Seventh Edition NetCord-FACT International Standards for Cord Blood Collection, Banking, and Release for Administration

Summary of Changes

This document summarizes the major changes made to the Seventh Edition *NetCord-FACT International Standards for Cord Blood Collection, Banking, and Release for Administration*. This summary does not list all changes made to the Standards; reorganization or clarified verbiage is not included unless intended to change the meaning of the Standard. Refer to the final Cord Blood Standards and the accompanying Accreditation Manual for all requirements.

To clearly identify new requirements, changes to the standards listed have been redlined.

Major Changes

1) Terminology
    a. The term "occurrence" was added to the Seventh Edition NetCord-FACT Cord Blood Standards. Where appropriate throughout the Standards, the generic term "occurrence" replaces "error, accident, deviation, adverse event, adverse reaction, or complaint."
    b. *Occurrence: An instance in which an action or circumstance results in an error, accident, deviation, adverse event, adverse reaction, or complaint.*

2) ISBT 128 and Eurocode Coding and Labeling
    a. The Sixth Edition NetCord-FACT Standards required that organizations be actively implementing ISBT 128 at a minimum. The Seventh Edition Standards requires that ISBT 128 or Eurocode be fully implemented. Appendix II was updated to convey requirements specific to both ISBT 128 and Eurocode. The changes are in Appendix II below.

        ~~If~~ Coding and labeling technologies shall be ~~have not yet been~~ implemented~~, the CBB shall be actively implementing~~ using ISBT 128 or Eurocode. (B6.1.2)

    b. Partial Label at Distribution for Administration

        The Seventh Edition Standards redefines the partial label used at the time of distribution for administration. A partial label must only be used if there are size constraints; otherwise, a full label must be applied. (A4, B6.6.5, Appendix II)

        For in-process identification of a CB unit, the Seventh Edition requires that, at a minimum, the CB unit be labeled at all times with the proper name of the product and the unique numeric or alphanumeric identifier. Before distribution to another entity, the CB unit must be labeled with a full label or a partial label with accompanying documentation that meets the requirements listed in Appendix II. (B6.6.2, D3.2.2)

c. Detached Segments (B6.2.6)

In the Sixth Edition, integrally attached segments were recommended to be labeled with an identifier linking the segments to the applicable CB unit. This recommendation is retained in the Seventh Edition. In addition, detached segments must include an identifier linking the segments to the applicable CB unit.

APPENDIX II

CORD BLOOD UNIT LABELING[1]

Applicable standard	B6.6.4	C7.6	B6.6.4	B6.6.4	B6.6.5	E5.3.6
Label Element	**At completion of collection**	**Outer container labeling at transport or shipping from collection**	**~~At Completion~~ Post processing prior to cryopreservation**	**At distribution ~~to~~ from the CBB to Clinical Program[7]**	**Partial label at distribution for administration[6]**	**Outer container labeling at distribution from the CBB to Clinical Program[8]**
Unique numeric or alphanumeric identifier	AF		AF	AF	~~A~~AF	
Proper name of product[2]	AF		AF	AF	~~A~~AF	
Product Code[2]			AF	AF	AF	
Product attributes (manipulations)[2]			AC	AC	AC	
Statement Related Donor[1]	~~A~~AF		AF	AF	~~A~~AF	
Statement "Autologous Use Only"[3]				~~A~~AF	AC	
Statement "Caution: New Drug – Limited by Federal (or United States) law to investigational use."[6]				~~A~~AC	AC	
Statement "Rx Only"[5] *(Rx = Prescription)*				~~A~~AC	AC	
Collection site identifier	~~A~~AC				AC	
Date of collection	~~A~~AC		AC	AC	AC	
Time of collection and time zone, if different from the CB Processing Facility	AC				AC	
Name and volume or concentration of additives			AC	AC	AC	
Name and volume or concentration of anticoagulants	AF		AC	AC	AC	
Recommended storage temperature	~~A~~AC		AF	~~A~~AC	AC	
Donor name (Related CB units)[3]	~~A~~AC		AT	~~A~~AC	AC	
Recipient family or individual name and unique identifier, if known	~~A~~AC		AT	~~A~~AC	AC	
Recipient's name and unique identifier				AC	AC	
Volume or weight of the CB unit at the end of collection			AC	AC	AC	
Volume or weight of the CB unit at the end of processing			AC	AC	AC	
Date of cryopreservation			AC	AC	AC	
ABO group and Rh type				AC	AC	
HLA phenotype				AC	AC	
Number of nucleated cells post processing			AC	AC	AC	
Gender of CB unit infant donor			AC	AC	AC	
Identity of the CBB[4]			AF	AF	AC	
Statement "Properly Identify Intended Recipient and Product"				AC	AC	
Statement "For Use By Intended Recipient Only" (Allogeneic CB units)[3]				AC	AC	
A statement indicating that leukoreduction filters should not be used				AC	AC	
Statement "Do Not Irradiate"				AC	AC	
Statement "For Nonclinical Use Only"[3]				AC	AC	
Biohazard legend and/or warning labels (see B6.6.3)[3]	AC		AC	AC	AC	
Donor eligibility summary. See Appendix III.				AC	AC	
Date and time of distribution				AC	AC	AF
Shipping facility name, address, phone number		AF				AF
Receiving facility name, address, phone number		AF				AF
Identity of person or position responsible for receipt of the shipment		AF				AF
Statement "Do Not X-Ray"[5]		AF				AF
Statements "Medical Specimen", "Handle With Care"[5] or equivalent as defined by Applicable Law		AF				AF
Statement indicating Cord Blood for Transplantation						AF
Shipper handling instructions[5]		AF				AF

3) Testing and Specification Requirements (Appendix IV and V)

Several changes were made to the testing and specification requirements shown in Appendix IV and V below:

a. The requirement for viability of CD45 positive cells was deleted. (Appendix IV and Appendix V)
b. The requirement for percent viability of CD34 positive cells was deleted for the following samples:
    i. CB unit samples obtained post-processing prior to cryopreservation. (Appendix IV)
    ii. Unrelated CB units post-processing prior to cryopreservation. (Appendix V)
    iii. Related CB units post-processing prior to cryopreservation. (Appendix V)
    iv. Related CB units thawed contiguous segment or representative sample prior to release to the Clinical Program. (Appendix V)
c. The requirement for viability of total nucleated cell count (TNC) was added for:
    i. CB samples obtained post-processing prior to cryopreservation and thawed contiguous segment or representative sample prior to release to the clinical program. (Appendix IV)
d. TNC viability thresholds were set for post-processing prior to cryopreservation samples at ≥ 85% for unrelated units and at ≥ 70% for related units.

APPENDIX IV

TESTING REQUIREMENTS

Test	CB Samples Obtained						Maternal Samples
	Pre-processing (end of collection)	Post-processing prior to cryo-preservation	Any time prior to cryo-preservation	On an appropriate sample type at any time prior to listing	Thawed contiguous segment or ~~thawed~~ representative sample prior to release to the Clinical Program	On an appropriate sample type at any time prior to release	Obtained within seven (7) days before or after CB collection
Cell Count							
CBC with differential	X						
Total nucleated cell count		X			Should be performed		
Nucleated red blood cell count		X					
Total CD34		X					
Total Viable CD34		X			Should be performed		
Viability							
% Viability of Total nucleated cell ~~or % viability CD45~~ count		X			X		
~~% Viability CD45~~					~~X~~		
% Viability of CD34		~~X~~			X		
CFU or other validated potency assay		Should be performed[1]			X		
HLA Tissue Typing							
Low Resolution: HLA-A, HLA-B, HLA-DRB1				X			
Low Resolution HLA-C				Should be performed			
High Resolution: HLA-A, HLA-B, HLA-DRB1						X	
High Resolution HLA-C						♦	
Verification Typing					X[2]		
Infectious Disease[3]							
HIV 1				X[4]			X
HIV 2				X[4]			X
Hepatitis B				X[4]			X
Hepatitis C				X[4]			X
HTLV I				X[4,5]			X[5]
HTLV II				X[4,5]			X[5]
Syphilis				X[4]			X
CMV				X[4]			X
Additional tests[3]				X[4]			X
Other							
Microbial culture		X					
ABO/Rh blood group			X				
Hemoglobinopathy						♦	

APPENDIX V

SPECIFICATION REQUIREMENTS FOR CORD BLOOD UNITS STORED FOR CLINICAL ADMINISTRATION[2]

Test	Unrelated Specification		Related Specification	
	~~Fresh~~ Post-Processing prior to cryopreservation Sample	~~Post-~~Thawed ~~Attached~~ contiguous segment or representative sample prior to release to the Clinical Program	~~Fresh~~ Post-Processing prior to cryopreservation Sample	~~Post-~~Thawed ~~attached~~ contiguous segment or representative sample prior to release to the Clinical Program
Total nucleated cell count	≥ 5.0 x 10^8		Enumerated	
Total nucleated cell recovery	Should be ≥60%		Should be ≥60%	
~~Total viability~~	~~≥ 85%~~		~~≥ 70%~~	
Viability of total nucleated cell count	≥ 85%		≥ 70%	
Viable CD34 count	≥ 1.25 x 10^6			
Viability of CD34 cells	~~≥ 85%~~	≥ 70%	~~≥ 85%~~	~~≥ 70%~~
~~Viability of CD45 cells~~		~~≥ 40%~~		~~≥ 40%~~
CFU (or other validated potency assay)[1]		Growth (or positive result for potency)		Growth (or positive result for potency)
~~Sterility~~ Microbial Screen	Negative for aerobes, anaerobes, fungus		Negative for aerobic and anaerobic bacteria and fungi – OR – identify and provide results of antibiotic sensitivities	
Donor screening and testing	Acceptable as defined by Applicable Law and NetCord-FACT Standards		Acceptable as defined by Applicable Law and NetCord-FACT Standards	
Identity		Verified		Verified

4) Accreditation of HLA Typing Laboratories

The CBB shall use HLA testing laboratories that are capable of carrying out DNA–based intermediate and high resolution HLA-typing and are appropriately accredited by the American Society for Histocompatibility and Immunogenetics (ASHI), European Federation for Immunogenetics (EFI), College of American Pathologists (CAP), or other accrediting organizations providing histocompatibility services appropriate for cord blood banking. (B5.6)

The College of American Pathologists (CAP) has been approved as an accrediting organization providing histocompatibility services appropriate for hematopoietic cellular therapy.

Changes Made to the Standards for Consistency

1) In the Seventh Edition, the following policies and SOPs were added to Part B for consistency:
    a. *Hand washing and sanitation* (B4.2.2)
    b. *Liquid nitrogen, including monitoring of oxygen levels.* (B4.2.6)
    c. *Latex allergy.* (B4.2.7)
    d. *Radiation safety, if applicable.* (B4.2.8)
2) Sixth Edition supply and reagent standards B8.4, B8.4.1, B8.6, and B8.6.1 were combined to form one (1) standard in the Seventh Edition:
    a. *Supplies and reagents that come into contact with the CB unit during collection, processing, or storage shall be sterile and of the appropriate grade for the intended use.* (B8.4)
3) In the Sixth Edition, a process to prevent the use of expired reagents and supplies was only explicit in Part C. In the Seventh Edition, this requirement was added to Part B: *There shall be a process to prevent the use of expired reagents and supplies.* (B8.10)
4) In the Sixth Edition (B1.5.1), the CBB must have an adequate number of qualified staff for its operations. In the Seventh Edition, the following standards were added to Part C and Part D for consistency:
    a. *The CB Collection Site shall have adequate staff to perform collection activities.* (C2.2)
    b. *The CB Processing Facility shall have an adequate number of qualified staff for its operations.* (D1.7)
5) In the Sixth Edition (B3.1.15), the CBB was required to establish and maintain policies or Standard Operating Procedures for acceptance criteria for CB unit receipt, processing, cryopreservation, and storage. In the Seventh Edition, the following requirement was added to Part D:
    a. *Acceptance criteria for CB unit ~~acceptance criteria~~ receipt, processing, cryopreservation, and storage.* (D2.1.1)

Changes to Cord Blood Bank Operational Standards

1) Quality Management (QM)
   In addition to revising standards to explicitly and consistently state requirements, the following changes and additions were made:
    a. *The CBB Director or designee shall be responsible for the Quality Management Plan*. (B2.2.1)
    b. Additional written agreement requirements include:
        i. *Agreements shall be established with external parties providing critical services that could affect the quality and safety of the CB unit or health and safety of the infant donor or mother.* (B2.4.1)
        ii. *Agreements shall have a defined effective date.* (B2.4.3)
        iii. *Agreements shall be ~~dated and~~ reviewed on a regular basis, at a minimum every two (2) years.* (B2.4.4)
    c. *Review and approval of the audit plan, audit report, results, and conclusion by the CBB Director or designee and the Quality Unit Manager or designee.* (B2.11.5)
    d. *Follow-up audits of the effectiveness of corrective and preventive actions shall be performed in a timeframe as indicated in the investigative report.* (B2.12.6.5)

e. *Review and approval of the validation plan, validation report, results, and conclusion by the CBB Director or designee and Quality Unit Manager or designee.* (B2.14.2.8)
f. *The Quality Unit Manager shall review and report ~~on~~ quality management activities, at a minimum, quarterly.* (B2.18)
    i. *Meetings shall have defined attendees, documented minutes, and assigned actions.* (B2.18.1)
    ii. *Review findings shall be reported to staff.* (B2.18.1.1)
g. *The annual report and documentation of the review findings shall be made available to key personnel.* (B2.19.1)

2) Policies and Standard Operating Procedures
    a. *Cleaning and sanitation procedures including identification of the personnel performing the activities.* (B3.1.36)
    b. In the Sixth Edition, a table of contents and standardized format were required as part of a Standard Operating Procedures manual. In the Seventh Edition: *The CBB shall maintain a detailed list of all controlled documents including title and identifier. ~~Standard Operating Procedures Manual that includes at a minimum:~~ (B3.2)*

3) Facilities and Safety
    a. *The facility shall provide adequate lighting, ventilation, sinks, and toilets, and shall be of adequate size, construction, and location to maintain safe operations, prevent contamination, and promote orderly handling.* (B4.1.1)

4) Equipment
    a. In the Sixth Edition, the CBB was required to identify qualify, calibrate, and maintain equipment and in the Seventh Edition these activities must be included in a policy or SOP: *The CBB shall establish policies and SOPs for the management of critical equipment including identification, qualification, calibration, and maintenance.* (B7.1)
    b. Sixth Edition Standards required that equipment records include identification of each CB unit for which the equipment was used (B7.3). Seventh Edition Standards explicitly require also that: *There shall be a mechanism to identify which piece of equipment was used for each CB unit.* (B7.3.1)
    c. *Equipment decommissioning or disposition shall be described and documented.* (B7.9)

5) Supplies and Reagents
    a. *If suitable clinical or pharmaceutical grade reagents are not use, reagents shall undergo lot-to-lot functional verification and shall include acceptance criteria to confirm that new lots perform as expected compared to the previous lots.* (B8.4.1)
    b. *Supplies and reagents shall be quarantined until they have been determined to meet criteria for release from quarantine.* (B8.8.1)
    c. *The lot number, expiration date, and manufacturer of supplies and reagents used for ~~the~~ collection, ~~and~~ processing, testing, cryopreservation, or storage of each CB unit shall be documented and linked to each CB unit.* (B8.9)
    d. *An expiration date shall be assigned to in-house prepared solutions or components.* (B8.10.1)
    e. *An expiration date shall be assigned to the collection kit, and shall be consistent with the first item in the collection kit set to expire.* (B8.10.2)

6) Inventory Transfer
    a. *For related CB units, the family should be made aware of the intent to transfer the units.* (B10.3)

Changes to Cord Blood Donor Management and Collection Standards

1) Personnel requirements
    a. *Initial training, competency, and retraining when appropriate in all procedures performed, quality management, and when applicable, good tissue practices and good manufacturer practices.* (B2.5.4.3)
    b. Training on the collection procedure must cover each aspect of the CB collection process. In the Seventh Edition Standards, training includes: *The appropriate storage, preparation, and use of the collection supplies and reagents.* (C2.4.1.1)
    c. All collections must be performed by health care professionals trained for the collection procedure. In the Seventh Edition Standards, the following are required:
        i. *The collecting health care professional's initial and continuous training shall be documented.* (C2.4.2)
        ii. *The minimum level of activity to maintain competency shall be specified.* (C2.4.3)

2) Informed consent
    a. Two new requirements were added for discussing all aspects of participation in CB donation with the mother in a language and with terms that she understands.
        i. *If an interpreter or translator is utilized, the identity of the interpreter or translator shall be documented.* (C4.2.1)
        ii. *Family members shall not serve as interpreters or translators.* (C4.2.2)
    b. The CBB must only perform steps in the CB banking process for which it has informed consent or a signed agreement from the mother, the Seventh Edition now includes: *Distribution.* (C4.3.5)
    c. A new requirement was added for the CBB's informed consent between the mother and the CBB.
        i. *The CBB's policies for disposition of related CB units in the event of cessation of operation.* (C4.5.12.4)

Changes to Cord Blood Processing Standards

1) Acceptance Criteria
    a. Minor changes were made to the acceptance criteria standards to provide clarity:
        i. *Upon receipt of a CB unit package into the CB Processing Facility, ~~the contents of,~~ the shipping container and contents shall be inspected and the records reviewed for the following ~~at a minimum~~:* (D3.1.1)
        ii. *The integrity of the outer container and the temperature ~~against validated parameters~~ during shipping is within a specified range.* (D3.1.1.2)
    b. A new standard was added: *Occurrences outside of acceptance criteria shall be evaluated.* (D3.1.2)

2) Conditions for Storage
    a. *If a warming event may have decreased the potency of a related CB unit, the unit shall only be made available for administration as a nonconforming unit after approval of the CBB Medical Director and the transplant physician.* (D6.5.2.3)
    b. *There shall be a written stability program to assess cryopreserved CB units for post-thaw ~~microbial contamination~~, potency, and container integrity.* (D6.6)
    c. *A minimum of three (3) CB units per manufacturing method and storage conditions shall be assessed annually.* (D6.6.1)
    d. *CB units with the longest storage duration for each manufacturing method shall be included in each annual assessment.* (D6.6.1.1)
    e. *Specifications for acceptance of stability results shall be defined.* (D6.6.2)
    f. *The stability program shall include requirements to assess additional CB units if a CB unit fails to meet specifications.* (D6.6.2.1)

3) Cord Blood Unit Testing
    a. *For related CB units, the results of positive microbial tests shall include identity and sensitivities of the organism(s). These results shall be reported to the ~~prospective Clinical Program~~ infant donor's mother and her physician, in accordance with Applicable Law and the CBB's policies and Standard Operating Procedures.* (D9.3.2.2)
    Notification of the Clinical Program is retained in E3.3.1.
4) Maternal testing
    a. A new standard was added to the Seventh Edition: *The CBB shall ensure samples are collected and stored for infectious disease testing.* (D10.1.1)

Changes to Cord Blood Listing, Search, Collection, Reservation, Release, and Distribution Standards

1) Policies and SOPs for related and unrelated use were separated as applicable and new requirements were added:
    a. For unrelated use:
        i. *Qualification for listing and search of the CB units.* (E1.2.2.2)
    b. For related use:
        i. *Continued storage and release.* (E1.2.3.2)
    c. For all units:
        i. *Review of records.* (E1.2.2.1, E1.2.3.1)
        ii. *A mechanism to ensure that CB units are released in accordance with Applicable Law and the agreement at the time of informed consent.* (E1.2.4)

2) Review of CB unit records
    a. The comprehensive review of CB unit records must now include:
        i. *Eligibility determination, if required by Applicable Law.* (E2.1.4)

3) The CBB shall ~~indefinitely retain~~ maintain documentation of requests for CB units, requests for samples, requests for and results of testing, and records of transportation and shipping of CB units and samples between facilities according to Applicable Law, institutional policy, or for a minimum of ten (10) years after the date of distribution or disposition, whichever is longer.

4) CB unit distribution to a clinical program
    a. *A CB unit with a positive microbial test result shall be released according to Applicable Law.* (E4.4)

5) Transportation and Shipping of cryopreserved CB units
    a. *The dry shipper shall be configured and labeled in a way to maintain an upright position.* (E5.3.4)

6) Clinical outcome data
    a. The request for information within the recommended time period for every CB unit released for administration for hematopoietic reconstitution must now include:
        i. *Method for thawing and any further processing prior to administration*. (E7.1.2)