MINISTRY OF HEALTH MALAYSIA

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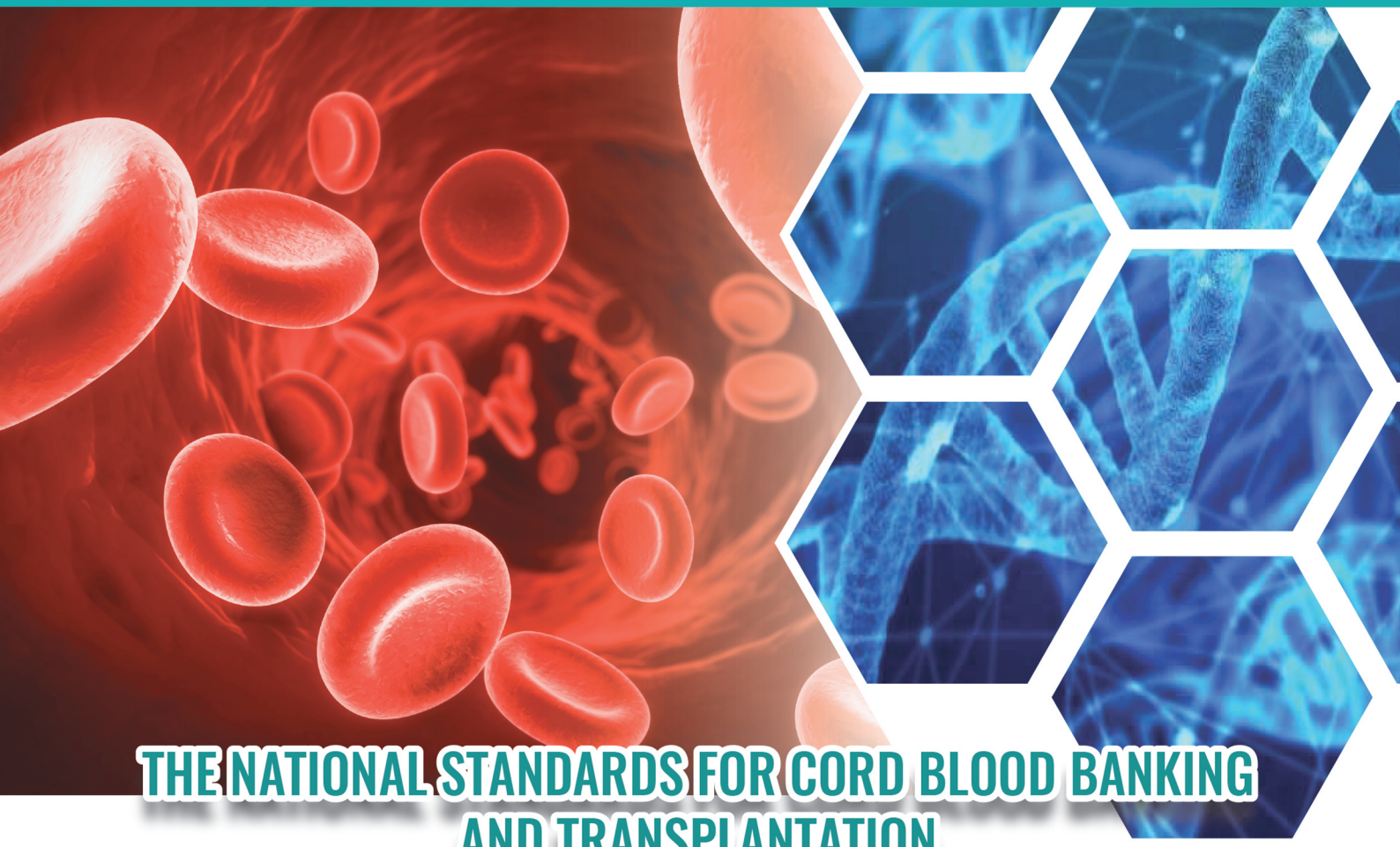
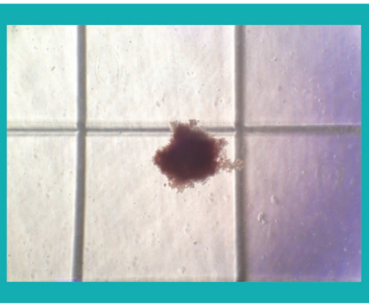
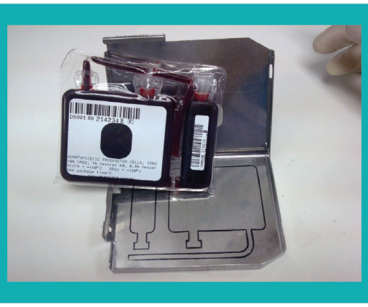


THE NATIONAL STANDARDS FOR CORD BLOOD BANKING AND TRANSPLANTATION

OCTOBER 2019



MEDICAL DEVELOPMENT DIVISION,
MINISTRY OF HEALTH, MALAYSIA

FOREWORD BY THE DIRECTOR GENERAL OF HEALTH MALAYSIA

The advancement of stem cell transplantation is a major breakthrough in medicine, offering hope to patients with blood cancers and other blood disorders where other treatment have failed. Among all haemopoietic stem cells sources, stem cells from cord blood stand a bright chance in championing both transplantation and stem cell based therapies. Internationally, advanced cellular molecular therapies using cord blood and adult derived stem cell for regenerative medicine, immunotherapy and tissue repair are also developing rapidly. At local arena, the extensive establishment of cord blood banking and transplantation requires a provision of clear guidance to undertake all activities in ensuring the quality of each collected stem cell unit.

This current edition of the National Standard for Cord Blood Banking and Transplantation is paramount to ensure quality and standardised laboratory practices throughout all essential phases of cord blood collection, processing, cryopreservation, selection and releasing to achieve consistent production of high quality and adequate yield of viable cells for a successful and efficient cord blood haematopoietic stem cells transplant with total quality management approach.

The review of this current Standard is a collaborative effort with commitment and by consensus from experts within the Ministry of Health Malaysia, academicians and other various stakeholders both from public and private sectors involved in various aspects of blood and bone marrow transplantation in Malaysia. It is based on the available technology and capability to the greatest extent possible concerning to issues of safety and effective cord blood stem cell therapy to be made available for patients. This Standard is designed to provide minimum guidelines for Cord Blood Banks and shall be adhered to by all personnel involved in the provision of cord blood haemopoietic stem cell transplantation services.

I would like to congratulate and express my gratitude in appreciating the working committee for the excellent effort and commitment in putting together this Standard. It is the responsibility of all health care providers to ensure that the foremost services are to be accorded for the benefit of the patients.

Datuk Dr. Noor Hisham Abdullah
Director General of Health Malaysia

FOREWORD BY CHAIRMAN OF THE STEERING COMMITTEE FOR NATIONAL STANDARDS FOR CORD BLOOD BANKING AND TRANSPLANTATION

Umbilical cord blood is an alternative source of haematopoietic stem cells to treat patients with diseases curable by haematopoietic cell transplantation. The first cord blood transplantation was successfully performed in France in October 1988 on a child with Fanconi Anaemia. The stem cell graft was obtained from the patient's newborn brother's cord blood. Since then, there has been tremendous progress in the field of cord blood banking and transplantation. Today, over 700,000 cord blood units have been stored in the cord blood banks worldwide and more than 30,000 cord blood transplantations have been performed. In the paediatric setting, both related and unrelated cord blood transplants have been performed with high rates of success for a variety of haematologic disorders, immunologic and genetic diseases.

In Malaysia, several private and 2 public cord blood banks have been established. Stem cell technology, utilising cord blood, has also gained national interest in view of its effectiveness in treating diseases as mentioned above and its potential utilisation in newer applications such as regenerative medicine. The first edition of the National Standards for Cord Blood Banking and Transplantation was published in 2008 to provide guidelines to ensure the collection and storage of standardised high quality cord blood units for transplantation. The review of the existing edition is necessary to update the requirements of this Standards in tandem with the developments occurring at international level covering the aspects of cord blood collection, processing, cryopreservation, selection and release of cord blood units. It is intended for use by management and technical personnel in cord blood banking services and may also be used for conduct of audits on cord blood bank services.

These Standards are in accordance with international best practices and the working group had referred to established international and other national standards which are based on published scientific literature. Both private and public cord blood banks in Malaysia should adhere to these Standards in carrying out their respective operations. It is hoped with the availability of these Standards, the quality of the stem cell units will further improve and contribute significantly to the success of the transplantation program in the country.

Dr. Noryati Abu Amin
Director (2014 – present)
National Blood Centre
Kuala Lumpur

Dato' Dr. Roshida Hassan
Director (2009 – 2014)
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SECTION 1 INTRODUCTION

The primary objective of publishing the National Standards of Cord Blood Banking and Transplantation is to promote quality medical and laboratory practices in both public and private Cord Blood Banks in Malaysia. Its first edition was published in 2008 and since then many advancements in the field of cord blood banking and services have occurred around the world. It is thus imperative that a new edition is made available for Malaysian CBB services to provide updated guidelines that conform to the national regulation and accepted current international practices.

As in the previous edition, these Standards cover cord blood cells collection, screening, testing, and eligibility determination of the maternal and neonate donor including all phases of processing, cryopreservation, and storage, listing, search and reservation process for selection of specific cord blood units and distribution of cord blood units. It is to be noted that the collection, processing and administration of erythrocytes, mature granulocytes, platelets, plasma or plasma-derived products intended for transfusion support are not within the scope of these Standards.

This second edition of the Standards were developed by consensus and collaboration by experts within the Ministry of Health Malaysia, universities and professionals involved in various aspects of blood and bone marrow transplantation in Malaysia. As cord blood banking is still an evolving field, every effort has been made to incorporate sound recommendations fostering quality medical and laboratory practices. The standards developed were based on the available international standards and published evidence-based science to the greatest extent possible.

These Standards are designed to provide minimum guidelines for facilities and individuals involved in all the processes as stated above. Each Cord Blood Bank and individual should analyse its practices and procedures to determine whether additional standards apply. Individual facility may exceed these Standards as deemed appropriate by the responsible personnel. In all cases, personnel must follow all applicable national regulations and directives.

This second edition of the Standard is effective from the date of publication.

SECTION 2 MANAGEMENT AND OPERATIONAL REQUIREMENTS

2.1 GENERAL REQUIREMENTS

2.1.1 The CBB shall consist of an integrated team responsible for CBB management; donor selection and management, collection, processing, testing, cryopreservation, storage, listing, search, selection, reservation, release and distribution of CBU; and recipient follow-up.

2.1.2 The CBPF and each CBCF shall operate in compliance with these Standards.

2.1.2.1 The CBB shall be registered and licensed as required by any Applicable Law for the activities performed.

2.1.2.2 Each CBB should plan for accreditation.

2.1.3 Claims made in advertising shall be supported by scientific evidence.

2.1.4 The CBB shall have a mechanism to list and distribute CBU for clinical use.

2.1.4.1 If the CBB utilises a registry to deliver services related to the listing, search, selection, reservation, release and/or distribution of a CBU:

2.1.4.1a The responsibilities of the registry shall be clearly documented.

2.1.4.1b The registry shall comply with these Standards.

2.1.5 If the CBB contracts with any other entity for services related to CBU donor management, collection, processing, testing, cryopreservation, storage, listing, search, selection, reservation, release, distribution and/or any other aspect of banking, the responsibility of each entity shall be clearly documented.

2.1.5.1 Each contracted entity shall meet these Standards with respect to its interaction with the CBB.

2.1.6 There shall be a CBB Director, a CBB Medical Director, CBCF Director(s), a CBPF Director and a Quality Unit Officer (QUO), responsible for the CBB operations and its overall compliance with these Standards including the CBB's policies and Standard Operating Procedures (SOP).

2.1.6.1 The CBB Director shall have an earned doctoral degree in medicine or in a related scientific field, with training and minimum of two (2) years of experience in immunogenetics of transplantation, basic or clinical immunology,

immunohaematology, basic or clinical haematology, transfusion medicine, blood or tissue banking, or cryobiology. The CBB Director has final responsibility for the CBB operations and its overall compliance with these Standards, including all components of the CBB's policies and SOP. The CBB Director shall participate regularly in educational activities related to the filed of CB banking and/or cellular therapy product collection, processing and administration.

2.1.6.1a If the CBB Director does not have specific training and expertise in HLA, the CBB shall confirm HLA expertise is available and utilised by the CBB.

2.1.6.2 The CBB Medical Director shall be a licensed physician with training in haematopoietic cell transplantation or blood or tissue banking. This individual is responsible for donor recruitment; donor eligibility; medical aspects of CB collection procedures, CB processing procedures, and review of the release and outcome data of the CBU; and compliance of the CBCF and CBPF with these Standards. The CBB Medical Director shall participate regularly in educational activities related to the field of donor safety, CB banking, and/or cellular therapy product collection, processing and administration.

2.1.6.3 The CBCF Director shall be a health care professional who is responsible for communicating with the CBB Medical Director regarding operations at an individual CBCF. The CBCF Director shall participate regularly in educational activities related to the field of donor safety, CB banking and/or cellular therapy product collection, processing and administration.

2.1.6.4 The CBPF Director shall be an individual with a relevant doctoral degree, qualified by training or experience for the scope of activities carried out in the CBPF. The CBPF Director is responsible for all operational aspects of all procedures related to receipt, testing, processing, cryopreservation, storage, release and distribution of CBU and administrative operations of the CBPF, including compliance with these Standards. The CBPF Director shall participate regularly in educational activities related to the field of CB banking and/or cellular product collection, processing and administration.

2.1.6.5 The QUO shall be an individual with relevant training in quality management. The QUO shall establish and maintain system to review, and implement all policies and SOP and monitor performance of the Quality Management Program, the quality of the CBU and compliance with these Standards.

2.1.6.5a The QUO shall be a different individual from the CBB Director, CBB Medical Director, CBCF Director and the CBPF Director.

2.1.6.5b The QUO shall participate regularly in educational activities related to the field of quality management, CB banking and/or cellular therapy product collection, processing and administration.

2.1.7 The CBB shall have an adequate number of qualified staff for its operations.

2.2 QUALITY MANAGEMENT PROGRAMME

2.2.1 The CBB shall establish and maintain a QMP that includes all key CBB functions including donor management, collection, processing, screening and testing, cryopreservation, storage, listing, search, selection, reservation, release, distribution and outcome analysis.

2.2.2 The CBB shall establish and maintain a written QMS that describes the QMP.

2.2.2.1 The CBB Director and the QUO shall participate in the establishment and maintenance of the QMS.

2.2.2.2 The QUO shall have responsibility for ensuring the QMP is effectively established and maintained.

2.2.2.3 The QUO shall report on quality management activities regularly.

2.2.2.4 The QUO shall report on the performance of the QMP on an annual basis, at a minimum.

2.2.3 The QMS shall include documentation of the relationship and interaction among all participating facilities and services, including, at a minimum, CBCF, CBPF, information technology services, testing laboratories, storage facilities, registries and outcome databases.

2.2.3.1 The QMS shall include an organisational chart of key positions, functions and interactions within the CBB, the CBCF and the CBPF.

2.2.4 The QMS shall include policies and SOP for establishment and maintenance of written agreements with external parties whose services impact the CBU.

2.2.4.1 Agreements shall include the responsibility of the external party performing any relevant aspect of CB collection, testing, banking or distribution for administration to comply

with these Standards and the requirements of other applicable accrediting agencies.

2.2.5 The QMS shall include or summarise a system for change control that includes at a minimum:

2.2.5.1 A description of the proposed change and who is affected.

2.2.5.2 Analysis of the change for compliance with these Standards.

2.2.5.3 Identification of risks of the change to the donor, CBU or recipient.

2.2.5.4 System for change approval, effective date and implementation.

2.2.5.5 Method for communication of the change and training.

2.2.6 The QMS shall include a system for document control inclusive of the following elements:

2.2.6.1 Current listing of all critical documents that shall comply with the document control system requirements that includes the following:

2.2.6.1a Policies and SOP.

2.2.6.1b Worksheets.

2.2.6.1c Forms.

2.2.6.1d Labels.

2.2.6.1e Educational, promotional and recruitment materials.

2.2.6.2 A Standard Operating Procedure for preparation, approval, implementation, review, revision and archival of all policies and SOP.

2.2.6.3 A procedure for document approval, including the approval date, signature of approving individuals and the effective date.

2.2.6.4 A procedure for document distribution to relevant personnel, including written confirmation that relevant personnel have received and read the document.

2.2.6.5 A system for document change control that includes description of the change, signature of approving individuals, approval date and effective date.

2.2.6.5a There shall be a system to protect controlled documents from accidental or unauthorised modification.

2.2.7 A system for document creation, assembly, review, storage, archival, retention and retrieval.

2.2.7.1 There shall be a standardised format indicating the date of document became effective and when it was archived.

2.2.7.2 Records of archived SOP, protocols and labels in their historical sequence including date of use, shall be maintained indefinitely.

2.2.8 The QMS shall include policies to support management of electronic record systems and electronic records and to maintain pertinent electronic records, if applicable.

2.2.9 The QMS shall include policies for actions to take in the event when CBB's operations are interrupted.

2.2.10 The QMS shall include a system to maintain confidentiality.

2.2.11 The QMS shall include a schedule for conducting audits of CBB key functions annually at minimum to verify compliance with elements of the QMS.

2.2.11.1 Key functions shall include donor management, collection, processing, testing, cryopreservation, storage, listing, search, selection, reservation, release, distribution and outcome analysis.

2.2.11.2 There shall be a written procedure for the management of external audits and inspections.

2.2.11.2a Documentation of results of inspection and accreditation visits shall be maintained indefinitely.

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

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

2.2.11.5 The results of audits shall be used to recognise problems, detect trends, identify improvement opportunities, implement corrective and preventive actions, and follow-up on the effectiveness of those actions.

2.2.11.6 Audit shall include documentation of the external facilities performing contracted services have met the requirements of the written agreements.

2.2.12 The QMP shall include a system to address errors, accidents, biological product deviations, adverse events, variances and complaints including the following activities at a minimum:

2.2.12.1 Detection.

2.2.12.1a There shall be a defined process improvement plan that includes the recognition of all issues that require corrective action.

2.2.12.1b There shall be a process for the regular review of records and assessment of record review to identify recurring problems, potential points of failure or need for improvement.

2.2.12.2 Investigation.

2.2.12.2a A thorough investigation shall be conducted by the CBB in collaboration with the CBCF, CBPF, registry and/or Transplantation Centre

2.2.12.3 Documentation.

2.2.12.3a All files of errors, accidents, product deviations, adverse events, variances and complaints shall be maintained indefinitely.

2.2.12.3b A written report of the investigation including conclusions, follow-up and corrective actions shall be prepared and linked to the particular CBU.

2.2.12.3c Records of all severe or unexpected adverse events or adverse reactions during CB collection and infusion shall be maintained.

2.2.12.3d Investigation reports shall be utilised in quality monitoring and tracking in order to analyse trends.

2.2.12.4 Tracking.

2.2.12.4a Errors, accidents, biological product deviations, adverse events, variances and complaints shall be tracked and trended in order to categorise and identify system problems and initiative corrective actions.

2.2.12.4b Investigation reports shall be utilised in quality monitoring and tracking in order to analyse trends.

2.2.12.5 Evaluation.

2.2.12.5a Planned deviations shall be pre-approved, as well as unplanned deviations shall be reviewed by the CBB Director and other staff as appropriate.

2.2.12.5b Unplanned deviations and associated corrective action, if necessary, shall be reviewed by the appropriate CBB Director and/or Medical Director, the QUO and other staff as appropriate.

2.2.12.5c All complaints shall be evaluated to determine if the complaint is related to a product deviation or adverse reaction.

2.2.12.6 Reporting.

2.2.12.6a When CBU is determined to be responsible for an adverse reaction, the reaction and results of the investigation shall be reported to the Transplant Centre, other parties involved in manufacturing of CBU, registries and governmental agencies as required by Applicable Law or these Standards.

2.2.12.6b Errors, accidents, biological product deviations, variances and complaints shall be reported to other parties involved in CBB functions on the affected CBU and to appropriate regulatory, registries or Ethics Committees as necessary.

2.2.12.7 Corrective action.

2.2.12.7a Corrective action shall be implemented and documented as indicated to address problem and to prevent the problem from recurring.

2.2.12.7b Corrective actions shall include the initiation of retraining and/or re-education of employees and performing follow-up audits of deficiencies as appropriate.

2.2.12.7c Documentation of the corrective action shall include the nature of the problem requiring corrective action and the identity and disposition of the affected CBU if indicated.

2.2.12.7d Documentation of the corrective action shall be maintained, including the dates of corrective action and a designated time frame at which the outcome of the corrective action shall be evaluated.

2.2.12.7e Corrective actions shall be evaluated by the appropriate Director and/or Medical Director or designee, the QUO and other appropriate staff.

2.2.13 The QMP shall include policies and procedures for selection of vendors, equipment, supplies, reagents and facilities.

2.2.13.1 Qualification studies shall be reviewed and approved by the CBB Director and the QUO.

2.2.13.2 Suppliers of critical supplies, reagents, services and equipment shall be qualified by a method that verifies they comply with these Standards.

2.2.14 The QMP shall include policies and SOP for validation of critical procedures of CBB functions.

2.2.14.1 Each validation shall include:

2.2.14.1a A validation plan.

2.2.14.1b Acceptance criteria.

2.2.14.1c Data collection.

2.2.14.1d Evaluation of data.

2.2.14.1e Summary of results.

2.2.14.1f Documentation of review and acceptance of the methodology.

2.2.14.1g Review and approval by the CBB Director or designee of the validation results and conclusions.

2.2.14.2 Changes to a process shall be verified or validated and documented.

2.2.15 The QMP shall include policies and procedures for CBU tracking, tracing and linkage that allow tracking from the neonate donor to the recipient or final disposition and tracing from the recipient or final disposition to the neonate donor.

2.2.15.1 Linkage of the CBU to the neonate donor and mother shall be retained confidentially and indefinitely.

2.2.15.2 Documentation of all facilities involved in each stage of CBU management shall be established and maintained.

2.2.16 The QMP shall include documented arrangement to trend, investigate and evaluate details of clinical outcome data and CBU characteristics.

2.2.16.1 The CBB shall obtain, maintain and analyse sufficient critical outcome data to verify that the procedures in use consistently provide a safe and effective product.

2.2.16.2 There shall be a written stability program that annually evaluates a minimum of three CBU per manufacturing method.

2.2.16.2a There shall be a plan for defining an expiration date.

2.3 PERSONNEL REQUIREMENTS

2.3.1 The QMS for personnel shall include education, experience and training requirements for each key position in the CBB. Personnel requirements shall include at a minimum:

2.3.1.1 Current position description for each staff member.

2.3.1.2 A system to document for each staff member:

2.3.1.2a Professional Qualification.

2.3.1.2b New employee orientation.

2.3.1.2c Initial training, training on each procedure performed and retraining as necessary.

2.3.1.2d Competency for each function performed.

2.3.1.2e Continued competency at least annually.

2.3.1.2f Continued education.

2.3.1.3 Trainer and training requirements for each position in the CBB including at a minimum:

2.3.1.3a A policy and/or SOP for personnel training and competency assessment.

2.3.1.3b A system that provides consistent training programs.

2.3.1.3c A description of minimal trainer qualifications.

2.3.1.4 Records of identification codes of personnel including methods to link the name and/or signature to the initials or other codes used to identify the responsible staff member. These records shall include dates of employment.

2.3.2 All personnel at the CBB, CBCF and CBPF shall follow the applicable policies and SOP established by the CBB.

2.4 OPERATIONAL POLICIES AND STANDARD OPERATING PROCEDURES

2.4.1 The CBB shall establish and maintain policies and/or SOP addressing critical aspects of operations and management in addition to those required in section 2.2. These documents shall include all elements required by these Standards and shall address the following aspects:

2.4.1.1 Cord blood donor management and collection.

2.4.1.2 Cord blood processing.

2.4.1.3 Cord blood listing, search, selection, reservation, release and distribution.

2.4.2 The CBB shall maintain a detailed and clearly written SOP to allow qualified staff to follow and complete the procedures successfully. The SOP shall include at a minimum the following:

2.4.2.1 A table of contents.

2.4.2.2 A standardised format for procedures, worksheet, forms and labels.

2.4.3 Standard Operating Procedures shall be sufficiently detailed and unambiguous to allow qualified staff to follow and complete the procedures successfully. Each individual SOP shall be written clearly and include the following elements.

2.4.3.1 Description of the objectives.

2.4.3.2 The personnel responsible for its execution.

2.4.3.3 A description of the facility, equipment, reagents and consumables required.

2.4.3.4 A stepwise description of the procedure.

2.4.3.5 Acceptable end-points and the expected range of results if applicable.

2.4.3.6 Reference to other SOP or policies required to perform the procedure.

2.4.3.7 A current version of worksheets, forms, reports and labels where applicable.

2.4.3.8 The date(s) and approval signature of the CBB Director, the QUO and relevant key personnel prior to implementation.

2.4.3.9 The date of review or revision and the approval signature of the CBB Director or designee, the QUO and relevant key personnel upon procedural modifications and at least every two years after implementation.

2.4.4 All policies and SOP shall comply with these Standards.

2.4.5 Copies of policies and SOP of the CBB relevant to the processes being performed shall be readily available to the CBB personnel.

2.4.6 All personnel at the CBB, CBCF and CBPF shall follow the applicable policies and SOP established by the CBB.

2.4.7 Review and/or training by a staff member shall be documented before staff is allowed to perform new and revised procedures.

2.5 FACILITIES AND SAFETY

2.5.1 The CBB space shall be of adequate size, construction and location to maintain safe operations, prevent contamination and promote proper handling.

2.5.1.1 The CBCF and CBPF space shall be maintained in a clean and orderly manner to prevent introduction, transmission or spread of communicable disease.

2.5.1.2 Separate areas shall be identified and maintained for processing and storage of CBU to prevent mislabelling, mix - ups, contamination and cross - contamination of CBU.

2.5.1.3 The CBB shall be secured to prevent the admittance of unauthorised individuals.

2.5.1.4 There shall be policies and SOP for biological chemical and radiation safety as appropriate including:

2.5.1.4a Communicable disease agents.

2.5.1.4b Chemical hygiene.

2.5.1.4c Hand washing.

2.5.1.4d Fire safety.

2.5.1.4e Radiation safety, if applicable

2.5.1.4f Latex allergy.

2.5.1.4g Power Failures.

2.5.1.4h Liquid nitrogen

2.5.1.4i Disposal of biological waste.

2.5.2 Where processes are not closed and there is an exposure of CBU to immediate room environment, measures should be in place including engineering and environment control on the basis of risk assessment principle.

2.6 CORD BLOOD BANK OPERATIONS

2.6.1 The responsibilities of each CBCF, CBPF, collecting health care professional and registry as they relate to the CBB shall be clearly defined and documented.

2.6.1.1 A CBB that includes multiple CBCF and/or CBPF shall employ coordinate policies and SOP, protocols, staff training and competency evaluation procedures and QMS.

2.6.1.2 A CBB that includes multiple CBCF and/or CBPF shall demonstrate evidence of regular interaction between these CBCF and/or CBPF and the CBB.

2.6.2 Records of each CBU shall be made concurrently with each stage of donor management and CBU collection, processing, testing, cryopreservation, storage, listing, search, selection, reservation, release, distribution and/or disposal in such a way that all steps may be accurately traced.

2.6.2.1 Records shall identify the person responsible for each step from collection to final disposition of the CBU include appropriate dates and times to provide a complete history of the work performed and to relate the records to a particular CBU.

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

2.6.3 The CBB shall have an established relationship with each CBCF to facilitate implementation and compliance with the CBB QMP and SOP.

2.6.4 The CBB shall incorporate CBCF activities into its QMP.

2.6.5 There shall be neonate donor and mother evaluation procedures in place to evaluate the risk of infectious and genetic disease transmission from CBU.

2.6.5.1 Maternal and neonate donor evaluation shall be reviewed by trained CBB personnel.

2.6.5.2 Maternal and neonate donor eligibility shall be determined based upon results of screening and testing.

2.6.5.3 Risks of genetic or malignant disease transmission from the CBU shall be determined based upon results of donor screening and testing.

2.6.5.4 When a mother does not meet the established screening criteria, the CBB Medical Director shall decide and document in the permanent record the nature of the nonconformance and the rationale for inclusion of the CBU.

2.6.6 The CBB should utilise a HLA testing laboratory that demonstrate the following:

2.6.6.1 Participate and scores well in external QAP Programme.

2.6.6.2 Establish and implement QMS.

2.6.6.3 Accredited by the internationally recognised or equivalent accrediting organisation.

2.6.7 All laboratories utilised by the CBB for testing of reference samples and maternal samples shall be accredited, certified or licensed to perform such testing in accordance with Applicable Law.

2.6.7.1 The CBB shall maintain documentation of the accreditation, certification or licensure of these laboratories to perform this testing.

2.6.7.2 When external laboratories are used for any aspect of reference sample or maternal 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.

2.6.8 Confidentiality.

2.6.8.1 There shall be a system to maintain the confidentiality of the neonate donor, receipient and their respective families according to these Standards and Ethics Committee. (Refer to the National Organ, Tissue and Cell Tranplantation Policy).

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

2.6.8.3 The CBB shall have written policies and SOP for circumstances where neonate donor, mother or neonate donor's legal guardian and appropriate medical personnel could be contacted.

2.6.9 Procedures shall be developed to monitor the continuing adequacy of the procedures, reagents, consumables and equipment used routinely by the CBB personnel.

2.6.9.1 The results of ongoing internal monitoring shall be documented, checked and analysed regularly.

2.6.9.2 If cord tissue is collected, procedures for tissue collection, processing and storage shall be fully integrated into the QMS.

2.6.10 Ethics Committee or Institutional Review Board Requirements.

2.6.10.1 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.

2.6.10.2 The CBB shall maintain documentation of all its research protocols, Ethics Committee or Institutional Review Board approval, investigational new drug or device exemptions, annual reports and any adverse events.

2.7 CODING AND LABELLING OF CORD BLOOD UNITS

2.7.1 Coding and Labelling.

2.7.1.1 CBU shall be identified according to the proper name of the unit, including appropriate modifiers and attributes as defined by the system used by the individual CBB.

NOTE: The ISBT 128 is the preferred system for coding and labelling. If the CBB has not fully implemented ISBT 128, an implementation plan for the usage of ISBT 128 coding and labelling shall be in place.

2.7.2 Label controls.

2.7.2.1 Pre-printed labels.

2.7.2.1a Labels shall be held upon receipt from the manufacturer pending review and proofing against a copy or template approved by the CBB Director or designee to confirm accuracy regarding identity, content and conformity.

2.7.2.1b Stocks of unused labels representing different products shall be stored and maintained in a controlled manner to prevent errors.

2.7.2.1c Unused obsolete labels shall be destroyed.

2.7.2.2 Print-on-demand label systems shall be validated to confirm accuracy regarding identity, content and conformity of labels to templates approved by the CBB Director or designee.

2.7.2.3 A system for label version control shall be employed.

2.7.2.4 Representative obsolete labels shall be archived indefinitely.

2.7.2.5 The label shall be validated as reliable for storage under the conditions in use.

2.7.3 Labelling Operations.

2.7.3.1 Labelling operations shall be conducted in a manner adequate to prevent mislabelling or misidentification of CBU, samples and associated documents.

2.7.3.2 There shall be processes to verify that all labels in use are accurate, legible and maintain physical integrity.

2.7.3.2a A system of checks in labelling procedures shall be used to prevent errors in transferring information to labels.

2.7.3.2b A controlled labelling procedure consistent with these Standards shall be defined and followed if container label information is transmitted electronically during a labelling process. This procedure shall include a verification step.

2.7.3.2c When the label has been affixed to the CBU, a sufficient area of the bag shall remain uncovered to permit inspection of the contents.

2.7.3.2d The information entered manually on the CBU bag label shall be verified by at least two (2) staff members prior to allowing the CBU to progress to the next stage of processing, storage or distribution.

2.7.3.2e All labelling shall be clear, legible and printed using ink that is indelible to all relevant agents.

2.7.3.2f Labels affixed directly to a CBU bag shall be applied using appropriate materials as defined by the applicable authority.

2.7.3.3 CBU that are subsequently re-packaged into new containers shall be labelled with new labels before they are detached from the original container.

2.7.3.3a The process to establish linkage between original and new labels shall be validated and maintained as a permanent part of the CBU record.

2.7.3.4 Integrally attached segments should be labelled with an identifier linking the segments to the applicable CBU.

2.7.4 Identification.

2.7.4.1 There shall be a human-readable system and a machine-readable system in operation for identification of the CBU samples and associated documents.

2.7.4.2 Each CBU shall be assigned a unique numeric or alphanumeric identifier by which it will be possible to trace any CBU to its maternal and neonate donor data, delivery information, family history, test results and to all records describing the handling and final disposition of the CBU.

2.7.4.2a There shall be processes to ensure that the CBU identifier is unique to prevent errors in identification.

2.7.4.2b If a single collection is stored in more than one fraction, there shall be a system to identify each fraction.

2.7.4.2c For multiple gestation deliveries, there shall be a system to link each neonate donor to the correct CBU.

2.7.4.3 If the CBB designates an additional or supplementary numeric or alphanumeric identifier to the CBU and/or samples, supplementary identifiers shall not obscure the original identifier.

2.7.4.3a No more than one supplementary identifier shall be visible on a CBU bag.

2.7.4.3b The facility associated with each identifier shall be documented.

2.7.5 The information provided on the label by the CB Clinical Site shall be maintained indefinitely as part of the CBU record.

2.7.6 Label Content.

2.7.6.1 The content of each label shall be compliant with these Standards.

2.7.6.2 Each label shall include at least the required information detailed in Cord Blood Unit Labelling table in Appendix 1.

2.7.6.3 A CBU bag with a partial label shall be accompanied by the required information detailed in the Cord Blood Unit Labelling table in Appendix I attached securely to the CBU on a tie tag or enclosed in a sealed package to accompany the CBU.

2.7.6.4 A partial label at a minimum shall be present on the CBU during all stages of processing.

2.8 EQUIPMENT

2.8.1 All critical equipment shall be defined, qualified and validated for the intended use.

2.8.1.1 Equipment should be used in accordance with the manufacturer's instruction.

2.8.2 Equipment shall be used in a manner that prevents CBU mix-ups, contamination and cross-contamination, and does not compromise function and integrity of the CBU.

2.8.3 Equipment shall conform to Relevant Law and Regulation.

2.8.4 Equipment records shall include manufacturer's name, serial number or other identifier, manufacturer's instructions, equipment location including the identification of each CBU for which the equipment was used.

2.8.4.1 Equipment records should be maintained for a minimum of 10 years after distribution of the CBU.

2.8.5 Calibration.

2.8.5.1 Equipment shall be observed, tested and calibrated on a regularly scheduled basis as recommended by the

manufacturer, after a critical repair or move and at a minimum annually.

2.8.5.2 All equipment with a critical measuring function shall be calibrated against a traceable standard, if available. Where no traceable standard is available, the basis for calibration shall be described and documented.

2.8.5.3 When equipment is found to be out of calibration or specification, there shall be a defined process for action required for CBU manufactured since the last calibration.

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

2.8.6 Maintenance and repairs.

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

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

2.8.6.3 There shall be a procedure that addresses the actions to take in the event of equipment malfunction or failure.

2.8.7 Cleaning and sanitation.

2.8.7.1 Equipment shall be cleaned and sanitised according to established schedules.

2.8.7.2 Records of equipment cleaning and sanitation shall be maintained.

2.8.8 Equipment shall be routinely inspected for cleanliness, sanitation and calibration to confirm adherence to equipment maintenance schedules.

2.9 SUPPLIES AND REAGENTS

2.9.1 All critical reagents and supplies shall be obtained from approved vendors.

2.9.2 Critical reagents and supplies shall be defined and qualified to function as expected.

2.9.3 Supplies and reagents shall not adversely affect the viability of the CBU and shall not permit the introduction of any agent for the transmission or spread of communicable disease.

2.9.4 Supplies and reagents that come into contact with the CBU shall be sterile.

2.9.4.1 Sterilisation of supplies and reagents prepared within the facility shall be documented.

2.9.5 Supplies and reagents should be used in a manner consistent with instructions provided by the manufacturer.

2.9.6 Supplies and reagents used for CB collection, processing or cryopreservation, whenever possible shall be of the appropriate grade for intended use and approved for human use.

2.9.7 Certificates of analysis shall be obtained and maintained indefinitely on file for all critical reagents.

2.9.8 Receipt, inspection, verification, acceptance and storage of supplies and reagents shall be documented.

2.9.8.1 The disposition of rejected supplies and reagents shall be documented.

2.9.9 The lot number, expiration date and manufacturer of supplies and reagents used shall be documented.

2.10 INVENTORY MANAGEMENT

2.10.1 The CBB shall establish the inventory management system to ensure traceability, security and safety of the CBU.

2.11 INVENTORY TRANSFER

2.11.1 The CBB shall establish a procedure for inventory transfer to another CBB.

2.12 DOCUMENTS AND RECORDS REQUIREMENTS

2.12.1 A record management system shall be established and maintained to allow for protection, preservation, integrity, disposal and ready retrieval of records.

2.12.1.1 Records shall be available for inspection by authorised individuals upon request from a regulatory or accrediting agency.

2.12.2 If records are maintained in more than one location and/or format, there shall be a system for prompt identification, location and retrieval of all records.

2.12.3 Identity and medical records of the infant donor and family shall be in a language understood by the CBB personnel, registry and/or Transplant Centre.

2.12.4 The following CBB records shall be maintained indefinitely:

2.12.4.1 Neonate donor and maternal records.

2.12.4.2 CBU records related to collection, processing, storage and distribution.

2.12.4.3 Quality management records.

2.12.4.4 Personnel records.

2.12.5 Facility cleaning and sanitation records shall be retained for three (3) years at a minimum.

2.12.6 Equipment maintenance, inspection, calibration and cleaning records shall be retained indefinitely.

2.12.7 Records in case of divided responsibility.

2.12.7.1 If two (2) or more facilities participate in donor management or the collection, processing, testing, cryopreservation, storage, listing, search, selection, reservation, release or distribution of the CBU, the records of each facility shall plainly show the extent of its responsibility.

2.12.7.2 The CBB shall maintain a listing of the names, addresses and responsibilities of other facilities that perform manufacturing steps on a CBU.

2.12.7.3 There shall be a system to allow the CBB access to information that tracks all manufacturing steps performed by other facilities.

2.12.7.4 Each participating facility shall furnish to the facility of final disposition a copy of CB collection and processing records related to the safety of the CBU.

2.12.8 Electronic Records Requirements

2.12.8.1 The CBB shall establish and maintain a current listing of all critical electronic record systems. Critical electronic record systems shall include at a minimum systems under the control of the CBB that are used in lieu of paper and to:

2.12.8.1a Make decisions.

2.12.8.1b Perform calculations.

2.12.8.1c Create and/or store information used in critical procedures.

2.12.8.2 For all critical electronic record systems, there shall be procedures to maintain the accuracy, integrity, identity and confidentiality of all records.

2.12.8.2a There shall be a means by which access to electronic records is limited to authorised individuals.

2.12.8.2b There shall be protection of the records to enable their accurate and ready retrieval throughout the period of record retention.

2.12.8.2c All critical electronic record systems shall ensure that all donor and CBU identifiers are unique.

2.12.8.3 For all critical electronic record systems, there shall be an alternative system to allow continuous operation of the CBB in the event that critical electronic record systems are not available. The alternative system shall be validated and CBB staff shall be trained in its use.

2.12.8.4 For all critical electronic record systems, there shall be written procedures for record entry, verification and revision.

2.12.8.4a A method shall be established or the system shall provide for review of data before final acceptance.

2.12.8.4b A method shall be established or the system shall provide for the unambiguous identification of the individual responsible for each record entry.

2.12.8.5 For all critical electronic record systems, there shall be the ability to generate true copies of the records in both human readable and electronic format suitable for inspection and review.

2.12.8.6 For all critical electronic record systems, there shall be validated procedures and documentation of:

2.12.8.6a Systems development.

2.12.8.6b Numerical designation of system versions, if applicable.

2.12.8.6c Prospective validation of system, including hardware, software and database.

2.12.8.6d Installation of the system.

2.12.8.6e Training and continued competency of personnel in systems use.

2.12.8.6f Monitoring of data integrity.

2.12.8.6g Back-up of the electronic records system on a regular schedule.

2.12.8.6h System maintenance and operations.

2.12.8.7 All system modifications shall be authorised, documented and validated prior to implementation.

2.13 INTERRUPTION OF OPERATIONS AT ESTABLISHED SITES

2.13.1 In the event that any CB collection or processing function is discontinued for a period exceeding six months, there shall be documentation of the training and continued competency of all staff to perform the duties assigned upon resumption of activities.

2.13.2 If CB collection activity is discontinued at any fixed CBCF for a period exceeding six months, the CBB Director or designee shall review and renew the CB collection contract with that site.

2.13.3 If a CBB discontinues processing of new CBU:

2.13.3.1 There shall be competent staff to oversee, maintain and distribute the inventory.

2.13.3.1a The staff shall maintain communication with all relevant registries and Transplant Centers, if applicable.

2.13.3.2 A process to distribute CBU contiguous segments and samples for testing shall be maintained.

2.13.3.3 All records of the entire inventory in storage shall be maintained.

2.13.4 Prior to the reestablishment of either CB collection or processing, as applicable, the following at a minimum shall be documented:

2.13.4.1 Review of all procedures to confirm that methods are consistent with current practices.

2.13.4.2 Inspection of all reagents and supplies to confirm none will be used after its expiration date.

2.13.4.3 Validation, calibration and maintenance of all equipment have been completed within the time periods specified in the SOP and manufacturer's instructions.

2.13.5 Cessation of CBB operations.

2.13.5.1 The CBB shall follow all contractual obligations that are specified in written agreements with CBCF, donor families, registries and other entities as applicable.

SECTION 3 CORD BLOOD DONOR MANAGEMENT AND COLLECTION

3.1 GENERAL REQUIREMENTS

3.1.1 These Standards shall apply to all CB donor management and collection procedures.

3.1.2 Written Agreements.

3.1.2.1 There shall be a written agreement outlining responsibilities for complying with CBB policies and SOP.

NOTE: Any formal arrangement within a legal entity in the form of request forms, circulars, formal letters, memos can be considered as a written agreement

3.1.2.2 There shall be documentation that a health care professional has agreed to perform the collection.

3.1.3 Cord Blood Collection Facilities:

3.1.3.1 The CBCF shall have processes to prevent the introduction, transmission, or spread of communicable diseases.

3.1.3.2 There shall be adequate space for the performance of the collection procedure.

3.1.3.3 There shall be secure storage of the CBU, associated samples, maternal samples, and documents until they are transported or shipped to the CBPF.

3.1.3.4 There shall be a designated area for appropriate and secure storage and preparation of the reagents, supplies, and equipment needed for the collection procedures as below:

3.1.3.4a Storage shall be according to the manufacturer's recommendations in an area and manner appropriate to protect their integrity and functionality.

3.1.3.4b Shipment from CBB to CBCF shall be in an outer container validated to maintain the designated temperature range.

3.1.3.4c Usage shall be prior to expiration dates

3.1.4 When a CB collection kit is prepared and sent from the CBB, adequate instructions and materials shall be provided to cover these areas of interest:

3.1.4.1 Storage and transportation/shipment of collection kit prior to transportation.

3.1.4.2 Collection, labelling, storage, packaging and transportation/shipment of the reagents and supplies, CBU, associated samples, and maternal samples to the CBB.

3.1.4.3 Transportation or shipment under conditions validated to maintain the designated temperature range from the time it leaves the CBB until it is received by the CBCF.

3.1.5 Records supplied to the CBB shall include the following at a minimum:

3.1.5.1 Identity of supplies and reagents including manufacturer, lot number, and expiration date.

3.1.5.2 Documentation of appropriate storage of all supplies, reagents, CBU, associated samples, and maternal samples.

3.2 CORD BLOOD COLLECTION FACILITY PERSONNEL REQUIREMENTS

3.2.1 All CBCF directors shall comply with these Standards.

3.2.1.1 Where there are CBCF that are not staffed by CBB director, there shall be a designated individual who is responsible for communication with the CBB Medical Director or designee.

3.2.2 All CB collection personnel shall have a defined line of communication with relevant CBB personnel.

3.2.2.1 At non-fixed CBCF, the CBB shall provide a mechanism for the collecting health care professional to communicate with the CBB Medical Director or designee for any problems with the collection.

3.2.3 All collections shall be performed by health care professionals trained for the collection procedure.

3.2.3.1 Training shall cover each aspect of the CB collection process, and must be documented. It shall include at a minimum:

3.2.3.1a The use of the collection supplies and reagents.

3.2.3.1b Cleaning of the umbilical cord to minimise the risk of contamination with microbes or maternal blood.

3.2.3.1c Use of the CB collection bag to avoid microbial contamination and clotting.

3.2.3.1d Labelling.

3.2.3.1e Verification of the identity of the donor.

3.2.3.1f Packaging, storage and shipping of the CBU as applicable.

3.2.3.1g Safety of the mother and neonate.

3.2.3.1h If applicable, review of medical records and physical examination of the mother and neonate donor for risks of communicable diseases.

3.2.3.2 Training shall be documented.

3.3 POLICIES AND STANDARD OPERATING PROCEDURES

3.3.1 There shall be the establishment and maintenance of policies and SOP addressing critical aspects of collection operations and management. These documents shall include all elements required by these Standards, be consistent with the policies and SOP of the CBB, and include at a minimum:

3.3.1.1 Donor education and recruitment.

3.3.1.2 Suitability assessment of maternal and neonate donor.

3.3.1.3 Informed consent.

3.3.1.4 Documentation of neonate donor's health at birth.

3.3.1.5 Maintenance of linkage of the CBU to the neonate donor and mother.

3.3.1.6 Collection of CBU, associated samples, and maternal samples.

3.3.1.7 Labelling of the CBU, associated samples, maternal samples, and documentation.

3.3.1.8 Storage and packaging of CBU, associated samples, maternal samples, and documentation at the CBCF.

3.3.1.9 Transport and shipping of the CBU, associated samples, maternal samples, and documentation to the CBPF.

3.3.1.10 Personnel and collector training.

3.3.1.11 Ordering, storage, security and use of supplies and reagents.

3.3.1.12 Equipment monitoring, qualification, and maintenance.

3.3.1.13 Facility management.

3.3.1.14 Cleaning and sanitation procedures.

3.3.1.15 Disposal of medical and biohazardous waste.

3.3.1.16 Emergency and safety procedures.

3.3.1.17 Disaster plan.

3.3.2 All collection personnel shall follow the policies and SOP established by the CBB and the CBCF related to their positions.

3.3.2.1 Review and training of an individual participating in CB collection shall be documented before the individual is allowed to perform new and revised policies and procedures.

3.3.2.2 Current versions of the policies and SOP relevant to the processes being performed shall be readily available to the personnel involved in the CB collection procedures at all times.

3.3.2.3 There shall be documentation of continued competency for the procedures performed.

3.4 MATERNAL AND NEONATE DONOR EVALUATION

3.4.1 There shall be written criteria for maternal and neonate donor evaluation and management.

3.4.1.1 There shall be a process for maternal and neonate donor identification and linkage.

3.4.1.2 There shall be criteria and evaluation procedures in place to protect the safety and confidentiality of the neonate donor and mother.

3.4.1.3 If a related CBU may potentially be used for unrelated donation, the evaluation process shall include all evaluation requirements for unrelated CBU at the time of donation.

3.4.1.4 There shall be a policy for follow-up donors for management of donation-associated adverse events.

3.4.1.5 Any abnormal result relevant to the health of the maternal or neonate donor shall be reported to the maternal donor or neonate donor's physician.

3.4.2 Maternal and neonate donor screening shall include an interview with the mother, review of medical records, and review of physical examination findings.

3.4.2.1 History shall be obtained and documented while the mother is able to concentrate on the information and is not distracted by aspects of labour

3.4.2.2 The history shall be obtained in a language the mother understands.

3.4.2.3 Family members shall not serve as interpreters or translators.

3.4.2.4 There shall be documentation that the mother, if applicable, affirmed that all the information provided is accurate to the best of her knowledge.

3.4.2.5 Maternal and neonate donor evaluation results shall be documented.

3.4.3 A medical and genetic history of the neonate donor's family (parents, grandparents, siblings, and parents' siblings) shall be obtained from the mother and documented.

3.4.3.1 The history shall include at a minimum genetic history, malignant disease, and inherited disorders that are transmissible to the recipient in the mother's and father's family including the neonate donor's grandparents, if known.

3.4.4 A history for the mother's communicable disease risk behavior shall be obtained and documented.

3.4.4.1 The mother's communicable disease risk behavior shall be obtained in a confidential manner.

3.4.4.2 The history shall include the mother's prenatal communicable disease testing, if known, and results of other general medical testing that could indicate a risk of communicable disease transmission.

3.4.4.3 If history for communicable disease risk was obtained in advance of the maternal donor's presentation for delivery, the history shall be updated to include information up to the time of delivery.

3.4.4.4 Questionnaire for human transmissible spongiform encephalopathy, including Creutzfeldt-Jakob disease, shall be documented.

3.4.2 Neonate Donor History

3.4.5.1 History of the current pregnancy and delivery shall be obtained and reviewed.

3.4.5.2 The neonate donor's birth data shall be obtained and documented, including gender, gestational age, other results of clinical examination, and if the neonate is free of any finding suggestive of disease potentially transmissible through administration of a CBU.

3.5 INFORMED CONSENT

3.5.1 Informed consent from the mother shall be obtained prior to delivery and steps in CB banking process shall only be performed once the consent is completed.

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

3.5.1.1a An explanation of the CB collection procedure.

3.5.1.1b The right of the mother to refuse without prejudice.

3.5.1.1c The mother shall have an opportunity to ask questions.

3.5.1.1d The mother will be approached at a later time for complete consent, including consent to bank the CBU and all of the elements.

3.5.1.2 Consent obtained for the CBU collection procedure prior to delivery shall be documented.

3.5.1.3 Informed consent shall be obtained and documented while the mother is able to concentrate on the information and is not distracted by aspects of labour. However, it is not encouraged during active labour.

3.5.2 All aspects of participation in the CBB shall be discussed with the mother in a language and with terms that she understands.

3.5.3 The informed consent process shall include:

3.5.3.1 The overall purpose of donation and participation of mother and neonate donor.

3.5.3.2 An explanation of the collection procedure and activities

3.5.3.3 The possible risk and benefits to the mother and/or neonate donor including medical and ethical concerns.

3.5.3.4 The possible alternatives to CB donation.

3.5.3.5 The right of the mother to refuse without prejudice.

3.5.3.6 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.

3.5.3.6a 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 neonate donor or the neonate donor's family at a later date.

3.5.3.6b 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 neonate donor.

3.5.3.6c If the CBU is intended for related use but may potentially be utilised for unrelated use, the mother shall be notified of the process for making the CBU available for unrelated use.

3.5.3.6d If the CBU may potentially be used for reasons other than the primary intent, including for purposes other than clinical administration, this shall be fully disclosed in the informed consent

3.5.3.7 The mother shall be provided with the information to contact the CBB if the neonate donor later develops a serious disease.

3.5.3.8 Collection of samples.

3.5.3.8a Blood samples from the mother for communicable disease and other testing as applicable.

3.5.3.8b Cord blood samples for communicable disease, genetic disease, and other testing as applicable.

3.5.3.9 Storage of reference samples from the mother and the CBU for future testing.

3.5.3.10 The CBB shall maintain linkage between the donor and CBU.

3.5.3.10a The CBB will notify the mother or her responsible physician and/or governmental agencies, when required of positive or indeterminate communicable disease.

3.5.3.10b The CBB retains the right to follow up with the mother or relevant healthcare provider at a future date.

3.5.3.10c Information related to neonate donor and family shall remain confidential.

3.5.3.11 Possible use of the CBU for research, quality control or validation studies.

3.5.3.12 The CBB policies for disposal of CBU including at least:

3.5.3.12a Nonconforming CBU.

3.5.3.12b Directed allogeneic or autologous CBU, if no longer required.

3.5.3.12c Agreed upon duration of storage for related CBU.

3.6 CORD BLOOD COLLECTION PROCEDURES

3.6.1 Cord blood collection practices and procedures shall protect the mother and the neonate donor and have no impact on obstetric practice or patient care.

3.6.1.1 Delivery practices shall not be modified in attempt to increase CB volume.

3.6.2 Collection of CB can be performed by two methods; *ex utero* or *in utero* techniques.

3.6.3 When *in utero* CB collection is performed, there shall be additional safeguards in place to protect the safety of the mother and the neonate donor.

3.6.3.1 Cord blood collections should only be performed *in utero* from documented singleton deliveries.

3.6.3.1a If CB collection is performed *in utero* in a multiple gestation pregnancy, all neonates shall be delivered before any CB collection begins.

3.6.3.1b *In utero* CB collections shall only occur in deliveries considered to be uncomplicated by the medical professional responsible for the delivery.

3.6.3.1c Cord blood units collected *in utero* shall only be obtained from neonate donor after at least 34 weeks gestation.

3.6.3.1d Related CBU collected *in utero* at less than 34 weeks' gestation shall be based on an evaluation of neonate donor safety by the health care professional responsible for the delivery.

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

3.6.4 Cord blood unit collection shall be performed according to written policies and SOP.

3.6.4.1 The identity of the collector shall be documented.

3.6.4.2 The identity of the maternal donor shall be verified.

3.6.4.3 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.

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

3.6.4.5 All reagents and supplies for collection that come into contact with the CB shall be sterile.

3.6.5 There shall be a unique identifier for the CBU, associated samples, maternal samples and associated documents.

3.6.6 There shall be a written policy at the CBCF for labelling of the CBU, associated samples, maternal samples and associated documents that permits tracking and tracing among the CBU, neonate donor, maternal donor, samples and documentation.

3.6.7 Upon completion of CB collection, the primary collection bag shall bear or be accompanied by the information required in Appendix I, Cord Blood Labelling Table.

3.6.8 There shall be a written policy for storage of CBU and associated samples at the CBCF prior to transport to the CBPF.

3.6.8.1 Cord blood units and samples shall be maintained in a secure environment.

3.6.8.2 Cord blood units shall be maintained in a temperature range validated to protect cell viability.

3.6.9 Records shall be maintained at the CBB of all reports of adverse events that occur during or immediately after CB collection.

3.7 TRANSPORTATION OF NON-CRYOPRESERVED CBU FROM THE CBCF TO THE CBPF

3.7.1 The methods of transportation of the CBU between the CBCF and the CBPF shall be designed to protect the integrity of the CBU being transported and the health and safety of personnel.

3.7.2 The primary CB collection bag shall be placed in a sealed secondary plastic bag to contain any leakage from the primary bag.

3.7.3 The CBU shall be transported or shipped with required accompanying records as defined in SOP.

3.7.4 Shipping container (Box).

3.7.4.1 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.

3.7.4.2 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.

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

3.7.5 Transportation and Shipping Records.

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

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

3.7.5.3 Transportation and shipping records shall identify:

3.7.5.3a The CBCF responsible for shipping the CBU.

3.7.5.3b The date and time of transport and shipment of the unit.

3.7.5.3c The identity of the courier.

3.7.5.3d The date and time of receipt of the package.

3.7.5.3e The condition of the package upon receipt.

SECTION 4 CORD BLOOD PROCESSING STANDARDS

4.1 CORD BLOOD PROCESSING FACILITY PERSONNEL REQUIREMENT

4.1.1 All CBPF personnel shall comply with these Standards.

4.1.2 All CBPF personnel shall be trained and competent.

4.2 CORD BLOOD BANK PROCESSING FACILITY REQUIREMENTS

4.2.1 The CBPF shall be registered, licensed, and/or accredited as required by the appropriate governmental authorities for the activities performed.

4.2.2 There shall be designated facilities of adequate design and location for the following activities:

4.2.2.1 Performance of processing activities and ancillary functions.

4.2.2.2 Preparation, safe, sanitary, and orderly manner for supplies, reagents and equipment needed for processing, testing, cryopreservation, storage and release.

4.2.2.3 Storage of CBU prior to release or distribution.

4.2.2.4 Maintenance of records.

4.2.3 The CBPF shall be secured in order to prevent the entrance of unauthorised personnel and protect daily operations, equipment, and records.

4.2.3.1 The CBPF shall have oversight of non-processing personnel visiting the CBPF to maintain compliance with these standards.

4.2.4 The CBPF shall provide adequate lighting, ventilation, access to hand decontamination and air quality to ensure adequate conditions for proper operations in compliance with Applicable Law.

4.2.5 The CBPF shall be maintained in a clean, sanitary, and orderly manner.

4.2.5.1 There shall be documentation of facility cleaning and sanitation.

4.2.6 Environmental conditions that affect the safety and potency of the CBU shall be defined, controlled, monitored and recorded to demonstrate ongoing compliance.

4.2.6.1 There shall be inspection of environmental control systems.

4.2.7 Critical CBPF parameters that may affect CBU processing, storage, or distribution shall be defined, controlled, monitored and recorded to demonstrate ongoing compliance.

4.2.8 Cord blood processing facility environmental conditions for temperature, humidity, ventilation and air pressure, filtration and classification shall be defined and if appropriate monitored for viable and nonviable particles.

4.2.9 Personnel safety requirements

4.2.9.1 The CBPF shall have procedures that utilise universal precautions and are designed to minimise risks to the health and safety of employees and visitors, including at least:

4.2.9.1a Blood borne pathogens.

4.2.9.1b Chemical hygiene.

4.2.9.1c Hand hygiene.

4.2.9.1d Fire safety.

4.2.9.1e Power failure.

4.2.9.1f Liquid nitrogen.

4.2.9.1g Latex allergy.

4.2.9.1h Radiation safety, if applicable.

4.2.9.2 Gloves and protective clothing shall be worn while handling biological specimens. Such protective clothing shall not be worn outside the work area.

4.2.9.3 The CBPF shall have written procedures for action in case of exposure to communicable disease agents or to chemical, biological, liquid nitrogen or if applicable, radiological hazards.

4.2.9.4 Medical waste shall be disposed in a manner to minimise hazard to facility, personnel and the environment in accordance with Applicable Law.

4.3 POLICIES AND STANDARD OPERATING PROCEDURES

4.3.1 The CBPF shall have clearly written policies and SOP that address all aspects of the processing operation. Section 2 is referred.

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

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

4.3.3.1 Cord blood unit acceptance criteria, processing, cryopreservation and storage.

4.3.3.2 Labelling of CBU, samples and associated documents.

4.3.3.3 Storage and retrieval of samples.

4.3.3.4 Acceptable levels of haemodilution of samples used for testing.

4.3.3.5 Communicable disease testing, microbial cultures, HLA typing, haemoglobinopathy testing, and other testing. Acceptance criteria for test results shall be described.

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

4.3.3.7 Criteria for qualification of CBU available for search and administration, including nonconforming CBU.

4.3.3.8 Personnel training and continued competency for the procedures performed.

4.3.3.9 Facility management.

4.3.3.10 Materials management.

4.3.3.11 Maintenance and monitoring of equipment.

4.3.3.12 Cleaning and sanitation procedures.

4.3.3.13 Disposal of medical and biohazardous waste.

4.3.3.14 Emergency and safety procedures.

4.3.3.15 A disaster plan to provide for continuous safe storage and transport and shipping, if applicable, of the CBU.

4.3.3.16 Disposal of a CBU.

4.3.3.17 Research carried out shall comply with National Organ, Tissue and Cell Transplantation Policies and Guidelines on Stem Cell Research.

4.4 CORD BLOOD PROCESSING

4.4.1 Acceptance Criteria.

4.4.1.1 Upon receipt of CBU package at the CBPF, the package shall be inspected for the following at a minimum:

4.4.1.1a The receipt of the package within an acceptable amount of time as defined by the CBB.

4.4.1.1b The integrity of the outer container and the temperature against validated parameters.

4.4.1.1c Verification of the contents of the package against the list of enclosed items.

4.4.1.1d The integrity of the collection bag.

4.4.1.1e The CBU for appropriate appearance, integrity, labelling, and identification.

4.4.1.1f The associated samples, maternal samples, and documents for appropriate labelling and identification.

4.4.1.2 For related CBU, there shall be a signed agreement with the donor family for collection, processing, testing, storage, and a name and contact information of the donor family.

4.4.1.3 For unrelated CBU, an appropriately signed consent authorising collection, processing, testing and storage and CBU samples for the intended purposes shall be confirmed before processing is completed.

4.4.2 Processing.

4.4.2.1 Only properly labelled and clearly identified CBU shall be accepted for processing.

4.4.2.2 Cord blood units during all stages of processing shall minimally contain an affixed in-process label with the CBU unique identifier at a minimum.

4.4.2.3 Information regarding processing steps that have been completed on a CBU shall accompany the CBU or be available electronically during all stages of processing.

4.4.2.4 Processing and cryopreservation of CBU shall be performed according to validated SOP to result in acceptable viability and recovery.

4.4.2.4a Critical control points shall be identified and their specifications defined.

4.4.2.4b Failure of the processing procedure to achieve specifications for critical control points shall be evaluated with appropriate action documented.

4.4.2.5 Method for processing shall employ aseptic technique and CBU shall be processed in a manner that minimises the risk of mix-ups and cross-contamination.

4.4.2.5a Where processing of CBU involves exposure to the environment, processing shall take place in an environment with specified air quality and cleanliness.

4.4.2.5b The effectiveness of measures to avoid contamination and cross-contamination shall be verified and monitored.

4.4.2.6 Cryopreservation of unrelated CBU shall be completed within 48 hours of collection provided storage and transportation conditions are in compliance.

4.4.2.7 Processing and cryopreservation of related CBU shall be completed within 72 hours of collection provided storage and transportation conditions are in compliance.

4.4.2.8 Cord blood unit processing shall be limited to volume reduction by depletion of erythrocytes and/or plasma.

4.4.2.9 More than minimal manipulation of a CBU shall be performed in accordance with Applicable Law and;

4.4.2.9a Using reagents and/or devices approved for that manipulation by the appropriate governmental agency or,

4.4.2.9b With an Ethics Committee or Institutional Review Board or approved protocol.

4.4.2.10 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.

4.4.3 At the completion of processing prior to cryopreservation, the freezing bag shall be labelled with the information as required by the Cord Blood Unit Labelling table in Appendix 1.

4.4.4 Records pertinent to the CBU shall be reviewed by the CBPF Director or designee and QUO and found to be acceptable prior to release from quarantine status.

4.5 SAMPLES AND CONDITIONS FOR STORAGE

4.5.1 Reference Samples.

4.5.1.1 At a minimum, the following reference samples shall be collected from CBU prior to cryopreservation.

4.5.1.2 Two (2) aliquots with minimum volume of 100 µL each sealed in the tubing that is integrally attached to the freezing bag.

4.5.1.2a The contents of each aliquot shall be representative of the CBU.

4.5.1.2b 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.

4.5.1.3 Additional samples may be collected for other purposes. At least two (2) vials containing 2 x 10^6 nucleated cells must be collected.

4.5.1.3a 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.

4.5.1.3b When cellular aliquots are stored in LN_2 vapor phase at -150°C or colder, the freezers shall be validated to show that all cellular aliquots are maintained at appropriate temperatures.

4.5.1.3c Cellular aliquots used for purposes other than viability or potency analysis shall be stored at -70°C or colder.

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

4.5.1.4a The serum or plasma should be stored at -70°C or colder.

4.5.1.4b Suitable material for preparation of at least 50 µg genomic DNA. This may be purified DNA, frozen cellular material or blots.

NOTE: Suitable material for preparation of at least 50 µg genomic DNA.

4.5.1.4c At least one retention sample from the CBU should be stored indefinitely.

4.5.2 Maternal Samples.

4.5.2.1 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.

4.5.2.2 From the genetic mother, suitable material for preparation of at least 50 µg of genomic DNA with the exception of egg or embryo donors.

4.6 CONDITIONS FOR STORAGE

4.6.1 Facilities storing CBU shall establish policies for the duration and conditions of storage and indications for discard, in line with these Standards:

4.6.1.1 There shall be a policy directing the validation of storage duration and the ongoing monitoring of product characteristics.

4.6.1.2 Refrigerators and freezers used for the storage of specimens, CBU, blood components, human cells, tissues, specimens or reagents shall not be used for any other purpose.

4.6.2 Procedures to minimise the risk of microbial cross-contamination of CBU shall be defined and maintained.

4.6.3 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.

4.6.3.1 Records shall indicate when a CBU was released from quarantine into permanent status.

4.6.3.2 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.

4.6.3.3 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.

4.6.4 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.

4.6.5 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.

4.6.6 Temperature.

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

4.6.6.1a When CBU are stored in LN_2 vapor phase at -150^{O}C or colder, the storage freezers shall be validated to show that all CBU are maintained at appropriate temperatures.

4.6.6.1b Transfer of cryopreserved CBU shall be validated and monitored.

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

4.6.6.2a The duration of warming events shall be documented, and the impact on the CBU shall be assessed.

4.6.6.2b If warming event may have potentially decreased the potency of an unrelated CBU, the unit shall not be made available for distribution or administration.

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

4.6.6.3.1a A procedure for notifying designated staff shall be placed at each remote alarm location and in the immediate area of the storage device.

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

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

4.7 CRYOPRESERVATION AND CORD BLOOD UNIT TESTING

4.7.1 Cord blood units shall be cryopreserved using a controlled rate freezing or an equivalent procedure validated to maintain cell viability and potency.

4.7.1.1 The time after addition of cryoprotectant prior to freezing shall be minimised and validated.

4.7.1.2 The duration from completion of freezing to storage at -150ºC or colder shall be minimised and validated.

4.7.2 Cryopreservation SOP shall specify that the following information is recorded for each CBU:

4.7.2.1 Total nucleated cell concentration within a defined range.

4.7.2.2 The cryoprotectant, its final concentration and the duration of cell exposure prior to freezing.

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

4.7.2.4 Cooling rate within a defined range.

4.7.2.5 Freezing curve parameters within a defined range.

4.7.2.6 Storage temperature.

4.7.3 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.

4.7.3.1 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.

4.7.3.2 Retention samples to be used for viability, potency, or stability study assays shall be cryopreserved and stored in the same manner as the CBU.

4.7.4 Processes shall minimise the risk of overfilling and underfilling freezing bags.

4.7.4.1 After filling, each freezing bag shall be visually inspected for possible leaking, overfilling or underfilling of the freezing bag, and breakage of seals. These inspections shall be recorded.

4.8 CORD BLOOD UNIT TESTING

4.8.1 The CBB shall define tests and procedures for CBU measurements and assays to determine their safety, viability, and integrity meet the predetermined release specifications. Results of above activity shall become part of the permanent record of the CBU.

4.8.2 Testing control procedures shall include:

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

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

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

4.8.2.4 Verification of new reagent lots to ensure comparable results to current lots or results in agreement with suitable reference ranges before or with introduction into service.

4.8.2.5 Where available, use of reference or quality control material with results within the defined established range.

4.8.2.6 Functional checks performed on the testing equipment, as appropriate, prior to testing.

4.8.2.7 Documentation of ongoing proficiency testing. The results shall be reviewed by the CBPF Director or designee and outcomes reviewed with the staff and QUO, if applicable.

4.8.3 The following assays shall be performed on a sample from each CBU as outlined in Testing Requirements in Appendix II.

4.8.3.1 Complete blood count with differential count shall include enumeration of neutrophils, lymphocytes, monocytes, and platelets. Parameters for each shall be defined as appropriate.

4.8.4 Microbial cultures of the CBU or product obtained using a system permissive for the growth of aerobic and anaerobic bacteria and fungi.

4.8.4.1 Cord blood units for unrelated use shall be free from microbial contamination.

4.8.4.2 For related CBU, organism(s) shall be identified and antimicrobial sensitivities shall be performed prior to release of the CBU for transplantation. These results shall be reported to the prospective Transplant Centre or the treating physician.

4.8.4.3 HLA Class I and Class II typing shall be performed by DNA-based methods.

4.8.5 Test results that are positive or outside of the established range and are relevant to the donor's health shall be informed to the neonate donor's mother or legal guardian and/or her physician according to Applicable Law and CBB policies and SOP.

4.9 MONITORING AND ALARM SYSTEMS, INVENTORY TRANSFER AND DISPOSITION

4.9.1 Refrigerator and freezer systems.

4.9.1.1 Refrigerators used for storage of CBU before cryopreservation of the CBU shall have a validated system to monitor the temperature continuously or record the temperature at a minimum every four hours.

4.9.1.2 Freezers used to store CBU where CBU are not fully immersed in liquid nitrogen shall have a validated system to monitor the temperature continuously or record the temperature every four hours at a minimum.

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

4.9.2 Alarm Systems.

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

4.9.2.2 Alarm systems shall have audible and visible signals.

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

4.9.2.3a A procedure for notifying designated staff shall be placed at each remote alarm location and in the immediate area of the storage device.

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

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

4.9.2.6 Any alarm event and its resolution shall be documented.

4.9.2.7 Contingency plans or storage devices of appropriate temperature shall be available for maintaining CBU and samples at the storage temperature in the event the primary storage device fails.

4.10 INVENTORY MANAGEMENT SYSTEM

4.10.1 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.

4.10.2 The inventory management system shall clearly distinguish related CBU from unrelated CBU.

4.10.3 The inventory management system for CBU shall allow each CBU and its samples and records to be located in a timely way. The inventory records shall include:

4.10.3.1 Cord blood unit unique identifier.

4.10.3.2 Maternal donor identifier.

4.10.3.3 Storage device identifier.

4.10.3.4 Location within the storage device.

4.10.4 The inventory management system shall be designed to prevent mix-ups, contamination of the CBU during storage, and the improper release of CBU.

4.10.4.1 The inventory management system shall be designed to address the duration of storage for cryopreserved CBU, including assigning an expiration date to CBU where appropriate.

4.10.5 The CBB shall have policies related to the return of CBU to the CBB Inventory.

4.10.5.1 Unrelated CBU shall not be returned to the CBB inventory after they have left the CBB premises.

4.10.5.2 If related CBU are returned to the CBB inventory, there shall be documentation of appropriate storage and transportation.

4.11 INVENTORY TRANSFER

4.11.1 If all or part of a CBU inventory is to be transferred to another CBB:

4.11.1.1 The CBB shall have policies and SOP describing the transfer of inventory.

4.11.1.2 There shall be a written agreement between the transferring and accepting CBBs that describes the responsibilities of each CBB, including the elements at a minimum.

4.11.1.3 The transferring CBB shall provide the receiving CBB with all records as mentioned in section 2.12: Documents and Records Requirements.

4.11.2 Responsibilities of the receiving CBB.

4.11.2.1 Records shall be in a language and form that can be understood by the accepting CBB personnel.

4.11.2.2 There shall be documentation of review of records of transferred inventory to verify that the CBU meet the requirements of the written agreement for transfer of inventory.

4.11.2.3 Transferred records shall include at a minimum:

4.11.2.3a Maternal consent.

4.11.2.3b Medical and genetic history.

4.11.2.3c A summary of records used to make the donor eligibility determination.

4.11.2.3d Identity and results of all maternal communicable disease tests, and if performed, the identity and results of all CBU communicable disease tests.

4.11.2.3e All results from testing performed on the CBU, including CBU cell counts and sterility testing.

4.11.2.3f Processing information.

4.11.2.3g Cryopreservation records, including freezing curve.

4.11.2.3h The manufacturer and approximate dimensions of the storage bag and canister.

4.11.2.3i Number of attached segments and other samples.

4.11.2.3j Other records as required to allow the receiving CBB to meet these Standards.

4.11.2.4 There shall be a process for inspecting incoming CBU for damage and contamination.

4.11.2.5 After the CBU have been transferred, but before the transferred inventory is made available for search:

4.11.2.5a The integrity and viability of thawed CBU shall be verified to confirm the transport or shipping method did not compromise CBU viability.

4.11.2.5b There shall be confirmation of the completeness of all records.

4.11.2.5c The accepting CBB shall determine whether to accept, reject, or place in quarantine incoming CBU based on established criteria designed to prevent the transmission of communicable disease.

4.11.2.6 If the CBB utilises a registry, the CBB shall use a validated process for uploading CBU information to the registry.

4.11.2.6a The CBB or registry shall have a validated electronic record system that enables search and match operations and reporting of results within a defined time frame.

4.11.2.6b If an outside agency is used for search and match functions, its electronic record system shall meet these Standards.

4.11.2.6c The CBB or registry shall have policies and SOP for the reservation and allocation of CBU.

4.11.2.6d There shall be a system to prevent simultaneous reservation of a CBU for more than one potential recipient or for more than one potential Transplant Centre.

4.11.2.6e At the time a CBU is removed from inventory, the CBB shall notify all registries on which the CBU is listed that it is no longer available.

4.12 DISPOSITION

4.12.1 The CBB shall have a policy regarding the disposition of a CBU, including at a minimum:

4.12.1.1 Cord blood units released for clinical use.

4.12.1.2 Cord blood units used for research and development.

4.12.1.3 Cord blood units used for quality assurance activities.

4.12.1.4 Cord blood units that are discarded.

4.12.2 Nonconforming CBU.

4.12.2.1 The CBB shall have a policy for the management of CBU that are not accepted into inventory.

4.12.2.2 The CBB shall have a written policy for the management of CBU that do not meet in-process or final endpoints and/or specifications.

4.12.2.3 The CBB shall have a written policy to address positive or indeterminate results found during the screening process and/or laboratory testing of samples.

4.12.3 Disposal.

4.12.3.1 There shall be a policy outlining personnel authorised to discard CBU.

4.12.3.2 If processing is initiated before obtaining a signed consent, the CBU shall be discarded if a signed consent is not obtained before processing is completed.

4.12.3.3 The records for discarded CBU shall indicate the unique numeric or alphanumeric identifier of the CBU; the reason, date, and method of disposal; and the individual who disposed of the CBU.

4.12.4 For related CBU disposal:

4.12.4.1 Disposal shall comply with the terms of disposal in the written agreement.

4.12.4.2 Reasons for disposal and the process of notification shall be identified at the time of the written agreement.

4.12.4.3 Notification of the neonate donor's family shall be documented.

SECTION 5 CORD BLOOD LISTING, SEARCH, SELECTION, RESERVATION, RELEASE AND DISTRIBUTION.

5.1 CORD BLOOD BANK FACILITY REQUIREMENTS

5.1.1 There shall be designated facilities properly located and designed to prevent mix-ups, mislabelling, or other errors in the procedures related to CBU listing, search, selection, reservation, release and distribution.

5.1.2 There shall be a defined process to prevent listing of related CBU for unrelated use.

5.1.3 The CBB shall have policies and SOP for the following at a minimum:

5.1.3.1 Listing, search, selection, reservation, release, and distribution of CBU to Transplant Centre.

5.1.3.2 Verification of HLA typing of the CBU.

5.1.3.3 For allogeneic use, verification that the neonate CB donor and the recipient are different individuals in the case of a complete HLA match.

5.1.3.4 For autologous use, verification of donor identity.

5.1.4 If the CBB utilises a registry, the CBB shall use a validated process for uploading CBU information to the registry.

5.1.5 The CBB or registry shall have a validated electronic record system that enables search and match operations and reporting of results within a defined time frame.

5.1.6 The CBB or registry shall have policies and SOP for the reservation and allocation of CBU.

5.1.6.1 There shall be a system to prevent simultaneous reservation of a CBU for more than one potential recipient or for more than one potential Transplant Centre.

5.1.6.2 At the time a CBU is removed from inventory, the CBB shall notify all registries on which the CBU is listed that it is no longer available.

5.1.7 For Public CBB in Malaysia, section 5.1.2 – 5.1.6 shall be carried out by the NSCCC at the National Blood Centre.

5.2 CORD BLOOD UNIT SELECTION AND RELEASE FOR ADMINISTRATION

5.2.1 The CBB shall retain indefinitely documentation of requests for CBU, requests for samples, requests for and results of testing, transportation and shipping of CBU and samples between facilities.

5.2.2 Before a CBU is released, a sample obtained from a contiguous segment of that CBU shall be tested to verify HLA typing and, if possible cell viability.

5.2.2.1 The CBU shall be tested to verify HLA typing at least once after a CBU is cryopreserved.

5.2.2.2 If a contiguous segment was never available, another validated method shall be used to identify the CBU.

5.2.2.3 Any histocompatibility discrepancy shall be resolved and communicated to the Registry and the Transplant Centre.

5.2.2.4 Where proof of identity has been obtained for the CBU, a copy of the report shall be provided to the Transplant Centre upon request for the CBU.

5.2.3 At the time of selection for administration, the CBB and/or NSCCC shall provide all technical data to the Transplant Centre, including at a minimum:

5.2.3.1 Results of tests outlined in the Testing Requirements table in Appendix II.

5.2.3.1a There shall be documentation of notification of the physician using the CBU of the results of all testing and screening as required by Applicable Law.

5.2.3.1b In the case of incomplete donor eligibility for related CBU, there shall be documentation that the donor eligibility was completed during or after use of the CBU and that the physician using the CBU was informed of the results of that determination as required by Applicable Law.

5.2.3.2 Gender of the neonate donor.

5.2.3.3 Risks of communicable and/or genetic diseases disclosed by the maternal medical and genetic screening or clinical chart review and the results of any investigation or further testing performed.

5.2.3.4 The method of CBU processing.

5.2.3.5 Any variances in collection, processing, testing, cryopreservation, storage, and/or transport or shipping procedures that may influence the integrity and/or quality of the CBU.

5.2.3.6 Physical characteristics of the CBU, including at a minimum the number and type of bags or compartments used for storage.

5.2.3.7 Information about the type of cassette in which the CBU will be shipped.

5.2.3.8 Instructions for storage of the CBU.

5.2.3.9 Instructions for thawing and administering the CBU, including expected range of results based upon CBB internal validation results or published documentation.

5.3 CORD BLOOD UNIT DISTRIBUTION TO A TRANSPLANT CENTRE

5.3.1 The CBB shall obtain in written or electronic form, a request from the transplant physician, designee, or registry for distribution of the CBU prior to release of the CBU.

5.3.2 The CBB Director or Medical Director or designee and the QUO shall conduct a comprehensive record review prior to distribution of a CBU to a Transplant Centre and document this review in accordance with Applicable Law.

5.3.3 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:

5.3.3.1 A CBU intended for allogeneic use that does not meet release or donor eligibility requirements shall be distributed only if there is documented urgent medical need for the CBU. Documentation shall include, at a minimum, the approval of the recipient's physician and the CBB Director or Medical Director.

5.3.3.2 The CBU shall not be released unless the CBB Director or Medical Director and the QUO give specific authorisation for release of the ineligible CBU in compliance with Applicable Law and documents the rationale for such authorisation.

5.3.4 At the time of distribution to a Transplant Centre, the CBU bag shall be labelled as required in the Cord Blood Unit Labelling table in Appendix 1.

5.3.5 A circular of information or package insert and instructions for handling, thawing, and using the CBU, including short-term storage and preparation for administration, shall accompany the CBU.

5.3.6 Elements detailed in the Accompanying Documents at Distribution to a Transplant Centre table in Appendix II shall accompany the CBU at distribution to a Transplant Centre according to Applicable Law.

5.3.7 The CBU should be received by the Transplant Centre prior to initiation of the recipient's preparative regimen unless approved by the transplant physician.

5.3.8 All communications between the public CBB and Transplant Centre should be carried out via NSCCC.

5.4 TRANSPORTATION AND SHIPPING OF CRYOPRESERVED CORD BLOOD UNITS.

5.4.1 Procedures for transportation and shipping of cryopreserved CBU shall be validated to protect the CBU and the health and safety of personnel involved.

5.4.2 The transit time between the CBB and other facilities shall be minimised.

5.4.2.1 There shall be written plans for alternative transportation or shipping in an emergency.

5.4.3 Cryopreserved CBU shall be transported or shipped in a liquid nitrogen cooled dry shipper that contains adequate absorbed liquid nitrogen and has been validated to maintain a temperature of -150ºC or colder for at least 48 hours beyond the expected time of arrival at the receiving facility.

5.4.3.1 The dry shipper shall contain an electronic data logger that continuously monitors temperature throughout the transportation or shipping period.

5.4.3.2 The transport or shipping methods shall conform to Applicable Law regarding the mode of transportation or shipping of such devices.

5.4.3.3 The dry shipper shall be labelled in accordance with Applicable Law regarding the cryogenic material used and the transportation or shipping of biologic materials.

5.4.3.4 All container lids shall be secured.

5.4.3.5 The outer container shall be labelled with the information required in the Cord Blood Unit Labelling Table in Appendix I.

5.4.4 The CBB shall have written policies and procedures to obtain the following data from the receiving facility about the CBU upon receipt:

5.4.4.1 Date and time of receipt.

5.4.4.2 Identity of the personnel receiving the CBU.

5.4.4.3 Integrity of the dry shipper.

5.4.4.4 Verification of appropriate temperature range.

5.4.4.5 Integrity of the CBU.

5.4.4.6 Verification that required documentation is available.

5.4.5 If an unrelated CBU has left the CBB premises, the CBU shall not be returned to the general CBB inventory.

5.5 TRANSPORTATION AND SHIPPING OF RECORDS REQUIREMENTS

5.5.1 Transportation and shipping records shall permit the tracking and tracing of the CBU from the CBB to its final destination.

5.5.2 The package shall include a list identifying the CBU, intended recipient, intended destination, transportation and shipping records, and any warnings and other associated documents.

5.5.3 Transportation and shipping records shall document:

5.5.3.1 The CBB responsible for transporting or shipping the CBU.

5.5.3.2 The date and time of packaging of the CBU at the CBB.

5.5.3.3 The date and time the package left the CBB.

5.5.3.4 The identity of the courier and tracking information.

5.5.3.5 The date and time of receipt of the package.

5.5.3.6 Maintenance of the temperature within the specified range throughout the period of transportation or shipment.

5.6 CLINICAL OUTCOME DATA

5.6.1 For every CBU released for administration, the CBB shall maintain details of clinical outcomes as necessary to confirm that the procedures in use in the CBB provide a safe and effective product.

5.6.1.1 The CBB shall obtain this information directly from the Transplant Centre or, if utilised, through a registry or outcomes database.

5.6.2 The CBB shall have a policy or procedure to request the following information within the recommended time period for every CBU released for administration. This information shall not be used for any misleading advertisement.

5.6.2.1 Cell yield results on the thawed CBU.

5.6.2.2 Adverse events associated with administration of the CBU in accordance with Applicable Law.

5.6.2.3 Serious adverse events related to the CBU in accordance with Applicable Law.

5.6.2.4 Time to neutrophil and platelet engraftment.

5.6.2.4a For allogeneic CBU only, data should include chimerism.

5.6.2.4b In the case of more than one CBU product used for administration, the CBB should collect and document that information and, if possible, which product engrafted.

5.6.2.5 Survival rates annually at a minimum.

5.6.2.6 GVHD results annually at a minimum.

5.6.2.7 All communications for outcome data between public CBB and Transplant Centre should be carried out via NSCCC.

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
Anti-	An antibody to the antigen designated
^{o}C	Degree Centigrade
CB	Cord blood
CBB	Cord Blood Bank
CBC	Complete blood count (Full blood count)
CBCF	Cord blood collection facility
CBPF	Cord blood processing facility
CBU	Cord blood unit
CFU	Colony forming unit
CMV	Cytomegalovirus
DNA	Deoxyribonucleic acid
EBV	Epstein-Barr virus
GVHD	Graft-vs-host-disease
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
HLA	Human Leukocyte Antigen
HTLV	Human T cell lymphotropic virus
IRB	Institutional Review Board
ISBT	International Society of Blood Transfusion
LN_2	Liquid nitrogen
µ*g*	Microgram
mL	Mililiter
NSCCC	National Stem Cell Coordinating Centre
QM	Quality Management
QMP	Quality Management Programme
QMS	Quality Management System
QUO	Quality Unit Officer
Rh	Rhesus system of human red blood cell types
SOP	Standard Operating Procedure

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.

Accrediting Organisation: An authorised agency responsible in granting an accreditation to HLA typing laboratory, e.g ASHI or EFI.

Administration: Infusion of a cord blood unit to the recipient.

Adventitious agent: Any extraneous microbiological, chemical, or radiological agents introduced into the CB unit during collection, processing, or administration.

Adverse event: Any unintended and unfavourable 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 a neonate donor and intended for infusion into a genetically distinct related or unrelated recipient.

Applicable Law: Any local, national, or international statute, regulation, or other governmental law that is applicable to cord blood donor management including recruitment or eligibility, or to cord blood collection, processing, testing, cryopreservation, storage, listing, search, selection, reservation, release, or distribution that is relevant to the location or activities of the Cord Blood Bank, Cord Blood Collection Facility, or Cord Blood Processing Facility.

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 a neonate donor and intended for infusion back into the same individual.

Available for distribution: The point at which the cord blood unit or any cellular therapy product has been determined to meet all release criteria.

Biological product deviation: A deviation from these Standards or other established specifications that relate to the prevention of communicable disease transmission or cord blood unit or any 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 cord blood unit or any 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 standard.

CD34: The glycoprotein antigen expressed by a small population of cord blood cells, that is defined by a specific monoclonal antibody (anti-CD34) using the standardised cluster of differentiation (CD) terminology. Haematopoietic progenitor cells are mostly present within the CD34 cell population of cord blood units.

Cellular therapy product: A somatic cell-based product, including cord blood, that is procured from a donor and intended for processing and administration.

Colony Forming Unit (CFU): 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 cord blood or any cellular therapy products, including labelling, regardless of technique or source.

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 established Standard Operating Procedures or instructions.

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

Consumables: For the purpose of these Standards, consumables include culture media, pipette tips, glass slides etc.

Contiguous segments: A sealed length of tubing integrally attached to the cord blood unit that contains a sample representative of the cord blood used for testing.

Cord Blood (CB): The neonate's blood present in the placenta and umbilical cord after the umbilical cord has been clamped.

Cord Blood Bank (CBB): An organisation responsible for cord blood donor management, cord blood collection and cord blood banking services, and consists of an integrated team headed by a Cord Blood Bank Director.

Cord Blood Banking: The processing, testing, cryopreservation, storage, listing, search, selection, reservation, release, and distribution of cord blood units intended for administration.

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

> *Ex utero:* The collection of cord blood cells from the placental and/or umbilical vessel after the placenta has been delivered.
>
> *In utero:* The collection of cord blood cells from the placental and/or umbilical vessels after the neonate donor has been delivered and separated from the umbilical cord, but before the placenta has been delivered.

Cord Blood Collection Facility (CBCF): The site where the neonate is delivered and the cord blood unit is collected.

Cord Blood Processing Facility (CBPF): The location where cord blood processing activities are performed in support of the Cord Blood Bank. A Processing Facility may be part of the same institution as the Cord Blood Bank or may be part of another institution and perform these functions through contractual agreement.

Cord Blood Standards: This document, "National Standards for Cord Blood Banking and Transplantation"

Cord Blood Unit: The nucleated cells including haematopoietic 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 cord blood unit in this document refers to all cord blood units 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.

Cryopreservation: A process using validated procedure in which cells or tissues are preserved by cooling to a very low temperature to maintain viability.

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

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

Disposition: The current status, location, or use of a cord blood unit.

Distribution: Any conveyance or shipment (including importation and exportation) of a cord blood unit and/or 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.

> *Neonate donor:* The neonate from whose placenta and/or umbilical cord the cord blood is obtained.
>
> *Maternal donor:* The mother who carries the neonate donor to delivery.
>
> *Unrelated donor:* The neonate donor whose cord blood is collected and stored for use by a person with no known genetic relationship.
>
> *Related donor:* The neonate donor whose cord blood is collected and stored for autologous use by the donor or for allogeneic use by a genetically related recipient.

Deviation: The action of departing from an established course or accepted standard.

> *Unplanned deviation:* Occurred without intent.
>
> *Planned deviation:* Was allowed to occur with documented approval as the best course of action when adherence to the established course or accepted standard was not feasible or possible.

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: A neonate donor and/or mother who meets all the donor screening and testing criteria for relevant communicable and/or genetic disease.

Engraftment: The reconstitution of recipient haematopoiesis or other cellular functions with cells from a donor.

Equipment: For the purpose of these Standards, laboratory equipment includes hardware and software of instruments, measuring systems, and laboratory information systems.

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 or 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 the patients, to review biomedical and behavioral research involving human subjects conducted at or supported by that institution.

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

High resolution typing: A high resolution typing result is defined as a set of alleles that encode the same protein sequence for the region of the HLA molecule called the antigen binding site and that excludes alleles that are not expressed as cell-surface proteins. The antigen binding site includes domain 1 and domain 2 of the class I α polypeptides, and domain 1 of the class II α and domain 1 of the class II β polypeptide chains.

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

Incomplete donor eligibility: A neonate donor and/or mother for whom the donor eligibility has not been completed in accordance with all donors screening and testing required by Applicable Law

Ineligible: A neonate donor and/or mother who does not meet any of the donor screening and testing criteria for relevant communicable and/or genetic disease.

Institutional Review Board: A Board or Committee established by an institution in accordance with Applicable Law to review biomedical and behavioral research involving human subjects conducted at or supported by that institution.

ISBT 128: The international information technology standard for transfusion medicine and transplantation. International Council for Commonality in Blood Banking Automation, Inc. (www.iccbba.org) is the organisation charged with the international maintenance of this database.

Key personnel: Personnel with responsibilities that significantly affect the provision, safety, and/or quality of a service or product.

Labelling: Steps taken to identify the cord blood unit collection and any products or product 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 neonate donor and/or mother.

Listing: The process of transferring information about a cord blood unit to be available for search.

Low resolution typing: A DNA-based typing result at the level of the digits comprising the first field in the DNA-based nomenclature. Examples include A*01; A*02. If the resolution corresponds to a serologic equivalent, this typing result should also be called low resolution.

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

> *Minimal manipulation:* Processing that does not alter the relevant biological characteristics of cells or tissues.
>
> *More than minimal manipulation:* Processing that does alter the relevant biological characteristics of cells or tissues.

Materials management: An integrated process for planning and controlling all steps in the acquisition and use of goods or supply items (materials) used for the collection or processing of cord blood units to determine whether these materials are of adequate quality and quantity and available when needed. The materials management system combines and integrates the material selection, vendor evaluation, purchasing, expediting, storage, distribution, and disposition of materials.

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

NETCORD: The international organisation of Cord Blood Banks that meet defined membership requirements of NETCORD. Further information on NETCORD is available at www.netcord.org.

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

Policy: Document that defines the scope of an organisation, explains how the goals of the organisation will be achieved, and/or serves as a means by which authority can be delegated.

Procedure: A document that describes in detail the process or chronological steps taken to accomplish a specific task. A procedure is more specific than a policy

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

Products: An output or result of a process or action. In this Standard, it refers to:

HPC, Cord Blood: Heamatopoietic progenitor cells obtained from the umbilical cord and/or placenta at the time of delivery.

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

Protocol: A written document describing steps of a treatment or procedure in sufficient detail such that the treatment or procedure can be reproduced repeatedly without variation.

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

Quality Audit: A documented, independent inspection and review of a facility's activities. The purpose of a quality audit is to verify, by examination and evaluation of objective evidence, the degree of compliance with those aspects of the Quality Programme under review.

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

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 Control: A component 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 cord blood units including testing and product release.

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

Quality Management System: A written document that describes the systems in place to implement the Quality Management Programme.

Quality Management Programme: An organisation's comprehensive system of quality assessment, assurance, control, and improvement. A Quality Management Programme is designed to prevent, detect, and correct deficiencies that may adversely affect the quality of the cord blood unit or increase the risk of communicable disease introduction or transmission.

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

Quarantine: The segregation of a cord blood unit to prevent cross-contamination or improper release. Quarantine can be temporal, physical, electronic, or a designation within the cord blood unit record.

Reagent: For the purpose of these Standards, reagents include reference materials, calibrators, and quality control materials.

Recipient: The individual into whom the cord blood unit was administered.

Registry: An organisation that publishes or makes available the description of cord blood units available for administration and may conduct searches of the available cord blood units, either exclusively or in conjunction with the Cord Blood Bank as defined in their agreement.

Release: The removal of a cord blood unit from quarantine or in-process status when it meets specified criteria.

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.

Sample: Biological material used for testing.

> *Associated sample:* Aliquot of biological material (e.g., blood, serum, plasma, tissue, Wharton's jelly, etc) derived from the neonate donor or maternal donor of the cord blood unit.
>
> *Maternal sample:* Aliquot of biological material (e.g., blood, plasma, serum, or cellular material) from the mother.
>
> *Reference samples:* Aliquots of biological material (e.g., cells, plasma, serum, or cellular material) from the cord blood unit, the umbilical cord, or the placenta that are used to confirm the identity, HLA typing, or genetic or transmissible disease information associated with a single cord blood unit. Such samples may or may not be contiguous segments.
>
> *Retention sample:* Aliquot replicate of the final cord blood unit that can be used to test for viability, potency or stability. This may be referred to as archive sample.

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 process of identification of a donor or cord blood unit according to defined criteria.

Standard Operating Procedures: Written detailed instructions required to perform a procedure.

Transplant Centre: An integrated medical team that evaluates and administers cord blood units or other source of haematopoietic stem cells for its patients.

Transplantation: The infusion of allogeneic or autologous CB progenitor cells with the intent of providing transient or permanent engraftment in support of therapy for disease.

Volume reduction: The manipulation of the CB unit 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.

Variance: A deviation from recommended practice or Standard Operating Procedure.

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

Verification typing: HLA typing performed on an independent sample (or, for a cord blood unit, from an attached segment or from the unit itself) with the purpose of verifying concordance of that typing assignment with the initial HLA typing results. Concordance does not require identical levels of resolution for the two sets of typing but requires the two assignments to be consistent with one another.

Viability assessment: The determination of the proportion of living cells using dye exclusion, flow cytometry, or progenitor cell culture methods.

REFERENCES

a) NETCORD-FACT International Standards for Cord Blood Collection, Processing, Testing, Banking, Selection and Release. Fifth Edition, July 2013.

b) Private Healthcare Facilities and Services Act 1998 (Act 586).

c) Guidelines on Stem Cell Research, *Medical Development Division, Ministry of Health Malaysia, July 2009.*

d) National Organ, Tissue and Cell Transplantation Policy, *Medical Development Division, Ministry of Health Malaysia, June 2007.*

e) ISBT 128 Standard Terminology for Blood, Cellular Therapy, and Tissue Product Descriptions, *Version 6.15, April 2016.*

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CORD BLOOD UNIT LABELLING TABLE

Label Element	Partial label	At completion of collection	Shipping container labelling for transport	At completion of processing and prior to cryopreservation	At CBU 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 CBU)	**AF**	**AF**		**AF**	**AF**	
Statement 'Autologous Use Only' (autologous CBU)	**AF**	**AF**		**AF**	**AF**	
Collection Facility Identifier		**AF**				
Date of Collection		**AF**		**AC**	**AC**	
Time of collection and time zone if different from the CBPF		**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 Autologus CBU)		**AF**		**AF**	**AF**	
Recipient's name, unique identifier of family (Directed Allogeneic and Autologous CBU)		**AF**				
Volume or weight of the CBU at the end of collection				**AC**	**AC**	
Volume or weight of the CBU 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 CBU donor				**AC**	**AC**	
Identity of the CBB				**AF**	**AF**	
Statement 'Properly Identify Intended Recipient and Product'					**AT**	
Statement 'For Use By Intended Recipient Only' (Allogeneic CBU)					**AT**	
A statement indicating that leukoreduction filters should not be used					**AT**	
Statement 'Do not Irradiate'					**AT**	
Statement 'For Non-clinical Use Only' (if applicable)					**AT**	
Biohazard legend and/or warning labels (if applicable)				**AC**	**AC**	
Donor eligibility summary					**AC**	
Date of distribution					**AC**	**AF**
Shipping facility name, address and phone number			**AF**			**AF**
Receiving facility name, address and 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 instruction						**AF**

NOTE : Each label shall include at least the elements detailed in the above table. The chart has minimum requirements only. A CBB may choose to be more inclusive.

AF = Affix, AT = Attach or Affix, AC = Accompany or Attach or Affix

TESTING REQUIREMENTS

		CB samples					Maternal samples
Specifications and tests	Pre processing	Post Processing prior to cryopreservation	Any time prior to Cryopreservation	Any time prior to listing	Post processing cryopreserved prior to release to the Transplant Centre	Any time prior to release to Transplant Centre	Obtained within seven (7) days before or after CB collection
Cell Count							
Total nucleated cell count	x	x					
CBC with differential	x	x					
Nucleated red blood cell count		x					
Viability							
Total viability		x					
Viable CD34		x					
CFU or other validated potency assay						x[1]	
ABO/Rh			x				
HLA							
Low resolution: HLA-A, B, DRB1.				x (unrelated)			
High resolution HLA-A, B, C, DRB1						x (unrelated)	
Verification of HLA typing results					x (contiguous segment-related and unrelated)		
Haemoglobinopathy						x[2]	x
Microbial culture		x					
Infectious Disease							
HIV				x[3]			x
Hepatitis B				x[3]			x
Hepatitis C				x[3]			x
CMV				x			x
Syphilis							x
*Additional Tests				x			x

Notes:

1. If testing was not performed historically, a potency assay must be performed prior to release for administration by the CBB.

2. DNA typing (molecular study) for haemoglobinopathy on CB samples any time prior to release if mother is a thalasaemia trait or haemoglobinopathy trait. Incase DNA not available for molecular, Transplant Centre will be informed.

3. Each CB unit should be tested for evidence of infection for communicable disease agents using licensed donor screening test when available according to Applicable Law.

4. *Additional tests for infectious transmissible agents may be required in accordance with Applicable Law or institutional policy. In certain circumstances, additional testing may be required depending on the donor's history and the characteristics of the tissue or cells donated (e.g., toxoplasma, HTLV, Malaria, EBV, etc.) and may include emergent disease testing.