity 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;
- (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;
- (i) length of expiry dates, if any, assigned for all final products;
- (I) 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 safe guard its mix-ups, receipt, issue, rejected and in-hand;

- (q) procedures of plasmapheresis, plateletpheresis 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, labeling, 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 organisations, 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 fulfill the following requirements, namely :-

- (a) the donor shall be in the age group of 18 to 60 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 pressures 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 a 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 (1)	PERIOD OF DEFERMENT (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	3 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
- c. Abnormal bleeding tendencies
- d. Unexplained weight loss
- e. Diabetes-controlled on Insulin
- f. Hepatitis infection
- g. Chronic nephritis
- h. Signs and symptoms, suggestive of AIDS
- i. Liver disease
- 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.
 - (ii) Capillary tube (1.3x1.4x96 mm or 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 seconds-hand) and a stop-watch.

4. For blood containers :

- (a) Only disposable PVC blood bags shall be used (closed system) as per the 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 separated blood components.

(i) Citrate Phosphate Dextrose Adenine solution (CPDA) or Citrate Phosphate Dextrose Adenine- 1 (CPDA-1) ----14 ml. Solution shall be required for 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. -- 15ml. Solution shall be required for 100ml of blood.
 - (iii) Additive solutions such as SAGM, ADSOL, NUTRICEL may be used for storing, and retaining Red Blood Corpuscles upto 42 days.

NOTE2. 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 percent 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 degree 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 6mmx50mm 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 EDT A 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.
- (5) ELISA or RPHA test kits for Hepatitis and HIV I & II.
- (6) Detergent and other agents for cleaning laboratory glasswares.

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 I 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 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.

NOTE:

- (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.

L. 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, hemoglobin, 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., Hepatitis B surface antigen and Hepatitis C virus antibody and irregular antibodies (if any), name and address of the donor with particulars, utilisation issue number, components prepared or discarded and signature of the Medical Officer Incharge.
- (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 cross-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 A.C.D./C.P.D/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 said 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
- (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	Color of the label
O	Blue
A	Yellow
B	Pink
AB	White

- (7) The results of the tests for 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 a typical 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 -

- (a) a licensed designated Regional Blood Transfusion Centre; or
- (b) a licensed Government blood bank; or
- (c) the Indian Red Cross Society ; or
- (d) a licenced blood bank run by registered voluntary or charitable organizations recognized by State or Union Territory Blood Transfusion Council.

NOTE:

- (i) "Designated Regional Blood Transfusion Centre" shall be a centre 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 centre 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 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/Organiser of the Camp;
 - (v) furniture and equipment arranged within the available place;
 - (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 120 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/matress.
10. Lancets, swab stick/tooth picks.
11. Glass slides.
12. Portable Hb meter/copper sulphate.
13. Test tube (big) and 12x100 mm (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 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 specifications, for preparing blood components depending on quantum of work load shall be as specified in item B under the heading "I. 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 Technician and Registered Nurse) shall be as specified in item C, under the heading "I. BLOOD BANKS/BLOOD COMPONENTS" of this Part.

(D) TESTING FACILITIES:

General: Facilities for A,B, AB and O groups and Rh(D) grouping.

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 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.
- (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 of 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 sample 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 21days, 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} (3.5×10 raised to the power of 10) and 4.5×10^{10} (4.5×10 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 percent 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.

- (d) 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 5 days, between 20 degree centigrade to 24 degree centigrade, with continuous gentleagitation 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 for 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.

- (iv) 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 CONCERNTRATES:

- (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. 1×10 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.

(6) 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 under the heading "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 donor is fit for apheresis and it shall be carried out by a trained person under supervision of the Medical Officer.

(A) PLASMAPHERESIS, PLATELET PHERESIS AND LEUCAPHERESIS:

The donors subjected to plasmapheresis, plateletpheresis and leucopheresis 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 a reference for subsequent Pheresis/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 validated Standard Operating Procedures.

NOTE:

- (i) At least 48 hours must elapse between successive apheresis and not more than twice in a week.
- (ii) Extracorporeal 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 cytappheresis 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 /100 ml.

(C) COLLECTION OF PLASMA:

The quantity of plasma separated from the blood of a 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 I of Schedule M shall apply mutatis mutandis to the manufacture of blood products.
2. Disposal of waste and infectious materials:
 - (i) The requirement as regards disposal of waste and infectious materials as contained in paragraph 1.1.4 of Part I 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, Hepatitis B (surface antigen and Hepatitis C virus antibody) through autoclaving, incineration or any other suitable validated methods.
3. Health, clothing and sanitation of 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 designed 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.
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 authorised personnel. Special procedures for entering and leaving of 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 minimise contamination and to take account of the comfort of personnels 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 validated 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 L 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 sterilised 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 sterilisation. 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 Hepatitis B surface antigen 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 Hepatitis B surface antigen and Hepatitis C virus antibody, HIV I and HIV II and if the 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 conditions. 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 authorised 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.

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 in Pharmacy (Microbiology), from a recognised 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 recognised 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 having 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.**

Maximum number of particles permitted per m³

	MAXIMUM NUMBER OF PARTICLES PERMITTED PER m3		MAXIMUM NUMBER OF VIABLE MICROORGANISM PERMITTED PER m3
GRADE	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 10000)	350000	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, 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 stabiliser 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 stabilisers 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, in writing for carrying out test and analysis.
- (2) To approve or reject raw material, components, containers, closures, in-process materials, packaging material, labeling 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.
- (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 thereunder 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 standard 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, 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.
- (iii) 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 labeled as specified in the Indian Pharmacopoeia, the British Pharmacopoeia or the United States 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 tests for 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 alongwith 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;
- (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 sterilising 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.

GUIDELINES FOR APPROVAL OF BLOOD AND/OR ITS COMPONENTS TO STORAGE CENTRES AND FIRST REFERRAL UNIT, COMMUNITY HEALTH CENTRE, PRIMARY HEALTH CENTRE OR ANY HOSPITAL

Ministry of Health & Family Welfare (Deptt. of Health) vide Notification No. GSR 909(E) dated 20th December, 2001 exempted blood storage centers run by FRU, Community Health Centre, PHC or any hospital from the purview of obtaining licence for operation. This notification has been inserted under Schedule K of Drugs & Cosmetics rules, 1945 under serial no. 5B. The main aim of this notification is to make abundant availability of whole human blood or its components to the said hospitals without taking licence. However, this exemption is applicable to those centers which are transfusing blood and/or its components less than 2000 units per annum.

In order to ensure the safety and quality of blood and/or its components to be stored in such blood storage centres, the following conditions are applicable before getting exemption from the purview of taking of a licence from the respective State Drugs Controllers:-

“5B. Whole Human Blood I.P. and / or its components stored for transfusion by a First Referral Unit, Community Health Centre, Primary Health Centre and a Hospital	The provisions of Chapter IV of the Act and the rules made thereunder which require obtaining of a licence for operation of a blood bank 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 or Whole Human Blood I.P. 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 and/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 or the Hospital shall apply for renewal to the State Licensing Authority three months
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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.
- (5) The First Referral Unit, Community Health Centre, Primary Health Centre and 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, specified equipments as specified in Part XII B of Schedule F shall also be provided.
- (6) The First Referral Unit, Community Health Centre, Primary Health Centre and Hospital shall maintain records and registers including details of procurements of Whole Human Blood I.P. and/or blood components, as required under Part XII B of Schedule F.
- (7) The First Referral Unit, Community Health Centre, Primary Health Centre and Hospital shall store samples of donors blood as well as patients sera for a period of seven days after transfusion.”

[No. X – 11014/3/2001-DMS & PFA]

(DEEPAK GUPTA)
JOINT SECRETARY OF SECRETARY OF INDIA

**GUIDELINES BEFORE GRANT OF APPROVAL FOR OPERATION OF
WHOLE HUMAN BLOOD AND/OR ITS COMPONENTS STORAGE CENTRES
RUN BY FIRST REFERRAL UNIT, COMMUNITY HEALTH CENTRE,
PRIMARY HEALTH CENTRE OR ANY HOSPITAL.**

The following guidelines may be followed before exempting the said institutions for obtaining of a licence for operation of a Blood Bank or processing Whole Human Blood / or its components :

1. The applicant shall be First Referral Unit, Community Health Centre, Primary Health Centre or any Hospital.
2. The applicant shall furnish an undertaking to the licensing authority that the captive consumption of Whole Human Blood or Components shall not be more than 2000 units annually.
3. The applicant shall enclose list of equipment needed for storage viz blood bank refrigerator with alarm system & temperature indicator. A separate list of equipments for blood components would be enclosed if proposed to be stored.
4. The applicant shall furnish the following :
 - a Name of the medical officer responsible for conducting operation of blood storage center.
 - b Attested certified copies of MBBS or MD qualification
 - c Name, certified copies of qualification and experience of the blood bank technician.
 - d Name, attested certified copies of qualification and experience of the blood bank technician having non-DMLT qualification
5. The applicant shall furnish the source of procurement of Whole Human Blood / Blood Components namely the name and address of the Blood Banks.
 - a. The source of procurement of blood / components shall be from licensed Blood Banks run by Govt. Hospitals / Indian Red Cross Society / Regional Blood Transfusion Centres only.
 - b. A letter of consent from the above Blood Banks who intend to supply Whole Human Blood / Blood Components to the Blood Storage Centres shall be furnished along with the application.
6. The applicant shall submit the plan of the premises. A minimum area of 10 sq. meter is essential for the Blood Storage Centre.

7. In order to satisfy the conditions and facilities, an inspection of the proposed Blood Storage Centre may be carried out by the respective State Drug Control Department.
8. The Inspection team shall also inspect the Blood Banks who have given consent letters for supply of Whole Human Blood / Components. The inspection team may verify whether the Blood Banks have sufficient quantity of blood units to be supplied to the Blood Storage Centres and also verify the mode of shipper or containers used for supply of blood units / components to ensure that the proper storage condition is maintained as per the pharmacopeia. The Blood Bank shall label the blood units / components as per the Drugs & Cosmetics Rules, 1945.
9. The Blood Banks who intend to supply the blood units / components shall test the following mandatory tests before supplying to Blood Storage Centres.
 - a. Blood Grouping
 - b. Anti Body Testing
 - c. Haemoglobin Content
 - d. HIV I & II Anti Bodies
 - e. Hepatitis B Surface antigen
 - f. Hepatitis C Anti Body
 - g. Malarial Parasite
 - h. Syphilis or VDRL

The label of the tested blood unit shall contain the above particulars with date of testing before supplying to Blood Storage Centres.

The Blood Bank shall maintain a separate register for supply of blood units / components to Blood Storage Centres with all necessary details.

10. The validity of approval shall be for a period of 2 years from the date of issue of the approval.
11. The State Licensing Authority shall forward the approved Blood Storage Centres to the concerned Zonal Officer immediately.
12. A format of the approval proforma is enclosed.

**CERTIFICATE OF APPROVAL TO BLOOD STORAGE CENTRE FOR
STORAGE OF WHOLE HUMAN BLOOD AND* / OR ITS COMPONENTS**

No. _____ Date _____ of _____ Issue

M/s _____ is hereby approved to store the following items on the premises situated at _____ under the supervision of the following technical staff :

1. Names of the approved medical officer _____ :
1. Names of the items _____ :
2. Name of the qualified Blood Bank Technician _____ :
3. Name & address of the licensed Blood _____ :
Bank from whom the blood units would be procured.
5. The approval shall be inforce from _____ to _____

Signature
Designation
Licensing Authority

Dated _____

* Delete whichever is not applicable.

CONDITIONS

The Blood storage center shall comply with the conditions as stipulated under item 5B of Schedule K of the Drugs and Cosmetics Rules which also includes as under :-

1. The captive conception of Whole Human Blood or its components in the above said center shall not be more than 2000 units annually.
2. In the event of any change in the technical staff shall be forthwith reported to the licensing authority.
3. In the event of any change in the name of the licensed blood bank from whom the blood units are procured, the same shall be intimated to the licensing authority for approval.
4. The center shall apply for renewal of the approval to the licensing authority three months prior to the date of expiry of the approval.

5. The center shall maintain records and registers including the details of procurement of blood* / its components.
6. The center shall store samples of donors' blood as well as patients' sera for a period of 7 days after transfusion.