5. –150 डिग्री सेल्सियस या उससे अधिक ठंडे तापमान पर भंडारित निम्नताप पर परिरक्षित कोर्ड ब्लड यूनिट को ऐसे किसी द्रव नाइट्रोजन द्वारा ठंडे शुष्क यान से परिवाहित किया जाएगा जिसमें पर्याप्त रूप से अवशोषित द्रव नाइट्रोजन हो और जिसको प्राप्ति सुविधा पर आगमन के प्रत्याशित समय से परे कम से कम 48 घंटे के लिए –150 डिग्री सेल्सियस से नीचे तापमान बनाए रखने के लिए मान्य किया गया हो।"

[फा. सं. एक्स. 11014/2/2008-डी.एफ.क्यू.सी.]

विनीत चौधरी, संयुक्त सचिव

पाद टिप्पण : मूल नियम, भारत के राजपत्र में अधिसूचना संख्या एफ-28-10/45 एच (एल), तारीख 21 दिसम्बर, 1945 द्वारा प्रकाशित किए गए थे और अंतिम बार अधिसूचना सा.का.नि. 45(अ) तारीख 21-1-2010 को संशोधित किए गए थे ।

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health)

NOTIFICATION

New Delhi, the 9th April, 2010

G.S.R. 304(E).—The following draft of certain rules to amend the Drugs and Cosmetics Rules, 1945, which the Central Government proposes to make, after consultation with the Drugs Technical Advisory Board, in exercise of the powers conferred by section 12 and section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), is hereby given that the said draft rules shall be taken into consideration on or after the expiry of a period of forty-five days from the date on which the copies of the Gazette of India containing these draft rules are made available to the public;

Objections or suggestions, if any, may be addressed to the Secretary (Health), Ministry of Health and Family Welfare, Government of India, Nirman Bhawan, New Delhi – 110011;

Any objection or suggestion which may be received from any person with respect to the said draft rules before the expiry of the period as specified above will be taken into consideration of the Central Government.

DRAFT RULES

1. (1) These rules may be called the Drugs and Cosmetics (3rd ----Amendment) Rules, 2010.

(2) They shall come into force on the date of their final publication in the Official Gazette.

2. In the Drugs and Cosmetics Rules, 1945, (hereinafter referred to as the said rules),-

(i) in rule 122EA, in sub-rule (1),-

(a) for the words. "and in Part XIIB and Part XIIC", the words, "Part XIIB, Part XIIBI and Part XIIC", shall be substituted.

(b) after clause (f), the following clause shall be inserted, namely:-

"(ff) 'cord blood bank' means a place or organization or unit for carrying out and responsible for operations of collection, processing, testing, banking, selection and release of cord blood units.";

(c) after clause (l), the following clause shall be inserted, namely:-

"(m) 'umbilical cord blood' is the whole blood including Hematopoietic Progenitor Cells (HPC) collected from placental and or Umbilical cord blood vessels after the umbilical cord have been clamped."

(ii) in rule 122F, after the words "processing of human blood for components" and "processing of whole human blood for components" wherever they are occurring, the words and symbols, "collection, processing, testing, storage, banking and release of Umbilical cord blood stem cells/" shall respectively be inserted;

(iii) in rule 122G,

(a) after the words "processing of whole human blood for components" wherever they occur, the words and symbols "processing of whole human blood for components /collection, processing, testing, storage, banking and release of Umbilical cord blood stem cells" shall be substituted;

(b) in Explanation II, after the words, "Schedule F, Part XIIB", the words ",Part XIIBI", shall be inserted;

(c) in Explanation III, after the words, "Schedule F, Part XIIB and /or", the words "XII-BI and/or", shall be inserted.

(iv) in rule 122-P,-

(a) after the words and letters "Schedule F, Part XIIB and Part XIIC" the Words and letters ",Schedule F, Part XIIB, Part XII-BI and Part XIIC", shall be substituted;

(b) in sub-rule (i)(b), for the words and letters "Schedule F, Part XII B and Part XIIC", the words and letters ",Schedule F, Part XIIB, Part XII-BI and Part XIIC shall be substituted;

(v) in Form 26G, in the heading after the words, "sale or distribution of its components" , wherever occurring, the words "or collection, processing, testing, storage, banking and release of umbilical cord blood", shall be inserted;

(vi) in Form 27C, in the heading after the words, "preparation of Blood Components", wherever occurring, the words "or collection, processing, testing, storage, banking and release of umbilical cord blood", shall be inserted;

(vii) in Form 28C, in the heading after the words, "its components for sale or distribution", the words " or collection, processing, testing, storage, banking and release of umbilical cord blood", shall be inserted;

(viii) in Schedule F, after Part XIIB the following "Part XIIB1" shall be inserted, namely:-

"PART XII BI

REQUIREMENTS FOR COLLECTION, PROCESSING, TESTING, STORAGE, BANKING AND RELEASE OF UMBILICAL CORD BLOOD DERIVED STEM CELLS

A. GENERAL REQUIREMENTS

1. *Location, Surroundings and Building*: The building (s) for storage of Umbilical cord blood shall be so situated and shall have such measures as to avoid risk of contamination from external environment including open sewage, drain, public lavatory or any factory which produces disagreeable or obnoxious odour or fumes, excessive soot, smoke, chemical or biological emissions.
2. *Building and premises:* The premises used for processing and storage shall be designed, constructed and adapted and maintained to ensure that the above operations and other ancillary functions are performed smoothly under hygienic conditions and in sterile areas wherever required. They shall also conform to the conditions laid down in the Factories Act, 1948 (63 of 1948)

The premises shall be:

(i) adequately provided with working space to allow orderly and logical placement of equipment, material and movement of personnel so as to maintain safe operations and prevent contamination.

(ii) designed/constructed/maintained to prevent entry of insects, pests, birds, vermins and rodents. Interior surfaces (walls, floors and ceilings) shall be smooth and free from cracks, and permit easy cleaning painting and disinfection. In aseptic areas the surfaces shall be impervious, non-shedding, non-flaking and non-cracking. Flooring shall be unbroken and provided with a cove both at the junction between the wall and the floor as well as the wall and the ceiling.

(iii) provided with light fitting and grills which shall flush with the walls and not hanging from the ceiling to prevent contamination.

(iv) provided with doors of non shedding materials in aseptic areas preferably of aluminium or steel.

(v) if provided, with fire escapes, these shall be suitably fastened to the walls without any gaps.

(vi) provided with the furniture in aseptic areas which is smooth, washable and made of stainless steel or any other appropriate material other than wood

(vii) provided with separate areas for processing and storage of products to prevent mix-ups, product contaminations and cross contamination.

(viii) provided with defined environmental conditions for temperature, humidity, ventilation, and air filtration. Classifications shall be defined and, if appropriate, monitored.

A periodical record of cleaning and renovating of the premises shall be maintained.

3. Disposal of waste and infectious materials:

3.1 Waste materials awaiting disposal shall be stored safely.

3.2 The disposal of sewage and effluents from the facility shall be in conformity with the requirements of the Environment pollution control Board.

3.3 All Bio- Medical waste shall be dealt with in accordance with the provisions of the Bio-medical Waste (Management and Handling) Rules, 1996.

4. Health, Clothing and Sanitation of personnel:

4.1 All personnel shall undergo medical examination prior to employment and shall be free from infectious and contagious diseases. Thereafter they should be medically examined periodically at least once a year. Records shall be maintained thereof.

4.2 All personnel, prior to and during employment, shall be trained in practices which ensure personal hygiene. A high level of personal hygiene shall be observed by all those engaged in the collection, processing, banking of umbilical cord blood.

4.3 All persons shall wear clean body coverings appropriate for their duties before entering the Processing Zone. Change Rooms with adequate facilities shall be provided prior to entry into any specific zone.

4.4 Smoking, eating drinking, is prohibited inside the Laboratory.

4.5 All personnel working in the Laboratory shall be vaccinated against Hepatitis B virus.

5 Requirements for Processing, Testing and Storage Areas for Umbilical cord blood stem cells

5.1 Separate enclosed areas specifically designed for the purpose and the workload shall be provided.

5.2 There shall be separate areas for designated work purposes, viz:

i. *Cord blood Reception*: Cord blood reception area with space for transient storage of units and physical examination shall have adequate facilities for registration, data entry and generation of bar-coded labels.

ii. *Cord blood processing area*: The room shall be clean and have an air handling System to provide a Class 10,000 environment. The room will house Class 100 biological safety cabinets for Umbilical cord blood processing. The temperature of the clean room shall be maintained 20 to 25°C and with a positive differential pressure of 10-15 pascals and Relative humidity of 50 - 60%

iii. *Haematology and Serology Laboratory*: The laboratory shall be equipped and utilized for the purpose of testing of Umbilical Cord Blood for ABO grouping and Rh Typing, Total Nucleated

Cell Count, Progenitor cell Count and viability test. The room shall be air-conditioned.

iv. *Transfusion Transmissible Disease Screening Laboratory:* The Laboratory shall be equipped and utilized for screening tests on maternal blood for infectious diseases viz. HIV I & II; Hepatitis B & C virus, syphilis and malaria. The room shall be air-conditioned.

v. *Sterility Testing Laboratory* : The laboratory shall be used for performing Sterility tests on Umbilical cord blood Unit. The premises may be classified depending on the testing method used. The room shall be air-conditioned.

vi. *HLA Typing Laboratory*: The Umbilical cord blood Unit shall have arrangements for HLA typing and genetic disease testing. In house testing can be done by providing a well departed Laboratory from the processing area for evaluation of possible genetic disease and HLA typing. The area shall have Class 100,000 environment and air conditioned.

vii. *Sterilization-cum-washing:* Appropriate facility shall be provided within the premises for proper washing and sterilization. This facility would be optional for Laboratories using entirely disposable items.

viii. *Records and Store Rooms:* There shall be designated record room(s) and store room(s). The access to record room shall be permitted only to authorized persons. The room will have adequate protective facilities as the documents and records are to be preserved for long years.

ix. *Cryogenic Storage room*: A minimum space of 200 sq feet shall be provided by the Licensee. The cryogenic storage room shall have provision for temperature monitoring of storage vessels, liquid nitrogen level in storage vessels and oxygen meter. The service space between each liquid nitrogen storage vessel, supply cylinders and connecting hose should be between 10 to 25 sq feet. Separate storage space for other accessories required shall be provided. The room shall be air-conditioned.

x. *General Storage area*: General storage area shall be provided to store all the consumables, under conditions deemed optimum for storage by manufacturers.

B. COLLECTION AND STORAGE OF PROCESSED UMBILICAL CORD BLOOD COMPONENT

1. *Collection:*

1.1 Umbilical cord blood specific for an individual will be collected after signing an agreement with the Parents, whose to be infant's Umbilical cord blood is to be collected, and the specific Processing, Testing and Storing Authority. Private and Public Umbilical Cord Blood Banking to have different agreements.

1.2 Umbilical cord blood shall be collected from hospitals, nursing homes, birthing centers and from any other place where a consenting mother delivers, under the supervision of the qualified Registered Medical Practitioner responsible for the delivery.

1.3 The cord blood shall be collected aseptically in a disposable PVC bag containing adequate quantity of sterile, pyrogen free anti-coagulant.

1.4 The Umbilical cord blood would be collected from a premises having a hygienic location to allow proper operation, maintenance and cleaning.

2. Transportation

2.1 Umbilical cord blood shall be transported from the birthing center to the designated laboratory under and as per procedure prescribed by the cord blood bank.
2.2 The Transportation procedure shall be validated to ensure optimum survival of the Stem Cells
2.3 The transportation temperature should be between 18 to 28°C.
2.4 The time period between Collection and processing shall not exceed 72 hours.

STORAGE:

a. The Umbilical cord blood shall be stored at room temperature between 20 to 25 °C in the processing area.
b. Samples pending tests for the Specific Transfusion Transmittable Infectious agents shall be stored in a segregated manner.

Note: - Maximum allowable temperature range shall be between 4 to 37 degrees Celsius, for the whole time period of transit. The effects, of deviation of transit temperature from the optimum, on the product shall be adequately explained by the licensee in the client education booklet.

C. PERSONNEL

Cord blood bank shall have following categories of whole time competent technical staff:-

1. *Medical Director*: The operation of cord blood bank shall be conducted under the active directions and supervision of a Medical Director who is a whole time employee and is possessing a Post Graduate degree in Medicine – MD (Pathalogy/Transfusion Medicine/Microbiology) and has experience / training in cord blood processing and Cryogenic Storage.
2. *Laboratory In-charge:* The laboratory in-charge shall have Post Graduate qualification in Physiology or Botany or Zoology or Cell Biology or Microbiology or Biochemistry or Life Sciences, or Graduate in Pharmacy and one year working experience in pathological laboratory licensed by the local health authority or any microbiology laboratory of a licensed drug manufacturing / testing unit and or experience / training in cord blood processing and cryogenic storage.
3. *Technical Supervisor (cord blood processing)* :- The technical supervisor shall have a:

    3.1 Degree in Physiology or Botany or Zoology, Pharmacy or Cell Biology or Bio Sciences or Microbiology or Biochemistry or Medical Laboratory Technology (M.L.T.) with minimum of three years of experience in the preparation of blood components and / or experience / training in cord blood processing and Cryogenic Storage, or

    3.2 Diploma in Medical Laboratory Technology (M.L.T) with five year's experience in the preparation of blood components. Experience / training in cord blood processing and Cryogenic Storage shall be essential.

4. *Cord Blood Bank Technician(s):*-The technicians employed shall have a:

    4.1 A Degree in Physiology or Botany or Zoology or Pharmacy or Cell Biology or Bio Science or Microbiology or Biochemistry or Medical Laboratory Technology (M.L.T.) with six months experience and or training in cord blood processing and cryogenic storage, or

    4.2 Diploma in Medical Laboratory Technology (MLT) with one year experience in the testing of blood and/or its components and / or experience / training in cord blood processing and Cryogenic Storage.

D. AIR HANDLING SYSTEMS

1. Air handling for sterile areas shall be different from those for other areas. The filter configuration in the air handling system shall be suitably designed to achieve the grade of air as given in the Table I. The environmental microbiological monitoring of clean areas shall be in accordance to the recommended limits given in Table II.
2. The Processing area shall be air-conditioned and fitted with HEPA Filters having Grade C (Class 10,000) environment as given in Table I.

3. The entire Processing would be done under a Biosafety hood conforming to Grade A (Class 100) Standard of Air Quality

TABLE I

AIR BORNE PARTICULATE CALSSIFICATIONS FOR MANUFACTURE OF STERILE PRODUCTS

Grade	Maximum number of permitted particles per cubic metre equal to or above			
	At rest (b)		In Operation (a)	
A	0.5 µm	5 µm	5 µm	5 µm
B (a)	3500	0	3500	0
C (a)	3,50,000	2000	35,00,000	20,000
D (a)	35,00,000	20,000	Not defined	Not defined

TABLE II

RECOMMENDED LIMITS FOR MICROGIOLOGICAL MONITORING OF CLEAN AREAS "IN OPERATION"

Grade	Air Sample cfu/m^3	Settle Plates (dia 90 mm) cfu/2 hrs.	Contact plates (dia.55mm) cfu per plate	Glove points (five fingers) cfu per glove
A	< 1	<1	<1	<1
B	10	5	5	5
C	100	50	25	-
D	500	100	50	-

E. QUALITY CONTROL

Facilities shall be provided for Quality Control such as Haematological, Microbiological and Instrumental testing. Following duties shall be performed under the function of quality control :

1. To prepare detailed instructions for carrying out such tests and analysis
2. To approve or reject raw materials and consumables, used in any step, on the basis of approved specifications
3. Haematological Tests like Total Nucleated Cell Counts, Mononuclear Cell Count, Enumeration of the population of Stem Cells, Stem Cell viability shall be performed on samples of Processed Umbilical cord blood Unit
4. Microbiological Tests shall be done on Maternal Blood samples for freedom from Hepatitis B Surface Antigen, Hepatitis C Virus antibody, HIV I and II antibodies. Syphilis and Malaria. Bacterial and Fungal Culture shall be done on the Umbilical Cord Blood Samples.
5. Instruments which would be used to process test and store the UCB unit would be validated before commissioning and calibrated from time to time to check their conformity to specific standards according to an approved and valid protocol.
6. The Environmental Monitoring of the Clean rooms would be done at periodic intervals according to an accepted and validated protocol.
7. All tests mentioned above shall be done in house except tests under item numbers 5, 6 and test for enumeration of Stem Cell Population, HLA typing and Genetic Disease Testing which may be outsourced to a competent third party.

F. SCREENING TESTS

1. The maternal Blood sample shall be tested for
   - i. Hepatitis B
   - ii. Hepatitis C
   - iii. HIV 1 & 2
   - iv. Syphilis
   - v. Malaria
2. The Umbilical Cord Blood shall be tested for
   - i. Total Nucleated Cell count
   - ii. Total Mononuclear Cell Count
   - iii. Progenitor Cell (CD34+) enumeration
   - iv. Cell Viability
   - v. ABO Group and Rh Type
   - vi. Sterility as regards Bacterial and Fungal contamination status
   - vii. HLA Matching (Only for allogenic Cord Blood Units)

G. STORAGE

1. The Umbilical cord blood shall be cryopreserved using a controlled rate freezing or equivalent validated procedures. The frozen storage shall be at minus 196°C and shall not be warmer than minus 150°C.
2. There will be no shelf life for this class of product.

H. REFERENCE SAMPLES

1. At least two reference samples shall be collected from cord blood unit product prior to cryopreservation and stored at minus 196°C and shall not be warmer than minus 150°C.
2. At least one additional reference sample shall be stored at minus 76 °C or colder for the purposes other than viability analysis.

I. LAELLING

1. Initial Label placed during collection shall specify:

   i. Human Umbilical Cord Blood
   ii. Approximate Volume or weight of contents in the collection bag (UCB + Anticoagulant)
   iii. Mother's Name
   iv. Place of Collection
   v. Date & Time of collection
   vi. Collected by
   vii. To be Labelled in bold, "ROOM TEMPERATURE ONLY- DO NOT REFRIGERATE, DO NOT IRRADIATE"

2. Label at completion of processing and before issue - Cryogenic Storage Label (Statutory label) shall indicate the following
   i. Name of Product :- Human Progenitor Cell(HPC) – Cord Blood
   ii. Volume or weight of contents
   iii. Percentage of Cryoprotectant (DMSO)
   iv. Percentage of any other additive/preservant
   v. Date of Collection (Birth) .....
   vi. Date of Processing.....
   vii. Name of Manufacturer :- .....
   viii. To be stored continuously not less than, – 196°C
   ix. Unique Traceability Number and / or BAR Code.

3. Issue Label at the time of release of Cord Blood Unit shall indicate the following:

   i. Name of manufacturer
   ii. Licence Number
   iii. All details of the Cryogenic Storage Label
   iv. The results of Total nucleated Cells, Progenitor Cell percentage (CD34+),Viability.
   v. Results of Transfusion Transmittable diseases testing on maternal blood.
   vi. ABO Group and Rh Type

vii. Date of processing
viii. Result of HLA typing (allogenic)
ix. Statement "Properly identify intended Recipient and Product"
x. A statement indicating that leukoreduction filters should not be used
xi. Statement "Do not irradiate".
xii. Name and address of receiving hospitals

J. RECORDS / DOCUMENTATION

1. The Licensee shall maintain the following records
   i. Client/donor enrollment/agreement record
   ii. Collection of unit and transportation record
   iii. Master record of stored unit
   iv. HLA Matching record
   v. Unit Release Register
   vi. Stock Register for Blood Collection Bag Cryoprotectant and Preservant, RBC Sedimentation Enhancer
   vii. Stock Register for Diagnostic Kits, Reagents and other consumables
   viii. Record on feedback after use of cord blood / Adverse reaction record
   ix. List of Standard Operating Procedures:
2. Standard Operating Procedures for the following shall be maintained:
   i. Umbilical cord blood collection
   ii. Transportation of the collected Umbilical cord blood unit
   iii. Processing of Umbilical cord blood unit
   iv. Cryogenic Storage of processed Umbilical cord blood unit
   v. Testing of maternal blood for transfusion transmittable infections
   vi. Testing of Umbilical cord blood for ABO Grouping and Rh Typing
   vii. Testing of Umbilical cord blood unit for Total Nucleated Cell Count, Mononuclear Cell Count, Progenitor Cell (CD34+) enumeration, and Viability.
   viii. Testing of Umbilical cord blood stem cell Unit for Sterility
   ix. Disposal of bio medical waste
   x. Dispensation of Umbilical cord blood unit.
   xi. Preventive maintenance Protocol for all Instruments
   xii. Acceptance / Rejection procedure of consumables
   xiii. Environment monitoring of classified areas.

K. CORD BLOOD RELEASE

1. There shall be designated area with adequate space for procedures and records related to cord blood unit selection and release.
2. The cord blood bank shall obtain written or electronic request from the transplant physician or designee for shipment of the cord blood unit.
3. Accompanying documentation at the time of issue from the cord blood bank shall include indications, contra-indications, caution, instruction for handling and use of the cord blood unit including short-term storage and preparation for transplantation.
4. Procedure for transportation of cryopreserved cord blood Unit within the facility shall be designed to protect the integrity of the unit and the health and safety of the personnel.
5. Cryopreserved cord blood unit stored at -150°C or colder shall be transported in a liquid nitrogen cooled dry shipper that contains adequate absorbed liquid nitrogen and has been validated to maintain temperature below -150°C for at least 48 hours beyond the expected time of arrival at the receiving facility."

[F. No. X. 11014/2/2008-DFQC]

VINEET CHAWDHRY, Jt. Secy.

Foot Note : The Principal rules were published in the Gazette of India vide notification No. F-28-10/45H (i), dated 21st December, 1945 and was last amended vide notification G.S.R. 45(E), dated 21-1-2010.

Printed by the Manager, Government of India Press, Ring Road, Mayapuri, New Delhi-110064
and Published by the Controller of Publications, Delhi-110054.