



ACCREDITATION MANUAL – Standards for Umbilical Cord Blood Progenitors (Chapter K)

EUROPEAN GROUP FOR ACCREDITATION AND
LIAISON OF BLOOD-TISSUES AND CELLS ESTABLISHMENTS



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INTRODUCTION

EGALiTE is a voluntary accreditation programme endorsed by the leading European Scientific Societies [European Eye Bank Association (EEBA), European Association of Tissue and Cell Banks (EATCB), and European Society for Blood and Marrow Transplantation (EBMT), and European Blood Alliance (EBA)].

The EGALiTE Standards are designed to provide guidelines for organisations, programmes, facilities, and individuals involved in activities pertaining to Substances of Human Origin (SoHO) - or providing support services for such activities – and who wish to apply for the European/EGALiTE Accreditation Program.

These Standards are designed by experts in the SoHO field for facilities wishing to demonstrate their commitment to quality medical care and best laboratory practice through an EGALiTE accreditation.

EGALiTE Standards are intended to apply to all actions performed by SoHO Entities in the preparation of SoHO, which include donor recruitment, selection, evaluation, testing, and SoHO collection, sampling, quality control, processing, preservation, storage, release and distribution for clinical application. The standards applicable to hematopoietic progenitor cells (HPC) activities are defined by FACT-JACIE (Foundation for the Accreditation of Cellular Therapy and Joint Accreditation Committee of the International Society for Cell and Gene Therapy and the European Society for Blood and Marrow Transplantation (EBMT))^{*} and the World Marrow Donor Association (WMDA)[†], and are not included in this guide.

The EGALiTE Standards were defined taking into account on the good practices defined by:

- European Directorate for the Quality of Medicines & HealthCare of the Council of Europe (EDQM) Guide to the quality and safety of tissues and cells for human application¹;
- EDQM Guide to the preparation, use and quality assurance of Blood Components²
- FACT-JACIE³;
- WMDA Standards⁴
- EuroGTP I and EuroGTP II⁵
- And other guidelines, namely related with the Good Manufacturing Practices (GMP)⁶ and quality management.

^{*} The scope of the FACT-JACIE Standards includes:

- HPCs defined as self-renewing and/or multi-potent stem cells capable of maturation into any of the hematopoietic 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).
- Nucleated cells or mononuclear cells from any hematopoietic tissue source (marrow, peripheral blood, umbilical cord, and placental blood) collected for therapeutic use other than as HPCs.
- Immune effector cells (IECs), defined as cells, in vitro modified or not, that have differentiated into a form capable of modulating or effecting a specific immune response.
- Genetically modified cells, defined as cells that have been modified by replacing a disease-causing gene with a health copy of the gene, inactivating a disease-causing gene that is not functioning properly, or introducing a new or modified gene into the body to help treat a disease.
- Clinical administration of the cellular therapy products derived from umbilical cord.

[†] WMDA standards cover all aspects of blood stem cell registry operations

These Standards are not intended to establish absolute best practice or include all procedures and practices that an organisation, programme, facility, or individual should implement if the standard of practice in the community or applicable governmental laws or regulations have determined additional requirements. Each organisation, programme, facility, and individual should analyse its practices and procedures to ascertain whether additional standards apply. In addition, compliance with these Standards is not an exclusive means of complying with the required standards of care as dictated by local, national, or international laws or regulations.

Compliance with the Standards does not guarantee compliance with Applicable Law. Governmental regulations must also be followed. It is the responsibility of the individual facility to determine which laws and regulations are applicable. In some cases, regulations of governmental authorities outside of the jurisdiction of the Donation Centre may apply; for example, when a facility is sending or receiving SoHO from outside of its immediate jurisdiction.

Compliance with other organisations' standards or governmental regulations does not ensure that the Standards have been met. Governmental regulations supersede any organisation's standards if those regulations set a higher standard or are inconsistent with a specific standard. However, if a standard is more rigorous than a governmental regulation, that standard must be followed.

Disclaimer

EGALiTE expressly disclaims any responsibility for setting maximum standards and additionally expressly disclaims any responsibility, liability, or duty to member programmes, directors, staff, or programme donors or patients for any such liability arising out of injury or loss to any person by the failure of member programmes, directors, or staff to adhere to the Standards or related guidance.

While the EGALiTE Accreditation Programme encourages the sharing of best practices and recommendations, it does not assume the role of a regulatory body or authority. The EGALiTE Accreditation Programme involves a peer review process designed to assess and evaluate the compliance of SoHO organisations with standards and criteria established in the present document, where experts in the field conduct assessments based on predetermined criteria. The peer review process is conducted with the utmost independence and impartiality to ensure a fair and unbiased evaluation, and the compliance with the best practices.

The EGALiTE Accreditation Programme is not responsible for informing National Competent Authorities of any non-compliance identified during the peer review process, including major non-compliances.

Participants voluntarily engage in this process to demonstrate their commitment to quality and best practices, and organisations participate in the EGALiTE Accreditation Programme voluntarily, acknowledging that the outcomes of the process are not intended for regulatory purposes.

ABBREVIATIONS[‡]

ADM	Acellular dermal matrix (ADM)
AM	Amniotic Membrane
aW	available water
CAPA	Corrective and Preventive Actions
CFU	Colony-forming units
CMV	Cytomegalovirus
CV	Cardiovascular
DALK	Deep anterior lamellar keratoplasty
DCD	Deceased donors after circulatory death
DMEK	Descemet membrane endothelial keratoplasty
DMSO	Dimethyl sulphoxide
DSAEK	Descemet stripping automated endothelial keratoplasty
EATCB	European Association of Tissue and Cell Banks
EBA	European Blood Alliance
EBMT	European Society for Blood and Marrow Transplantation
EBV	Epstein–Barr virus
ECDC	European Centre for Disease Prevention and Control
EDQM Blood	Guide to the preparation, use and quality assurance of Blood Components (20 th Edition)
EDQM Guides	<i>Guide to the quality and safety of tissues and cells for human application</i> and <i>Guide to the preparation, use and quality assurance of Blood Components</i>
EDQM Tissue and Cells	Guide to the quality and safety of tissues and cells for human application (5 th Edition)
EDQM	European Directorate for the Quality of Medicines and Healthcare
EEBA	European Eye Bank Association
EK	Endothelial keratoplasty
EM	Electron microscopy
EU	European Union
EuroGTP II	Good Practices for demonstrating safety and quality through recipient follow-up - Good Practices for evaluating quality, safety and efficacy of novel tissue and cellular therapies and products (EU Project 709567)
FMEA	Failure mode and effects analysis
FMECA	Failure mode, effects and criticality analysis
FMT	faecal microbiota transplantation
FTSG	Full-thickness skin graft

[‡] For practical reasons, the present list includes the abbreviations and acronyms utilized in other chapters of the EGALiTE Standards.

GAPP JA	Facilitating the Authorisation of Preparation Process for blood, tissues and cells, Joint Action
GMP	Good Manufacturing Practice
HACCP	Hazard analysis and critical control points
HM	Human Milk
HMB	human milk bank
HoP	Holder pasteurisation
HV	Heart valve
IDM	infectious disease marker
JACIE	Joint Accreditation Committee of the ISCT (International Society for Cellular Therapy) and the EBMT
MiRCA	Microbiological Risk of Contamination Assessment tool for tissues and cells
MSK	Musculoskeletal Tissues
ORHA	Organisations for Human Application
PK	Penetrating keratoplasty
PPA	Preparation Process Authorisation
PQR	Product Quality Review
PRF	Platelet-Rich fibrin
PRP	Platelet-Rich Plasma
QM	Quality Manager
rCDI	<i>Clostridioides</i> (formerly <i>Clostridium</i>) <i>difficile</i> infection
RP	Responsible Person
SARE	Serious Adverse Reaction and Event
SED	Serum Eye Drops
SMF	Site Master File
SoHO	Substances of Human Origin
SOP	Standard Operating Procedure
TED	Tissue Establishment Dossier
TGOT	Technical Guidelines for Ocular Tissue
TNC	Total nucleated cell
UCB	Umbilical Cord Blood
URS	User-requirement specifications
VMP	Validation Master Plan
WMDA	World Marrow Donor Association

DEFINITIONS[§]

Audit	means a systematic and independent examination to determine whether activities and the related results of such activities comply with legislation and planned arrangements and whether such arrangements are applied effectively and are suitable to achieve the objectives ⁷
Collection	means a process by which SoHO are obtained from a person, including any preparatory steps, such as hormone treatment, needed to facilitate the process at, or under the supervision of, a SoHO entity ⁷
Donation Centre	A SoHO Entity that carries out one or more of the activities: SoHO donor history review and eligibility assessment; SoHO testing of donors for eligibility or matching purposes; collection of SoHO from donors or patients.
Donor recruitment	means any activity aimed at informing persons about activities related to SoHO donation or at encouraging them to donate SoHO ⁷
Must (or shall)	Indicates an absolute requirement. Compliance with the statement is mandatory, and failure to meet this requirement is considered a violation of the standard.
Processing	All operations involved in the preparation, manipulation, preservation, storage and packaging of SoHO intended for human application. ¹ means any operation involved in the handling of SoHO, including, but not limited to, washing, shaping, separation, decontamination, sterilisation, preservation and packaging, except for the preparatory handling of SoHO for immediate human application during a surgical intervention, without the SoHO being removed from the surgical field before they are applied ⁷ .
Qualification	According to European Union Good Manufacturing Practice (EU GMP) ^{6,8} , the action of proving that any equipment works correctly and actually leads to the expected results. More generally, qualification is applied to the inputs to a process, i.e. equipment, facilities, materials and software (and their suppliers), as well as to operators and the relevant written procedures ¹
Quality Management System	The organisational structure, with defined responsibilities, procedures, processes and resources, for implementing quality management, including all activities that contribute to quality, directly or indirectly ¹
Risk assessment	Identification of potential hazards with an estimation of the likelihood that they will cause harm and of the severity of the harm should it occur ¹ .

^{§ §} For practical reasons, the present list includes the definitions referred in other chapters of the EGALiTE Standards.

Should	Indicates a recommendation. While it is not mandatory, adherence to this statement is strongly advised to ensure the best outcomes. Non-compliance is not a violation of the standard but may affect the overall effectiveness or quality of the implementation.
SoHO Entity	Means an organisation legally established in the Union that carries out one or more of the SoHO activities that have a direct impact on the quality, safety or effectiveness of SoHO, as follows: (i) SoHO donor registration; (ii) SoHO donor history review and medical examination; (iii) testing of SoHO donors or of persons from whom SoHO are collected; (iv) collection; (v) processing; (vi) quality control; (vii) storage; (viii) release; (ix) distribution; (x) import; (xi) export; (xii) human application; (xiii) clinical-outcome registration. ⁷
SoHO establishment	means a SoHO entity that carries out any of the following SoHO activities: (a) both processing and storage; (b) release; (c) import; (d) export. ⁷
SoHO preparation	means a type of SoHO that: (a) has been subjected to processing and, where relevant, one or more other SoHO activities referred to in Article 2(1), point (c) of the EU SoHO Regulation; (b) has a specific clinical indication; and (c) is intended for human application to a SoHO recipient or is intended for distribution. ⁷
SoHO Regulation	Regulation (EU) 2024/1938 of the European Parliament and of the Council of 13 June 2024, on standards of quality and safety for substances of human origin intended for human application and repealing Directives 2002/98/EC and 2004/23/EC.
Substance of Human Origin (SoHO)	means any substance collected from the human body, whether it contains cells or not and whether those cells are living or not, including SoHO preparations resulting from the processing of such substance ⁷
Validation	Documented evidence giving a high degree of assurance that a specific process or system, including pieces of equipment or the environmental conditions, will perform consistently to deliver a product meeting its pre-determined specifications and quality attributes, based on intended use (EU Directive 2006/86/EC ⁹) ¹ . or Confirmation, through the provision of objective evidence, that the requirements for a specific intended use or application have been fulfilled (ISO9000:2015 ¹⁰) ¹
Verification	Preferred term for the validation or qualification of IT systems/software. Or, Confirmation, through the provision of objective evidence, that specified requirements have been fulfilled (ISO9000:2015 ¹⁰) ¹

INDEX/STANDARDS STRUCTURE

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		A.2. DECEASED DONATION	G. AMNIOTIC MEMBRANE
	B. COLLECTION		H. SKN
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	C. PROCESSING, STORAGE AND RELEASE OF SoHO		J. MUSCULOSKELETAL
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PART I.1.: Umbilical Cord Blood Progenitors (UCB)

Recruitment of potential donors, identification and consent

STANDARD:

K.1.001 Donor recruitment may start during pregnancy, with information given by the woman's healthcare provider, or occur as late as at admission into the maternity unit, as soon as parents are informed about this possibility and the mother is in good condition for signing an informed consent.

Explanation:

Information leaflets or brochures to inform mothers about UCB banking are an important part of the recruitment plan. This, supported by the right information, may clearly bring parents to decide the final application of their donation. Information should include at a minimum:

- a. donor exclusion criteria;
- b. the potential benefits and risks of UCB donation;
- c. testing to be performed;
- d. potential use (transplantation or other proven clinical use);
- e. UCB unit exclusion criteria;
- f. data protection.

Any claims made in recruitment material should be supported by scientific evidence.

It is during pregnancy that expectant mothers are encouraged to gather information and ask questions about the UCB collection procedure. Motivated personnel at collection sites are an important way to approach potential maternal donors. Training of physicians and health professionals on this step is essential to make sure that information provided to parents is accurate and that all their questions can be answered.

STANDARD:

K.1.002 The consent that mothers must sign must cover in writing all aspects related to the donation.

Explanation:

Normally, there are questions about performing infectious disease marker (IDM) tests, contacting the maternal donor in case an IDM test is positive, using units for research, checking medical notes, etc.

STANDARD:

K.1.003 Asking for informed consent and providing information about it must not be done during active labour in order to avoid distraction linked to physical and emotional stress.

Explanation:

Consent can be obtained in a single step prior to collection, when the donation process is initiated early in the pregnancy, or in two steps: a pre-consent followed by a full consent before the UCB unit is placed into a clinical inventory.

STANDARD:

K.1.004 The following criteria are absolute contraindications that must be taken into account when evaluating a potential donor (non-exhaustive list):

- a. autoimmune diseases if the mother received treatment in the last 12 months;
- b. malignancy (except basal cell carcinoma and in situ cancer treated and cured);
- c. inflammatory bowel disease (e.g. Crohn's disease and ulcerative colitis);
- d. if the mother has received donated eggs or embryos since 1980;
- e. evidence of active or chronic infection;
- f. live immunisation (vaccination) during this pregnancy;
- g. myasthenia gravis;

- h. *myelodysplastic or myeloproliferative syndrome;*
- i. *unexplained night sweats;*
- j. *animal bite;*
- k. *organ recipient.*

STANDARD:

K.1.005 A medical and genetic history of the infant donor's family must also be obtained to prevent the transmission of malignant diseases and inherited disorders

Explanation:

The questionnaire must include questions to obtain at a minimum genetic history, malignant disease and inherited disorders that may be transmissible to the recipient.

STANDARD:

K.1.006 The medical history evaluation must be obtained while the mother is able to concentrate on the answers to the questionnaire and is not distracted by aspects of labour

Explanation:

The language used must be understood by the donor herself. It is not recommended that either family or friends serve as interpreters or translators. Confidentiality must be preserved. The results of this evaluation must be documented in the clinical history and reviewed by trained personnel.

STANDARD:

K.1.007 If responses obtained during the medical history evaluation generate medical concerns, the collection must be rejected or cancelled. The mother's travel history to endemic areas must be obtained and documented, and eligibility determined according to national regulations

Explanation:

Trained personnel must determine the donor's eligibility. It is important to ensure that the donation is safe for future recipients. Maternal and infant donor eligibility must be determined on the basis of the results of screening and testing in accordance with national regulations.

Evidence:

Donor eligibility criteria defined in the Standard Operating Procedure (SOP).

STANDARD:

*K.1.008 IDM tests on maternal blood samples must be performed within seven days before or after collection of the UCB unit.
At a minimum, prior to release for administration, the maternal donor of each UCB unit must be tested for evidence of infection*

Explanation:

Maternal blood obtained within 7 days before or after the collection of the unit is used as a surrogate test for IDMs, and is strongly reflective of the infectious status of the UCB units due to the shared circulation during gestation.

These samples will be tested for evidence of infection of HIV1, HIV2, hepatitis B, hepatitis C, syphilis and any additional markers according to local regulations. Assays used for testing must be validated for use in volunteer blood or tissue donations. According to the EU regulation, if initial IDM tests do not include nucleic acid tests for HIV, HBV and HCV, then a second IDM test 180 days after donation must be performed. Testing the UCB unit for IDM provides an additional degree of safety.

Evidence:

Donor eligibility criteria defined in the SOP .

STANDARD:

K.1.009 In the case of a woman who gives birth to an infant donor not genetically hers, her communicable disease risk history must be obtained

Evidence:

Evidence of requirement described in the donor recruitment/selection SOP.

STANDARD:

K.1.010 Mechanisms for donor counselling must be in place if there is a positive test result for any IDM (other than Cytomegalovirus), an abnormal haemoglobinopathy screening or any other abnormal test finding.

The UCB bank must have policies for handling specific cases

Explanation:

Every effort should be made to notify the mother, and/or her physician.

Evidence:

SOP must detail the procedures/mechanisms in place to handle these situations.

Collection

STANDARD:

K.1.011 The procurement procedure must include the definition of the following steps:

- a. The umbilical cord is clamped as distal from the placenta as possible. No interference with labour and delivery must occur in order to protect mother and newborn safety;*
- b. A section of the cord is cleaned with a suitable disinfectant;*
- c. A needle that is attached to the collection bag is inserted into the umbilical cord vein;*
- d. The collection bag is filled by gravity until the cord looks 'white' and all the blood from the placenta and umbilical cord is drained into the bag;*
- e. The collection bag must be appropriately labelled.*

Explanation:

Nowadays, many obstetrical medical associations recommend delayed clamping. Evidence suggests that an acceptable time of 1 minute is compatible with public UCB banking.

Evidence:

Associated SOP.

STANDARD:

K.1.012 Individuals performing the collection must be adequately trained

STANDARD:

K.1.013 The collection bag must contain an adequate volume of anticoagulant (i.e. CPD) to prevent clotting

STANDARD:

K.1.014 A report describing the labour phase, listing the events to be evaluated for acceptance of the unit, such as presence of fever, complications, type of delivery, etc must be completed by a health care provider

STANDARD:

K.1.015 Before temporary storage, there is an opportunity to check the units and decide whether to transport them to the lab for processing and storage. If for example the TNC count is too low, it could be a criterion for not shipping a UCB from a collection site to the banking site. This decision must be documented.

STANDARD:

K.1.016 A maximum time between collection and the start of processing must be established: unrelated UCB units must be initiated as soon as possible within 48 h and cryopreservation of related units within 72 h

Explanation:

Progressive loss of HPC viability occurs during non-frozen storage. Nevertheless, UCB should be temporarily stored in non-frozen conditions after collection, during transportation to the processing facility. Cell viability decreases, and the risk of bacterial growth increases during storage at room temperature as well as in refrigerators. The distance from the collection and the processing facilities may be considerable.

STANDARD:

K.1.017 The UCB procurement bag must be identified with the following labels and paperwork:

- a. unique UCB and maternal codes;*
- b. product name;*
- c. procurement site name or identifier;*
- d. date/time of collection;*
- e. name and volume/concentration of anticoagulants;*
- f. recommended storage temperature;*
- g. biohazard sign and/or other warning labels, following national regulations;*
- h. statement 'Related donor' where applicable;*
- i. donor name for related UCB units;*
- j. recipient family or individual name if known*

STANDARD:

K.1.018 Storage containers with tamper-evident seals must be used

STANDARD:

K.1.019 Shipping method (transport between collection site and UCB Bank) must be validated and must meet transport regulations for this type of product.

Processing, preservation and storage

STANDARD:

K.1.0020 Upon receipt, the integrity of the UCB units and their containers must be checked, and any deviation must be recorded within the processing records.

Explanation:

On receipt of a UCB unit, checks must be performed on the unit, on the associated samples and on the accompanying documentation, to verify and determine whether specific acceptance criteria are met. These include parameters such as:

- a. volume,
- b. total nucleated cell (TNC) content,
- c. correct documentation and labelling,
- d. signed maternal donor consent,
- e. appropriate transport temperature,
- f. Absence of large/multiple clots,
- g. transport conditions and acceptable time in transit from procurement centre to processing laboratory.

Once a UCB unit meets the initial acceptance criteria it will continue on to be processed.

STANDARD:

K.1.021 The equipment and reagents used must not adversely affect the viability of the cells, that the process does not allow the introduction of adventitious agents or the transmission of communicable disease, and that the method be validated to allow optimal recovery of the fraction of interest.

Explanation:

The final product volume and cellular characteristics are dependent on the starting product as well as the processing/separation technique.

The selection of a suitable protocol for cryopreservation of UCB is critical to optimise the recovery of functionally viable HPC.

Potential causes of cell damage include type and concentration of cryoprotectant, cell concentration, and cooling and warming rates, as well as level of control of storage conditions.

Over the past decade three major methods have been used in large-scale banking which produce reproducible results that could be standardised. These include the manual method using hydroxyethyl starch for RBC sedimentation or other proprietary reagents, the semi-automated bottom-and-top method, and newer fully automated and programmable closed systems.

STANDARD:

K.1.022 SOPs related to cryopreservation must specify that the following information is recorded for each unit:

- a. TNC concentration within a defined range;*
- b. the type of cryoprotectant, its final concentration and the duration of the cell exposure prior to freezing;*
- c. method of freezing and end-point temperature of cooling;*
- d. cooling rate within a defined range;*
- e. freezing curve parameter within a defined range;*
- f. storage temperature.*

STANDARD:

K.1.023 UCB units must be stored in freezing bags designed and approved for the cryopreservation of human cells and placed into metal cassettes to provide protection during freezing, storage, transportation and shipping.

After filling, each freezing bag must be visually examined for possible leaks and breakage of seals.

STANDARD:

K.1.024 Storage temperature must be maintained at -140°C or colder.

Explanation:

Both vapour or liquid phases can be used, but the use of an overwrap bag for prevention of cross-contamination is required if the units are immersed in liquid nitrogen.

STANDARD:

K.1.025 Reference samples of each freezing bag must have integrally attached, at minimum, two segments of adequate volume to assess identity and potency of the UCB cells prior to release.

STANDARD:

K.1.026 UCB units must be cryopreserved using a controlled-rate freezer with a validated freezing programme.

Example(s):

The majority of UCB banks use cooling rates of $1\text{--}5^{\circ}\text{C}/\text{min}$ in order to allow the cells to slowly dehydrate as the ice phase progresses and the extracellular solute concentration increases.

STANDARD:

K.1.027 Prolonged addition of cryoprotectant to initiation of freezing must be minimised and the maximum time allowed must be validated by the bank.

Explanation:

As the exposure of cells to DMSO can result in damage to cells. It is therefore essential that the duration from Cryoprotectants used for UCB are those generally established for other HPC sources.

In general, a concentration of 10 % DMSO is considered optimal for UCB. When used in conjunction with DMSO, other cryoprotectants, like Dextran-40, enhance the cryoprotective effect by allowing stabilisation of the cell membrane. While alternatives have been proposed, it is generally considered that a combination of 10 % DMSO and 1 % Dextran-40 is considered to ensure the best recovery rates for TNC, CD34+ and colony-forming units (CFU).

STANDARD:

K.1.028 The following samples must be available for each banked unit, in addition to the two contiguous segments:

- a. (at least) 2×10^6 TNC divided in two vials, suitable material for preparation of genomic DNA, and plasma; and,*
- b. from the maternal donor, serum and/or plasma and suitable material for preparation of genomic DNA.*

All the samples must be stored at -70°C or colder. Representative samples intended for viability or potency analysis must be stored under the same conditions as the UCB unit.

Explanation:

In addition to the, it is necessary to store several samples. Netcord-FACT International Cord Blood Standards require, from each UCB unit.

STANDARD:

K.1.029 All clinical and biological information pertaining to donor identification, screening and recruitment must be kept, along with all information pertaining to processing and distribution. This information must remain as a permanent part of the preparation and release file.

STANDARD:

K.1.030 The primary packaging must be sterile and made of a biologically compatible material. Cryopreservation requires the use of liquid-nitrogen-resistant bags and labels

STANDARD:

K.1.031 Labelling must allow the UCB bank to ensure the link between the UCB unit and its samples and records.

Each label must include at least the unique identifier, the proper name of product, the intended recipient (if known), the type of manipulation, the anticoagulants and additives used and the conditions under which the cells are to be stored and distributed

Explanation:

Because UCB bags are normally too small for a standard-size label, a partial label at distribution is acceptable and must include at least a unique numeric or alphanumeric identifier, the proper name of the product and the product code. Additional information can be included in a tie tag and/or in the accompanying documentation.

STANDARD:

K.1.032 UCB banks must have an inventory management system to ensure that each UCB unit and its associated reference samples, maternal samples and records can be located in a timely manner.

Explanation:

This inventory management system should prevent mix-ups or contamination of the UCB units during storage, and address the duration of the storage for cryopreserved UCB units.

STANDARD:

K.1.033 The UCB banks must establish and validate the duration and conditions of storage.

Explanation:

The effects of long-term storage on the viability, potency and sterility of the UCB cells should be evaluated in a stability protocol.

Evidence:

Validation study.

STANDARD:

K.1.034 A procedure for quarantine to minimise the risk of microbial cross-contamination of UCB units must be in place.

Explanation:

Refrigerators and freezers used for the storage of UCB units and all associated reference products should not be used for any other purpose, in order to minimise the risk of cross-contamination.

STANDARD:

K.1.035 Release of a UCB unit from quarantine must be based upon the evaluation of the testing and screening results pertinent to that UCB unit, in accordance with applicable national laws and regulations.

STANDARD:

K.1.036 The UCB bank must assess the potential risk of transient warming events during processing and/or storage.

Explanation:

UCB units are intended for long-term storage and must be stored at -140°C or colder.

Examples of these events include transfer of UCB units from the controlled-rate freezer to the cryostorage tank, removal of segments for HLA verification testing or other tests required and storage of UCB units in vapour vessels that may exhibit unstable temperatures when open. Each step should be validated to show that the viability and potency of the UCB unit have not been compromised.

Quality Controls

STANDARD:

K.1.037 Microbial testing must be performed using a system validated for the growth of aerobic and anaerobic bacteria and fungi

STANDARD:

K.1.038 UCB units for unrelated use must be shown to be free of microbial contamination.

STANDARD:

K.1.039 For related UCB units, the results of positive microbial tests must include identity and antibiogram(s) of the organism(s), and these results must be reported to the prospective clinical programme.

STANDARD:

K.1.040 Prior to release for administration, each UCB unit must have undergone haemoglobinopathy screening, regardless of the family's ethnic background or history.

STANDARD:

K.1.041 Unless justified by the result of a risk assessment the following quality controls must be performed, either in routine or in the context:

- *Total nucleated cell count*
- *Viable CD34+ cell enumeration*
- *Viability of CD45+ and CD34+ cells*
- *ABO Rh blood group and verification HLA typing*
- *Measurement of residual ABO incompatible red cell volume*
- *CFU or other validated potency assay*

Explanation:

The three tests must be performed by the bank before a UCB unit can leave storage premises:

- verification of donor identity;
- potency assessment; and safety evaluation

The 7th edition of the Netcord–FACT standards provides a list of reference values to determine the quality of a UCB unit stored for clinical administration.

Meeting UCB quality specifications and having very good banking practice will ensure a successful UCB transplantation

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The 7th edition of the Netcord–FACT standards provides a list of reference values to determine the quality of a UCB unit stored for clinical administration.

Meeting UCB quality specifications and having very good banking practice will ensure a successful UCB transplantation

Verification of donor identity: UCB unit identity can be verified by performing HLA-typing using a contiguous segment physically attached to the freezing bag containing cryopreserved UCB cells. The UCB bank must have a policy in place for the cases where there are no remaining attached segments. Verifying the maternal HLA haplotype would add additional safety requirements to validate HLA typing and to ensure maternal testing and assessment corresponds to the product selected.

Potency assessment:

It is a requirement to assess the functional capacity of the UCB unit prior to release to the transplant centre. CFU assay is the surrogate potency usually used and its ability to predict engraftment should be validated. CFUs are grown from functionally viable cells and the results of this assay increase confidence in UCB unit quality and ability to engraft. It is recommended to perform CFU assay from a frozen contiguous segment prior to release for administration since 8-12 days are needed for the read-out of cellular growth.

Safety evaluation

IDM testing of the maternal samples is understood to be a surrogate test, and strongly reflective of the infectious status of the UCB unit. Prior to release for administration the results of maternal donor screening must be available. Because of differing national regulations, testing for additional infectious agents by IDM test may be required by the transplant centres.

Cellularity/viability:

Cell dose will depend on clinical indication, age and patient's body-weight. It is suggested to increase cell dose if there is HLA mismatch increase or if the patient has a non-malignant disorder

Cellularity/viability Minimum: recommended cell dose for a single UCB transplantation: TNC > 3E7/kg;
CD34 > 1.5E5/kg

Microbiological criteria are defined in the standards K1.037, K1.038, K1.039

Distribution

STANDARD:

K.1.042 The UCB bank must receive a formal request from the transplant centre before the work-up starts. Return of unrelated UCB units is generally not permitted

STANDARD:

K.1.043 The recipient must be identified (but not the donor) when cells are distributed for administration.

STANDARD:

K.1.044 Methods of transportation and shipping must be described in operating procedures. Internal and external transport or shipping must be controlled, and records must allow tracking and tracing of the UCB unit from UCB bank to the transplant centre. For shipment of the cryopreserved UCB units, a dry-shipper must be used, and the temperature monitored and recorded to detect temperature excursions

Evidence:

Validation Studies should be evaluated to determine the compliance of this requirement.

STANDARD:

K.1.045 Container validation and courier qualification must be performed periodically

STANDARD:

K.1.046 Transport containers must be appropriately labelled and secured with tamper-evident seals, and must conform to applicable regulations.

Evidence:

SOP and practical observation of materials used can be assessed.

Example(s):

Information related with the SOPs and materials used may be submitted as evidence of compliance

STANDARD:

K.1.047 A plan for alternative transportation or shipping in an emergency must be in place.

Evidence:

Contingency plans should consider this requirement.

Example(s):

SOP or contingency plan may be submitted as evidence of compliance

STANDARD:

K.1.048 Transportation records must be maintained by the shipping facility and shared with the receiving facility.

Evidence:

Examples of such records can be evaluated.

Example(s):

SOP and/or examples of these registries may be submitted as evidence of compliance.

STANDARD:

K.1.049 Appropriate training of the personnel in charge of transportation must be documented

Evidence:

Training registries and plans.

Example(s):

Training registries and plans may be submitted as evidence of compliance.

STANDARD:

K.1.050 The UCB bank must provide handling instructions, and information about indications, contraindications and cautions, to the transplant units. In addition UCB banks must be able to provide instructions for a validated thawing method of their UCB unit.

Explanation:

It is important to ensure that the transplant centre receives information on how to handle and use the UCB unit.

Units that have not been red cell reduced prior to cryopreservation should be washed, as recommended by FACT-JACIE, while a buffy coat enriched UCB unit can be simply diluted

In case of ABO incompatibility, red cell volume should be less than 1 mL/kg recipient body weight. If not, a washing step is recommended before infusion.

Evidence:

Example of handling instructions (SOP, Flyer/leaflet) should be evaluated.

Example(s):

Informative documentation and/or SOP may be submitted as evidence of compliance.

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