



MINISTRY OF HEALTH MALAYSIA

MOH/P/PAK/131.07 (BP)



NATIONAL STANDARDS FOR CORD BLOOD BANKING AND TRANSPLANTATION

JANUARY 2008



MEDICAL DEVELOPMENT DIVISION,
MINISTRY OF HEALTH, MALAYSIA





Y.BHG. TAN SRI DATUK
DR. HJ. MOHD ISMAIL
MERICAN

Bone marrow transplantation has become an established procedure in the treatment of a variety of haematological malignancies, solid tumours and bone marrow aplasia. In the absence of the bone marrow from the family and HLA-compatible unrelated donors, umbilical cord blood, which is also a rich source of hematopoietic stem cells, can be used for transplantation.

Stem cell technology, especially from cord blood, has gained national interest in view of its potential in effectively treating several genetic, hematologic, immunologic, metabolic and oncologic disorders. Cord Blood Banks around the world face a constant challenge in providing high quality products and effective services towards improving the quality of lives of patients who depend on bone marrow transplantation for survival. Malaysia will face major challenges over the next few years in supplying stem cells for treatment of patients. The establishment of cord blood banks in Malaysia will provide stem cells from all ethnic groups. For the Malays, this may be the only source of stem cell.

The publication of these national standards on cord blood banking transplantation is timely, to give guidance and ensure consistency in quality of the stem cells derived from

cord blood for the purpose of transplantation. These standards are in accordance with international best practices.

Both Private and Public Cord Blood Banks in Malaysia will have to adhere to these standards in carrying out their respective operations.

The Ministry of Health continues to provide stewardship in providing good quality healthcare services and will continue to support other healthcare providers in ensuring that all Malaysians enjoy high quality health care services.



TAN SRI DATUK DR. HJ. MOHD ISMAIL MERICAN
Director General of Health, Malaysia



Y.BHG. DATO' DR.
NOORIMI HJ. MORAD

The health delivery system of the country has progressed at a tremendous pace in line with the advancement of medical knowledge and technology, including the use of cord blood in management of certain medical conditions. Cord blood is a rich source of stem cells which have the capability of differentiating into other types of cells needed by the body.

One of the Expert Committees set up under the National Transplantation Council is the National Stem Cell Committee, responsible for drawing up the National Standards for Cord Blood Banking. Cord blood banking is a process of saving the cord blood from the umbilical cord after the delivery of a newborn. The process involves collection, processing, storage and issue of stem cells from cord blood for bone marrow transplantation.

These National Standards for Cord Blood Banking shall ensure the welfare, safety and confidentiality of the parties involved, namely the mothers, the newborns and the recipients. To ensure that the standards are holistic and comprehensive, experts in related fields and academicians are involved in drawing up the standards.

These standards are necessary to ensure the production of quality stem cells for the benefit of patients. It places significant responsibility on the cord blood bank for implementation of systems and process that ensures high quality cord blood units.

A handwritten signature in black ink, consisting of several vertical and diagonal strokes, positioned above the name of the signatory.

DATO' DR. NOORIMI HJ MORAD

Deputy Director General of Health, Malaysia (Medical)



Dato' Dr Yasmin Ayob

Stem cells transplantation has now been recognized as a valuable form of therapy for a variety of haematological and non haematological conditions. Cord blood has been shown to be abundant in stem cells and is recognized as a valid alternative to other sources of haemopoietic progenitor cells for marrow replacement therapy.

The implementation and management of cord blood banks has the potential to provide high quality cord blood units for treatment of patients in need of haemopoietic reconstitution. The approaches are partially derived from those developed in transfusion medicine. However Cord Blood banking requires more additional process and procedures because of the metabolic nature and long-term storage of the stem cells. This includes not only additional testing but a quality system to ensure faultless traceability and viability of the cryopreserved cells to be stored for many years.

Therefore specific requirements including organisation, personnel, facility, equipment, supplies and reagent, process control, safety, testing, inspection, documents and records are included in The National Standards for Cord Blood

Banking. Strict unavoidable requirements are included to ensure the collection and storage of standardized high quality cord blood units for transplantation.

The Working Group for the National Standards for Cord Blood Banking and Transplantation were faced with a challenging task as the field of cord blood banking is evolving rapidly. To facilitate the development of these Standards the Working Group had referred to established international and other national standards which are based on published scientific literature. It is hoped that these Standards would contribute significantly to the success of the transplantation programme in the country.

A handwritten signature in black ink, appearing to read 'Yasin Ayob', with a large, stylized loop at the beginning.

DATO' DR YASMIN AYOB

Chairman of the Working Group National Standards
for Cord Blood Banking and Transplantation

WORKING GROUP FOR THE NATIONAL STANDARDS FOR CORD BLOOD BANKING AND TRANSPLANTATION

Advisors : Dato' Dr Noorimi Hj Morad
Deputy Director General of Health Malaysia
(Medical)
Ministry of Health Malaysia

Dato' Dr. Azmi Shapie
Director
Medical Development Division
Ministry of Health Malaysia

Chairman : Dato' Dr. Yasmin Ayob
Director
National Blood Centre

Secretariat : Dr. Norhanim Asidin
Deputy Director II
National Blood Centre

Pn. Zuraidah Yusoff
Senior Scientific Officer
National Cord Blood Bank
National Blood Centre

Dr. Noor Aziah Zainal Abidin
Senior Principal Assistant Director
O&G / Paediatric Services Unit
Medical Development Division
Ministry of Health Malaysia

Dr. Sabrina Che Ab Rahman
Senior Principal Assistant Director
Diagnostic / Clinical Support Services Unit
Medical Development Division
Ministry of Health Malaysia

Dr. Jafanita Jamaludin
Assistant Director
O&G / Paediatric Services Unit
Medical Development Division
Ministry of Health Malaysia

Dr. Hirman Ismail
Assistant Director
Surgical / Emergency Services Unit
Medical Development Division
Ministry of Health Malaysia

Members : Dr Teng Seng Chong
Senior Deputy Director
Medical Development Division
Ministry of Health Malaysia

Datin Dr Rusnah Hussin
Deputy Director
Medical Professional Development Section
Medical Development Division
Ministry of Health Malaysia

Datin Dr. Rugayah Bakri
Deputy Director
Health Technology Assesment Section
Medical Development Division
Ministry of Health Malaysia

Dr. Shahnaz Morad
Director
Institute for Medical Research

Dr. Mohd Farouk Abdullah
O&G Consultant & Head of O&G Department
Hospital Tengku Ampuan Rahimah, Klang

Dr. Ravichandran Jeganathan
O&G Consultant & Head of O&G Department
Hospital Sultanah Aminah, Johor Bahru

Dr. Roshida Hassan
Consultant Pathologist
Hospital Kuala Lumpur

Dr. Zubaidah Zakaria
Head of Haematology Division
Institute for Medical Research

Dr. Zubaidah Wahab
Consultant Pathologist
Hospital Sg. Buloh

Dr. Jasbir S. Dhaliwal
Research Officer
Allergy and Immunology Research Centre
Institute for Medical Research

Prof. Dr. Cheong Soon Keng
Haematologist
International Medical University

Prof Gan Gin Gin
Haematologist
University of Malaya

Dr. Ahmad Razid Salleh
Senior Principal Assistant Director
Private Medical Practice Control Section
Medical Practice Division
Ministry of Health Malaysia

Dr. Md Khadzir Sheikh Ahmad
Senior Principal Assistant Director
Private Medical Practice Control Section
Medical Practice Division
Ministry of Health Malaysia

Dr. Afifah Hassan
Consultant Pathologist
Head, Immunogenetic & Histocompatibility Unit
National Blood Centre

Cik Zuliza Mohamed
Senior Scientific Officer
Immunogenetic & Histocompatibility Unit,
National Blood Centre

CONTENT

Foreword By Director General Of Health Malaysia	1-2
Foreword By Deputy Director General Of Health Malaysia (Medical)	3-4
Foreword By Chairman Of The Working Group For The National Standards For Cord Blood Banking And Transplantation	5-6
Working Group For The National Standards For Cord Blood Banking And Transplantation	7-9
Content	11-13
Section 1 - Introduction	15
Section 2 - Definition Of Cord Blood Bank	16
Section 3 - Organizational Structure	17-18
Section 4 - Facilities And Safety	19
Section 5 - Equipments, Supplies And Reagents	20-21
Section 6 - Cord Blood Bank Operational Standards	
6.1 Cord Blood Bank Personnel Requirements	23
6.2 Policies And Standard Operating Procedures	23-26
6.3 Cord Blood Bank Operations	26-28
6.4 Equipment	28
6.5 Supplies and Reagents	28

6.6	Labelling	28-30
6.7	Documents and Records Requirements	30-33

Section 7 - Cord Blood Donor Management And Collection

7.1	Cord Blood Collection Personnel Requirements	35
7.2	Cord Blood Collection Facilities	35-36
7.3	Policies and Standard Operating Procedures	36-37
7.4	Maternal and Infant Donor Evaluation	37-38
7.5	Informed Consent	38-40
7.6	Cord Blood Collection Procedures	40-41
7.7	Transportation of Non-Cryopreserved Cord Blood Units Between Cord Blood Collection Facility and the Cord Blood Processing Facility	41-42

Section 8 - Cord Blood Processing Standards

8.1	Cord Blood Bank Processing Facility Personnel Requirements	43
8.2	Cord Blood Bank Processing Facility Requirements	43-44
8.3	Policies and Standard Operating Procedures	44-45
8.4	Cord Blood Processing	45-46
8.5	Reference Samples	46-47
8.6	Cryopreservation	47-48
8.7	Conditions for Storage	48-49
8.8	Monitoring and Alarm Systems	49-50
8.9	Inventory Management Systems	50
8.10	Disposal	50
8.11	Quality Management Program	50
8.12	CBU Assays	50-52
8.13	Maternal Testing	52-53

Section 9 - Cord Blood Selection And Release Standards

9.1	Cord Blood Bank Facility Requirements	55
9.2	General Requirements for Unrelated Allogeneic, Directed Allogeneic and Autologous Cord Blood Units	55-56

9.3	Cord Blood Selection for Unrelated Allogeneic, Directed Allogeneic And Autologous Cord Blood Transplantation	56-57
9.4	Cord Blood Selection for Directed Allogeneic and Autologous Cord Blood Transplantation	57
9.5	Cord Blood Unit Release	57-58
9.6	Transportation of Cryopreserved Cord Blood Units	58-59
9.7	Documents and Records Requirements	59-60
9.8	Clinical Outcome Data	60

Section 10 - Cord Blood Bank Quality Management

10.1	Quality Management Program	61-63
10.2	Personnel Requirements	63
10.3	Documents and Records Requirements	63-65
10.4	Monitoring, Quality Assessments and Audits	65-66
10.5	Errors, Accidents, Biological Product Deviations, Adverse Events, Variances and Complaints	66-68
10.6	Validation and Qualification Requirements	68
10.7	Equipment, Supplies and Reagents	68-70
10.8	Inventory Management	70
10.9	Process Control	70-71
10.10	Identification, Labelling and Product Tracking	71
10.11	Outcome Analysis	71
10.12	Facilities And Safety	71-72
10.13	Infant Donor Eligibility Determinations	72
	National Stem Cell Committee	73
	Glossary	75-86
	Terminology	
	Definitions	
	References	87
	Acknowledgement	88
	Appendix 1	89-90

- 1 • Introduction
- 2 • Definition of Cord Blood Bank
- 3 • Organizational Structure
- 4 • Facilities and Safety
- 5 • Equipment, Supplies and Reagents





SECTION 1: INTRODUCTION

The National Standards for Cord Blood Banking and Transplantation were developed by consensus and collaboration by individual members within the Ministry of Health Malaysia, universities and professionals active in blood and bone marrow transplantation in Malaysia. These Standards are for Cord Blood Collection, Processing, Testing, Banking, Selection and Release. They do not address the collection, processing and administration of erythrocytes, mature granulocytes, platelets, plasma or plasma-derived products intended for transfusion support.

The main objective of these Standards is to provide guidelines to ensure good quality medical and laboratory practices in cord blood banking. Every effort has been made to incorporate sound recommendations fostering quality medical and laboratory practices. Attempts have also been made to ensure these Standards conform to the existing worldwide clinical practices. In all cases, personnel must follow all applicable national regulations and directives. These Standards are designed to provide minimum guidelines for facilities and individuals performing cord blood collection, processing, testing, banking, selection and release or providing support services for such procedures. Each Cord Blood Bank and individual should analyze its practices and procedures to determine whether additional Standards apply. Individual facility may exceed these Standards as deemed appropriate by the responsible personnel. These Standards will be reviewed and revised as and when necessary.



DEFINITION OF CORD BLOOD BANK

SECTION 2:

- 2.1 Cord Blood Bank (CBB) means any premises used or intended to be used for the collection, processing, testing, banking, selection and release of CBU.
- 2.2 Cord Blood Unit (CBU) means the nucleated cells including stem and hematopoietic progenitor cells harvested from placental and umbilical cord blood vessels from a single placenta after the umbilical cord has been clamped. Unless otherwise specified, the term CBU in this document refers to all CBU regardless of method of collection or intended use.



ORGANIZATIONAL STRUCTURE

SECTION 3:

- 3.1 The organization shall have all participating facilities and service including, Collection Facilities, Processing Facilities and Testing Laboratories which shall be indicated in the organizational chart.
- 3.2 The key personnel shall include at least the following:
 - 3.2.1 CBB Director
 - 3.2.1.1 The CBB Director shall be a registered medical practitioner, with training and experience in immunogenetics of transplantation, basic or clinical immunology, immunohematology, blood or tissue banking, or cryobiology. The CBB Director has final responsibility for the CBB scientific and clinical performance and its overall compliance with these Standards. The CBB Director should participate regularly in educational activities related to the field of hematopoietic progenitor cell collection, processing, transplantation and/or Cord Blood banking of the collection procedures and of the CBB Processing Facilities, and compliance of the Collection and Processing Facilities with these Standards. The CBB Director shall participate regularly in educational activities related to the field of donor safety, CB banking, and/or hematopoietic progenitor cell collection, processing, and transplantation.
 - 3.2.2 CBB Collection Manager
 - 3.2.2.1 There shall be a CBB Collection Manager who is a registered medical practitioner who is responsible for the medical aspects of cord blood collection procedures and compliance of the Cord Blood Collection Facility with these Standards. The CBB Collection Facility Manager

shall participate regularly in educational activities related to the field of donor safety, cord blood banking and/or hematopoietic progenitor cell collection, processing, and transplantation.

3.2.2.2 Where there are collection facilities that are not staffed by the CBB Personnel, there shall be a designated individual who is responsible for the daily operation of the Collection Facility and communication with the CBB Director.

3.2.2.3 At Collection Facilities where individual healthcare practitioners perform CB collections, the individual healthcare practitioner may be the contact person.

3.2.3 CBB Processing Laboratory Manager.

3.2.3.1 There shall be a CBB Processing Laboratory Manager who is an individual with a relevant, qualified by training or experience for the scope of activities carried out in the CBB Processing Facility. The CBB Processing Laboratory Manager is responsible for all operational aspects of all procedures related to receipt, testing, processing, cryopreservation, storage, release for shipment of cord blood units, and administrative operations of the CBB Processing Laboratory, including compliance with these Standards. The CBB Processing Laboratory Manager shall participate regularly in educational activities related to the field of cord blood banking and/or hematopoietic progenitor cell collection, processing and transplantation.

3.2.3.2 The CBB Processing Laboratory Manager may also serve as the CBB Director if appropriately credentialed.

3.2.4 CBB Quality Manager.

3.2.4.1 There shall be a CBB Quality Manager approved by the CBB Director. Section 10.1.3 also applies.

3.3.3 The CBB shall have adequate staff with appropriate qualifications and training. Continuing education and continued competency for the performance of all assigned operations shall be documented for all staff.



FACILITIES AND SAFETY

SECTION 4:

- 4.1 The CBB space shall be of adequate size, construction and location to maintain safe operations, prevent contamination and ensure orderly handling.
- 4.2 Environmental conditions for temperature, humidity, ventilation and air filtration and classification shall be defined and, if appropriate, monitored.
- 4.3 Separate areas shall be maintained for processing and storage of products to prevent mix-ups, product contamination and cross-contamination.
- 4.4 The CBB shall be secured to prevent the admittance of unauthorized individuals.
- 4.5 Dedicated CBB Facilities shall be maintained in a clean, sanitary and orderly manner to prevent introduction, transmission or spread of communicable disease and to facilitate operations and cleaning.
- 4.6 There shall be procedures for biological and chemical safety as appropriate including:
 - 4.6.1 Communicable Disease Agents.
 - 4.6.2 Chemical Hygiene.
 - 4.6.3 Hand Hygiene.
 - 4.6.4 Fire Safety.
 - 4.6.5 Power Failures.
 - 4.6.6 Liquid Nitrogen.



EQUIPMENT, SUPPLIES AND REAGENTS

SECTION 5:

- 5.1 The CBB shall have adequate and appropriate equipments for all procedures performed to ensure safety and quality of the CBU.
 - 5.1.1 All equipment shall be identified and records maintained, including manufacturer's name, serial number or other identifier, manufacturer's instructions, equipment location and use of each piece of equipment, including the identification of each CBU for which the equipment was used.
 - 5.1.2 Calibration.
 - 5.1.2.1 Equipment shall be tested, calibrated and validated on a regularly scheduled basis as recommended by the manufacturer or at a minimum annually.
 - 5.1.2.2 Calibration acceptance criteria shall be defined.
 - 5.1.2.3 Records of the dates and copies of calibration results shall be maintained.
 - 5.1.3 Maintenance and repairs.
 - 5.1.3.1 Equipment shall be maintained in a clean and orderly manner and located so as to facilitate cleaning and maintenance according to established schedules.
 - 5.1.3.2 Records shall be maintained of the maintenance schedule, maintenance performed and damage, malfunction, modification or repair to equipment.

5.1.4 Cleaning and sanitation.

5.1.4.1 Equipment shall be cleaned and sanitized according to established schedules.

5.1.4.2 Records of equipment cleaning and sanitation shall be maintained.

5.1.5 Inspections.

5.1.5.1 Equipment shall be routinely inspected for cleanliness, sanitation and calibration and to ensure adherence to applicable equipment maintenance schedules.

5.2 The CBB shall have procedures to address management of critical supplies and reagents used in the collection, processing and/or storage of CBU.

5.2.1 Critical reagents and supplies shall be verified to function as expected and to meet specifications designed to prevent the spread of communicable disease.

5.2.2 Approved suppliers for all critical reagents and supplies shall be identified and utilized.

5.2.3 Records of receipt, inspection, verification, acceptance and storage of supplies and reagents shall be maintained.

6 • Cord Blood
Bank Operational
Standards





CORD BLOOD BANK OPERATIONAL STANDARDS

SECTION 6:

6.1 CORD BLOOD BANK PERSONNEL REQUIREMENTS

- 6.1.1 The CBB Director has final responsibility for the CBB scientific and clinical performance and its overall compliance with these Standards. The CBB Director should participate regularly in educational activities related to the field of hematopoietic progenitor cell collection, processing, transplantation and/or CB banking. Section 3.2.1 applies
- 6.1.2 There shall be a CBB Collection Manager. Section 3.2.2 applies.
- 6.1.3 There shall be a CBB Processing Laboratory Manager. Section 3.2.3 applies.

6.2 POLICIES AND STANDARD OPERATING PROCEDURES

- 6.2.1 The CBB shall have clearly written policies and Standard Operating Procedures that are precise and unambiguous and address all aspects of the operation.
 - 6.2.1.1 Each individual Standard Operating Procedures shall include:
 - 6.2.1.1.1 An appropriate title.
 - 6.2.1.1.2 A standardized format for procedures, including worksheets, reports and forms.
 - 6.2.1.1.3 A standardized system of numbering.
 - 6.2.1.1.4 The objective addressed.
 - 6.2.1.1.5 The personnel responsible for its execution.

- 6.2.1.1.6 The facility, equipment and supplies required.
 - 6.2.1.1.7 The expected range of results, if applicable.
 - 6.2.1.1.8 A reference section listing appropriate literature, if applicable.
 - 6.2.1.1.9 Examples of current worksheets, forms, reports and labels, where applicable.
 - 6.2.1.1.10 The date(s) of initial implementation and the signature of the CBB Director.
 - 6.2.1.1.11 The date of review or revision and the signature of the CBB Director or designee.
- 6.2.1.2 There shall be policies and Standard Operating Procedures to cover at least the following CBB operations:
- 6.2.1.2.1 Preparation, approval, implementation and revision of Standard Operating Procedures.
 - 6.2.1.2.2 Donor recruitment, maternal and infant donor screening, collection criteria and consent.
 - 6.2.1.2.3 Maintenance of linkage of the CBU to the infant donor and the recipient or the final distribution of the CBU.
 - 6.2.1.2.4 CBU collection, storage and transport to the CBB Processing Laboratory Facility.
 - 6.2.1.2.5 Cord blood processing, cryopreservation and storage.
 - 6.2.1.2.6 Documentation of who performs each steps from collection to final disposition of the CBU.
 - 6.2.1.2.7 Labeling of the CBU, reference samples and associated documents.
 - 6.2.1.2.8 Communicable disease testing, HLA typing, testing for hemoglobinopathies and other testing.
 - 6.2.1.2.9 Storage of maternal and CBU samples for testing.

- 6.2.1.2.10 Notification of mothers or their responsible physicians of positive or indeterminate communicable disease and/or genetic test results.
- 6.2.1.2.11 Search, selection and release of CBU.
- 6.2.1.2.12 Quality management. Section 10 applies.
- 6.2.1.2.13 Data management.
- 6.2.1.2.14 Confirmatory of HLA typing of the CBU.
- 6.2.1.2.15 Personnel training and documentation of continued competency for the procedures performed.
- 6.2.1.2.16 Discard and disposal of CBU.
- 6.2.1.3 When an electronic system is used, there shall be validated procedures for:
 - 6.2.1.3.1 System development.
 - 6.2.1.3.2 Prospective validation of the system(s), including hardware, software and database.
 - 6.2.1.3.3 Installation of the system(s).
 - 6.2.1.3.4 Training and continuing competency of personnel in use of the system(s).
 - 6.2.1.3.5 Backup of the electronic record system(s) on a regular schedule.
 - 6.2.1.3.6 Electronic record entry, verification and revision including review of data before final acceptance.
- 6.2.2 Policies and standard operating procedures management requirements.
 - 6.2.2.1 All policies and standard operating procedures shall comply with these Standards.
 - 6.2.2.2 The policies and Standard Operating Procedures shall be reviewed and approved by the CBB Director or designee prior to implementation, signed and dated at least annually and after each revision.

- 6.2.2.3 The CBB Director or designee shall review all deviations or variances from the CBB policies and/or Standard Operating Procedures or from these Standards. This review shall be documented.
- 6.2.2.4 The appropriate staff shall read new and revised policies and Standard Operating Procedures prior to performing the task. This review and associated training shall be documented.

6.3 CORD BLOOD BANK OPERATIONS

- 6.3.1 The responsibilities of each CBB Collection Facility, CBB Processing Facility and Registry as they relate to the CBB shall be clearly defined and documented.
- 6.3.2 The CBB shall be responsible for all components of the CBU production process, including at least donor recruitment; maternal and infant donor screening, testing and eligibility determination; and CBU collection, processing, testing, storage and release from inventory. The CBB shall ensure that all CBU are collected using Standard Operating procedures that meet these Standards.
 - 6.3.2.1 For collection of unrelated donor CBU, there shall be an established relationship between the collection facility and the CBB such that the CBB ensures implementation of and compliance with its QM Program and Standard Operating Procedures for obtaining and documenting informed consent, maternal and infant donor screening and testing, completion of medical history and the collection, labeling and shipment of the CBU and maternal samples.
 - 6.3.2.2 For collection of directed allogeneic or autologous CBU, the CBB shall have a contract with the infant donor family and shall have communicated with the collecting physician, midwife or either healthcare professional. the CBB shall provide the appropriate policies and standard operating procedures for collection, labeling and shipment of the CBU and maternal samples and shall monitor the quality of the CBU collections through its QM Program.
- 6.3.3 The CBB shall utilize an HLA testing laboratory that participate and scores well in QA Program and has accreditation recognized either by the American Society of Histocompatibility and Immunogenetics (ASHI) or, European Foundation for Immunogenetics (EFI) or, Australian and South East Asian Tissue Typing Association or a similar organization.

6.3.4 All laboratories utilized by the CBB for testing of mother and infant donor samples shall be certified to perform such testing.

6.3.4.1 When external laboratories are used for any aspect of CBU or sample testing, the CBB shall maintain a record of all samples sent to such laboratories, including the identifiers, results, date sent and date results are received.

6.3.5 Confidentiality

6.3.5.1 There shall be a system to maintain the confidentiality of the infant donor, recipient and their respective families according to these Standards and Ethics Committee. (Refer to National Organ, Tissue and Cell Transplantation Policy)

6.3.5.2 Confidential information shall be secured such that data are available only when needed and only to authorized personnel.

6.3.5.3 The CBB shall have written policies and Standard Operating Procedures for circumstances where infant donor, mother or infant donor's legal guardian and appropriate medical personnel could be contacted.

6.3.6 Clinical Outcome Data Requirements.

6.3.6.1 The CBB shall maintain sufficient critical outcome data to assure that the procedures in use in the CBB consistently provide a safe and effective product.

6.3.6.2 For unrelated allogeneic, directed allogeneic and autologous CBU, data shall include neutrophil and platelet engraftment or recovery and survival rates.

6.3.6.3 For allogeneic CBU only, data should include chimerism and Graft-Vs-Host-Disease results.

6.3.7 Ethics Committee Requirements

6.3.7.1 In compliance with these Standards, the CBB shall have formal review of investigational protocols and maternal consent for CB banking and related activities by a mechanism that is approved by the Ministry of Health Malaysia.

- 6.3.7.2 The CBB shall maintain documentation of all its research protocols, Ethics Committee approvals, investigational new drug or device exemptions, annual reports and any adverse events.

6.4 EQUIPMENT

- 6.4.1 Equipment used shall not adversely affect the viability of the CBU and shall not permit the introduction of adventitious agents or the transmission or spread of communicable disease. Section 5 applies.

6.5 SUPPLIES AND REAGENTS

- 6.5.1 Supplies and reagents used shall not adversely affect the viability of the CBU and shall not permit the introduction of adventitious agents or the transmission or spread of communicable disease. Section 5 applies.
- 6.5.2 Supplies and reagents that come into contact with the CBU shall be sterile.
- 6.5.3 Supplies and reagents used for CB collection, processing or cryopreservation whenever possible, shall be sterilized.
- 6.5.4 Certificates of analysis shall be obtained and maintained on file for all critical reagents.

6.6 LABELLING

- 6.6.1 Labelling Operations.
 - 6.6.1.1 Labelling operations shall be conducted in a manner adequate to prevent mislabeling of CBU and reference samples.
 - 6.6.1.2 There shall be a bar-coding or equivalent human and machine-readable system of identification for the maternal samples, the CBU reference samples and associated documents.
 - 6.6.1.3 The labelling operation shall include at least the following controls:
 - 6.6.1.3.1 Labels shall be held upon receipt from the manufacturer pending review and proofing against an approved copy to ensure accuracy regarding identity, content, and conformity.
 - 6.6.1.3.2 Stocks of unused labels representing different components shall be stored and maintained in a manner to prevent errors. Stocks of obsolete labels shall be destroyed.

- 6.6.1.3.3 A system of checks and verification in labelling procedures shall be used to prevent errors in transferring information to labels.
- 6.6.1.3.4 All labelling shall be clear and legible and printed using indelible ink.
- 6.6.1.3.5 The labelling system shall be validated as reliable for storage under the conditions in use.
- 6.6.1.4 When the label has been affixed to the bag, a sufficient area of the bag shall remain uncovered to permit inspection of the contents.
- 6.6.2 Identification
 - 6.6.2.1 There shall be a written policy for labeling of the CBU, reference samples and associated documents.
 - 6.6.2.2 Each CBU shall be assigned a unique numeric or alphanumeric identifier by which it will be possible to relate any CBU to its maternal and infant data, delivery information, family history, test results, and to all records describing the handling and final disposition of that CBU.
 - 6.6.2.3 Facilities may designate an additional or supplementary unique numeric or alphanumeric identifier to the CBU or to a test-aliquot. supplementary identifiers shall not obscure the original identifier. No more than one supplementary identifier shall be visible on a CBU bag.
- 6.6.3 The information provided on the label by the initial Collection Facility shall be maintained indefinitely as part of the CBU record.
- 6.6.4 Label Content.
 - 6.6.4.1 Each label shall include at least the elements detailed in Appendix I, Cord Blood Unit Labeling Table.
 - 6.6.4.2 Minimally, the partial label shall be present on the CBU during all stages of processing.
 - 6.6.4.3 Any CBU bag bearing a partial label shall be accompanied by the full information in Appendix I attached securely to the CBU on a tie tag or closed in a sealed package.

6.6.5 Documentation of donor eligibility shall accompany the CBU at distribution and shall include:

6.6.5.1 A statement that the donor has been determined to be eligible or ineligible based on the results of donor screening and testing.

6.6.5.2 A summary of records used to make donor eligibility determination in compliance with these Standards including:

6.6.5.2.1 Identification of the laboratory performing communicable disease testing.

6.6.5.2.2 A listing and interpretation of the results of all communicable disease screening and testing performed.

6.6.5.2.3 The name of establishment that made the donor eligibility determination.

6.7 DOCUMENTS AND RECORDS REQUIREMENTS

6.7.1 General Record Requirements.

6.7.1.1 Records of each CBU shall be made concurrently with each stage of the CB collection, processing, testing, banking, selection, release, transplantation and/or disposal; identify the person immediately responsible for each step; and include appropriate dates and times to provide a complete history of the work performed and to relate the records to a particular unit.

6.7.1.1.1 Records shall be as detailed as necessary for a clear understanding by a person experienced in CBB procedures.

6.7.1.2 Records pertinent to the CBU shall be reviewed by the CBB Director and/or by the CBB Processing Facility Director or designee.

6.7.1.3 Records shall be available at the CBB or Collection Facility from which to determine that the lot number, expiration date and manufacturer of supplies and reagents used for the collection and processing of each CBU.

6.7.1.4 A record management system shall be established and maintained to assure protection, preservation and ready retrieval of records.

6.7.2 CBB records shall be maintained indefinitely including the following:

6.7.2.1 Infant donor and parental records.

6.7.2.1.1 Mother's full name, address and neonatal delivery date and if available, infant donor's full name and address and father's full name and address.

6.7.2.1.2 Medical history of the genetic mother, the birth mother and the medical history of the genetic father if available.

6.7.2.1.3 Copies of consent forms.

6.7.2.1.4 Results of maternal screening, maternal testing and results of infant donor testing if performed.

6.7.2.1.5 Records of physical assessment of the mother and infant donor.

6.7.2.1.6 Records of maternal or infant donor adverse reactions, complaints and reports, including results of all investigations and follow-up.

6.7.2.2 CBU records.

6.7.2.2.1 Identity of all facilities and personnel involved in the collection, processing, testing, banking, selection and release of the CBU.

6.7.2.2.2 CBU processing worksheets.

6.7.2.2.3 Supplies and reagents used including name of manufacturer or supplier, lot numbers, expiration dates and relevant verification, including test results or a certificate of analysis from the vendor.

6.7.2.2.4 CBU bag and canister characteristics, including appropriate dimensions.

6.7.2.2.5 Records of the cryopreservation procedures including the record of the cooling rate.

6.7.2.2.6 Records of storage conditions throughout the history of the CBU.

6.7.2.2.7 Documentation of receipt, distribution and disposition including destruction of CBU, integrally attached segments and all related CBU samples.

- 6.7.2.2.8 CBU transport records.
- 6.7.2.2.9 Reasons for exclusion of CBU collected but not banked.
- 6.7.2.3 Directed allogeneic and autologous recipient and parental records.
 - 6.7.2.3.1 A copy of mother's consent for collection and if available, a copy of the father's consent for collection.
 - 6.7.2.3.2 A contract specifying duration of storage and possible uses of the CBU and reference samples.
 - 6.7.2.3.3 Documentation of the agreement for disposition at the end of the contract and the final disposition of the CBU.
- 6.7.2.4 Directed allogeneic recipient and parental records.
 - 6.7.2.4.1 HLA typing of infant donor, mother, father and recipient to include at least A, B and DRB1, when performed.
- 6.7.2.5 Quality assurance records.
 - 6.7.2.5.1 Periodic performance checks of equipment and reagents.
 - 6.7.2.5.2 Proficiency test results.
 - 6.7.2.5.3 Validation studies.
- 6.7.2.6 General records.
 - 6.7.2.6.1 Personnel employed by the CBB responsible for CBU collection or processing, including signature, initials and inclusive dates of employment for each.
 - 6.7.2.6.2 Technical personnel training, continuing education and periodic competency testing.
 - 6.7.2.6.3 Errors, accidents and corrective action taken.
 - 6.7.2.6.4 Equipment including maintenance, cleaning and sanitization and calibration records.
 - 6.7.2.6.5 Facilities including records of cleaning and sanitation.

6.7.2.6.6 Sterilization of supplies and reagents prepared within the facility, including date, time interval, temperature and method used.

6.7.3 Electronic records

6.7.3.1 If an electronic record-management system is used, there shall be a system to ensure the authenticity, integrity and confidentiality of all records throughout the period of record retention.

6.7.3.1.1 There shall be a system to make legible records readily accessible by authorized individual.

6.7.3.2 There shall be the ability to generate true copies of the records in both paper and electronic forms suitable for inspection and review.

6.7.3.3 There shall be a back-up or alternative system for all electronic records that ensures continuous operation in the event that primary electronic data are not available.

6.7.3.4 There shall be a system that limits access to the electronic records to authorized individuals.

7 • Cord Blood Donor Management and Collection



CORD BLOOD DONOR MANAGEMENT AND COLLECTION

SECTION 7:

7.1 CORD BLOOD COLLECTION PERSONNEL REQUIREMENTS

- 7.1.1 There shall be a CBB Collection Manager. Section 3.2.2 applies.
- 7.1.2 There shall be adequate staff whose training, continuing education and continued competency for the performance of all assigned operations shall be documented.
- 7.1.3 Collection of cord blood shall be performed by registered medical practitioner or registered nurse trained in the collection procedure and to practice in the jurisdiction where the collection takes place.

7.2 CORD BLOOD COLLECTION FACILITIES

- 7.2.1 The Collection Facility is the site where the infant donor is delivered and the CBU is collected.
- 7.2.2 There shall be adequate space for the performance of the collection procedures.
- 7.2.3 There shall be adequate space for the secure storage of the CBU, associated reference samples and documents until they are transported to the CBB Processing Facility.
- 7.2.4 Cord Blood Collections.
 - 7.2.4.1 There shall be documentation describing the agreement and interaction between the Collection Facility and the CBB.

7.2.4.2 There shall be a designated area for appropriate storage and preparation of the reagents, supplies and equipment needed for the collection procedures.

7.2.4.2.1 Reagents and supplies shall be stored according to the manufacturer's recommendations and manner appropriate to protect their integrity and functionality.

7.2.4.2.2 When a collection kit is prepared and sent from the CBB, there shall be a mechanism to record the temperature of the kit from the time it leaves the CBB to the return of the kit to the CBB.

7.2.4.3 Temporary storage of the CBU, associated reference samples and documents shall be secure until they are transported to the CBB Processing Facility.

7.2.5 When directed allogeneic or autologous CBU are collected in a Fixed Collection Facility, Section 7.2.4 applies.

7.3 POLICIES AND STANDARD OPERATING PROCEDURES

7.3.1 The Collection Facility shall have clearly written policies and procedures. Section 6.2 that are precise and unambiguous and that address all applies.

7.3.2 All Collection Facility personnel shall follow the policies and Standard Operating Procedures established by the CBB.

7.3.3 There shall be SOP to cover at least the following:

7.3.3.1 Preparation, approval, implementation and revision of SOPs.

7.3.3.2 Donor recruitment, maternal and infant donor screening, collection criteria and consent.

7.3.3.3 CB collection, storage, and transport of the CBU to the CBB Processing Facility.

7.3.3.4 Labeling of the CBU, reference samples, maternal samples and associated documents.

7.3.3.5 Storage of maternal and CBU samples for testing.

- 7.3.3.6 Personnel training and documentation of continued competency for the procedures performed.
- 7.3.3.7 Facility management including supplies, maintenance and monitoring of equipment, sterility and sanitation procedures, disposal of medical and biohazardous waste, emergency and safety procedures and disaster plan.

7.4 MATERNAL AND INFANT DONOR EVALUATION

- 7.4.1 There shall be donor evaluation procedures in place that protect the recipient against transmitted disease and also protect the safety and confidentiality of the CB donor and mother. Both the potential for disease transmission from the infant donor to the recipient and the risks to the infant donor and mother from the collection procedure shall be assessed.
 - 7.4.1.1 Maternal and infant donor eligibility shall be determined based upon results of screening and testing in accordance with these Standards.
- 7.4.2 Maternal Screening.
 - 7.4.2.1 There shall be written criteria for maternal screening.
 - 7.4.2.1.1 When a mother does not meet the criteria below, the CBB Director shall document and maintain in the permanent record the nature of the variances and the rationale for inclusion of that CBU.
 - 7.4.2.2 A medical and genetic history of the infant donor's family (parents, grandparents, sibling, if applicable) shall be obtained and documented.
 - 7.4.2.2.1 The history shall include the infant donor's ethnicity and the potential presence of inherited disorders that are transmissible to the recipient.
 - 7.4.2.2.2 The CBU shall not be accepted for unrelated donor transplantation if there is a family history of a genetic disease that may affect the recipient.

7.4.3 Maternal Testing

7.4.3.1 Blood sample from the birth mother shall be obtained for communicable disease testing within 7 days before or after collection of the CBU.

7.4.3.1.1 This maternal blood sample shall be tested for evidence of communicable disease as defined in Section 8.13.

7.4.4 Infant Donor Screening and Testing

7.4.4.1 History of the current pregnancy and delivery, and infant's birth data shall be obtained and documented, including gender, gestational age, and if available, other results of clinical examination and any finding suggestive of disease potentially transmissible through transplantation.

7.4.4.2 Haemoglobinopathy testing on the infant donor or the CBU shall be performed prior to release of the CBU. Section 8.12.17 applies.

7.4.5 Maternal and Infant Donor Follow-up

7.4.5.1 Maternal and infant donor follow-up shall be carried out after six weeks of delivery.

7.4.5.2 The mother shall be enquired with regards of her health and her infant's health to exclude any reason that may make it inappropriate for the CBU to be transplanted.

7.5 INFORMED CONSENT

7.5.1 Informed consent shall be obtained from the mother prior to delivery and within 7 days after delivery of the infant donor.

7.5.1.1 If complete consent has not been obtained prior to delivery, at least the following information shall be provided to the mother:

7.5.1.1.1 An explanation of the CB collection procedure.

7.5.1.1.2 The right of the mother to refuse without prejudice.

7.5.1.1.3 The mother will be approached at a later time for complete consent, including consent to bank the CBU and all of the elements in Section 7.5.3.

- 7.5.1.2 Consent obtained for the CBU collection procedure prior to delivery shall be documented.
- 7.5.1.3 Informed consent shall not be obtained while the mother is in active labour.
- 7.5.2 All aspects of participation in the CBB shall be discussed with the mother in a language that she understands.
- 7.5.3 The informed consent process shall include at least the following:
 - 7.5.3.1 The overall purpose.
 - 7.5.3.2 The possible risk and benefits to the mother and/or infant donor including medical and ethical concerns.
 - 7.5.3.3 The possible alternatives to CB donation.
 - 7.5.3.4 The right of the mother to refuse without prejudice.
 - 7.5.3.5 Donation of the CBU for use in transplantation and specifying the intent of the donation for either unrelated use or for directed allogeneic or autologous use.
 - 7.5.3.5.1 If the collection is intended for unrelated allogeneic transplantation, the CBU is a donation that will be made available to other individuals and will not necessarily be available to the infant donor or the infant donor's family at a later date.
 - 7.5.3.5.2 If the collection is intended for directed allogeneic or autologous transplantation, the release of the CBU will be limited respectively to the family, intended recipient(s) or the infant donor.
 - 7.5.3.6 Interview for personal and family medical history.
 - 7.5.3.7 Review of the medical record of the mother and infant.
 - 7.5.3.8 An explanation of the CB collection procedure.
 - 7.5.3.9 Collection of reference samples:
 - 7.5.3.9.1 Blood sample from the mother for communicable disease and other testing as applicable.

- 7.5.3.9.2 CBU samples for communicable disease, genetic disease and other testing as applicable.
- 7.5.3.10 Storage of reference samples from the mother and the CBU for future testing.
- 7.5.3.11 Maintenance of linkage for the purpose of notifying infant donor family of communicable disease whenever possible.
 - 7.5.3.11.1 The CBB retains the right to contact the mother at any time.
 - 7.5.3.11.2 Information related to infant donor and family shall remain confidential.
- 7.5.3.12 Possible use of the CBU for research, quality control or validation studies.
- 7.5.3.13 The CBB policies for disposal of CBU including at least:
 - 7.5.3.13.1 Nonconforming CBU.
 - 7.5.3.13.2 Directed allogeneic or autologous CBU, if no longer required.
 - 7.5.3.13.3 A format for withdrawal of consent shall be established.

7.6 CORD BLOOD COLLECTION PROCEDURES

- 7.6.1 There shall be emergency medical care available for the mother and infant donor.
- 7.6.2 Procedures and practices in CB collection shall be performed to protect the health and safety of the mother and infant donor.
 - 7.6.2.1 Delivery practices shall not be modified in attempt to increase CB volume.
 - 7.6.2.2 CB collections should only be performed *in utero/ex utero* from documented singleton deliveries.
 - 7.6.2.2.1 If CB collection is performed *in utero* in a multiple gestation pregnancy, all infants shall be delivered before any CB collection begins.

7.6.2.2.2 *In utero* CB collections shall only occur in deliveries considered to be uncomplicated by the medical professional responsible for the delivery.

7.6.2.2.3 CBU collected *in utero* shall only be obtained from infant donor after at least 34 weeks gestation.

7.6.2.3 For directed allogeneic or autologous collections, the decision to collect from infant donors who are less than 34 weeks gestation shall be based on an evaluation of infant donor safety by the medical professional responsible for the delivery.

7.6.3 CBU collection shall be performed according to written policies and SOPs.

7.6.3.1 The identity of the collector shall be documented.

7.6.3.2 Methods for collection shall employ aseptic technique and shall use procedures validated to result in acceptable progenitor cell viability, recovery and microbial culture negativity rates.

7.6.3.3 The primary CB collection bag shall be approved for use with human blood and shall be used and sealed in a manner that minimizes the risk of cell loss and of microbial contamination.

7.6.3.4 All reagents and supplies for collection that come into contact with the cord blood shall be sterile.

7.6.4 On completion of collection, the primary collection bag shall bear or be accompanied by the information required in Appendix I, Cord Blood Labeling Table.

7.6.5 There shall be a written policy for storage of CBU and reference samples at the collection facility prior to transport to the CBB processing facility.

7.6.5.1 CBU and reference samples shall be maintained in a secure environment.

7.7 TRANSPORTATION OF NON-CRYOPRESERVED CORD BLOOD UNITS BETWEEN CORD BLOOD COLLECTION FACILITY AND THE CORD BLOOD PROCESSING FACILITY

7.7.1 Transportation of the CBU shall be in compliance with these Standards.

7.7.2 The methods of transportation of the CBU between the Collection Facility and the CBB processing facility shall be designed to protect the integrity of the CBU being transported and the health and safety of personnel.

7.7.3 Shipping container (Box)

7.7.3.1 The shipping container shall maintain a designated temperature range to protect cell viability during CBU transport as documented by prior validation of the shipping container, or by a continuous recording of the temperature of the shipping container during transport, or another method to document maintenance of temperature within the accepted range.

7.7.3.2 The outer shipping container shall be made of material adequate to withstand leakage of contents, shocks, pressure changes and other conditions incident to ordinary handling in transportation.

7.7.3.3 The shipping container shall bear the information required in Appendix I, Cord Blood Unit Labeling Table.

7.7.4 Transport Records

7.7.4.1 Transport records shall permit the tracing of the CBU from the collection facility to its final destination.

7.7.4.2 A shipping list identifying each CBU, reference sample and associated documents that are enclosed in a package shall be included.

7.7.4.3 Transport records shall identify:

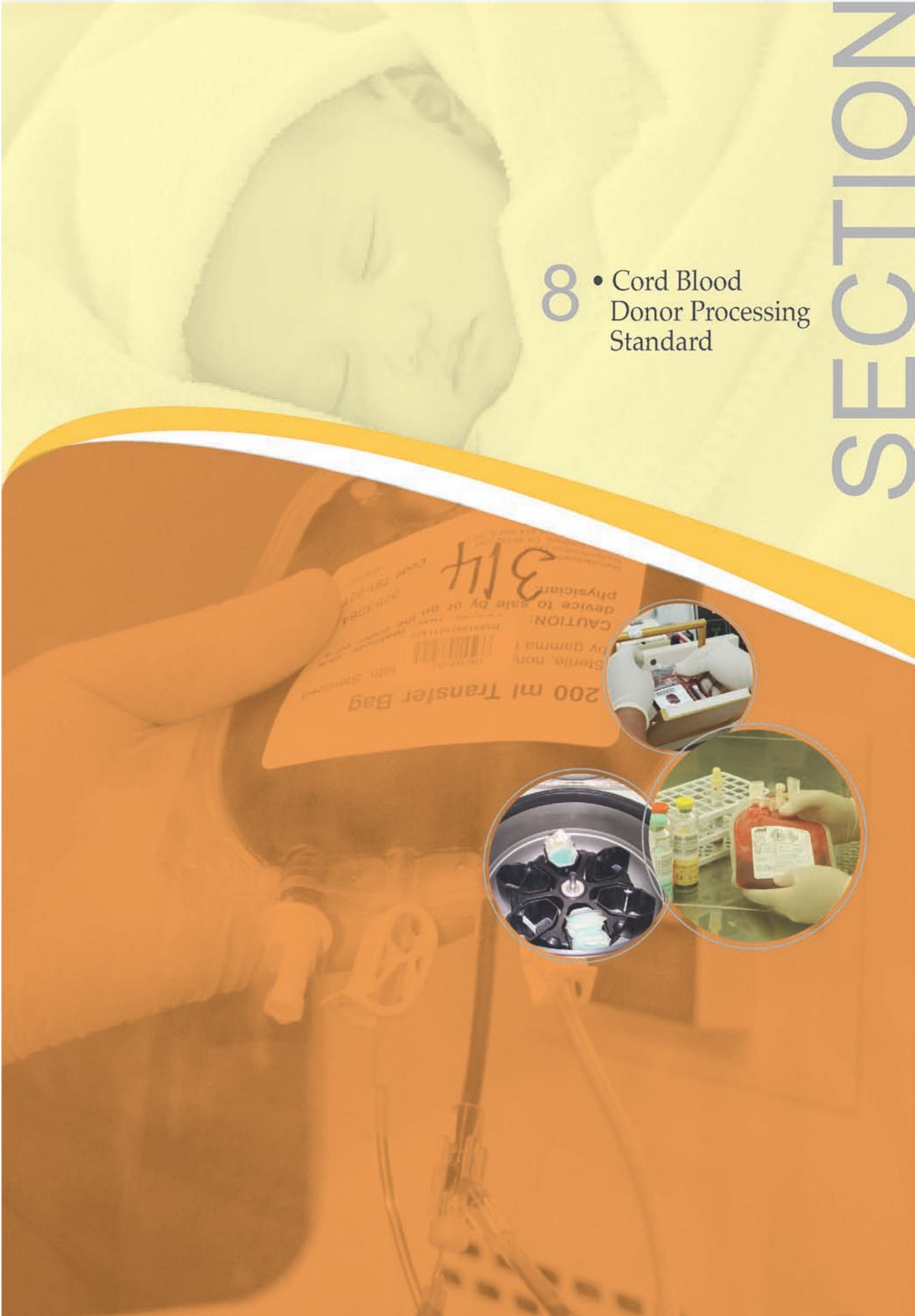
7.7.4.3.1 The collection facility responsible for shipping the CBU.

7.7.4.3.2 The date and time of shipping and the unit.

7.7.4.3.3 The identity of the courier.

7.7.4.3.4 The date and time of receipt of the package.

8 • Cord Blood Donor Processing Standard





CORD BLOOD PROCESSING STANDARDS

SECTION 8:

8.1 CORD BLOOD BANK PROCESSING FACILITY PERSONNEL REQUIREMENT

8.1.1 There shall be a CBB Processing Laboratory Manager. Section 3.2.3 applies.

8.1.2 There shall be adequate staff. Section 6.1.4 applies.

8.2 CORD BLOOD BANK PROCESSING FACILITY REQUIREMENTS

8.2.1 There shall be a designate facility with adequate space for performance of processing activities; the preparation and safe, sanitary, orderly storage of the reagents and equipment needed for CB processing, testing, banking and release and for records.

8.2.2 Facility Safety Requirements.

8.2.2.1 The CBB processing facility shall have programs operating in compliance with these Standards that are designed to minimize risks to the health and safety of employees and visitors.

8.2.2.2 There shall be procedures for biological and chemical safety as appropriate, including:

8.2.2.2.1 Blood borne pathogens.

8.2.2.2.2 Chemical hygiene.

8.2.2.2.3 Hand hygiene.

8.2.2.2.4 Fire safety.

8.2.2.2.5 Power failure.

8.2.2.2.6 Liquid Nitrogen.

8.2.2.2.7 Latex Allergy.

8.2.2.3 The CBB Processing Facility shall have written procedures for action in case of exposure to communicable disease or to chemical, biological, radiological or liquid nitrogen hazards.

8.2.2.4 Decontamination and disposal techniques for medical waste shall be described. Human tissue shall be disposed in such a manner as to minimize hazard to facility personnel and the environment.

8.3 POLICIES AND STANDARD OPERATING PROCEDURES

8.3.1 The CBB processing facility shall have clearly written policies and SOP that are precise and unambiguous and address all aspects of the processing operation. Section 6.2.1.1 and 6.2.2 also apply.

8.3.2 All personnel shall follow the policies and SOP established by the CBB.

8.3.3 There shall be policies and SOP to cover at least the following:

8.3.3.1 Preparation, approval, implementation and modification of SOP.

8.3.3.2 Maintenance of documentation of who performs steps from collection to final disposition of the CBU.

8.3.3.3 CB processing, cryopreservation, storage.

8.3.3.4 Labeling of the CBU, reference samples and associated documents.

8.3.3.5 Communicable disease testing, HLA typing, hemoglobinopathy testing and other testing.

8.3.3.6 Storage of maternal and CBU reference samples for testing.

8.3.3.7 Criteria for release of CBU from quarantine, including nonconforming CBU.

8.3.3.8 Criteria for qualification of CBU available for search and transplantation, including nonconforming CBU.

- 8.3.3.9 Quality management. Section 10 applies.
- 8.3.3.10 Personnel training and documentation of continued competency for the procedures performed.
- 8.3.3.11 Facility management of supplies, maintenance and monitoring of equipment, cleaning and sanitation procedures, disposal of medical and biohazardous waste, emergency and safety procedures and a disaster plan.
- 8.3.3.12 Transport and alternate place of storage of CBU in the event of a disaster
- 8.3.3.13 Discard and disposal of CBU.
- 8.3.3.14 Research carried out shall comply to National Organ, Tissue and Cell Transplantation Policies and Guidelines on Stem Cell Research.

8.4 CORD BLOOD PROCESSING

8.4.1 General Principles.

- 8.4.1.1 Section 6.3 applies.
- 8.4.1.2 In the case of directed allogeneic or autologous infant donors, a signed agreement from the requesting family shall be obtained including the name of the intended recipient, if known.
- 8.4.1.3 Processing and cryopreservation of CBU shall be performed according to validated SOP.
- 8.4.1.4 Failure of the processing procedure to achieve acceptable end-points shall be evaluated and documented.
- 8.4.1.5 Equipment, supplies and reagents used shall not adversely affect the viability of the CBU and shall not permit the introduction of adventitious agents or the transmission or spread of communicable disease.
- 8.4.1.6 Processing and cryopreservation of CBU shall be completed within 48 hours of collection provided storage and transportation condition are in compliance with the standards in section 7.7.

8.4.1.7 CBU processing shall be limited to volume reduction by depletion of erythrocytes and/or plasma.

8.4.2 Label at the completion of processing.

8.4.2.1 At the completion of processing, the freezing bag shall bear or be accompanied by the information required in Appendix I, Cord Blood Unit Labeling Table.

8.4.3 Records pertinent to the CBU shall be reviewed by the CBB Processing Laboratory Manager or designee.

8.5 REFERENCE SAMPLES

8.5.1 At a minimum, the following reference samples shall be collected from unrelated allogeneic, directed allogeneic or autologous CBU prior to cryopreservation.

8.5.1.1 Two (2) reference aliquots with minimum volume of 100 μ L each sealed in the tubing that is integrally attached to the freezing bag.

8.5.1.1.1 The contents of each aliquot shall be representative of the CBU.

8.5.1.1.2 One (1) segment shall be used for confirmatory typing and the other shall be used for cell viability analysis when the CBU is requested for confirmatory typing.

8.5.1.2 Additional samples may be collected for other purposes.

8.5.1.2.1 All cellular aliquots that will be used for viability analysis should be stored at -196°C and shall not be stored warmer than -150°C .

8.5.1.2.2 When cellular aliquots are stored in LN2 vapor phase at -150°C or colder, the freezers shall be validated to show that all cellular aliquots are maintained at appropriate temperatures.

8.5.1.2.3 Cellular aliquots used for purposes other than viability analysis shall be stored at -80°C or colder.

8.5.1.3 Two (2) vials of serum or plasma from non-heparinized samples with a minimum volume of two (2) mL each for future relevant testing when available.

- 8.5.1.3.1 The serum or plasma should be stored at -70°C or colder.
- 8.5.1.4 Suitable material for preparation of at least 50 µL genomic DNA. This may be purified dna, frozen cellular material or blots.
- 8.5.2 The following reference samples for unrelated allogeneic CBU shall be collected from the infant donor's mother within seven (7) days before or after the time of CBU collection, but prior to release of that CBU.
 - 8.5.2.1 From the birth mother, serum or plasma from non-heparinized samples of at least two (2) vials, two (2) mL each. this serum or plasma shall be stored at -70°C or colder to be used for future relevant tests when available.

8.6 CRYOPRESERVATION

- 8.6.1 CBU shall be cryopreserved using a controlled rate freezing or equivalent procedure validated to maintain viability.
 - 8.6.1.1 The time after addition of cryoprotectant prior to freezing shall be minimized.
- 8.6.2 Cryopreservation SOP shall specify the following:
 - 8.6.2.1 Total nucleated cell concentration within a defined range.
 - 8.6.2.2 Hematocrit within a defined range.
 - 8.6.2.3 The cryoprotectant, its final concentration and the duration of cell exposure prior to freezing.
 - 8.6.2.4 Method of freezing and endpoint temperature of cooling.
 - 8.6.2.5 Cooling rate within a defined range.
 - 8.6.2.6 Freezing curve parameters within a defined range.
 - 8.6.2.7 Storage temperature.
- 8.6.3 Frozen CBU shall be stored in approved freezing bags designed for the cryopreservation of human cells and placed into metal canisters to provide protection during freezing, storage and transportation.

- 8.6.3.1 Each CBU freezing bag and its satellite container(s), if any, shall be examined visually for damage or possible contamination prior to its use and immediately after filling. Such examination shall include inspection for breakage of seals. The results of this inspection shall be documented.

8.7 CONDITIONS FOR STORAGE

- 8.7.1 Facilities storing CBU shall establish policies for the duration and conditions of storage and indications for discard, in line with these Standards:-
- 8.7.1.1 There shall be a policy directing the validation of storage duration and the ongoing monitoring of product characteristics.
- 8.7.1.2 Refrigerators and freezers used for the storage of specimens, CBU, blood components, human tissues, or reagents shall not be used for any other purpose.
- 8.7.2 Procedures to minimize the risk of microbial cross-contamination of CBU shall be defined and maintained.
- 8.7.3 Each CBU shall be maintained in quarantine status until the CBB Director or designee has approved the release of the CBU from quarantine status based upon review of maternal communicable disease risk history, other medical history, maternal test results and CBU sterility test results as required by these Standards.
- 8.7.3.1 Records shall indicate when a CBU was released from quarantine into permanent status.
- 8.7.3.2 Unrelated allogeneic CBU shall not be released for transplantation if the unit or maternal samples have positive or indeterminate screening test results for human immunodeficiency virus, hepatitis C virus, hepatitis B virus and syphilis.
- 8.7.3.3 If directed allogeneic and autologous CBU associated maternal samples have positive or indeterminate communicable disease test results, such units shall be kept in a separate storage device separated from negative CBU until disposal.
- 8.7.4 For CBB that stores both unrelated and related directed CBU there shall be a defined process to prevent listing of directed allogeneic and autologous CBU for unrelated use.

8.7.5 The CBU storage device shall be located in a secure area. The device and/or the area shall have locking capability that is used, at least, when the area is not occupied.

8.7.6 Temperature

8.7.6.1 Frozen storage should be at -196°C and shall not be warmer than -150°C and shall be within a temperature range determined to be appropriate for the cryoprotectant and defined in the SOP.

8.7.6.1.1 When CBU are stored in LN₂ vapor phase at -150°C or colder, the storage freezers shall be validated to show that all CBU are maintained at appropriate temperatures.

8.7.6.2 Significant warming events at any time in the process of cryopreservation, storage and/or shipment shall be minimized.

8.8 MONITORING AND ALARM SYSTEMS

8.8.1 Freezers for CBU storage shall have a system to monitor the temperature continuously and to record the temperature at least every four (4) hours.

8.8.1.1 For CBU fully immersed in liquid nitrogen, continuous temperature monitoring is not required.

8.8.1.2 Liquid nitrogen freezers shall have a mechanism to ensure that levels of liquid nitrogen are monitored and that adequate levels are maintained.

8.8.2 Alarm Systems

8.8.2.1 Storage devices shall have alarm systems that are continuously active.

8.8.2.2 Alarm systems shall have audible and visible signals.

8.8.2.3 The alarm system shall be capable of notifying designated personnel 24 hours a day.

8.8.2.3.1 A procedure for notifying designated staff shall be placed at each remote alarm location and in the immediate area of the storage device.

8.8.2.4 Alarm parameters shall be set to allow staff sufficient time to salvage CBU and/or reference samples.

8.8.2.5 Alarm systems shall be checked periodically for function. the records of such checks shall be maintained and be available for inspection.

8.9 INVENTORY MANAGEMENT SYSTEM

8.9.1 There shall be an inventory management system in operation that ensures each CBU, its associated reference samples, maternal samples and records can be located in a timely way. Section 10.9 also applies.

8.10 DISPOSAL

8.10.1 The records for discarded CBU shall indicate the unique numeric or alphanumeric identifier of the unit, and the reason, date of disposal.

8.10.2 Before a directed allogeneic and autologous CBU is discarded:

8.10.2.1 There shall be written documentation of no further need for the CBU by the treating/requesting physician.

8.10.3 Disposal of any CBU shall be documented.

8.11 QUALITY MANAGEMENT PROGRAM

8.11.1 CBB processing facility control procedures shall include:

8.11.1.1 The use of established and validated appropriate assays, standards and test procedures for the evaluation of the CBU.

8.11.1.2 Adequate provisions for monitoring the reliability, accuracy, precision and performance of the laboratory test procedures and instruments.

8.11.1.3 Adequate identification and handling of all test samples so that they are accurately related to the specific CBU being tested, to its infant donor, or to the specific recipient, as applicable.

8.12 CBU ASSAYS

8.12.1 The following assays shall be performed on a sample from each CBU.

8.12.1.1 Total nucleated cell count from the final CBU at end of processing prior to cryopreservation.

8.12.1.2 Viability from the final CBU at end of processing prior to cryopreservation.

- 8.12.1.3 Total number of CB34-positive cells at end of processing prior to cryopreservation.
- 8.12.1.4 Microbial cultures of the CBU or product obtained after processing prior to cryopreservation using a system permissive for the growth of aerobic and anaerobic bacteria and fungi.
 - 8.12.1.4.1 For CBU with results of positive microbial tests, the organism(s) shall be identified and antibiotic sensitivities for aerobic bacteria shall be performed prior to release of the CBU for transplantation. These results shall be reported to the prospective clinical transplant program or the treating physician.
- 8.12.1.5 ABO group and Rh type.
- 8.12.1.6 Human leukocyte antigen (HLA) type before listing for unrelated allogeneic CBU or for directed allogeneic CBU, before release of the CBU to the Clinical Transplant Program.
 - 8.12.1.6.1 HLA-A, B and DRB1 loci shall be determined.
 - 8.12.1.6.2 HLA-C And DQB should be determined.
 - 8.12.1.6.3 HLA Class II and Class II typing shall be performed by DNA-based methods.
- 8.12.1.7 Hemoglobinopathy screening for unrelated allogeneic and directed allogeneic shall be performed on the maternal sample.
 - 8.12.1.7.1 If the mother is found to be a trait for haemoglobinopathy, paternal sample shall be tested prior to transplantation. In the absence of paternal sample, the infant shall be tested after six months.
 - 8.12.1.7.2 If the paternal sample is found to be normal, the CBU may be stored and information shall be documented and made available to the treating physician.
 - 8.12.1.7.3 In situation where both parents are found to be traits for haemoglobinopathy, infant sample may be tested after six months, before the CBU is discarded.

- 8.12.2 Prior to release for transplantation, each CBU shall be tested for evidence of infection by at least the following communicable disease agents. These tests shall be performed on each CBU:
- 8.12.2.1 Human immunodeficiency virus, type 1
 - 8.12.2.2 Human immunodeficiency virus, type 2
 - 8.12.2.3 Hepatitis B virus
 - 8.12.2.4 Hepatitis C virus
 - 8.12.2.5 *Treponema pallidum* (syphilis).
 - 8.12.2.6 Any additional agents required applicable standards and regulations approved by the Ministry of Health Malaysia and/or the Ethics Committee at the time of release of the CBU.
- 8.12.3 The CBB shall have a written policy for the management of positive or indeterminate results found during the screening process and/or laboratory testing of CB samples.
- 8.12.4 Positive or indeterminate test results shall be communicated to the mother and/or her physician in accordance with these Standards and the Ethics Committee.
- 8.12.5 If the CBU is collected for directed allogeneic or autologous use but then was subsequently released for unrelated allogeneic use, reference samples shall meet full unrelated allogeneic banking criteria as described above. Sections 6, 7, and 8 apply.

8.13 MATERNAL TESTING

- 8.13.1 The maternal blood samples obtained within seven (7) days before or after collection of the CBU shall be tested for evidence of infection by the following communicable disease agents utilizing assays required for volunteer tissue donations.
- 8.13.1.1 Human immunodeficiency virus, type 1
 - 8.13.1.2 Human immunodeficiency virus, type 2
 - 8.13.1.3 Hepatitis B virus

- 8.13.1.4 Hepatitis C virus.
- 8.13.1.5 *Treponema pallidum* (syphilis).
- 8.13.1.6 Cytomegalovirus (unless previously documented to be positive)
- 8.13.1.7 Actual virus detection test shall be performed on the maternal and infant donor samples for HBV, HCV and HIV prior to release.
- 8.13.1.8 Any additional agents required applicable standards and regulations approved by the Ministry of Health Malaysia and/or the Ethics Committee at the time of release of the CBU.
- 8.13.2 The CBB shall have a written policy directing response to positive or indeterminate results found during the screening process and/or laboratory testing of maternal samples.
- 8.13.3 Positive or indeterminate test results, excluding cytomegalovirus, shall be communicable to the mother and/or her physician.
- 8.13.4 All maternal samples should have negative or non-reactive test results with the exception of:
 - 8.13.4.1 Cytomegalovirus antibody
 - 8.13.4.2 Hepatitis B core antibody.
 - 8.13.4.2.1 Maternal samples that are hepatitis B core antibody positive may be accepted if they are hepatitis B virus negative by Nucleic Acid Amplification Technique.
 - 8.13.4.3 *Treponema pallidum* (syphilis)
 - 8.13.4.3.1 Maternal samples that are *Treponema pallidum* (syphilis) screen positive but negative using a specific confirmatory test may be accepted.

9 • Cord Blood Selection and Release Standards





CORD BLOOD SELECTION AND RELEASE STANDARDS

SECTION 9:

9.1 CORD BLOOD BANK FACILITY REQUIREMENTS

9.1.1 There shall be designated facilities with adequate space for procedures and records related to CBU selection and release.

9.2 GENERAL REQUIREMENTS FOR UNRELATED ALLOGENEIC, DIRECTED ALLOGENEIC AND AUTOLOGOUS CORD BLOOD UNITS

9.2.1 The CBB shall have policies and SOP for:

9.2.1.1 Selection, release and transport of the CBU to Clinical Transplant Programs.

9.2.1.1.1 If the CBB utilizes a Registry for any of these functions, these Standards apply to that Registry.

9.2.1.2 Verification of confirmatory HLA typing of the CBU.

9.2.1.3 Verification that the infant donor and the recipient are different individuals in the case of complete HLA matches.

9.2.2 The CBB shall retain documentation of requests for CBUs, requests for maternal and/or CBU reference samples, requests for and results of testing, and transportation of CBU and samples between facilities.

9.2.3 Once a CBU is identified for potential use, a sample obtained from a contiguous segment of that CBU shall be tested to verify HLA type and cell viability.

9.2.3.1 Any histocompatibility discrepancy shall be resolved and communicated to the Clinical Transplant Program.

- 9.2.3.2 The identified CBU for use shall be assigned to the clinical transplant programme unless no longer required.
- 9.2.4 The CBU should be received by the Clinical Transplant Programme or transplant physician accordance to existing protocols .
- 9.2.5 The CBB or Registry shall maintain records of each search request.
- 9.2.6 The CBB or Registry shall have an electronic record system that enables search and match operations for unrelated allogeneic CBU.
 - 9.2.6.1 If an outside agency is used for search and match functions, its electronic record system shall meet these Standards.
- 9.2.7 The CBB or Registry shall utilize validated procedures for the performance of donor-recipient matching and for reporting results within a defined time limit.
- 9.2.8 Each CBB shall maintain a policy for the allocation and reservation of CBU.
 - 9.2.8.1 Reservation of a CBU shall not be in place for more than one patient.

9.3 CORD BLOOD SELECTION FOR UNRELATED ALLOGENEIC, DIRECTED ALLOGENEIC AND AUTOLOGOUS CORD BLOOD TRANSPLANTATION

- 9.3.1 Prior to release of a CBU, the CBB shall provide the following processing data, assay results and infant donor and maternal medical history to the Clinical Transplant Program and if applicable to the Registry.
 - 9.3.1.1 HLA Class I and II typing results.
 - 9.3.1.2 Total nucleated cell count from the final CBU at the end of processing, prior to cryopreservation.
 - 9.3.1.3 Viability from the final CB product at the end of processing prior to cryopreservation.
 - 9.3.1.4 Total number of CB34-positive cells at the end of processing prior to cryopreservation.
 - 9.3.1.5 Communicable disease testing results performed on the maternal sample and on the CBU.

- 9.3.1.6 Risks of communicable and/or genetic disease disclosed by the maternal medical and genetic screening or clinical chart review and the results of any investigation or further testing performed.
- 9.3.1.7 The method of CBU processing.
- 9.3.1.8 Any variances in collection, processing, testing, storage and/or transport procedures that may influence the integrity and/or quality of the CBU.

9.4 CORD BLOOD SELECTION FOR DIRECTED, ALLOGENEIC AND AUTOLOGOUS CORD BLOOD TRANSPLANTATION

- 9.4.1 Samples of DNA (or material to isolate DNA) from the requested CBU shall be provided to the Clinical Transplant Program if available and if requested.
 - 9.4.1.1 If confirmatory HLA typing is performed, the CBB shall obtain, review and archive the results. These results may be used in the future to support the identity of the CBU and sample when offering the CBU to another Clinical Transplant Program.
- 9.4.2 Microbial testing results of the CBU obtained at the end of processing prior to cryopreservation shall be reviewed.
 - 9.4.2.1 If aerobic bacteria are documented in the CBU, antibiotic sensitivities shall be provided.

9.5 CORD BLOOD UNIT RELEASE

- 9.5.1 The CBB shall obtain a written request from the transplant physician, designee or Registry for shipment of the CBU.
- 9.5.2 The CBB Director or designee shall review the record of each CBU before its release including processing, test results and medical history. Section 10.4.5 also applies.
- 9.5.3 When the maternal medical and/or genetic screening history indicates potentially transmissible disease or when there is a positive or indeterminate communicable disease test result:
 - 9.5.3.1 The CBU shall not be released unless the CBB Director gives authorization for release of the non-conforming CBU and documents the rationale for such authorization.

- 9.5.3.2 There shall be documentation of the consent to use the CBU from the transplant physician.
- 9.5.3.3 CBU deemed non-conforming as a result of the risk for transmission of communicable disease by donor screening or testing shall bear an appropriate biohazard labels.
- 9.5.4 At the time of issue for transplantation, a CBU shall bear or be accompanied by the information required in Appendix I, Cord Blood Unit Labeling Table.
 - 9.5.4.1 Such information shall be attached securely to the CBU on a tie tag or enclosed in a sealed package to accompany the CBU.
- 9.5.5 Accompanying documentation at time of issue from the CBB shall include indications, contradictions, cautions and instructions for the handling and use of the CBU including short-term storage and preparation for transplantation.

9.6 TRANSPORTATION OF CRYOPRESERVED CORD BLOOD UNITS

- 9.6.1 Transport within facility.
 - 9.6.1.1 Procedures for transport of cryopreserved CBU within the facility shall be designed to protect the integrity of the CBU and the health and safety of facility personnel
- 9.6.2 Transport between facilities.
 - 9.6.2.1 Procedures for transport of cryopreserved CBU shall be designed to protect the integrity of the CBU and the health and safety of personnel.
 - 9.6.2.2 The transit time between the CBB and remote facility shall be minimized. There shall be plans for alternative transportation in an emergency.
 - 9.6.2.3 Cryopreserved units 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 at least 48 hours beyond the expected time of arrival at the receiving facility.
 - 9.6.2.3.1 The dry shipper shall contain a device that monitors temperature throughout the shipment period.

- 9.6.2.3.2 The shipping methods shall conform to the standard or specification that is applicable regarding the mode of transport of such device.
- 9.6.2.3.3 The dry shipper shall be labeled in accordance to these Standards regarding cryogenic material used and transportation of biologic materials.
- 9.6.3 The shipping container shall bear the information required in Appendix I, Cord Blood Unit Labeling Table.
- 9.6.4 The CBB shall obtain the following data from the receiving clinical transplant program about the CBU upon receipt:
 - 9.6.4.1 Time of receipt.
 - 9.6.4.2 Internal temperature of the shipper.
 - 9.6.4.3 Integrity of the CBU.
 - 9.6.4.4 Integrity of the shipper.
- 9.6.5 Once an unrelated CBU has left the CBB premises it shall not be returned to general CBB inventory.

9.7 DOCUMENTS AND RECORDS REQUIREMENTS

- 9.7.1 Section 6.7 applies.
- 9.7.2 Transport Records.
 - 9.7.2.1 Transport records shall permit the tracing of the CBU from the CBB to its final destination.
 - 9.7.2.2 A shipping list identifying each CBU and document enclosed in a package shall be included.
 - 9.7.2.3 Transport records shall document:
 - 9.7.2.3.1 The CBB responsible for shipping the CBU.
 - 9.7.2.3.2 The date and time of packaging of the CBU at the CBB.

9.7.2.3.3 The date and time the package left the facility.

9.7.2.3.4 The identity of the courier.

9.7.2.3.5 The date and time of receipt of package.

9.7.2.3.6 Maintenance of the temperature within the specified range throughout the period of transportation.

9.8 CLINICAL OUTCOME DATA

9.8.1 For every unrelated allogeneic, directed allogeneic or autologous CBU released, the CBB shall maintain details of clinical outcome as necessary to assure that the procedures in use in the CBB provide a safe and effective component.

9.8.1.1 The CBB shall obtain this information directly from the Clinical Transplant Program/transplant physician or through the Registry, if utilized.

9.8.2 The CBB shall have a policy or procedures to obtain the following information within the recommended time period for unrelated allogeneic, directed allogeneic and autologous CBU:

9.8.2.1 Adverse events associated with transplantation of the CBU should be reported to the CBB within six weeks of transplant.

9.8.2.2 Time to neutrophil and platelet engraftment should be reported to the CBB within 100 days of transplant.

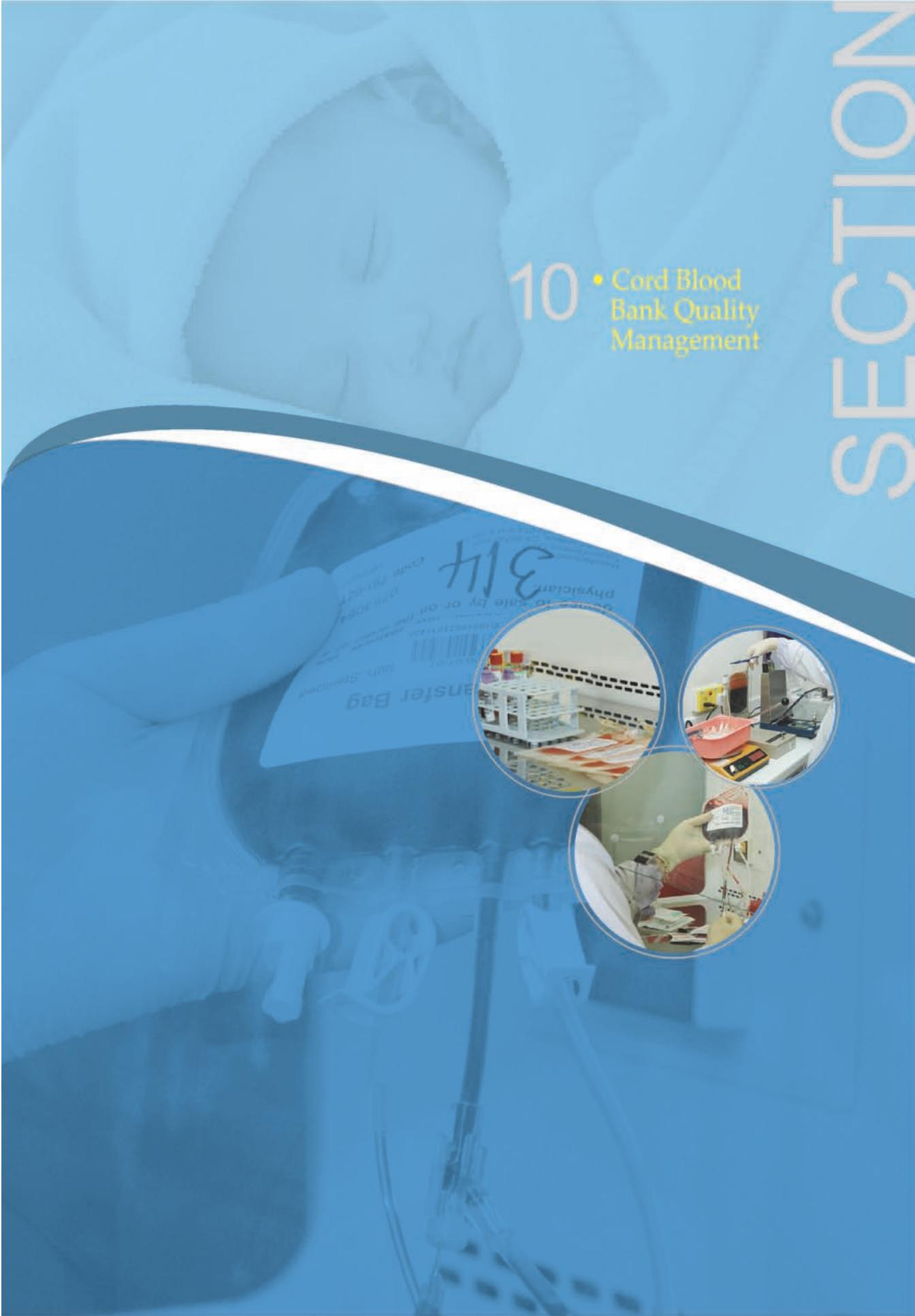
9.8.2.3 Survival rates should be reported to the CBB annually at a minimum.

9.8.2.4 For allogeneic CBU only, data should include chimerism and GVHD results that should be reported to the CBB annually at a minimum.

9.8.3 In the case of more than one graft product used for transplantation, the CBB shall collect and document that information.

9.8.4 The CBB shall collect viability and cell yield results on the thawed CBU from the Clinical Transplant Program.

10 • Cord Blood Bank Quality Management





CORD BLOOD BANK QUALITY MANAGEMENT

SECTION 10:

10.1 QUALITY MANAGEMENT PROGRAM

- 10.1.1 The CBB shall establish and maintain a Quality Management System (QMS) that shall cover all aspects of infant donor and maternal screening and testing, cord blood collection, processing, cord blood testing, banking, making CBU available for search, selection, release, and outcome analysis.
- 10.1.2 There shall be a Quality Manager (QM) appointed by the CBB Director, to establish and maintain system to review, modify as necessary, approve and implement all Standard Operating Procedures related to QMS and to monitor compliance with these Standards.
 - 10.1.2.1 The QM shall be a different individual from the CBB Director, or the CBB Processing Laboratory Manager.
 - 10.1.2.2 The QM shall report on the performance of the Quality Management Program at least on an annual basis.
 - 10.1.2.3 The QM shall not have oversight of his/her own work if this person also performs other task in the CBB.
 - 10.1.2.4 The QM shall participate regularly in educational activities related to the field of quality management, CB banking, and/or hematopoietic cell transplantation.
- 10.1.3 The CBB shall maintain a written QMS Plan that describes the QMS, including at a minimum:
 - 10.1.3.1 Organizational structure.

- 10.1.3.1.1 The QMS Plan shall include an organizational chart of all participating facilities and service including at least, Collection Facilities, Processing Facilities and testing laboratories.
- 10.1.3.2 A CBB that have multiple Collection Facilities shall employ coordinated policies and Standards Operating Procedures, protocols, staff training and competency evaluation procedures, and quality assessment systems; and shall demonstrate evidence of regular interaction between these Collection Facilities and the CBB.
- 10.1.4 Personnel requirements, qualifications, training and competency.
- 10.1.5 Documents and records.
 - 10.1.5.1 Policy and procedure development, implementation and review.
 - 10.1.5.2 Records creation, review, control and maintenance.
- 10.1.6 Quality control procedures shall be developed to monitor the continuing adequacy of the procedures, reagents, equipment and supplies as used under routine operating conditions by the CBB personnel.
- 10.1.7 Monitoring, quality assessments and audits. Section 10.5 applies.
- 10.1.8 Detection, investigation, reporting, corrective action and follow-up of errors, accidents, biological product deviations, adverse events and complaints.
- 10.1.9 Equipment, supplies and reagents.
 - 10.1.9.1 Validation and qualification.
 - 10.1.9.2 Calibration and maintenance.
 - 10.1.9.3 Vendor qualification
- 10.1.10 Inventory control
 - 10.1.10.1 Materials, supplies and reagents.
 - 10.1.10.2 CBU, reference CBU samples, maternal samples and records.

10.1.11 Process control

10.1.11.1 Product specifications.

10.1.11.2 Nonconforming products.

10.1.12 Identification, labelling and product tracking.

10.1.12.1 Labelling process.

10.2 PERSONNEL REQUIREMENTS

10.2.1 The QMS Plan shall include personnel requirements for each position in the CBB. Personnel requirements shall include at least :

10.2.1.1 Current position description for each staff.

10.2.1.2 A system to document for each staff member:

10.2.1.2.1 Initial qualifications.

10.2.1.2.2 Initial training.

10.2.1.2.3 Competency for each function performed.

10.2.1.2.4 Continued competency evaluation at least annually.

10.2.1.2.5 Continue education, training and retraining.

10.3 DOCUMENTS AND RECORDS REQUIREMENTS

10.3.1 The QMS Plan shall include a system to maintain confidentiality of infant donor, mother and recipient; of all records and communications among the Collection Facilities, Processing Facilities, CBB, Registry and/or Clinical Transplant Program; and of staff and employee records.

10.3.2 The QMS Plan shall contain a system to ensure uniformity of the Standard Operating Procedures and related forms.

10.3.2.1 There shall be a documented process for the development, approval, implementation, review, revision, archival, storage, retention and retrieval of policies, Standard Operating Procedures, protocols, forms, CBU and sample labels, educational and promotional materials and other documents.

- 10.3.2.2 Records of archived Standard Operating Procedures, protocols and labels, in their historical sequence including dates of use, shall be maintained indefinitely.
- 10.3.3 The QMS Plan shall include a process for regular assessment of records including, but not limited to collection, processing, storage and transportation of CBU.
- 10.3.4 The QMS Plan shall include a process for the regular assessment of record review to identify recurring problems, potential points of failure, or need for continuous process improvement.
- 10.3.5 The QMS Plan shall include a process for the comprehensive review of product records prior to making a CBU available for search, including at least:
 - 10.3.5.1 CBU total nucleated cell count.
 - 10.3.5.2 CBU total number of CB34-positive cells.
 - 10.3.5.3 CFU total number and/or CBU viability.
 - 10.3.5.4 CBU ABO group and Rh type.
 - 10.3.5.5 Microbial cultures of the CBU obtained after processing.
 - 10.3.5.6 For unrelated allogeneic CBU, HLA type.
 - 10.3.5.7 Infant donor's ethnicity.
 - 10.3.5.8 Infant donor's gender.
 - 10.3.5.9 Maternal risk factors for transmission of communicable disease.
 - 10.3.5.10 Maternal communicable disease testing results.
 - 10.3.5.11 Family medical history for transmissible genetic diseases.
 - 10.3.5.12 Consents.
 - 10.3.5.13 Processing and cryopreservation parameters as defined in the Standard Operating Procedures:
 - 10.3.5.13.1 Total nucleated cell concentration within defined range.
 - 10.3.5.13.2 Hematocrit within defined range.
 - 10.3.5.13.3 The cryoprotectant, its final concentration, and the duration of cell exposure prior to freezing.

10.3.5.13.4 Method of freezing and end-point temperature of cooling.

10.3.5.13.5 Cooling rate and freezing curve within defined range.

10.3.5.13.6 Storage temperature.

10.3.6 The QMS Plan shall include a process for comprehensive product review prior to release of a CBU from inventory for transplantation and for documentation of this review in accordance with these Standards.

10.3.7 The QMS Plan shall include a process for retention of records as required by Section 6.7 of these Standards.

10.3.8 The QMS Plan shall include policies and Standard Operating Procedures to support management of electronic record systems and electronic records, to maintain pertinent electronic records, and to ensure continuous operations in the event that the electronic record system ceases to function, including a plan for data backup and to ensure compliance with these Standards.

10.3.9 The QMS Plan shall include policies and procedures to ensure that the records of each facility involved in the collection, processing, testing, storage, transportation, search, or transplantation of the CBU shall show plainly the identity of each facility and the extent of its responsibility.

10.4 MONITORING, QUALITY ASSESSMENT AND AUDITS

10.4.1 The QMS Plan shall include a process for assessing the CBB functions at predefined intervals, at a minimum, on an annual basis.

10.4.1.1 The results of ongoing monitoring shall be documented, reviewed and trends shall be analyzed on a regular basis.

10.4.1.2 Corrective action shall be implemented and documented as indicated. Corrective action shall include both short-term action to address the immediate problem and long-term action to prevent the problem from recurring. Section 10.6.2 also applies.

10.4.1.3 Opportunity for continuous quality improvement shall be identified, reviewed, implemented as appropriate and documented.

10.4.2 The QM System Plan shall include a process for conducting independent internal quality audits of significant CBB activities to verify compliance with elements of the QM Program under review.

10.4.2.1 Quality audits shall include aspects of all CBB functions, including at least:

10.4.2.1.1 Maternal screening and testing.

10.4.2.1.2 Infant donor eligibility determinations.

10.4.2.1.3 CBU collection.

10.4.2.1.4 CBU transportation.

10.4.2.1.5 CBU processing.

10.4.2.1.6 CBU labeling.

10.4.2.1.7 CBU storage.

10.4.2.1.8 CBU release for transplantation.

10.4.2.1.10 CBU records.

10.4.2.1.11 CBU disposition. Section 8.10 and 9.10 also apply.

10.4.2.2 Quality audits shall be conducted by an individual with sufficient expertise to identify problems, but who is not directly responsible for the process being audited.

10.4.2.3 The results of audits shall be used to recognize problems, detect trends and identify continuous improvement opportunities.

10.4.2.4 Collection and analysis of data related to the audit shall be reviewed, reported and documented at a minimum, on an annual basis.

10.4.3 The QM Plan shall include a written procedure for the management of external audits and inspections.

10.5 ERRORS, ACCIDENTS, BIOLOGICAL PRODUCT DEVIATIONS, ADVERSE EVENTS, VARIANCES AND COMPLAINTS.

10.5.1 The QMS Plan shall include procedures for monitoring, detecting, documenting, evaluating and reporting errors, accidents, biological products deviations, adverse events, variances and complaints. These shall be evaluated by the appropriate Director and/or Medical Director together with staff involved in the QMP and other appropriate staff.

10.5.1.1 The QMP shall review all occurrences and trend the errors, accidents, adverse events and variances related to:

- 10.5.1.1.1 Collection.
- 10.5.1.1.2 Transportation.
- 10.5.1.1.3 Processing.
- 10.5.1.1.4 Cryopreservation.
- 10.5.1.1.5 Storage.
- 10.5.1.1.6 Thawing.

10.5.2 Corrective actions shall be implemented as appropriate. Documentation shall be maintained and shall include:

- 10.5.2.1 The nature of the problem requiring corrective action.
- 10.5.2.2 The identity and disposition of the affected CBU.
- 10.5.2.3 The dates of corrective action, including a designated time at which the outcome of the corrective action shall be evaluated.
- 10.5.2.4 Performing reaudits of deficiencies as necessary.

10.5.3 A thorough investigation of all reported severe or unexpected adverse events or reactions shall be made by the independent body in collaboration with the CBB, Collection Facility, Processing Facility, Registry and/or Clinical Transplant Program, as appropriate. A written report of the investigation including conclusions, follow-up and corrective action, if applicable shall be:

- 10.5.3.1 Prepared and maintained as part of the record for that final CBU.
- 10.5.3.2 Maintained in the CB adverse event aggregate file.
- 10.5.3.3 Utilized in quality monitoring and analysis of trends.
- 10.5.3.4 When it is determined that the CBU was responsible for the adverse reaction, results of the investigation shall be shared with the Clinical Transplant Program and/or other appropriate organization(s) involved.

10.5.4 The QMS Plan shall include a process for the review, evaluation and documentation of complaints.

10.5.4.1 Each complaint shall be evaluated to determine if the complaint is related to a product deviation or adverse reaction. Corrective action shall be initiated when appropriate.

10.5.4.2 A complaint management system shall be maintained.

10.6 VALIDATION AND QUALIFICATION REQUIREMENTS

10.6.1 Procedures shall be developed, implemented and documented for the validation or qualification of significant aspects of the CBB functions.

10.6.2 Determination of which elements of collection, transportation, testing, processing, cryopreservation, storage and thawing are to be validated or qualified shall be made by the CBB Director in collaboration with representatives of the QM Program.

10.6.3 Validation studies shall be reviewed and approved by the CBB Director or designee from the QM Program.

10.6.4 Records shall be maintained to document that procedures have been validated to achieve the expected end-points, including viability of the CB cells and product integrity.

10.6.5 All critical equipment shall be validated and/or qualified for its intended use.

10.6.6 Quality control procedures shall be developed to monitor the continuing adequacy of the procedures, reagents, equipment and supplies as used under routine operating conditions by the facility personnel.

10.7 EQUIPMENT, SUPPLIES AND REAGENTS

10.7.1 The QMS Plan shall include the following procedures for equipment used in collection, processing or storage of CBU.

10.7.1.1 All equipment shall be identified and records maintained, including manufacturer's name, serial number or other identifier, manufacturer's instructions, equipment location and use of each piece of equipment, including the identification of each CBU for which the equipment was used.

10.7.1.2 Calibration.

10.7.1.2.1 Equipment shall be observed, tested and calibrated on a regularly scheduled basis as recommended by the manufacturer or at a minimum annually.

10.7.1.2.2 Calibration acceptance criteria shall be defined.

10.7.1.2.3 Records of the dates and copies of calibration results shall be maintained.

10.7.1.3 Maintenance and repairs.

10.7.1.3.1 Equipment shall be maintained in a clean and orderly manner and located so as to facilitate cleaning and maintenance according to established schedules.

10.7.1.3.2 Records shall be maintained of the maintenance schedule, maintenance performed and damage, malfunction, modification or repair to equipment.

10.7.1.4 Cleaning and sanitation.

10.7.1.4.1 Equipment shall be cleaned and sanitized according to established schedules.

10.7.1.4.2 Records of equipment cleaning and sanitation shall be maintained.

10.7.1.5 Inspections.

10.7.1.5.1 Equipment shall be routinely inspected for cleanliness, sanitation and calibration and to ensure adherence to applicable equipment maintenance schedules.

10.7.2 The QMS Plan shall include procedures to address management of critical supplies and reagents used in the collection, processing and/or storage of CBU.

10.7.2.1 Critical reagents and supplies shall be verified to function as expected and to meet specifications designed to prevent the spread of communicable disease.

- 10.7.2.2 Approved suppliers for all critical reagents and supplies shall be identified and utilized.
- 10.7.2.3 Records of receipt, inspection, verification, acceptance and storage of supplies and reagents shall be maintained.
- 10.7.3 Quality control procedures shall be developed to monitor the continuing adequacy of the procedures, reagents, equipment and supplies as used under routine operating conditions by the CBB Personnel.

10.8 INVENTORY MANAGEMENT

- 10.8.1 The QMS Plan shall include a process for inventory management that encompasses all materials, supplies, reagents and labels.
- 10.8.2 The QMS Plan shall include an inventory management system for CBU that ensures each CBU, its associated reference samples, maternal samples and records can be located in a timely way.
 - 10.8.2.1 The inventory management system shall be designed to prevent mix-ups, contamination of the CBU during storage and the improper release of quarantine CBU.
- 10.8.3 The QMS Plan shall include policies related to the return of CBU to the CBB inventory.
 - 10.8.3.1 Unrelated allogeneic CBU shall not be returned to the CBB inventory.
 - 10.8.3.2 Directed allogeneic and autologous CBU may be returned to the CBB inventory with documentation of appropriate storage and transportation.

10.9 PROCESS CONTROL

- 10.9.1 The QMS Plan shall include a process for controlling and monitoring the collection, processing and storage of CBU to ensure that the products conform to specifications, are not contaminated or cross-contaminated and maintain function and integrity.
 - 10.9.1.1 Donor eligibility requirements that meet these Standards shall be defined, implemented and documented to include maternal health history screening, maternal testing and CBU testing.

- 10.9.1.2 CBU from two (2) or more infant donors shall not be placed in physical contact or mixed in a single container.
- 10.9.1.3 Any change to a standard operating procedure shall be verified or validated, approved by the CBB Director or designee before implementation and be communicated to appropriate personnel.
- 10.9.2 There shall be a mechanism to identify, review, segregate if indicated and document nonconforming CBU that do not fully meet these Standards, CBB requirements and/or CBB requirements for donor eligibility.
 - 10.9.2.1 The CBB shall maintain a record of nonconforming CBU that are banked and/or released.
 - 10.9.2.1.1 The nature of the nonconformity shall be communicated to the Clinical Transplant Program, either directly or through the Registry, at the time of initial consideration of the CBU for clinical use.

10.10 IDENTIFICATION, LABELING AND PRODUCT TRACKING

- 10.10.1 The QMS Plan shall include processes to ensure that each CBU is assigned a unique numeric or alphanumeric identifier by which it will be possible to link that CBU to its maternal and infant donor data, delivery information, family history, test results and to all records describing the handling and final disposition.
- 10.10.2 The QMS Plan shall include processes for product tracking that allow tracking of the CBU from the infant donor to the recipient or final distribution.
 - 10.10.2.1 Linkage of the CBU to the infant donor and mother shall be retained indefinitely.

10.11 OUTCOME ANALYSIS

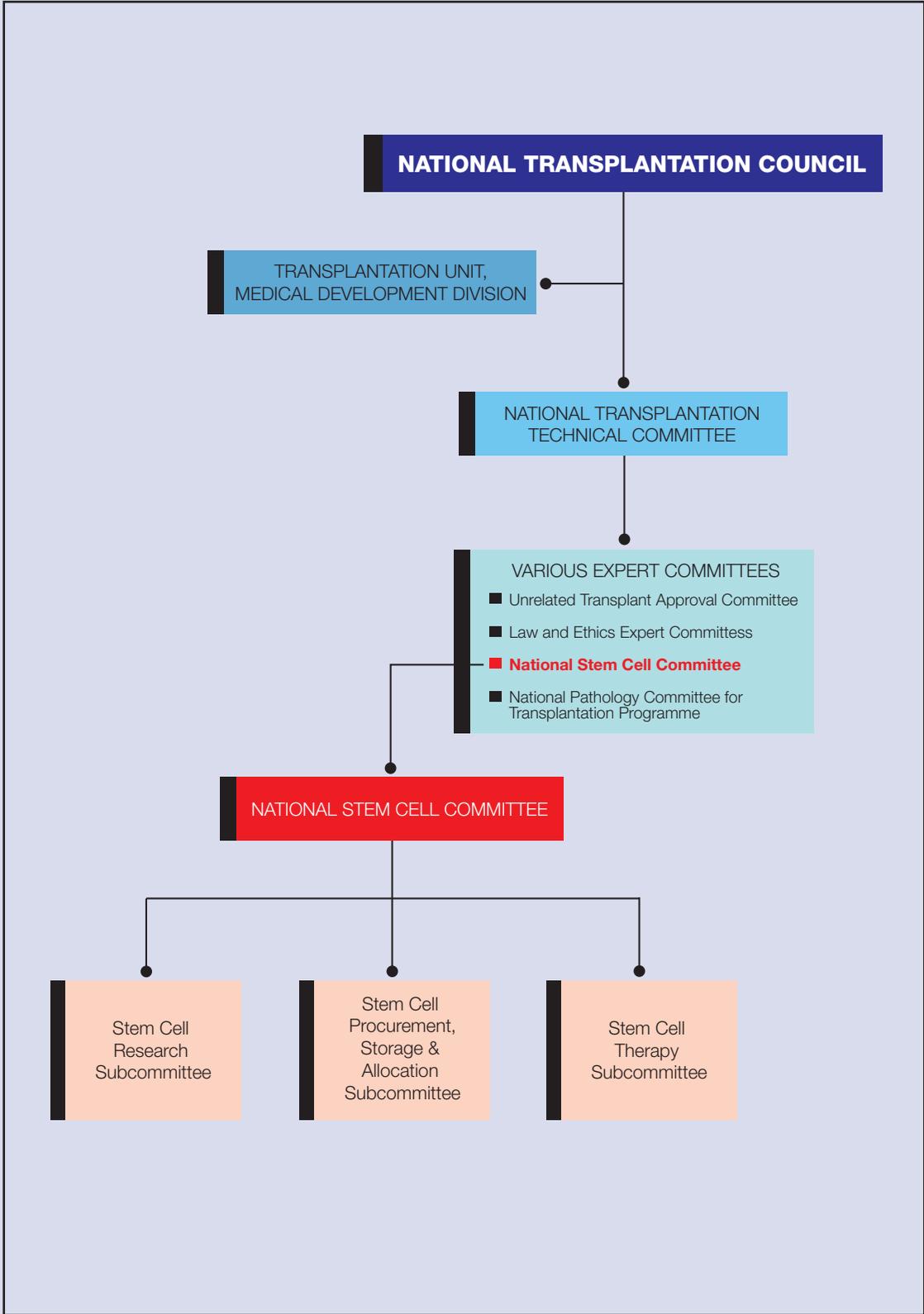
- 10.11.1 The QMS Plan shall include processes to maintain and evaluate details of clinical outcome as necessary to ensure that the procedures in use in the CBB continuously provide a safe and effective product.

10.12 FACILITIES AND SAFETY

- 10.12.1 The QMS Plan shall include processes to ensure safe, sanitary and adequate environmental workplace conditions.
 - 10.12.1.1 The CBB space shall be of adequate size, construction and location to maintain safe operations, prevent contamination and ensure orderly handling.
 - 10.12.1.2 Environmental conditions for temperature, humidity, ventilation and air filtration and classification shall be defined and, if appropriate, monitored.
 - 10.12.1.3 Separate areas shall be maintained for processing and storage of products to prevent mix-ups, product contamination and cross-contamination.
 - 10.12.1.4 The CBB shall be secured to prevent the admittance of unauthorized individuals.
 - 10.12.1.5 Dedicated CBB Facilities shall be maintained in a clean, sanitary and orderly manner to prevent introduction, transmission or spread of communicable disease and to facilitate operations and cleaning.
- 10.12.2 There shall be procedures for biological and chemical safety as appropriate including:
 - 10.12.2.1 Communicable disease agents.
 - 10.12.2.2 Chemical hygiene.
 - 10.12.2.3 Hand hygiene.
 - 10.12.2.4 Fire safety.
 - 10.12.2.5 Power failures.
 - 10.12.2.6 Liquid nitrogen.

10.13 INFANT DONOR ELIGIBILITY DETERMINATIONS

- 10.13.1 There shall be procedures for determining infant donor eligibility based on infant donor and maternal screening and testing in accordance with these Standards.



NATIONAL TRANSPLANTATION COUNCIL

TRANSPLANTATION UNIT,
MEDICAL DEVELOPMENT DIVISION

NATIONAL TRANSPLANTATION
TECHNICAL COMMITTEE

- VARIOUS EXPERT COMMITTEES
- Unrelated Transplant Approval Committee
 - Law and Ethics Expert Committeess
 - **National Stem Cell Committee**
 - National Pathology Committee for Transplantation Programme

NATIONAL STEM CELL COMMITTEE

Stem Cell
Research
Subcommittee

Stem Cell
Procurement,
Storage &
Allocation
Subcommittee

Stem Cell
Therapy
Subcommittee

GLOSSARY



GLOSSARY

TERMINOLOGY

For purposes of these Standards, the term *shall* means that the Standard is to be complied with at all times. The term *should* indicates an activity that is recommended or advised, but for which there may be effective alternatives. The term *may* is permissive, indicating that the practice is acceptable, but not necessarily recommended.

ABBREVIATIONS

The following abbreviations are used in these Cord Blood standards:

ABO	Major human blood group system
AC	Accompany
AF	Affix
AG	Antigen
ANTI-	An antibody to the antigen designated
ASBMT	American Society for Blood and Marrow Transplant
ASHI	American Society for Histocompatibility and Immunogenetics
°C	Degree Centigrade
CB	Cord Blood
CBB	Cord Blood Bank
CBU	Cord Blood Unit
CMV	Cytomegalovirus
DNA	Deoxyribonucleic Acid
EBMT	European Group for Blood and Marrow Transplantation
EBV	Epstein-Barr Virus
FACT	Foundation for the Accreditation of Cellular Therapy

GVHD	Graft-Vs-Host-Disease
HLA	Human Leukocyte Antigen, the Major Histocompatibility System in Humans
HBc	Hepatitis B Core Antigen
HBsAg	Hepatitis B Surface Antigen
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HLA	Human Leukocyte Antigen
HPC	Hematopoietic Progenitor Cells
HTLV	Human T Cell Lymphotropic Virus
ISCT	International Society for Cellular Therapy
ISHAGE	International Society for Hematotherapy and Graft Engineering
LN2	Liquid Nitrogen
QMP	Quality Management Program
Rh	Rhesus System of Human Red Blood Cell Types

DEFINITIONS

The following terms are used in this document with the following definitions:

Accompany: To go or be together with, but not attached. information that must accompany the cord blood unit in a sealed package may alternatively be attached or affixed.

Adventitious Agent: Any extraneous microbiological, chemical, or radiological agents introduced into the CBU during collection, processing, or infusion.

Adverse Event: Any unintended and unfavorable sign, symptom, abnormality, or condition temporally associated with an intervention, medical treatment, or procedure. adverse reaction is a type of adverse event.

Adverse Reaction: A noxious and unintended response to the collection or infusion of any cellular therapy product for which there is a reasonable possibility that the cellular therapy product caused the response.

Affix: To attach in physical contact with the cord blood unit container.

Allogeneic: Cord Blood unit obtained from an infant donor and intended for infusion into a genetically distinct recipient.

Unrelated Allogeneic: Cord Blood unit obtained from one infant donor and intended for transplantation into another individual who is not genetically related to the infant donor.

Related Allogeneic: Cord Blood unit collected and stored for use by an identified individual or family that is biologically linked to the cord blood donor.

Aseptic Technique: Practices designed to reduce the risk of microbial contamination of products, reagents, specimens, patients, or donors.

Attach: To fasten securely to the cord blood unit container by means of a tie tag or comparable alternative. any information required to be attached to a container may alternatively be affixed.

Audit: Documented, systematic evaluation to determine whether approved policies or procedures have been properly implemented and are being followed.

Autologous: Cord Blood unit obtained from an infant donor and intended for infusion back into the same individual.

Available For Distribution: The point at which the cellular therapy product has been determined to meet all release criteria.

Biohazard Legend: The universal biohazard symbol.

Biological Product Deviation: A deviation from these, standards or other established specifications that relate to the prevention of communicable disease transmission or cellular therapy product contamination; or an unexpected or unforeseeable event that may relate to the transmission or potential transmission of a communicable disease or may lead to cellular therapy product contamination.

Calibrate: To set measurement equipment against a known standard.

Calibration: Periodic scheduled activity to check and maintain the accuracy of measurements against a known standards.

Cd34: The 115 kD glycoprotein antigen, expressed by 1-2% of normal bone marrow mononuclear cells, that is defined by a specific monoclonal antibody (anti-CD34) using the standardized cluster of differentiation (cd) terminology. the vast majority of CB progenitors, including those cells that give rise to hematopoietic colonies in vitro, are contained in the population of cells expressing the CD34 antigen.

Colony Forming Unit: A clonogenic cell able to produce colonies in vitro under specific conditions in the presence of appropriate colony stimulating factors and defined by the type of mature progeny that develop.

Collection: Any procedure for harvesting cellular therapy products, including labeling, regardless of technique or source.

Collection Facility: The site where the infant is delivered and the CBU is collected.

Communicable Disease: A disease or disease agent for which there may be a risk of transmission by a cord blood unit either to a recipient or to the people who may handle or otherwise come in contact with the cord blood unit.

Competency: Ability to adequately perform a specific procedure or task according to directions.

Complaint: Any written, oral, or electronic communication about a problem associated with a distributed cellular therapy product or with a service related to the collection, processing, storage, distribution, or infusion of a cellular therapy product.

Component: Cord Blood unit that is being processed, at any stage of the processing.

Contiguous Segments: A sealed lengths of tubing integrally attached to the CBU that contains a sample representative of the cord blood used for testing.

Cord Blood: The whole blood including hematopoietic progenitor cells collected from placental and/or umbilical cord blood vessel after the umbilical cord has been clamped.

Cord Blood Bank: Means any premises used or intended to be used for the collection, processing, testing, banking, selection and release of cord blood units; and consists of an integrated team, under a director.

Cord Blood Collection: The procurement of CB for banking and transplantation before and/or after the placenta is delivered.

Ex Utero: The collection of CB cells from the placental and/or umbilical vessel after the placenta has been delivered.

In Utero: The collection of CB cells from the placental and/or umbilical vessels after the infant donor has been delivered and separated from the umbilical cord, but before the placenta has been delivered.

Cord Blood Cryopreserved: The CB that has been frozen using devices, supplies, and techniques validated for that purpose.

Cord Blood Standards: These document, “National standards for Cord Blood Banking and Transplantation”

Cord Blood Unit: The nucleated cells including stem and hematopoietic progenitor cells harvested from placental and umbilical cord blood vessels from a single placenta after the umbilical cord has been clamped. Unless otherwise specified, the term CBU in this document refers to all CBU regardless of method of collection or intended use.

Corrective Action: Action taken to eliminate the causes of an existing discrepancy or other undesirable situation to prevent recurrence.

Designee: An individual with appropriate experience or expertise who is given the authority to assume a specific responsibility.

Depletion: The manipulation of CB that results in the loss of specific targeted cell population(s) using validated techniques.

Director: For purposes of these standards includes individuals with the following qualifications:

CBB Director: A registered medical practitioner with training and experience in immunogenetics of transplantation, basic or clinical immunology, immunohematology, blood or tissue banking, or cryobiology.

The CBB Director has final responsibility for the CBB scientific and clinical performance and its overall compliance with these Standards. The CBB Director should participate regularly in educational activities related to the field of hematopoietic progenitor cell collection, processing, transplantation and/or CB banking.

CBB Collection Manager: A registered medical practitioner with training and experience in cord blood collection, processing and transplantation.

The CBB Collection Manager is responsible for the medical aspects of cord blood collection procedures and compliance of the cord blood collection facility with these Standards. The CBB Collection Facility Medical Director shall participate regularly in educational activities related to the field of donor safety, cord blood banking and/or hematopoietic progenitor cell collection, processing, and transplantation.

CBB Processing Laboratory Manager: A registered medical practitioner or technical staff with a relevant, qualified by training or experience for the scope of activities carried out in the CBB Processing Facility.

The CBB Processing Laboratory Manager is responsible for all operational aspects of all procedures related to receipt, testing, processing, cryopreservation, storage, release for shipment of cord blood units, and administrative operations of the CBB Processing Facility, including compliance with these standards. The CBB Processing Facility director shall participate regularly in educational activities related to the field of cord blood banking and/or hematopoietic progenitor cell collection, processing, transplantation.

Distribution: Any conveyance or shipment (including importation and exportation) of a cellular therapy product that has been determined to meet all release criteria.

Donor: A person who is the source of cells or tissue for a cellular therapy product.

Electronic Record: Any record or document consisting of any combination of text or graphic or other data that is created, stored, modified, or transmitted in digital form by a computer.

Eligible: An infant donor and/or mother who meet all donor screening and testing requirements related to transmission of communicable disease.

Engraftment: The reconstitution of recipient hematopoiesis with white blood cells, red blood cells and platelets from the donor.

Errors And Accidents: Any unforeseen or unexpected deviations from these standards, or other established Standards or specifications that may affect the safety, purity, or potency of a cord blood unit.

Ethics Committee: A Board of Committee established by an institution in accordance with the regulations of the Ministry of Health Malaysia and the guidelines on stem Cell Research Ministry of Health, to safeguards of the patients, to review biomedical and behavioral research involving human subjects conducted at or supported by that institution.

Facility: A location where activities covered by these standards are performed. such activities include determination of donor eligibility or suitability, product collection, processing, storage, selection and release.

Guidelines On Stem Cell Research Ministry Of Health: Guidelines developed by consensus and collaboration by the local scientist and clinicians to prevent unethical research and unethical use of stem cell, to keep abreast of current advances in science, to improve the quality of stem cell research and hence can be benefited to all.

Healthcare Professional: Includes a medical practitioner, dental practitioner, pharmacist, clinical psychologist, nurse, midwife, medical assistant, physiotherapist, occupational therapist and other allied healthcare professional and any other person involved in the giving of medial, health, dental, pharmaceutical or any other healthcare services under jurisdiction of the ministry of health.

Hematopoietic Progenitor Cells: Self-renewing and/or multi-potent stem cells capable of maturation into any of the hematopoietic lineages, lineage-restricted pluri-potent progenitor cells, and committed progenitor cells, regardless of tissue source (bone marrow, umbilical cord blood, peripheral blood, or other tissue source).

Hpc, Cord Blood: Hematopoietic progenitor cells obtained from the umbilical cord and/or placenta at the time of delivery. HPC, Cord Blood is the proper name of a cord blood unit.

Identifier: A numeric or alphanumeric sequence used to designate a cord blood unit.

Ineligible: An infant donor and/or mother who does not meet all donor screening and testing requirements related to transmission of communicable disease as defined in these standards.

Infant Donor: The infant from whose placenta and/or umbilical cord the cord blood is obtained.

Directed Infant Donor: The infant whose cord blood is collected and stored for use by an individual or family that is genetically related to the infant donor. directed infant donors could be directed allogeneic or autologous infant donors.

Labelling: Steps taken to identify the original hematopoietic progenitor cell collection, any components, and any component modifications; to complete the required reviews; and to attach the appropriate labels.

Linkage: The basic demographic information including name, that would allow identification of the CB donor and/or mother.

Manipulation: Ex vivo procedure(s) that selectively removes, enriches, expands or functionally alters hematopoietic progenitor cells.

Minimally Manipulated: Processing that does not alter the relevant biological characteristics of cells or tissues.

More Than Minimally Manipulated: Processing that does alter the relevant biological characteristics of cells or tissues.

Microbial: Related to infectious agents including bacterial and fungal organisms.

Mother: Any of the following:

Biologic Mother: The woman from whose egg the infant donor develops; the egg donor.

Birth Mother: The woman who carries the infant to its delivery; may be the biologic mother or surrogate mother.

Mother: When used unmodified, the term mother is intended to include all of the above individuals.

NETCORD: The international organization of CB banks that meet defined membership requirements of NETCORD. NETCORD cord blood accreditation is determined by evaluation of written information provided by the applicant and by on-site inspection. all inspections are conducted by persons qualified by training and experience in haematopoietic progenitor cell therapy and cord blood banking, who have attended cord blood bank inspector training, and who have a working knowledge of the netcord standards and of their application in the various cord blood banking activities. NETCORD standards for cord blood do not cover the clinical transplantation of cord blood cells. further information on NETCORD accreditation is available at www.netcord.org.

Nonconforming Cord Blood Unit: Any CBU that does not completely meet the requirements specified by these Standards, the CBB, and/or the requirements for the donor eligibility.

Partial Label: The minimum essential elements that must be affixed at all times to all cord blood unit containers.

Positive Selection: The manipulation of CB such that a specified cell population(s) is enriched.

Processing: All aspects of manipulation, cryopreservation, packaging, and labeling cellular therapy products regardless of source, including microbial testing, preparation for storage, and removal from storage. processing does not include collection, donor screening, donor testing, storage or distribution.

Processing Facility: The location where cord blood processing activities are performed in support of the CBB. A processing facility may be part of the same institution as the CBB or may be part of another institution and perform these function through contractual agreement.

Product Modifications:

B-Cell-Reduced: Cells processed by negative selection for B lymphocytes.

Buffy Coat Enriched: Cells remaining after removal of a portion of the mature erythrocytes and plasma by centrifugation and/or sedimentation using devices, supplies, and techniques validated for the procedure(s).

Cd34-Enriched: Cells processed by positive selection for CD34-antigen bearing cells.

Cryopreserved: Cells frozen using devices, supplies, and techniques validated to maintain viability.

Plasma And Rbc Reduced: Cells remaining after removal of a portion of the mature erythrocytes and plasma by sedimentation and/or centrifugation using devices, supplies and techniques validated for the procedure(s).

Plasma Reduced: Cells remaining after removal of a portion of the plasma by sedimentation or centrifugation using devices, supplies and techniques validated for the procedure(s).

RBC Reduced: Cells remaining after removal of a portion of the mature erythrocytes by sedimentation, centrifugation, or lysis using devices, supplies, and echniques validated for the procedure(s).

Proficiency Test: A test to ensure the adequacy of testing methods and equipment and the competency of personnel performing testing.

Quality: Conformance of a product or process to pre-established specifications or standards.

Quality Assurance: The actions, planned and performed, to provide confidence that all system and elements that influence the quality of the product are working as expected individually and collectively.

Quality Assessment: The actions, planned and performed, to evaluate all systems and elements that influence the quality of the product or service.

Quality Control: A components of a quality program that includes the activities and controls used to determine the accuracy and reliability of the establishment's personnel, equipment, reagents and operations in the manufacturing of hematopoietic progenitor cell progenitor cell components, including testing and product release.

Quality Improvement: The actions planned and performed to develop a system to review and improve the quality of a product or process.

Quality Management: An integrated program of quality assessment, assurance, control and improvement.

Quality Management Supervisor: A qualified individual designated by the CBB Director, to establish methods to review, modify, approve and implement all procedures intended to maintain quality in the operation of the CBB, and to monitor compliance with these Standards.

Quarantine: The identification or is storage of CB in a physically separate area clearly identified for such use, or using other procedures, such as automated designation to prevent improper release before infectious disease testing results are reviewed.

Reference Samples: Aliquots of cells, plasma, serum, or cellular material from the CBU or blood from the mother that are used to confirm the identity, HLA typing, or genetic or transmissible disease information associated with a single CBU. such samples may or may not be contiguous segments.

Rh: The abbreviation for the Rhesus system of human red cell antigens, is used in this document to refer to the Rh(D) antigen only unless otherwise specified.

Safety: Relative freedom from harmful effects to persons affected, directly or indirectly, by a product when prudently administered, taking into consideration the character of the product in relation to the condition of the recipient at the time.

Selection: The dynamic process of identification of a CBU for transportation that meets recipient-defined criteria.

Standard Operating Procedures Manual: A compilation of written detailed instruction required to perform procedures.

Surrogacy: In a surrogate arrangement a women agrees to becomes pregnant and bear a child for another person/persons and to surrender it at birth. the above practice is not acceptable to most of the major religions in this country. such a surrogate pregnancy can also potentially lead to many legal dilemmas for the persons involved. surrogacy is not allowed in malaysia.

Technical Staff: Means a medical laboratory technologist or scientific officer or any other person with the qualifications, training and experience recognized by the Director General of Health.

Transplantation: The infusion of allogeneic or autologous CB progenitor cells with the intent of providing transient or permanent engraftment.

Volume Reduction: The manipulation of the CBU that results in loss of CB volume without significant loss of nucleated cells.

Validation: Confirmation by examination and provision of objective evidence that particular requirements can consistently be fulfilled. A process is validated by establishing by objective evidence that the process consistently produces a cord blood unit meeting its predetermined specification.

Verification: The confirmation of the accuracy of something or that specified characteristics have been fulfilled.

Viability: Living cells as defined by dye exclusion, flow cytometry, or progenitor cell culture.

REFERENCES

- A) Foundation for the Accreditation of Cellular Therapy (Fact) Standards, Accreditation Manual. Second Edition, 2002.
- B) NETCORD-FACT International Standards for Cord Blood Collection, Processing, Testing, Banking, Selection and Release. Third Edition, December 2006.
- C) FACT-JACIE International Standards for Cellular Therapy Product Collection, Processing and Administration.
- D) Guide To The Preparation, Use And Quality Assurance Of Blood Components, 10th Edition. Council Of Europe Publishing.
- E) Private Healthcare Facilities and Services Act 1998 (Act 586)
- F) Guidelines on Stem Cell Research, *Medical Development Division, Ministry of Health Malaysia, April 2007.*
- G) Guidelines on Importation and Exportation of Human Tissues and/or any Body Part (Garispanduan Pengimportan dan Pengeksportan Tisu Manusia atau Mana-Mana Bahagiannya), *Disease Control Division, Ministry of Health Malaysia, August 2006.*
- H) Malaysian Medical Council on Assisted Reproductive Technique, *Ministry of Health Malaysia, 2007.*
- I) National Organ, Tissue and Cell Transplantation Policy, *Medical Development Division, Ministry of Health Malaysia, June 2007.*

ACKNOWLEDGEMENT

Ministry of Health Malaysia would like to express our deepest gratitude and appreciation to :-

- The Medical Development Division, Ministry of Health Malaysia for their support and services rendered.
- Netcord - FACT for allowing us to adopt some of their standards for our use in cord blood banking services.
- And last but not least to all those who provided valuable input and feedback to make this publication a success.

Cord Blood Unit Labeling Table

Appendix I

Label Element	Partial Label	At the completion of	Shipping Container labeling for transport	At completion of processing and	At CB unit release	Dry shipper
Unique barcode number	AF	AF		AF	AF	
Proper name ‘Cord Blood’	AF	AF	AF	AF	AF	
Statement “Directed Donor” (Directed Allogeneic and “Autologous CB units)	AF	AF		AF	AF	
Statement “Autologous Use Only” (Autologous CB units)	AF	AF		AF	AF	
Collection Centre Identifier		AF				
Date of Collection		AF		AC	AC	
Time of collection and time zone, if different from the CBB Processing Facility		AC				
Name and volume or concentration of anticoagulant and other additives		AF		AC	AC	
Recommended storage temperature		AT		AF	AF	
Donor name (Directed Allogeneic and Autologous CB units)		AF		AF	AF	
Recipient’s name, unique identifier, of family (Directed Allogeneic and Autologous CB units)		AF				
Volume or weight of the CB unit at the end of collection				AC	AC	
Volume or weight of the Cb unit at the end of processing				AC	AC	
Date of cryopreservation				AC	AC	
ABO group and Rh type				AC	AC	
HLA phenotype				AC	AC	
Number of nucleated cells post processing				AC	AC	
Gender of CB unit infant donor				AC	AC	
Identity of the CBB				AF	AF	

continued

Label Element	Partial Label	At the completion of	Shipping Container labeling for transport	At completion of processing and	At CB unit release	Dry shipper
Statement “Properly Identify Intended Recipient and Product”					AT	
Statement “For Use By Intended Recipient Only” (Allogeneic CB units)					AT	
A statement indicating that leukoreduction filters should not be used					AT	
Statement “Do not Irradiate”					AT	
Statement “For Nonclinical Use Only: (if applicable)					AT	
Biohazard legend and/or warning labels (if applicable)				AC	AC	
Date of distribution					AC	AF
Shipping facility name, address, phone number			AF			AF
Receiving facility name, address, phone number			AF			AF
Identity of person or position responsible for receipt of the shipment			AF			AF
Statement “Do Not X-Ray”						AF
Statement “Medical Specimen”. Handle With Care						AF
Statement indicating Cord blood for Transplantation						AF
Shipper Handling instructions						AF

Each label shall include at least the elements detailed in the following table:

AF=Affix, AT=Attach or Affix, AC=Accompany or Attach or Affix The chart has minimum requirements only. A CBB may choose to be more inclusive.

