Guide and recommendations for Cord Blood Banking

ARTHIQS – Deliverable 9
WP 5
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1. Introduction

This Guide of recommendations for cord blood banking has been developed by the European Joint Action project entitled Assisted Reproductive Technologies and Haematopoietic stem cells Improvements for Quality and Safety throughout Europe - ARTHIQS (www.arthiqs.eu). ARTHIQS is a European Joint Action funded by the European Commission under the 2008-2013 Health Programme. It has lasted four years, from May 1st 2014 till April 30th 2018. This project was focused on Assisted Reproductive Technologies and Haematopoietic Stem cells for transplantations. A total of 16 partners and 9 collaborators from 18 different Member States participated in the ARTHIQS consortium.

The ARTHIQS project was organised in five Work Packages, each led by a member state, as follows: WP1 Coordination (France), WP2 Dissemination (Czech Republic), WP3 Evaluation (Sweden), WP4 Assisted Reproductive Technologies (France), WP5 Haematopoietic Stem cells for Transplantation. WP5 was co-led by the Ministry of Health of the Republic of Croatia (Croatia) and Centro Nazionale de Trapianti – Instituto Superiore di Sanita (Italy).

The following Member States and organisations participated in this WP:

**Associated Partners:**
Agency for Biomedicine (France), The Health and Social Care Inspectorate (Sweden), State Institute for Drug Control (the Czech Republic), The Portuguese Institute of Blood and Transplantation (Portugal), Hellenic Transplant Organisation (Greece), Federal Agency for Medicines and Health Products (Belgium), Bulgarian Executive Agency for Transplantation (Bulgaria), Ministry of Health, Welfare and Sport (The Netherlands), National Centre for Tissue and Cell Banking (Poland), National Transplant Organisation of Slovakia (the Slovak Republic).

**Collaborative partners:**
World Marrow Donor Association (WMDA), Hungarian National Blood Transfusion Service, European Society for Blood and Marrow Transplantation (EBMT), NetCord Foundation*, Cord Blood Europe, Vilnius University Hospital (Lithuania), Ministry of Health Cyprus, Clinical University Hospital Virgen de la Arrixaca (Spain)

* Activities of NetCord Foundation is integrated into WMDA (effective January 1, 2017)

1.1 Aim and scope

Specific objectives of WP5 were to
1. set up a model for the haematopoietic donor follow-up registry,
2. the definition of standards for safety and quality for cord blood banks, derived from EU tissues and cells directives and compatible with other standards,
3. to provide the basic guidance and training for cord blood banking inspectors

The purpose of these guidelines is to provide cord blood banks not accredited by international organisations, as well as tissues and cells competent authorities, with basic principles relating to the collection, processing, testing and distribution of cord blood. Guidelines are applicable both to CB units intended for public use and CB units stored for autologous or family use in the future in the Member States which allow that activity. The guidelines aim to be a starting tool for harmonisation.
of the authorisation procedure for cord blood banking at EU level, in order to increase quality, safety and transparency in the field of cord blood banking. This document does not intend to replace well-established standards like NETCORD-FACT or AABB, but rather provides a comprehensive view on where and how some requirements of these standards can be used.

Aiming to reach its objective, WP5 produced two complementary guiding documents: (1) this Guide of Recommendations for Cord Blood Banking and (2) the Guide for the Inspection of Cord Blood Banks.

1.2 Acronyms

AABB: Advancing Transfusion and Cellular Therapies Worldwide (former American Association of Blood Banks)
AHCTA: Alliance for Harmonisation of Cellular Therapy Accreditation
ATMP: Advanced therapy medicinal product
BM: Bone Marrow
CA: Competent Authority
CAPA: Corrective Action and Preventive Action
CB: Cord Blood
CBB: Cord Blood Bank
CE: Conformité Européenne (“European Conformity”)
CFU: Colony-forming unit
cGMP: Current Good Manufacturing Practice
CNS: Italian National Blood Centre
CNT: Italian national Transplant Centre
CT: Cellular Therapy
DG SANTE: Directorate General for Health and Food Safety
EBMT: European Society for Blood and Marrow Transplantation
EC: European Commission
EDQM: European Directorate for the Quality of Medicines and HealthCare
EAA: European Economic Area
EU: European Union
EUTCD: European Union Tissues and Cells Directive
FACT-NETCORD: Foundation for the Accreditation of Cellular Therapy
GVHD: Graft versus host disease
HLA: Human Leukocyte Antigen
HPC: Haematopoietic Progenitor Cells
IBMDR: Italian Bone Marrow Donor Registry
IPA: Instrument for Pre-Accession Assistance
ISO: International Organization for Standardization
JACIE: Joint Accreditation Committee-ISCT & EBMT
MS: Member state
QS: Quality system
SAE: Serious adverse event
SAR: Serious adverse reaction
SEC: Single European Code
SOP: Standard Operative Procedure
TCD: Tissues and Cells Directive
TNC: Total nucleated cells
TWE: Transient warming event
VISTART: Vigilance and Inspection for the Safety of Transfusion, Assisted Reproduction and Transplantation
Cord blood (CB) is a source of rare but precious haematopoietic progenitor cells (HPC) that can reconstitute the haematopoietic and immune systems in patients with malignant and non-malignant disorders treated with myeloablative or non-myeloablative therapy. CB cells possess high capacity for progenitor cell proliferation and self-renewal in vitro. Usually the CB is regarded as a waste product, of no usage to the child or mother and therefore discarded after the delivery. Thus, the blood remaining in the delivered placenta can easily be collected from the cord and stored safely. The predominant collection procedure currently practiced involves a relatively simple venipuncture, followed by gravity drainage into a standard sterile anti-coagulant-filled blood bag, using a closed system, similar to the one utilized for whole blood collection. After aliquots have been removed for routine testing, the units are processed, cryopreserved and stored at a low temperature. After decades of clinical experience, it is currently accepted that CB transplants, both related and unrelated, are equivalent to or might compare favourably with other HPC sources, especially in children. Initial studies of long-term survival in children with both malignant and non-malignant hematologic disorders, who were transplanted with CB from a sibling donor, demonstrated comparable or superior survival to children who received BM transplantation. One factor that limits the use of CB transplantation in adult patients is the relatively limited number of Total Nucleated Cell Count (TNC) per cord blood unit that may be collected from the umbilical cord, resulting in a longer time to engraftment. In order to speed up the engraftment time, strategies such as multiple CB transplants have been applied. Despite prolonged periods of aplasia, the apparent reduction in the incidence and severity of graft versus host disease (GVHD) may in turn underline comparable rates of survival in some series comparing CB to adult-donor sources. Due to the immune naivety of the CB cells, less stringent HLA compatibility requirements can be applied, extending the access to many patients in need, who would otherwise not be able to find a match.

2. The regulatory framework

In EU Member States, cord blood banking is regulated by national regulation based on the EU Tissues and Cells Directives (EUTCD). The directives establish the minimum requirements of quality and safety for activities connected with cord blood banking, namely donation, procurement, testing, processing, preservation, storage, distribution, coding and import.

In cases when CB cells are substantially manipulated, Regulation 1394/2007 on advanced therapy medicinal products should be applied in addition to the TCDs’ requirements for donation, procurement and testing. This is stated only as information and will not be further described since ATMP is not the subject of this Guidelines.

The regulatory framework is detailed below:


The aforementioned legislation refers to all cord blood cells and tissue regardless of the intended use (autologous or allogeneic) and ownership structure of the facility. Namely, all cord blood units intended for any kind of human application must meet at minimum quality and safety criteria set in the legislation cited above. In the same way, in performing their activities all CB banks must meet Tissues and Cells Directives’ requirements irrespective of the banking model. In addition to the TCD requirements, Member States may impose additional requirements.

In order to ensure the compliance of activities connected with cord blood banking with EU legislation, Member States are obliged to designate a competent authority (CA) responsible for implementing legal requirements. The CA should carry out inspections, as well as ensure that all activities undertaken have been accredited, designated, authorised or licensed by the competent authority.

3. Standards and guides

While requirements emanating from legislation are mandatory, there are documents developed with the purpose of improving quality and safety. Implementation is optional, but contributes to the improvement and harmonization of the field. Those are standards specifying requirements to be fulfilled for the purpose of accreditation. They have been developed by professional societies on different levels, so they can be global, regional or national. Usually, the standards are established by consensus of a critical number of professionals and are based on contemporary evidence-based science.

Furthermore, standards can be adopted into legislation and in that way become legally mandatory.

Many aspects of worldwide standards for cord blood banking are common for all models of cord blood banking; related and unrelated allogeneic and autologous, and the majority of requirements from the standards can be applied to all of them. Issues specific to one type of CBB are indicated separately.

The common aspects of standards which are applicable to all types of cord blood banks concern:

- collection
- transport from the maternity clinic to cord blood bank
- labelling
- processing
- storage
- quality control
- infectious disease testing
- distribution
- maternal and infant donor follow-up
In the field there are different professional organisations that have established an accreditation programme. Alliance for Harmonisation of Cellular Therapy (ACHTA), a standing committee of the Worldwide Network for Blood and Marrow Transplantation (WBMT), prepared and published extensive document comparing cellular therapy standards. It can be found on-line at address: http://www.ahcta.org/documents.html or at www.wbmt.org.

3.1 NetCord-FACT standards

The Foundation for the Accreditation of Cellular Therapy (FACT) and the International NetCord Foundation established the NetCord-FACT International Standards for Cord Blood Collection, Banking, and Release for Administration. These Standards apply to cord blood units intended for unrelated and related allogeneic use as well as for autologous use. Active cord blood banks with inventory of 500 or more stored units can apply for accreditation. The first edition of the NetCord-FACT standards was released in 2000. Concurrently, a global network of inspectors was established based on these Standards, and inspections began in 2001. The standards are updated according to the latest developments and requirements in approximately three-year intervals. Accredited banks are re-inspected every 3 years.

The NetCord-FACT Standards cover all phases of cord blood collection, banking, testing and release for application:

- Donor management, including screening, testing and eligibility determination of infant and maternal donors
- Collection, regardless of the methodology or site of collection
- Processing
- Testing and characterization of the unit
- Cryopreservation
- Storage
- Listing, either directly or through a search registry
- Search, selection, and reservation
- Release
- Distribution to clinical programmes, whether fresh or cryopreserved


Organisation web site: http://www.factwebsite.org/cbstandards/
A list of the FACT-NetCord accredited cord blood banks is available on: http://www.factwebsite.org/CordSearch.aspx?

3.2 AABB Standards

AABB standards set requirements for donor eligibility and the collection, processing, storage and application of any type of cellular therapy product. The standards provide the basis for the AABB Accreditation programme that accredits both public and family cord blood banks.

In 2001 AABB (former American Association of Blood Banks) published the 1st edition of the Standards for Cord Blood Services which included ISO9000 standards. In 2005, standards for haematopoietic stem cells and cord blood were merged into the Standards for Cellular Therapy

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Services. The latest, 8th edition of Standards has been effective since July 2017. The standards are revised every 24 months in response to the changing scientific and/or regulatory environment.

Standards aim to aid facilities to maintain and enhance the quality and safety of procurement, processing, storage and clinical administration of cellular products, and they cover:

- Organizational issues of CT facility and resources
- Process control, including management of materials, methods and operational controls, development and change of processes and procedures
- Donor evaluation, management and testing
- Product collection, labelling and traceability
- Processing, testing, cryopreservation
- Transport and shipping
- Stability of products
- Discard and disposal
- Documents and records
- Deviations, nonconforming products or services and adverse events
- Internal and external assessment
- Process improvement
- Safety policies and environmental controls

Organisation website: [http://www.aabb.org](http://www.aabb.org)


3.3. Council of Europe/EDQM Guide to the quality and safety of Tissues and Cells

The European Directorate for the Quality of Medicines and HealthCare, which is a Directorate of the Council of Europe, develops guidance and proposes ethical, safety and quality standards for the transplantation of organs, tissues and cells. EDQM approaches tissue and cell transplantation in compliance with the principles of non-commercialisation and voluntary donation of materials of human origin. Because of the work of leading European experts in the field, EDQM publishes the Guide to the Quality and Safety of Tissues and Cells for Human Application. It constitutes a common European standard, based on the long-standing expertise and knowledge of the EDQM.

The Guide contains general requirements applicable to all establishments involved in the donation, procurement, testing, processing, preservation, storage and distribution of tissues and cells, and specific guidelines and requirements for the different tissue and/or cell types. The chapter on haematopoietic stem cells covers specificities within the following issues:

- donor evaluation
- collection
- processing
- quality control
- storage
- packaging and labelling
- vigilance and surveillance

### 3.4 Comparison of standards

A comparison between the EUTCD, NetCord –FACT and AABB requirements regarding some, but not all, of the CB specific issues are listed in Table 1. From this comparison, it should be noted that certain CB-specific aspects that are essential for the quality and safety of CB derived HPC are not covered by the EUTCD. In addition, if the CBB aims at accreditation by NetCord-FACT or AABB, they need to have had some prior activity. In EU, it is mandatory to have authorization / licensing for the intended activity in order to collect, store or distribute human tissues and cells to be used for human application. Accordingly, the CA needs to have basic knowledge in the area of CB and HPC to be able to guarantee quality and safety of the activity until an accreditation by more CB specific standards can be reached.

<table>
<thead>
<tr>
<th>Requirements</th>
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<th>NetCord-FACT 6th ed</th>
<th>AABB 8th ed</th>
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</thead>
<tbody>
<tr>
<td><strong>Donation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Voluntary and unpaid</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Consent</td>
<td></td>
<td></td>
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<tr>
<td>Obtained by licensed physician or other health care provider familiar with the collection procedure</td>
<td>X</td>
<td>Trained individual at collection site</td>
<td></td>
</tr>
<tr>
<td>Mother donating cord blood informed to contact CBB if infant donor develops serious disease post donation</td>
<td>-</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td><strong>Donor Evaluation</strong></td>
<td></td>
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<tr>
<td>Laboratory testing by laboratory accredited or licensed in accordance with applicable laws and regulations using tests approved or cleared by relevant governmental authority</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

*Table 1 Partial comparison of standards and recommendations in the context of CB (Adapted from [www.ahcta.org/docs/crosswalks/](http://www.ahcta.org/docs/crosswalks/))
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<th>NetCord-FACT</th>
<th>AABB</th>
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<tbody>
<tr>
<td>Donor evaluation (cont)</td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>History obtained and documented from maternal</td>
<td>-</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>cord blood donors at a time when the mother is</td>
<td></td>
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<tr>
<td>able to concentrate on the information and is</td>
<td></td>
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<tr>
<td>not distracted by aspects of labor</td>
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<tr>
<td>Infant donor of Cord Blood data to include</td>
<td>-</td>
<td>X</td>
<td>-</td>
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<tr>
<td>history of pregnancy and delivery, birth</td>
<td></td>
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<td></td>
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<tr>
<td>data including gestational age, gender, and</td>
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<td>results of clinical examination, and any</td>
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<td>indication suggestive of potentially transmissible</td>
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<tr>
<td>disease</td>
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<tr>
<td>Maintain linkage of the CB unit to the infant</td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>donor and mother</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Traceability from donor to recipient is</td>
<td></td>
<td></td>
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<td>required but not specified to the mother in the</td>
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<td>case of CB</td>
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<tr>
<td>Collection</td>
<td></td>
<td>X</td>
<td></td>
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<tr>
<td>Cord Blood collection kit reagents and supplies</td>
<td>-</td>
<td>X</td>
<td>X</td>
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<tr>
<td>shipped to collection site in validated</td>
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<tr>
<td>container and stored at site according to</td>
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<td>manufacturer's recommendations.</td>
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<tr>
<td>Environmental conditions controlled and</td>
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<td>-</td>
<td>X</td>
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<tr>
<td>documented?</td>
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<td></td>
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<tr>
<td>For initial accreditation cord blood banks,</td>
<td></td>
<td>X</td>
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<tr>
<td>need a minimum number of units collected and</td>
<td></td>
<td>X</td>
<td></td>
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<tr>
<td>banked</td>
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<td></td>
<td></td>
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<tr>
<td>Must be authorized before operation</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Must have 500 units banked</td>
<td></td>
<td>X</td>
<td></td>
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<tr>
<td>Minimum time in operation: 6 months</td>
<td></td>
<td>X</td>
<td></td>
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<tr>
<td>Processing</td>
<td></td>
<td>X</td>
<td></td>
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<tr>
<td>Minimal product testing prior to infusion or</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>cryopreservation to include use of a validated</td>
<td></td>
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<tr>
<td>assay for:</td>
<td></td>
<td></td>
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<tr>
<td>TNC and viability assessment</td>
<td>-</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Assessment of CD34 content for HPC products</td>
<td>-</td>
<td>X</td>
<td></td>
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<tr>
<td>Product sterility</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
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</table>

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<thead>
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<th>NetCord-FACT</th>
<th>AABB</th>
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</thead>
<tbody>
<tr>
<td>Processing (cont)</td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>When processing alters the final cell population, the target cell population should be assessed before and after processing</td>
<td>-</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Test procedures performed by the processing facility must be monitored for reliability, accuracy, precision, and performance.</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Ongoing proficiency testing required for tests performed by the processing facility</td>
<td>-</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Communicable disease testing shall be performed using laboratories and testing reagents or kits approved in accordance with applicable laws and regulations</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Cryopreserved HPC(CB) products must contain minimally 2 segments integrally attached to bag and containing approximately 200 microliters of representative sample</td>
<td>-</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>One integrally attached segment must be used to verify HLA typing, and should be used to verify viability and potency for banked HPC(CB)</td>
<td>-</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Serum or plasma samples (not heparinized) of &gt;3.6 mL stored -70 C or colder in at minimum 2 vials stored</td>
<td>-</td>
<td>X</td>
<td>Also from maternal sample</td>
</tr>
<tr>
<td>Minimally sample sufficient to obtain 50 microgram genomic DNA required from banked HPC(CB)</td>
<td>-</td>
<td>X</td>
<td>Also from maternal sample</td>
</tr>
</tbody>
</table>

3.5 **ISO standards**

The International Organization for Standardization, ISO, develops and publishes international standards. Draft standards, are developed by an experts’ technical committee, and are adopted by ISO members.

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Although there is no ISO standard dedicated specifically to cord blood banking in contrast to the previously mentioned ones, there are many ISO standards applicable to CB banking activities. Examples of those are following series: 03.100.70: Management systems, 03.120.01: Quality in general, 03.120.10: Quality management and quality assurance, 11.080: Sterilization and disinfection, 13.040.35: Clean rooms and associated controlled environments comprising 14644 (1-15) standards.

It is easy to conclude that the implementation of ISO standards in CBB demonstrates an awareness of the concept of quality and efforts made towards higher product safety. Data on holding relevant ISO certificates is informative for CAs in preparation for the authorisation and inspection process of a particular CBB.

### 4. Current situation in member states in the area of Cord Blood Banking

#### 4.1. CBB models

Across the European Union, cord blood banks are established based on different models:

**A) According to the genetic lineage of donors and recipients:**

- Allogeneic and autologous
- Allogeneic can be related or unrelated
  - related allogeneic can be used for families with medical indication (for potential use in treatment of a diseased sibling) or for potential use within the family of the donor, without medical indication at the moment of collection – family cord blood banks
  - unrelated is intended for use in therapy of any patient in the world

*Figure 1. Schematic illustration of CBB types according to the genetic lineage of donors and recipients*
**B) According to the ownership of the facility:**
- Public or private

**C) According to the intended use:**
- Allogeneic use related with medical indication
- Allogeneic use unrelated, i.e. public use
- Allogeneic use related without medical indication
- Autologous use

*Figure 2. Showing the relationship of ownership of the facility and use of CB units with the aim to elucidate different contexts of the use of the terms “private” and “public”.*

**D) Hybrid or mixed model**
- Where donations primarily for autologous use are also on disposal for public use when needed (fig 4.3) e.g. Spain, foreseen in Belgian law.
- Alternatively, donation is split between the bank for public use and the family bank. This model is known as the Virgin Health Bank (VHB) model – such a CBB model operates in the United Kingdom (fig 4.4).

*Figure 3. Hybrid CBB model*

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4.2. Initial survey – existing CBB in member states

As a start, this WP launched a short and simple survey on standardization in the CBB field among European Union Member States’ and EEA countries’ competent authorities for tissue and cells in 2015. Member States were asked about the number of cord blood banks and the number of cord blood banks authorized or licensed by the competent authority. In addition, the types of standards used to accredit their CBBs – national or international. Competent authorities from twenty-six Member States and two EEA countries answered. The summarised results from the survey, presenting the state of the play in 2015 are shown below (Figures 4.5 – 4.9).

It should be noted that this is a rapidly expanding field and according to the EU- coding platform, in November 2017 there were >300 tissue establishments authorized for storage of CB https://webgate.ec.europa.eu/eucoding/.

![Figure 5. The number and types of cord blood banks (CBB) across EU. *Other: CBB without authorisation for distribution/marketing (banking only authorisation)](image-url)
Figure 6. Number of cord blood banks authorised by Competent Authorities. From numbers of CBBs shown in Fig.3.5: CAs authorised 96% allogeneic, 95% family and 88% hybrid banks.

Figure 7. Number of CBBs accredited according to various standards. The most common accreditation among accredited allogeneic CBBs is NetCord-Fact standard (69% of all accreditations).
Besides accreditation by international accreditation programmes, 32 CBBs for allogeneic use, 12 CBBs for family use and 4 hybrid CBBs are accredited according to national standards. The framework of these national standards may vary between Member States.

Even from this elementary survey it could be concluded that a variety of technical standards coexists in this field and a substantial portion of the CBBs work according to a variety of national standards. Six Member States reported their allogeneic CBBs work according to national standards, five reported their family CBBs work according to national standards and four have hybrid CBBs that work according to national standards.

This diversity of approaches supports the usefulness of the harmonisation effort in the field.
4.3. Member states approaches

In the project’s later phase, another, more complex survey was launched with the purpose of investigating Member States’ standpoints in relation to cord blood banking. A questionnaire targeting the main descriptors of the cord blood banking activity was circulated among WP5 partners. Complete data from the survey with a graphical representation of the results can be found in the annex 1.

General approaches of some EU Member States to cord blood banking are presented here, including an overview of legislative framework.

4.3.1 Italy

Cord blood banking in Italy is organized in a national network of 18 Cord Blood Banks (CBB) that are located in 14 different Italian regions. Only public and hospital–based facilities of CBBs exist. The purposes of the CBB network are:

- to promote allogeneic unrelated voluntary CB donation in order to meet the national and international demand of CB units for haematopoietic stem cells transplantation;
- to guarantee the related allogeneic and autologous collection, storage and distribution of CB units (family use) only for appropriate and evidence-based clinical indications; this activity is governed by the national health care system;
- to implement common requirements in compliance with national legislation and commonly accepted international standards;
- to annually collect and send activity data to the Italian National Blood Centre (CNS) and the Italian National Transplant Centre (CNT);
- to perform research projects in the field of collection, processing, testing and banking of CB units.

Inspection activities aimed at the official authorization/licensing of CBBs are the remit of the regional competent authorities, which have to take into account the minimum requirements and guidelines laid down by the national competent authorities (CNS and CNT). The legal framework of CBB activities is defined by the following legislation:

- AGREEMENT between government and regions about the minimum organizational, structural and technological requirements for the activities of the CBBs (Rep. Atti n. 184/CSR del 29 ottobre 2009).
Guidelines for the accreditation, designation, authorisation or licensing of CBBs

The guidelines define the requirements of donation, procurement, testing, processing, preservation, storage and distribution of cord blood units for human application. They are in line with NETCORD-FACT standards, the operational standards of the Italian Bone Marrow Donor Registry (IBMDR) and the standard of the World Marrow Donor Association (WMDA) on the selection and release of unrelated CBUs for national and international patients.

The guidelines apply to the CBBs and maternity units in charge of the collection activities, which shall be performed under the technical control of the responsible CBB.

4.3.2 Belgium

In Belgium, the collection and storage of CB (but also of other tissues and cells) for autologous or allogeneic deferred use in a given and identified recipient is forbidden, except in cases where:

a) the intended recipient of the body material at the time of the procurement or collection presents a scientifically proven high risk for development of pathologic status for which the usefulness of application is scientifically proven, or is already suffering from such a pathologic status

b) or where the cord blood (or tissues and cells) will be available for therapeutic use in a third party and is registered for this purpose.

In the latter case, law lays down detailed rules for the registration and availability, including requirements regarding the information to be provided to the donor by the tissue establishment before collection. In the event that the tissues and cells are used for therapeutic purposes in third parties, the cord blood bank (tissue establishment) has to refund the donor the amount equal to that paid at the time of collection, after adjustment to the consumer price index.

Activities related to cord blood banking are regulated within the scope of:

- Human body material law (19 DECEMBRE 2008. — Loi relative à l’obtention et à l’utilisation de matériel corporel humain destiné à des applications médicales humaines ou à des fins de recherche scientifique article 8,§1, 4°).

4.3.3 Croatia

Activities of cord blood banking in Croatia are performed in a single national multi-tissue bank. The bank is responsible for collection, processing and storage of CB for allogeneic unrelated use, allogeneic related use in cases of medical indication and also family use. It is a public, hospital-based bank. Collection sites are in maternity hospitals, or wards within hospitals, all under the contract with the bank. Currently, the bank collects from 24 collection sites.

In 2016 the CBB applied for NetCord accreditation after a preparatory process, supported, among the other means, through the two EU IPA1 Projects.

The Competent Authority for cord blood is within the Ministry of Health, consisting of two units: an inspection unit and a regulatory and authorisation unit.

Legislation for cord blood is within the tissues and cells legislation:

- Act on application of human tissues and cells (Official Gazette 144/12, from 19 December 2012).
- Ordinance on requirements regarding premises, personnel, equipment and quality system for performing procurement, testing, processing, preservation, storage and distribution of human tissues and cells (Official Gazette 54/13, from 17 June 2013).

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- Ordinance on ways of monitoring serious adverse events and reactions in the area of application of human tissues and cells, on records keeping and deadlines for the annual report form (Official Gazette 54/13, from 17 June 2013),
- Ordinance on requirements for professional qualifications and training of inspectors and on inspections in the area of application of human tissues and cells (Official Gazette 54/13, from 17 June 2013).

According to the above-mentioned legislation, any foreign CBB collecting cord blood (or cord tissue) in Croatia and storing abroad shall be inspected by CA in the same manner as the Croatian bank in order to obtain authorization.

4.3.4 Sweden

Sweden has only two cord blood banks, one National CBB for public use and one private for family use. Both are authorized according to the same criteria, under the EUTCD, by the Competent Authority (The health and Social Care Inspectorate IVO) and the National CBB is also accredited by FACT according to NetCord standards. The agreement between the CBB for family use and the mother also includes information how to end or extend the storage when the child reach adult age.

5. Authorization

Each cord blood bank, regardless of the model or ownership of the facility (i.e. intended use of the units), shall be authorised/licensed by the competent authority, or authorities, for each activity it performs in accordance to the requirements from the EU T&C directives, as a minimal standard.

CA does not need to authorise collection sites separately; it is acceptable if collection sites are authorised as a responsibility of the CBB. However, collection sites must be inspected either at regular intervals or based on risk assessment.

It is strongly recommended that authorization should only be granted based on on-site inspection carried out by an inspector(s) with knowledge in the field of HPC and their clinical use.

Inspection of a CBB and/or collection site can be performed by only one CA or can be carried out as joint inspection of interested CAs (e.g. CA of MS in which CBB is situated, CAs of MSs in which collection sites are situated). The EU Joint Action project VISTART (https://vistart-ja.eu/about-vistart) covers conduct of MSs CAs’ joint inspections.

The cord blood bank shall not undertake any substantial changes to its activities without prior approval of the CA.

If the CBB contracts any other entity for a service related to CB collection and banking, each activity shall be authorised according to EU Directives and national legislation and written agreements are required.

The laboratory tests for transmittable diseases required for donor clearance must be performed by a laboratory authorized/ accredited by the relevant national CA. In an exercise conducted in 2015 by the DG SANTE of the European Commission, Member States’ CAs mapped more stringent donor testing measures in the EU. The results of this mapping are publicly available on the following website:

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A CBB which collects in Member States other than the Member State in which it is registered shall comply with all national legislative requirements of Member States from whose citizens the CBB collects in addition to EU T&C directives requirements. That is, cord blood should be collected and treated under the conditions required in the donor’s MS, when such requirements exist. The CA of that MS shall be informed about the activities in its country.

Figure 10. Illustration of cumulative fulfilling of more stringent/different requirements

Cord blood units are often collected in one MS, processed and stored in another or others. For the purpose of quality, safety and traceability assurance, all Member States’ CAs on whose territories a CBB performs any of the activities should cooperate in surveillance closely and in confidence. Cooperation should include exchange of information on inspection and control measures carried out, and all inspection findings relevant to quality and safety. It is recommended that the CA (or CBB) of the member state on whose territory the CBB is located inform other collection MS on that activity.

The CBB shall submit to the CA an annual report on its activities, which shall be made public. CBBs shall be part of national tissue establishment registers and the list of collection sites should be publicly available.

Member States can make decisions to prohibit or restrict the collection and/or banking of CB for autologous use or family banks. Countries within the EU that prohibit such type of banking are Italy and France. Other countries in the EU allow autologous use and family banks applying various models.

CBBs can use this project’s complementary Inspection Guidance - Cord Blood Banks to perform a self-assessment prior to authorisation application and/or inspection

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5. Quality system

The CBB shall establish and maintain a quality system based on the principles of good practice. The quality system has to ensure that all key CBB functions and stored CB products meet the necessary requirements.

The CBB should enable second-party audits, i.e. customer audits, of its facility and processes. A CBB for public use, should be audited by a clinic to which the bank distributes CB for transplant(s). In the case of a family CBB, this would be an audit by customers or potential customers. The CBB should inform the second party about the right to perform an audit clearly and in written form.

5.1. Organisation

Organisational aspects within the quality system for CBB should follow general principles for tissues and cells. Here is a reminder of the key requirements.

The CBB shall establish a quality system with a precisely defined network of working positions, relations between them, job descriptions, responsibilities and accountabilities.

There shall be persons specifically designated for:

➢ medical affairs (such as medical director)
➢ collection site(s)
➢ processing
➢ quality assurance

The CBB shall designate a responsible person who meets the requirements from Directive 2004/23. The CBB shall provide to the CA with accurate data on the responsible person (name, contact) and the possible temporary replacement during the absence of the responsible person.

5.2 Documentation

The CBB shall ensure that the quality system includes at minimum the following documentation:

➢ quality manual,
➢ policies and procedures,
➢ training records,
➢ reporting forms,
➢ maternal and infant records
➢ information on traceability from collection to the final destination of the cells.

The CBB shall have written policies and procedures containing at minimum the following topics:

A) Policies and procedures specific for CB banking

➢ donor selection and evaluation shall encompass:
  The genetic mother, and in the case of surrogacy, the surrogate mother:
Interview with the mother,
review of medical records
physical examination
medical history
risk behaviour related to communicable disease
travel history
delivery data

From the family of the infant donor:
medical history including genetic history

➢ the safety of the mother and infant donor
➢ follow-up on the new born donor

The CBB shall have a policy on donor follow-up. The status when discharged from hospital should be recorded. The health status of the mother and infant donor should be re-reviewed and evaluated 6 months after cord blood donation and/or before distribution for clinical use. The health status could be reviewed via telephone call to the mother and/or family doctor.

➢ donor testing on transmissible diseases including infectious and genetic diseases
➢ ABO, Rh testing
➢ Other relevant laboratory assays specific for CB (CD34, CFU, CD45, TNC)
➢ HLA typing; minimum of HLA-A,-B,-DRB1 (not for autologous use, unless is nationally required)

The CBB shall ensure data protection and confidentiality

B) Generic tissue banking policies and procedures that should be adapted for CB banking

➢ maternal or parental donor consent
➢ collection
➢ coding and labelling
➢ packaging
➢ transportation
➢ traceability
➢ processing
➢ storage
➢ distribution
➢ reference samples
➢ quality control
➢ import/export
➢ non-conformities in the recording, monitoring and implementation of CAPAs
➢ SAE and SAR notification
➢ internal audits
➢ external audits (including second-party audits) / inspections
➢ procedure validation
➢ equipment qualification and maintenance
➢ critical equipment and incoming material/media/reagents monitoring
➢ facility and premises monitoring
➢ cleaning, disinfection, sterilisation procedures
➢ release of the product for clinical use, with criteria
➢ exceptional release
➢ contingency events: the CBB shall have agreements and procedures in place to ensure that, in the event of termination of activities for whatever reason, stored CB shall be transferred to other CBBs or establishments authorised in accordance with EUTCD
This documentation shall be available for inspection by the CA. A system for keeping data to ensure traceability should be in place. Policies and procedures shall be designed and regularly updated in compliance with scientific and technical progress. Modifications of the processes shall be validated and documented.

5.3 Quality reports

CBBs shall establish a quality report for each collected unit. Family CBBs should submit the quality report to the parents. In the report, the utility of the stored number of cells shall be clearly explained based on the data obtained from the unit and the demonstrated applications at the time of collection.

The report should contain at minimum data on:

- infectious diseases tests;
- sterility (bacterial and fungal cultures) tests;
- total nucleated cells (TNCs);
- viable CD45+, CD34+ cells;
- volume;
- the method of red cell reduction.

The final quality report shall accompany the CB unit to the transplant centre upon request for CB units for allogeneic use, as well as for autologous use. It should comprise of all the elements of the abovementioned quality report and additionally data on:

- HLA testing (minimum HLA-A, -B, -DRB1);
- viability results on contiguous segment after thawing;
- ABO Rh grouping;
- haemoglobinopathy testing;
- donor suitability, as donor eligibility is part of medical history.

5.4 Quality Assurance

5.4.1. Infectious disease testing

For infectious diseases testing, a blood sample shall be collected from the mother before or within 7 days of birth. The blood sample shall be tested at minimum to the extent specified in the Annex II of Directive 2006/17 (annexed). Additional national testing requirements that are to be met can be found online in the Commission’s exercise mapping ‘More Stringent Requirements’ (MSR) in the EU 28 Member States (web link in chapter 4).

Having in mind that intra-venous infusions of fluids may have taken place even within the normal labour, data on that activity shall be collected, documented and assessed, and the necessity of haemodilution evaluation must not be forgotten.
5.4.2 Quality control

CBBs shall establish quality control of their processes and products, in order to be able to document quality and safety. For that purpose, a list of critical parameters to be controlled shall be set up, and an acceptable range of values determined. All the parameters, their values and procedures for performing controls shall be based on scientific references and/or validated by the bank. A policy with a threshold for the various parameters of the CBBs shall be established for the initial acceptance of units (depending on the time that elapsed after collection), volume or number of cells. Reference samples should be available at the CBB

Minimum parameters for quality control:

- number of stored TNCs
- number of CD34+ cells
- cell viability (also after freezing)
- microbiological testing

Samples in addition to the CB unit:
Prior to cryopreservation, at minimum the following samples shall be collected:

1. Cord blood unit samples
   - two segments attached to the freezing bag, at minimum 100 µL each
   - additional two segments attached to the freezing bag or in vials with at minimum $1 \times 10^6$ nucleated cells each (one for viability testing stored at -150°C, the other for other tests prior to release for human application stored at ≤ -70°C)
   - at minimum two vials of serum or non-heparinised plasma with a total volume of 3.6 mL stored at ≤ -70°C
   - suitable material for preparation of at minimum 50 µg genomic DNA

2. Maternal samples obtained at the time of donation or within seven days after collection of the CB unit
   - at minimum two vials of serum or non-heparinised plasma with a total volume of 3.6 mL stored at ≤ -70°C
   - suitable material for preparation of at minimum 50 µg genomic DNA from the biological mother

5.5 Third party agreements

The CBB shall have written agreements with a third party whenever a third party performs one or more of the following activities/procedures for the CBB, and vice versa:

- collection
- any processing procedure
- testing
- preservation
- storage
- transport
- distribution
- quality control
- supply of critical equipment, material/reagents
- provision of any service that can affect the quality and safety of CB
The CBB shall have a documented procedure in place for the selection of third parties, taking into consideration, in the first line, their compliance with the requirements of EU Directives and national legislation if it is more stringent than the directives.

The CBB shall keep a complete list of the agreements established with third parties. Agreements between the CBB and third parties shall specify the responsibilities of the third parties and detailed procedures. The CBB shall be able to provide copies of agreements with third parties at the request of the CA.

5.5.1 Agreement with the collection facility

It is important to establish that the CBB is responsible for all aspects of quality and safety at the collection sites even if a third party is performing the activity.

The CBB shall have a written agreement with each collection site, which includes at minimum:
- agreement for auditing obligation of education and training of collection personnel
- provisions for donor safety (e.g. assurance of no deviation from standard delivery procedure)
- list of trained personnel performing activities related to collection
- specification of the procedures to be followed
- specification of samples for testing to be obtained

6. Collection

6.1. General

Prior to the collection, the consent of the donor’s mother (or both parents, depending on national legislation and CBB policy) shall be obtained. The consent shall be in written form and should follow written information given by the health care professional in an understandable way.

If the CB, in case of not fulfilling the requirements for human application, is going to be used for research or quality control purposes, consent must be obtained for that use.

Information to the donor should include at a minimum:
- donor exclusion criteria;
- the potential benefit and risks of CB donation;
- testing to be performed;
- potential use (transplantation or other use)

In 2015, the Committee on Organ Transplantation (CD-P-TO) of the Council of Europe developed and published the brochure “Umbilical Cord Blood Banking – A Guide for Parents” (in annex).

The Guide covers aspects of collection, use, cord blood banking models, differences between storage for public and family use. The guide can be used by CA as material for raising awareness and a model for an information leaflet, or for the content of the written information prior to consent.

Personnel responsible for donor selection should be designated by the collection facility and trained for this task. The collection of CB shall be performed by personnel who completed a training program specified by the CBB, including training on the use of instruments and devices for collection.

There shall be written procedures for the verification of:

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➢ the donor’s identity (maternal and newborn donor)
➢ details of the consent given by the donor’s parent(s)
➢ donor selection criteria
➢ the collection of laboratory samples required for donors

The CBB shall establish donor suitability criteria for autologous donors as well, which may differ from allogeneic donor criteria.

In the case when CB originally stored for autologous use may also be used for related or unrelated allogeneic transplantation, all requirements must be met to the same extent as for an allogeneic donor.

Cord blood collection must not change standard obstetric practice or interfere with the delivery and patient care.

Collection methods shall employ aseptic techniques, using single use sterile materials when possible and reusable instruments should be sterilized according to validated procedures. The training of the personnel performing collection should include aseptic vein-puncture of the cord. A designated space for the collection should be available.

Collection should be performed in a way to ensure safety and quality of the donation including traceability of materials and equipment.

6.2. Transport conditions from maternity to the tissue establishment (bank)

Transport conditions of the unit from maternity to the bank must be specified in the CBB’s QS documentation. Time- and temperature- limits during transport should be established after validation where the properties of the CB unit are preserved. All parameters shall be monitored and documented.

A minimal set of parameters determines transport conditions:
➢ maximum time period from collection to reception at the bank
➢ temperature during transport
➢ transport packaging
➢ mode of transport
➢ labelling

In the case of crossing country borders, transport shall be organised in compliance with national/local legislation requirements of all the countries involved.

6.3. Unit reception at the bank

At reception at the CBB it should be verified and documented that the received unit is:
➢ packed;
➢ labelled;
➢ transported in the appropriate conditions;
➢ accompanied by the documentation and samples as described in the bank’s written procedures

If any non-compliances are observed they shall be noted, documented and properly investigated and the risk of influencing the quality of the unit shall be assessed. The CBB should have written procedures
for information and advice to the customer/parents regarding possible outcomes concerning quality and quality defects of the CB unit.

Following reception at the bank, the unit shall be quarantined until donor-screening tests have been completed and all data describing acceptance criteria gathered. The person responsible for accepting the unit for long-term storage must review the information and document the decision.

7. Processing

For each processing activity the bank performs, written procedures must be in place. Each procedure shall be validated. Written procedures shall exist at minimum for:

- the processing method (the nucleated cells enrichment/red cell depletion)
- sample collections
- cryopreservation
- storage
- the release procedure

All open processing activities that might affect the quality and safety of the product shall be performed in an environment with air quality classified as A in a laminar flow cabinet, with the background classified at minimum as D according to cGMP.

It is strongly recommended to use a functionally closed processing system of bags.

To prepare the CB unit for storage at -150°C or lower, a cryopreservation process should be performed by controlled rate freezing method using a cryoprotectant. The process must not damage the properties of stem cells and at minimum the following procedures must be validated:

- maximum time period from collection to storage;
- maximum time of exposure to the cryoprotectant till the beginning of freezing
- maximum time from completed freezing till storage

Also, all critical materials used in the process must be validated. The list of critical materials shall comprise all those materials that have a direct impact on the viability, quality and identity of the CB unit; at minimum cryo bags, overwrap bags, cryoprotectant and labels.

The SOP for cryopreservation shall contain requirements for documenting information on cryopreservation for each CB unit:

- TNC concentration
- cryoprotectant used, with its final concentration
- end-point temperature of freezing
- freezing rate
- record of continuous temperature monitoring during freezing
- storage temperature
- adequate samples accompanying the unit
- existence of contiguous segment

8. Labelling
All cord blood units should be identified with a unique identifier in order to ensure traceability. Labels and printing ink shall be validated for conditions of processing and storing in (liquid or vapour) nitrogen.
The use of pre-printed labels is strongly recommended for donor identification.

As of 29 April 2017, labels on the CB unit should contain the Single European Code (SEC) when these units are distributed from the tissue establishment (CBB) to the organisation responsible for human application. Also for transport across national borders, units shall be identified according to Directive EC/2015/565.
Although not mandatory, it might therefore be useful and practical to apply the TE-identification and donation sequence part of SEC when already when transporting CB units from the site of collection to the tissue establishment.
Units that were stored before 29 October 2017 can still be distributed without the SEC until 29 October 2021. However, as of 29 April 2017, the full SEC should appear in the accompanying documentation for such cases.

Units donated for family use with medical indication should be labelled with the name of the intended recipient.

9. Storage

CB units can be stored in the liquid or vapour phase of liquid nitrogen.
Liquid phase storage offers a uniform temperature of -196°C, but there is a possibility of both sample contamination and cross-contamination in the case of leakage.
Vapour phase storage has to provide -150°C or lower. It cannot provide uniform temperature across the whole height of the container and, although the temperature gradient can be reduced, it cannot be eliminated. The CBB should demonstrate an adequate temperature at the top of the storage container when storing in vapour phase.
Continuous temperature monitoring shall be in place and policies to prevent undesired warming events must be in place.
For the selection of storage phase, a risk assessment procedure should be applied and documented.
It is advisable to use overwrap bags to ensure leakage protection.
Oxygen concentration in the room with liquid nitrogen containers shall also be monitored to alert and protect personnel in case of nitrogen leakage.
The storage room should have restricted access.

Storage of units with positive microbiological tests
The storage of units with positive microbiological tests is justified only in the case of related donation for immediate medical need and in case of non-obligatory pathogenic bacteria where the unit could still be used for transplantation. In the family bank setting, there is usually no immediate medical need, but the possibility remains. It is a prerequisite to provide the family with clear information.
Any decision regarding the disposition of an autologous cord blood unit with positive cultures must be made by the family after information by the CBB considering the type of contamination, antibiotic sensitivity pattern and the potential benefits and risks of using the unit. The application of such a unit requires the recipient’s consent.

The bank needs to confirm the stability of long-term storage and the quality of long-term stored products.
Example of Stability Protocol

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The bank can select CB products (attached samples) for testing from those produced in the first year of implementation of each manufacturing method. In addition, for each subsequent year, the bank selects CB products from the same time/method cohorts for testing. Products are thawed according to SOP and evaluated. The bags are examined for overall integrity (label, closures, tubing and tubing seals) and the content is tested for sterility, identity and potency. The obtained results should be within the bank’s acceptance criteria.

While stored, CB units can experience transient warming events (TWE); brief periods of exposure to environment temperature, usually when taking units out of the container or placing them inside. TWE can also occur during shipment to the end user. It has been demonstrated\(^2\) that in relation to the extent of the temperature rise and number of occurrences, TWEs can reduce CD34+ cell viability and the colony-forming unit (CFU) count.

Although studies that are more recent suggest that frozen CB units are resistant to transient temperature changes,\(^3\) CBBs should make every effort to minimise TWE. TWEs shall be documented (number of events and duration), and the impact on cryopreserved CB units shall be assessed.

10. Traceability

The CBB must ensure traceability from the donor to the recipient and vice-versa for each unit. In addition, it should be possible to relate all critical materials, reagents, media, tests and critical equipment with each unit.

All data necessary to ensure traceability at all stages shall be kept by the CBB for a minimum of 30 years after clinical use. Data may be stored in electronic form.

11. Notifications of SAR and SAE

CBBs must take part in the Member State’s system for reporting, investigating and transmitting information about serious adverse events and reactions (SAE and SAR) which may influence the quality and safety of CB.

The CBB shall ensure that an accurate, rapid and verifiable procedure is in place that will enable it to recall from distribution any product which may be related to an adverse event or reaction.

A relevant overview of SAE and SAR attributable to cord blood can be found on the web pages of another project – NOTIFY LIBRARY, a publicly accessible database; \textit{http://www.notifylibrary.org/}.

The Notify Library is a joint global initiative, co-sponsored by the World Health Organization (WHO) and the Italian National Transplant Centre (CNT) as its Collaborating Centre. The library describes all types of documented reactions or events, which are analysed by groups of international experts and might have teaching value and assist in the estimation of risk.

Furthermore, the Joint Action project VISTART (\textit{https://vistart-ja.eu/about-vistart}) within the EU Health Programme 2014-2020 manages tissue vigilance issues from two aspects: one work package is dedicated to reporting of SAR/E and the other to international collaboration for vigilance communication.

\(^2\) Dobrila L, Coelho P, Rubinstein P. Transient Warming Events and Cell Viability of Placental/Umbilical Cord Blood (CBU), ISHAGE June 2001, Quebec, Canada

\(^3\) Zbigniew R. Mrowiec, Adla Angelina, Julio Laluf, Ceyhan Yildirim, Frances Verter Transient warming events and cryogenic storage of cord blood mononuclear cells for stem cell transplantation, Journal of Transfusion Medicine 2012, tom 5, nr 4, ISSN 1689–6017

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12. Import / Export of Cord Blood for/from family banks

According to EUTCDs, the import/export activity means the movement of tissues and cells across the borders of the Union, i.e. from/to third countries. The movement of tissues and cells between EU Member States is considered as distribution, unless differently defined by national regulation, which lays down measures that are more stringent.

Directive 2015/566 sets procedures for verifying equivalent standards of the safety of imported tissues and cells. Allogeneic CB units intended for immediate transplantation are not in the scope of this Directive. Import/export of such units is usually performed through registries that work in close collaboration with transplant centres. Registries provide quick and thorough searches for matching units. It is recommended that public CBB register in the national registries or directly in the global database of haematopoietic stem cell donors (www.bmdw.org) to make their inventory visible to transplant centres and to increase the probability of finding matching units.

The import and/or export of CB units for/from family CBBs, fresh or cryopreserved, must be authorized by the CA and can be performed only by the cord blood bank. The family shall import CB units from third countries only from banks meeting EU tissue and cells directives’ criteria and authorised by the local dedicated CA. It has to be possible to trace also the Imported CB units from the donor to the CBB and vice-versa. The CBB that receives imported CB from third countries shall ensure that they meet standards of quality and safety equivalent to the ones laid down in EU Directives. The CBB shall ensure that it exports CB units, fresh or cryopreserved, to third countries’ banks that meet standards of quality and safety equivalent to the ones laid down in EU Directives. For this the same requirements/agreements as for import may be used or adapted.

In case a future collaboration is foreseen between an authorized CBB in EU and one CBB in a third country, the Directive 2015/566/EC lays down the requirements for written agreements in order to ensure quality and safety. In case of a single import occasion (i.e. one-off import in Directive), less documentation may be needed depending on national measures. If the CBB does not hold an accreditation according to any international or national standards the minimum requirements to ensure quality and safety is:
- traceability from donor to recipient and vice versa must be guaranteed
- the imported CB unit must not be used for any other than the intended recipient

13. Ethical issues

At the 884th meeting of the Ministers’ Deputies on 19 May 2004, the Committee of Ministers of the Council of Europe adopted Recommendation Rec(2004)8 of the Committee of Ministers to Member States on autologous cord blood banks.

If a member state allows cord blood banking for autologous use or family banks, it is recommended to set a legal framework regulating issues that are specific for this type of banking and different from banking for altruistic allogeneic use.

Specific ethical and legal issues appear in the field of cord blood banking for autologous use or family banking.
Some, but not all, special issues that should be considered before authorization of a CBB for autologous use are listed:

- destiny of CB units after the expiration of the contract for storage
- destiny of units in case bank activities are stopped
- storage of CB not meeting quality criteria
- ownership of the unit - child or mother?
- prolongation of contract
- possibility of conflict of interest for the personnel simultaneously working in a CB bank for allogeneic use and in a CB for family use.

### 14. Bibliography

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Annexes

1. Survey data

2. Directive 2006/17, Annex II
