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D3.1 Public webpages with cord blood banking practices

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Abbreviations

- AABB = American Association of Blood Banks
- CBB = Cord Blood Bank
- FACT = Foundation for the Accreditation of Cellular Therapy
- ION = Issuing Organisation Number
- WMDA = World Marrow Donor Association
- WO = WMDA Organisation

1. Preface

This report describes the background information for Deliverable *D3.1 Public webpages with cord blood banking practices* as part of the 2019 work programme of the World Marrow Donor Association (WMDA) for the EU Third Health Programme (2014-2020).

First in *Chapter 2,* an introduction to cord blood transplantation and cord blood banking is given.
In the final *Chapter 3*, an example profile: WO-XXXX Cord Blood Bank, including the WO-XXXX Cord Blood Banking Specifics and the WO-XXXX Cord Blood bank Operation Specifics is shown. This provides readily accessible and up-to-date information relating to good and best practices in relation to cord blood banking. This knowledge-bank will support cord blood banks across the EU to review and re-engineer their practices to reflect internationally accepted best practice, leading in time to improved quality and efficiency in cord blood banking. The Cord Blood Banking Technical Survey of Anthony Nolan (AN – United Kingdom) was used as best example for WMDA's cord blood documents, which resulted in the creation of two separate documents: Cord Blood Banking Specifics and the Cord Blood bank Operation Specifics.

The complete online cord blood bank (CBB) databases of the Organisation Information Public Access – hosted by WMDA – can be accessed via:

Cord Blood Bank Database

The Cord Blood Banking Specifics and the Cord Blood bank Operation Specifics were established by the WMDA Cord Blood Steering Committee, consisting of experts from cord blood banks worldwide. During monthly conference calls the progress of the creation of these two documents, based on the cord blood files that are used by Anthony Nolan, was developed.

Early 2019, the Anthony Nolan Cord Blood Bank and Cell Therapy Centre performed a successful pilot study where they investigated barriers in the search process for cord blood units. They worked with their internal customers to improve processes and reduce turnaround times. For external research, they surveyed transplant centres through their registry to identify the external customer's needs. It turned out the best way to serve their customers is by offering improved streamlined processes and paperwork around search, selection and provision. Furthermore, they offered better support in all aspects of search, selection, data interpretation, shipment, thawing and infusion. All these components build confidence for the usage of cord blood units and makes it easier to choose for a cord blood product instead of a living stem cell donor.

It turned out that transplant centres that had better support services of the cord blood banks, reported finding the processes around cord usage simpler. In addition, there was an increase in usage of Cord Blood for their patients compared to 12 months prior to the study. The Anthony Nolan Cord Blood Bank presented their findings during the WMDA-NetCord & FACT Cord Blood Day in September in Miami (USA).

Based on this experience the Cord Blood Steering Committee decided to implement a service for transplant centres where they can easily find the Cord Blood Banking Specifics.

To have complete information about the operation of the cord blood bank and the cord blood units significantly reduces the time to transplant.

2. Background

(Source: https://share.wmda.info/x/UoDFAg)

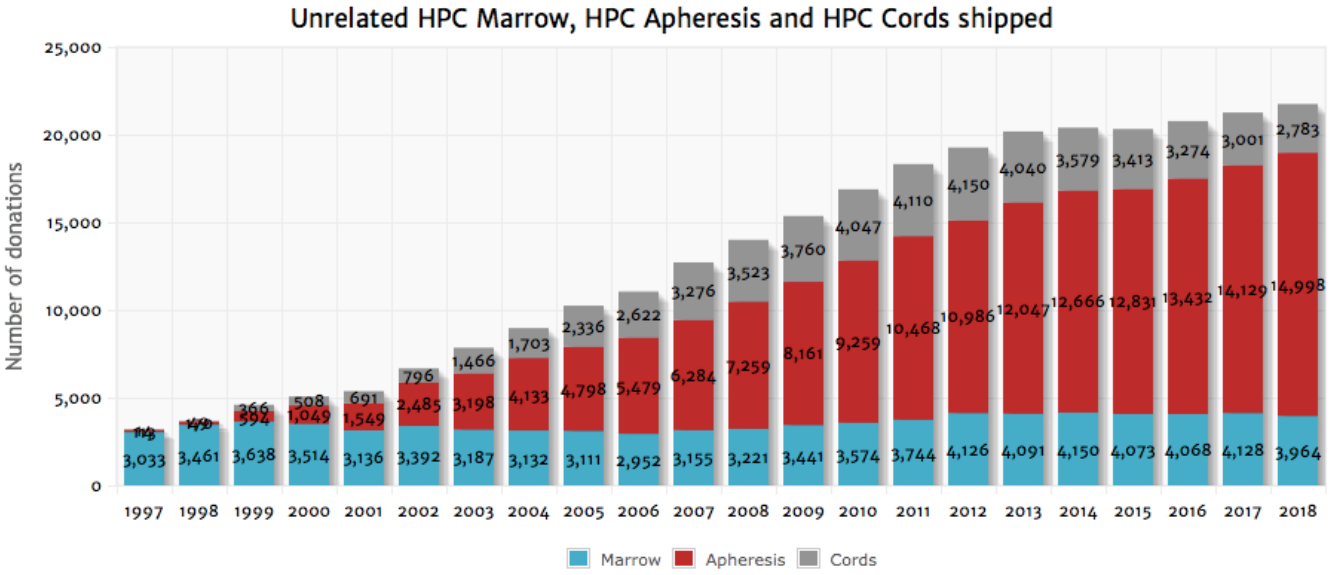
2.1 Introduction to cord blood transplantation

The first successful umbilical cord blood transplant was performed in 1988 – the patient was a five-year-old boy with Fanconi's anaemia. Since that time, umbilical cord transplantation has become recognised as an effective form of therapy for an increasing number of both malignant and non-malignant disorders, and an established method of haematopoietic reconstitution.

Cord blood units increase the donor pool availability

Umbilical cord blood transplantation has expanded the pool of available donor possibilities for patients needing a stem cell transplant, as shown in *Figure 1*.

Figure 1. Number of cord blood units shipped for adults and children in 1997-2018



According to the World Marrow Donor Association (WMDA) 2017 Annual Report, more than 47,000 unrelated cord blood units have been shipped for transplantation between 1999 and 2017. Currently, more than 700,000 units are registered in the global Search & Match Service of WMDA. There are several advantages to the use of cord blood units (CBUs) as a source of stem cells for unrelated transplantation. Cord blood units are a ready-to-use cellular product and, clinically, result in a low incidence of Graft vs. Host Disease (GvHD) and increased match tolerance, which expands the donor pool availability.

However, the number of stem cells in a cord blood unit is relatively low for use in adult patients, which can delay engraftment, and in principle there is no possibility to use a donor lymphocyte infusion after

transplantation. The delay in myeloid recovery that is observed following cord blood transplantation remains a critical barrier to successful outcomes.

Many novel approaches are currently under investigation, with the aim of enhancing engraftment in cord blood recipients. These approaches range from increasing the number of cells obtained at collection to increasing the number of stem cells available at the time of infusion, through double cord transplant or ex-vivo expansion. Other areas of research include enhancing the homing capacity of the cells that are available. As an example, therapy has been extended to older patients using reduced toxicity conditioning and the double graft approach.

2.2 Cord blood bank

A cord blood bank is a multi-disciplinary structure that is responsible for the recruitment and subsequent management of maternal donors as well as the collection, processing, testing, cryo-preservation, storage, listing, reservation, release, and distribution of cord blood units. Public cord blood banks aim to store cord blood for allogeneic transplantation purposes. These cord blood banks are typically not-for-profit entities where units are cryo-preserved and stored at no cost to the donor and family. They may be independent stand-alone cord blood banks but are often affiliated with a registry that offers cord blood units from multiple cord blood banks using a defined search algorithm and sophisticated matching programmes.

In addition to public cord blood banks, a large number of private cord blood banks have also been established. These cord blood banks aim to store cord blood for autologous or family use. Newly explored models of public-private partnership, the so-called hybrid banks, are currently being proposed, driven by the need to improve the financial viability and sustainability of cord blood banks.

For the purpose of this report, the focus will be on the collection activities in public cord blood banking.

2.3 Challenges of cord blood banking

Typically, cord blood is not only searched by HLA-matching – cell dose and quality are important selection factors, as they are critical issues affecting the clinical outcome of transplants. The high cost of providing good-quality cord blood units is a challenge cord blood banks must face. As the standards for what is considered to be an acceptable quality of cord blood have risen, the percentage of units deemed viable for banking has decreased. This high rate of cord blood units being discarded has added to the overall cost per unit.

Next to HLA matching, cell dose and quality are important selection factors

Total inventory numbers must be balanced with a need to maximise the ethnic representation and diversity of the cord blood bank. The rapid growth in the global inventory has resulted in a proportional decrease in the number of cord blood units released by each cord blood bank – making public banking activities economically challenging.

2.4 Regulatory framework

The regulatory framework of cord blood collection has evolved considerably over the past 25 years. What began as an effort to broaden the available transplant options has developed into an expensive industry with robust regulation.

Cord blood has become the first Food and Drug Administration (FDA) licensed tissue product in the United States. Prior to this, concerns about safety and efficacy led the industry to develop voluntary standards, mainly set out by Foundation for the Accreditation of Cellular Therapy and AABB accreditation programmes.

The WMDA, as part of its registry accreditation standards, has provided a specific status for cord blood banks that are accredited by NetCord-FACT or AABB and wish to apply for WMDA accreditation.

2.5 Cord blood bank management and evaluation

Cord blood banks can list their cord blood units directly in an international database or have an established relationship with a national registry in their country. The majority of cord blood banks operate in close association with their national registry. In such cases, all processes related to the listing and search of the cord blood units should be performed in agreement with the registry.

The cord blood bank should have policies and standard operating procedures (SOPs) for the review of the cord blood unit records, prior to the unit being listed by the registry. Once the units are HLA-typed and have been medically qualified, the cord blood bank submits the cord blood unit data to their registry. Upon request from a transplant centre or a patient's registry, the cord blood bank registry provides an initial search report containing information about the units that have the highest grade of HLA-matching with the patient. The registry also lists the cord blood units in the global database, the Search & Match Service of WMDA (search.wmda.info).

2.5.1 Forms

After reviewing the available data in the Search & Match Service of WMDA, the transplant centre can request additional. The cord blood bank should have appropriate forms to ensure that all screening questions are documented, along with results of all testing which has been carried out. The WMDA provides a comprehensive standard cord blood unit report template, which can be used by any cord blood bank in the world. The template, as well as a supplementary cord blood unit report template, can be found on the WMDA website in the forms section.

A standard cord blood unit report template can be found on the WMDA website

2.5.2 Communication

The cord blood bank should use a validated electronic records system for uploading cord blood unit information to the registry. The cord blood bank must update the data of the cord blood units listed by the registry on a continuous basis. When a cord blood unit is removed from the bank's inventory, this

change must be reported immediately to the registry. The cord blood bank must have adequate information technology support to ensure such a system is in place.

Cord blood banks must respond to cord blood unit report requests, and to requests for additional information, within a time period which is in line with WMDA recommendations. The WMDA recommendations are:

- For urgent cord blood verification typing requests: time from request received to results reported to the transplant centre should be 7 calendar days for 80% of the requests received.
- For standard cord blood verification typing requests: time from request received to results reported to the transplant centre should be 13 calendar days for 80% of requests received.

Access within the cord blood bank to information about the infant or maternal donor, as well as the transmission of this information to the registry, must be restricted. Access to and transmission of data should be structured in a way that prevents accidental or unauthorised access, destruction or modification of data and which guarantees confidentiality. Search requests for cord blood units listed by a national registry are to be accepted and processed by the responsible registry only.

The readily accessible and up-to-date information of the cord blood banks worldwide, including their good and best practices in relation to cord blood banking are publicly accessible via the WMDA Share website (under type CBB).

2.5.3 Challenges in cord blood selection

As the way how cord blood units are processed may change over time, it is complex for transplant centres to access the quality of the cord blood unit. Therefore, Cord Blood Banking Specifics and the Cord Blood bank Operation Specifics, are a way to reduce the complexity for transplant centres to select an unit.

3. Example profile: WO-XXXX Cord Blood Bank

Example profile: WO-XXXX Cord Blood Bank

Created by [redacted] (administrator), last modified on Nov 28, 2019

Cord Blood Bank

Country	
Contact details	
Visit address	Street Postal code City
Invoice address	Street Postal code City
Primary phone	+xxx xxxxx
Secondary phone	+xxx xxxxx
Fax	+xxx xxxxx
Email	cordbloodbank@test.com
Website	www.cordbloodbank.com
Location	
Registry details	
ION	XXXX
WO-Id	WO-XXXX
Affiliation	ION-XXXX
WMDA membership	
WSMS listed	
WSMS registration date	
WSMS shortcode	COUNTRY-ABB
EMDIS Code	CBB
Accreditation	
Accreditation	
Year first status	
Current status from	
Current status to	
CBB Accreditation	FACT

Additional pages

Information about additional documents

Some, but not all organisations have additional pages.

Although all resources are listed, member documents are only accessible to WMDA members.

- Example profile: WO-XXXX Cord Blood Banking Specifics
- Example profile: WO-XXXX Cord Blood Bank Operational Specifics

Additional data

You are watching a public page.
WMDA Members may visit the Member version of this page: WO-XXXX
You may be asked to login.

Example profile: WO-XXXX Cord Blood Banking Specifics

Example profile: WO-XXXX Cord Blood Banking Specifics

Section 1 General Info

Question	CBB answer
Name of the cord blood bank:	
Number of cord blood units the cord blood bank plans to store for public use (unrelated patients):	

Section 2 Cord Blood Units in Inventory

Question	CBB answer
Current processing method(s):	
Plasma and RBC reduced (automatic)	☐
Plasma reduction only	☐
Plasma and RBC reduced (manual)	☐
RBC reduction only	☐
Total Nucleated Cell Count (x10E7) of your cord blood units stored for Unrelated Patients (Public Use).	
< 125 :	
125 - 149 :	
150 - 199 :	
200 - 250 :	
> 250 :	

Section 3 Cord Blood Collection

Question	CBB answer
Current practice for collecting cord blood:	
Current antiseptic:	
Collection bag:	
Agitation during collection:	

Section 4 Conditioning and transport from Collection Centre to cord blood bank

Question	CBB answer
Secondary bag used by the cord blood bank (sealed, plastic bag or similar to avoid any leakage):	
Transport conditions:	
Insulating transport container	☐
Active refrigeration system	☐
Passive refrigeration system (gel, blocks)	☐
Electronic temperature probe	☐
Non-electronic temperature probe	☐
Qualified transporter	☐
Unqualified transporter	☐
Air transport	☐
Ground transport	☐
Other,	☐
Temperature range for storage and transportation of fresh product:	

Section 5 Evaluation

Question	CBB answer
Pre-processing Evaluation: Current threshold for accepting a cord blood unit for public use in the cord blood bank:	
Net weight in grams (excluding bag and anticoagulant) before processing	
TNC (10E7) before processing	
Viability CD45 positive cells (%)	
Viability CD45 positive cells (method)	
Viability CD34 positive cells (%)	
Viability CD34 positive cells (method)	
Criteria that are completed before accepting a cord blood unit for public use in the cord blood bank:	
Medical History	☐
Collection Report	☐
Informed Consent	☐
Maternal IDM results	☐
Temperature and integrity of the bag	☐
Other,	☐
Used method for CD34 enumeration:	
The cord blood banks uses external proficiency testing for QC of the cord blood banks FACS lab:	
The cord blood bank performs post processing/pre-freeze CD34 cell count:	
Acceptable time from collection to processing:	

Section 6 Processing-Packaging

Question	CBB answer
The pre-freeze processing method(s) cord blood bank uses at any stage in time:	
AXP	☐
SEPAX	☐
Optipress	☐
Prepacyte	☐
Manual- plasma and red cell reduction	☐
RBC/plasma reduction with HES	☐
Ficoll sedimentation	☐
Centrifugation and volume reduction	☐
No processing	☐
Manual- plasma reduction only	☐
Other,	☐
The current pre-freeze processing method(s):	
AXP	☐
SEPAX	☐
Optipress	☐
Prepacyte	☐
Manual- plasma and red cell reduction	☐
RBC/plasma reduction with HES	☐
Ficoll sedimentation	☐
Centrifugation and volume reduction	☐
No processing	☐
Manual- plasma reduction only	☐
Other,	☐
Additives currently in use in addition to anticoagulants and DMSO during processing:	
HES	☐
Prepacyte	☐
Plasmalyte	☐
Albumin	☐
Isotonic salt solution NaCl (saline)	☐
No additive	☐
Other,	☐
Cryoprotectant additives currently in use:	
Cryopreservation method currently in use:	
BioArchive	☐
MVE 1850 Vapor freezer	☐
Programmed cryopreservation with Air Liquid program (FREEZAL)	☐
Programmed freezer	☐
Two-step (equilibrium) freezing	☐
Cryobag currently in use:	
Currently used packaging when a unit is stored:	
Segments currently stored with the unit by the cord blood bank:	
One attached segment	☐
Two or more attached segments	☐
Separate segments detached from the bag, but stored with the CBU	☐
Other samples	☐
None	☐

Section 7 Testing

Question	CBB answer
Does your cord blood bank currently store extra material?	
Cord blood DNA	☐
Cord blood material for DNA extraction	☐
Plasma/cord blood	☐
Maternal DNA	☐
Maternal material for DNA extraction	☐
Maternal plasma/serum	☐
HLA typing at time of listing:	
HLA-A	
HLA-B	
HLA-C	
HLA-DRB1	
HLA-DRB2	
HLA-DPB1	

Section 8 Storage

Question	CBB answer
The following type(s) of storage container is currently used by the cord blood bank:	
BioArchive tank	☐
Conventional storage tank-Vapor phase	☐
Conventional tank-Liquid phase	☐
Double walled liquid Nitrogen	☐
Type following type(s) of storage monitoring is currently by the cord blood bank:	
Alarm on individual tanks only	☐
Centralized system-local	☐
Centralized system-remote monitoring	☐
LN2 level	☐
Lid opening	☐
System default	☐
Temperature monitoring	☐
No temperature monitoring	☐

Section 9 Adverse Events Reporting

Question	CBB answer
Adverse Event Reporting used by the cord blood bank:	
Competent authority	☐
Internal report	☐
National registry	☐
Transplant centre	☐
WMDA	☐

Example profile: WO-XXXX Cord Blood Bank Operational Specifics

Example profile: WO-XXXX Cord Blood Bank Operational Specifics

General

Question	CBB answer
Name of the Cord Blood Bank:	

Verification typing and extended typing requests

Question	CBB answer
Extended/verification typing is performed at an ASHI, EFI or CAP accredited lab:	
The average turnaround time for extended HLA typing results is:	
The Cord Blood Bank does currently use an attached (contiguous) segment (if available) for confirmatory/verification HLA typing:	
The Cord Blood Bank does list cord blood units that do NOT have attached segments and have NOT previously been confirmatory typed on attached segments:	
The percentage of cord blood units in the Cord Blood Bank inventory that will be sent with attached segment is:	
The Cord Blood Bank performs confirmatory/verification HLA typing on cord blood units prior to release with the following resolution:	
The DNA sample will be send to Transplant Centre if requested prior to shipment request:	

Reservation policy

Question	CBB answer
At what point is a cord blood unit reserved for a patient and not available for other patients?	
At time of cord blood unit report request	☐
At time of HLA typing request	☐
At time of reservation request	☐
At time of shipment request	☐
Other,	☐
The length of time that a cord blood unit can be reserved is:	
There is a fee to reserve a cord blood unit:	
The Cord Blood Bank allows for an extension on a reservation of a cord blood unit:	
Will your Cord Blood Bank provide a cord blood unit report on a cord blood unit that is already reserved for another patient (and thus not available) without specifying that the cord blood unit is already reserved?	
If the Cord Blood Bank releases a cord blood unit from a patient's search (as opposed to the transplant centre indicating that the cord blood unit may be released), the transplant centre will be informed by the Cord Blood Bank of the release:	

The list below, indicates which tests are currently performed by the Cord Blood Bank on a thawed attached segment and at which stage:

	VT	TNC count	Total viable CD34 count	% viability of CD34	% viability of CD45	CFUs
As standard when verification typing is performed	-	-	-	-	-	-
As standard when CBU is reserved	-	-	-	-	-	-
Upon request when CBU is reserved	-	-	-	-	-	-
Upon request when verification typing is performed	-	-	-	-	-	-
Only once shipment is requested	-	-	-	-	-	-
Upon request at any point	-	-	-	-	-	-
Not performed	-	-	-	-	-	-

	VT	TNC count	Total viable CD34 count	% viability of CD34	% viability of CD45	CFUs
Will this incur a charge?		-	-	-	-	-

Question	CBB answer
If any of the above tests are requested prior to shipment, this will result in automatic reservation of the CBU:	

Shipment request and release of Unit

Question	CBB answer
The Cord Blood Bank performs hemoglobinopathy screening before release:	

Criteria to allow a Cord Blood Unit to be shipped to transplant centres. See Appendix V of FACT Netcord Standards 6th Edition.			
	Acceptable range of values	**Please provide method**	**Please provide additional information**
Viability/cell count:	-	-	-

Question	CBB answer
Criteria to allow a cord blood unit to be shipped to transplant centres. See Appendix V of FACT Netcord Standards 6th Edition. At the time a cord blood unit is released to be shipped to a transplant centre the following will be performed:	
Current packaging for shipment to transplant centre.	
How many segments do you currently send with the unit?	
How much time is required from the date the shipment order is placed until the unit is shipped?	
The Cord Blood Bank validates its dry shippers to ensure they maintain the temperature at ≤ - 150°C at least 48 hours beyond the expected arrival time at the receiving facility:	
All dry shippers that are used by your Cord Blood Bank, contains an electronic temperature data logger:	
Typically the courier company for international transports is chosen by:	
The shape of the transport container the Cord Blood Bank currently uses:	

Cancellation policy

Question	CBB answer
There is a fee to cancel the reservation for a cord blood unit in the absence of a subsequent request for shipment:	
There a fee for cancellation of shipment:	

IDMs performed before release

IDM	Maternal sample	Cord blood sample
CMV anitbodies IgG Cytomegalovirus antibodies IgG	-	-
CMV antibodies IgM Cytomegalovirus antibodies IgM	-	-
CMV antibodies total Cytomegalovirus antibodies total	-	-
EBV antibodies IgG Epstein Barr Virus antibodies IgG	-	-
EBV antibodies IgM Epstein Barr Virus antibodies IgM	-	-
EBV antibodies total Epstein Barr Virus antibodies total	-	-
HBV-NAT Hepatitis B Virus - Nucleic Acid Amplification Technique	-	-
HCV-NAT Hepatitis C Virus - Nucleic Acid Amplification Technique	-	-
HBsAg Hepatitis B surface antigen	-	-
Anti-HBc Hepatitis B core antibody	-	-
Anti-HBs Hepatitis B surface antibody	-	-
Anti-HCV Hepatitis C antibody	-	-
HIV-1 P24 Human Immunodeficiency Virus p24 antigen	-	-
HIV-NAT Human Immunodeficiency Virus - Nucleic Acid Amplification Technique	-	-
Anti-HIV 1/2 Human Immunodeficiency Virus 1/2 antibody	-	-
Anti-HTLV 1/2 Human T-Lymphotropic Virus 1/2 antibody	-	-
HTLV-NAT Human T-Lymphotropic Virus - Nucleic Acid Amplification Technique	-	-
Anti-HIV 1/2 Human Immunodeficiency Virus 1/2 antibody	-	-
Anti-HTLV 1/2 Human T-Lymphotropic Virus 1/2 antibody	-	-
HTLV-NAT Human T-Lymphotropic Virus - Nucleic Acid Amplification Technique	-	-
STS Syphilis serologic test	-	-
T. Cruzi antibody Trypanosoma Cruzi anitbody (Chagas Disease)	-	-
TOXO antibodies IgG Toxoplasmosis antibody IgG	-	-
TOXO antibodies IgM Toxoplasmosis antibody IgM	-	-
TOXO antibodies total Toxoplasmosis antibody total	-	-
Anti-WNV West Nile Virus antibody	-	-
WNV-NAT West Nile Virus - Nucleic Acid Amplification Technique	-	-