Australian Government
Department of Health
Therapeutic Goods Administration

Consultation Paper:

Revision of TGO 75 Standard for Haematopoietic Progenitor Cells Derived from Cord Blood

Version 1.0, May 2017

TGA Health Safety Regulation

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Contents

Background and purpose of consultation

The *Therapeutic Goods Act 1989* provides for the establishment and maintenance of a national system of controls for the quality, safety, efficacy and timely availability of therapeutic goods that are supplied, imported, exported or manufactured in Australia.

Blood and blood components, including hematopoietic progenitor cells (HPCs) derived from cord blood, are therapeutic goods within the meaning of section 3 of the Act.

Subsection 10(1) of the Act provides that the Minister may, by legislative instrument, make an order determining that matters specified in the order constitute a standard for therapeutic goods or a class of therapeutic goods identified in the order.

The *Therapeutic Goods Order No. 75 Standard for Haematopoietic Progenitor Cells Derived from Cord Blood* (TGO 75) is made under subsection 10(1) of the Act in order to establish a ministerial standard for HPCs derived from cord blood.

TGO 75 has been in force since 1 August 2007. In accordance with the *Legislation Act 2003*, legislative instruments (such as TGO 75) are automatically repealed after a fixed period of time (subject to some exceptions). This automatic repeal is called sunsetting. TGO 75 is due to sunset on 1 October 2017. Accordingly, the Therapeutic Goods Administration (TGA) is considering options for remaking an order under subsection 10(1) of the Act which specifies a standard for HPCs derived from cord blood. A new Order would ensure that HPCs derived from cord blood continue to be the subject of an applicable ministerial standard following the automatic repeal of TGO 75.

This consultation provides an opportunity for cord blood banks (CBB) and other stakeholders to comment on the proposed options, including the development of the new Order. Specifically, the TGA is seeking feedback from manufacturers and CBBs on the potential impact that either of the proposed options may have on their operations.

Overview of NetCord-FACT International Standards

TGO 75 specifies that HPCs derived from cord blood must meet the requirements of the 3rd edition of the Foundation for Accreditation of Cellular Therapy (FACT) and NetCord document titled *International Standards for Cord Blood Collection, Processing, Testing, Banking, Selection, and Release* (NetCord-FACT International Standards 3rd Edition). The NetCord-FACT International Standards 3rd Edition was published in December 2006 and was the current edition when TGO 75 was made on 1 August 2007.

FACT and NetCord publish updated editions of the international standards every three years. The 6th edition titled *International Standards for Cord Blood Collection, Banking, and Release for Administration* (NetCord-FACT International Standards 6th Edition) was published in July 2016 and is the current edition. This edition is available for free download from the FACT website at http://factwebsite.org/.

As part of the sunsetting of TGO 75 and related activity of making the new Order under subsection 10(1) of the Act, the TGA is considering whether to specify the requirements of the NetCord-FACT International Standards 6th Edition for HPCs derived from cord blood. (The TGA chose not to adopt the changes made in the 4th and 5th editions of the international standards as those changes related mainly to the structure of the document and included only minor amendments to matters relating to Good Manufacturing Practice (GMP)).

Specifying the requirement of the NetCord-Fact International Standards 6th Edition would align cord blood regulation in Australia with international best practice and maintain consumer confidence in the regulation of these products.

Manufacturing principles

Subsection 36(1) of the Act provides that the Minister may determine written principles to be observed in the manufacture of therapeutic goods for use in humans. Compliance with these manufacturing principles forms an important consideration in the granting of a manufacturing licence in accordance with paragraph 38(1)(e) of the Act. Unless an exemption applies, manufacturing licenses are subject to the statutory conditions that the holder of the licence will conform to any standard applicable to the goods and observe the manufacturing principles in carrying out any steps in the manufacture of the goods.

The *Therapeutic Goods (Manufacturing Principles) Determination No. 1 of 2013* is made under subsection 36(1) of the Act and determines manufacturing principles applicable to specific therapeutic goods, including blood, blood components, biologicals, plasma and HPCs. The Manufacturing Principles Determination stipulates that manufacturers of HPCs must submit a Technical Master File (TMF) which demonstrates compliance with applicable standards as part of an application for a manufacturing licence.

The two ministerial standards specified in the Manufacturing Principles Determination are TGO 75 and *Therapeutic Goods Order No. 88 Standards for donor selection, testing and minimising infectious disease transmission via therapeutic goods that are human blood and blood components, human tissues and human cellular therapy products* (TGO 88). This means that, at present, TMFs submitted with an application for a manufacturing licence must demonstrate compliance with the NetCord-FACT International Standards 3rd Edition to ensure the quality and safety of the Cord Blood Units (CBUs) under the licence.

The Manufacturing Principles Determination also requires HPCs to be manufactured in compliance with the Australian Code of Good Manufacturing Practice for human blood, blood components, human tissues and human cellular therapy products (cGMP) dated April 2013 and published by the TGA on its website.

Consequential amendments would need to be made to the Manufacturing Principles Determination as part of the making of any new Order for HPCs derived from cord blood.

The problem

TGO75 is due to sunset at the end of September 2017 and the current mandated standards no longer represent industry or international best practice on the quality of CBUs.

In addition, the Australian cord blood sector is currently divided between CBBs complying with either the 3rd edition or the 6th edition of the international standards. TGO 75, which specifies the NetCord-FACT International Standards 3rd Edition, no longer represents industry or international best practice on the quality of CBUs. The new requirements outlined in the NetCord-FACT International Standards 6th Edition represent improvements to the quality and safety of the CBUs, and should be considered for uniform implementation in Australia.

As the practices of some CBBs may not be consistent with the requirements of the NetCord-FACT International Standards 6th Edition, the TGA is seeking feedback from CBBs in relation to the proposal to mandate these requirements in a new order.

Differences between the 3rd and 6th editions of the NetCord-FACT International Standards

There are many differences between the 3rd edition and the 6th edition of the NetCord-FACT International Standards. Some of these differences were first implemented in the 6th edition while others were implemented in the previous editions (4th and 5th editions). Changes implemented in the 4th – 6th editions of the Standards are documented at Attachments 1-3. The attached documents are released by FACT with each new edition of the Standards and provide a comprehensive list of the changes introduced to the relevant edition. Note that it is the responsibility of each manufacturer to compare the 3rd and the 6th editions against their current practices). The main differences between the 3rd and 6th edition of the NetCord-FACT International Standards are outlined below.

1. CB Unit Specification Requirements

The 6th edition requires that CBUs stored for clinical administration meet certain specifications. (D8.2)

a. Required specifications are outlined in Appendix V of the 6th edition.

b. Separate requirements exist for unrelated and related CBUs.

For related CBUs, if specifications are unmet, the CBB at a minimum must follow its processes for deviations and nonconforming CBU in the event a customer insists on storage.

2. Testing Requirements

Appendix IV in the 6th edition contains the detailed testing requirements. Several changes were made to the requirements as outlined below. This list does not include every instance in which a test must be performed. Review the appendix for complete requirements.

a. Total Viable CD34 should be performed on a thawed segment or thawed representative sample prior to release to the Clinical Program.

b. % Viability of CD45 must be performed on a thawed segment or thawed representative sample prior to release to the Clinical Program.

c. % Viability of CD34 must be performed post processing prior to cryopreservation and on a thawed segment or thawed representative sample prior to release to the Clinical Program.

d. CFU or other validated potency assay should be performed post processing prior to cryopreservation and must be performed on a thawed segment or thawed representative sample prior to release to the Clinical Program.

3. Accreditation of Human Leukocyte Antigen (HLA) Typing Laboratories (B5.6)

a. Prior editions of Standards have required accreditation by American Society for Histocompatibility and Immunogenetics (ASHI), European Federation for Immunogenetics (EFI), or equivalent. Due to the difficulty of defining " equivalent," a joint FACT/NMDP consultative committee of histocompatibility experts established guidelines for appropriate standards and accreditation for HLA laboratory services.

b. If a CBB wishes to use an HLA laboratory accredited by an organization other than ASHI or EFI, that accrediting organization must demonstrate that it meets the guidelines established by this committee.

c. An accredited CBB contemplating a change in HLA laboratory service provider must confirm appropriateness of accreditation prior to discontinuing services of an ASHI- or EFI-accredited HLA typing laboratory.

4. Scope of Standards

a. The scope of the Standards in the 6th edition includes only the use of cord blood for clinical use.

b. Collection of Cord Tissue

i. For cord tissue storage, these Standards only apply to tissue samples retained for testing or research purposes. Collection and storage of cord tissue for therapeutic intent fall under the scope of the FACT Common Standards for Cellular Therapies.

ii. The Standards explicitly added "for testing" to clearly state why cord tissue is referenced. (B5.9.2)

c. The Cord Blood Bank (CBB) must have a policy or procedure to request the following information (in addition to previous requirements) for every CBU released for administration for hematopoietic reconstitution: (E7.1)

i. Viable nucleated cell yield results on the thawed CB unit. (E7.1.1)

ii. Complaints associated with the CB unit. (E7.1.2)

iii. Microbial screening. (E7.1.7)

iv. Administered cell dose. (E7.1.8)

d. The CBB must have a policy to request outcome data that is relevant to other uses for which the CBU was released. (E7.2)

5. Haemodilution assessment of maternal samples used for infectious disease testing (B3.1.18 of the 6th edition).

6. Educational, promotional, and recruitment materials (B1.6, B2.7.1.5) must be supported by scientific evidence. This requirement is implemented in the 5th edition, but was made more specific and detailed to clearly delineate the types of materials to which the Standard applies in the 6th edition. Because CBB is promoted directly to lay people, CBBs have an obligation to truthfully describe the potential uses of CBUs for various diseases.

7. The CBB Medical Director must give specific authorization to accept CBUs if the genetic or medical history of a first-degree relative of the infant donor is unknown, in accordance with Applicable Law. (B5.5.4.1)

8. Specific reference to the issue of CBUs with unavailable medical history is new in this edition, and is relevant in cases such as sperm or egg donor, absent father, etc. If allowed by Applicable Law, the CBB Medical Director may decide if the incomplete genetic or medical history precludes banking of the CBU.

9. Coding and Labelling of Cord Blood Units

a. ISBT 128 Coding and Labelling. (B6.1.2)

i. The 5th edition required organizations to have a plan for ISBT 128 coding and labelling technology implementation. The 6th edition requires that organizations be actively implementing ISBT 128 coding and labelling technologies.

ii. "Actively implementing" could be demonstrated by registration with ICCBBA, identification or creation of appropriate product codes, label designs, label validation, and/or use of scanned information.

b. A system for label reconciliation must be employed to prevent mix-up of labels and also to detect when a label was used for an incorrect CBU. Label reconciliation applies to any label that includes unique identifier(s) or name(s). (B6.2.2)

c. Barcoding may negate the need for verification of label information by two people. The verification now may be conducted by two qualified people or by one qualified person using a validated process. (B6.3.2.4)

10. Informed Consent (C4)

a. Throughout this section, standards were reorganized to accommodate the variety of methods used by CBBs to obtain and document informed consent. Consent requirements for all donations were delineated, and distinguished from those requirements specific for unrelated donations or unique to related donations.

b. References to an agreement between the mother and the CBB were added throughout the section to provide clarity that these agreements could serve a role in the consent process.

i. CBBs collecting only related donor units often perform the informed consent process in conjunction with the written agreement, and this language is intended to enhance comprehension of the requirements.

ii. All potential CB banking participants, including those involved in related donor banking, must be fully informed of the banking processes, the risks and benefits, and be allowed to ask questions, decline to participate, or to affirm agreement to bank the infant donor's cord blood.

c. The CBB must only perform steps in the CB banking process for which it has informed consent or a signed agreement from the mother. Testing was added to the list of steps that must have specific consent or be included in a signed agreement. (C4.3, C4.3.3)

d. Cryopreserved related CB units lacking a signed consent must be maintained in quarantine status until consent has been obtained. (D8.4.2.2)

11. Maternal and Infant Donor Evaluation

a. Any abnormal result relevant to the health of the maternal or infant donor must be reported to the relevant healthcare provider, maternal donor, and governmental authority according to Applicable Law. The previous standard required only notification of relevant healthcare provider OR the maternal donor. (C5.1.6)

b. Maternal and infant donor screening must include a medical history, review of medical records, and review of physical examination findings. (C5.2)

12. Cord Blood Collection

a. In utero collection requirements were modified to allow health care professionals more decision-making authority. (C6.2)

i. In the 5th edition, in utero CB collections were only allowed to occur in uncomplicated deliveries as determined by the licensed health care professional responsible for the delivery. In the 6th edition, this requirement is limited to in utero CB collections for unrelated donations.

ii. CBUs collected in utero at less than 34 weeks gestation must be based on an evaluation of infant donor safety by the licensed health care professional responsible for the delivery. Previously, collection at less than 34 weeks gestation was not allowed for unrelated donations. The 6th edition leaves this decision up to the health care professional following an evaluation of infant donor safety. (C6.2.3)

b. CBUs, associated samples, and maternal samples at collection sites must be maintained at a defined temperature range. (C6.7.1)

c. The chain of custody of the CB unit must be maintained from collection to receipt at the CBB. (C6.8)

13. Transportation and shipping of unmanipulated CBUs between the Cord Blood Collection Site and the Cord Blood Processing Facility

a. The process for transport and shipping must be validated to maintain a designated temperature range in the immediate environment of the CB unit. (C7.5.2)

b. When a CB unit is shipped, the temperature inside the immediate environment must be continuously monitored, or the CB unit must be shipped in a rigorously validated container. (C7.5.3)

i. The term “rigorously” was intentionally added to stress that compliance with this option requires an extremely robust validation that accounts for several worst-case scenarios (i.e., delays, temperature excursions) in all modes of transportation or shipping used (e.g., car, airplane).

ii. It will be incumbent on the CBB to demonstrate through data and validation summaries to the inspector and Accreditation Committee that the container was rigorously validated.

c. Specific validation requirements are listed in the Accreditation Manual.

d. The CBB must have acceptance criteria for all CB units prior to processing.

e. If related donor CB units are received that do not meet acceptance criteria, the CBB must notify the family donors.

14. Cord Blood Processing

a. For related CB units, the 5th edition required a signed agreement with the donor family for collection, processing, testing, and storage of the CB unit. The 6th edition also requires that disposal be included in the agreement. (D3.1.3).

b. Processing and cryopreservation of CB units must be performed according to Standard Operating Procedures validated to result in acceptable potency in addition to acceptable viability and recovery. (D3.2.4)

15. Samples

a. When a CB unit is initially requested, a minimum of one (1) contiguous segment must be used to verify the results of HLA typing. Sixth edition Standards require HLA

verification typing when a CB unit is initially released compared to the fifth edition requirement at the time of release. (D4.1.1.2)

b. When a CB unit is initially requested for clinical use, potency must be tested in accordance with the Testing Requirements table in Appendix IV and must meet the specifications outlined in the Specification Requirements table in Appendix V. (D4.1.1.3). These are new requirements.

c. At the time of removal for testing, one (1) qualified person using a validated process or two (2) qualified people must verify the identity of the segment. (D4.1.1.4)

d. The Standards define representative and retention samples to clarify that the retention sample is not intended to be used for routine testing, but is intended to be maintained after the CB unit was released for potential future uses. (D4.1.2).

   i. Representative sample: Aliquot of the final cord blood product that is stored under the same conditions as the CB unit, and can be used to test for viability, potency, or stability. (D4.1.2.1).

   ii. Retention sample: Aliquot of the final CB unit saved for future use, such as investigation of adverse events or retroactive quality control activities. (D4.1.2.2)

e. To address the newly-defined representative samples, the 6th edition states that representative samples (in addition to retention samples) intended for viability or potency analysis must be stored under the same conditions as the CB unit. (D4.1.2.1)

f. Samples of plasma from the CBU must be collected, rather than "serum or plasma." Collection of serum alone is no longer in compliance with the Standards, although CBBs may choose to collect serum in addition to the required minimum total volume of 3.6 mL of plasma. (D4.1.3)

g. Use of heparin in plasma samples is no longer restricted. (D4.1.3)

16. Cryopreservation

    a. Total Nucleated Cell (TNC) recovery should be ≥ 60% after processing prior to cryopreservation. (D5.1.1)

    b. CB units must be placed into individual metal canisters for protection; a single canister may not be used for multiple units. (D5.3)

17. Conditions for Storage

    a. Samples, in addition to CB units, must be stored in a secure area. (D6.1)

    b. Warming events at any time after cryopreservation must be minimized. The prior requirement was "at any time after the process of storage," which led to some confusion. (D6.5.2)

    c. The details and purpose of the stability program are expanded and codified in the 6th edition.

       i. There must be a written stability program to assess cryopreserved CB units for post-thaw microbial contamination, potency, and integrity. (D6.6)

          § Because CB units cannot easily be tested prior to release, the CBB must develop a stability program that annually tests CB units of various storage duration and manufacturing methods for viability and potency.

- § The length of CB unit storage is unknown, so data must be accumulated to demonstrate that the conditions of cryopreservation and storage results in CB units that can provide acceptable hematopoietic reconstitution.

ii. A minimum of three CB units per manufacturing method must be assessed annually. (D6.6.1)

18. Cord Blood Unit Testing

For CBC differentials, defined parameters for monocytes are no longer required. (D9.3.1)

19. Key Personnel Requirements (Appendix 1)

In the 5th edition Cord Blood Standards, the requirements for the CBB Director, CBB Medical Director, CB Collection Director, CB Processing Facility Director, and Quality Manager were defined in Part B. In the sixth edition, these requirements are defined in a table in Appendix I.

20. Cord Blood Unit Labelling (Appendix II)

a. The following label elements were changed from affixed to attached or affixed:

i. Partial label

1. Unique numeric or alphanumeric identifier
2. Proper name of product

ii. At completion of collection

1. Collection site identifier
2. Date of collection
3. Donor name (Related CBUs)
4. Recipient family or individual name and unique identifier, if known

iii. At completion of processing prior to cryopreservation

1. Donor name (Related CBUs)
2. Recipient family or individual name and unique identifier, if known

iv. At distribution to Clinical Program

1. Donor name (Related CB units)
2. Recipient family or individual name and unique identifier, if known

b. The following label elements were changed from attached or affixed to accompanied:

i. At distribution to Clinical Program

1. Statement “Properly Identify Intended Recipient and Product”
2. Statement “For Use By Intended Recipient Only” (allogeneic CB units)
3. A statement indicating that leukoreduction filters should not be used
4. Statement “Do Not Irradiate”
5. Statement “For Nonclinical Use Only”

21. Accompanying Documents at Distribution (Appendix III)

    a. This table was expanded to more completely describe the US regulations for documentation of incomplete donor eligibility.

    b. Instructions for reporting serious adverse reactions or events to the distributing facility were also explicitly added to Appendix III. This is required of all cellular therapy products regardless of donors' eligibility status.

22. Additional changes to GMP requirements include: management of change control (B2.6.5), assessment and review of records (B2.11.3.1), assessment and review of non-conformances by the quality staff (B2.12.53); the use of aseptic techniques extended from collection procedures to processing (D3.2.5); clarified training requirements for collection personnel (C2); the Cord Blood Processing Facility requirements for environmental conditions that affect the safety and potency of the CBU (D1.6); and the validation of electronic record systems including verification of calculations and algorithms (B11.9.6.1).

23. Change to the volume of maternal blood samples collected within 7 days before or after collection from at least two vials, 2 mL each to a minimum total volume of 3.6 mL of serum and/or plasma divided into at least two vials (D8.2 of the 3rd edition and D4.3 of the 6th edition).

24. Changes to the time frames for processing and cryopreservation of CBUs. The 3rd edition requires all CB units (related and unrelated) from processing to cryopreservation to be completed within 48 hours. The 6th edition requires different time frames for initiation of the processing and cryopreservation for the unrelated (48 hours) and related (72 hours). (D2.3.6 and D2.3.7, respectively).

Consultation options

The proposed consultation options should be considered in light of the objectives for regulating HPCs, which include:

1. minimising public health and safety risks;
2. maintaining consumer confidence in the regulation of therapeutic goods, specifically the national system of controls relating to the quality, safety, efficacy and timely availability of therapeutic goods;
3. aligning, as far as possible, with international best practice; and
4. minimising unnecessary regulatory burden.

Two options are proposed for the remaking of an order under subsection 10(1) of the Act which specifies a standard for HPCs derived from cord blood.

Option 1: Remake TGO 75 as a new order maintaining the requirements of the 3rd edition

Under this option, the new Order would continue to specify the requirements of the NetCord-FACT International Standards 3rd Edition. In addition, it is proposed that the new Order would include additional definitions and provisions which clarify the scope of the order to ensure best regulatory practice and to minimise unnecessary regulatory burden. These clarifications include:

1. The inclusion of definitions that align with the NetCord-FACT International Standards 3rd Edition definitions for cord blood and HPCs.
2. The application and scope of the new Order would be detailed. Specifically, the new Order would only apply to HPCs derived from cord blood. It would not apply to HPCs derived from other sources, including bone marrow and peripheral blood, or blood that is processed beyond minimal manipulation.
3. Provisions would be included which stipulate that the scope of the new Order does not extend to matters outside the ambit of the Act. For example, requirements in relation to documentation of maternal consent specified in the NetCord-Fact International Standards 3rd Edition, which are only relevant to state law, would not be dealt with by the new Order.

The advantages for adopting Option 1 are:

- All currently licensed CBB are in compliance with the NetCord-FACT International Standards 3rd Edition.
- The proposed additional definitions and provisions which clarify the scope of the new Order would provide greater clarity for the regulation of cells derived from cord blood and ensure best regulatory practice.

The disadvantages of adopting Option 1 are:

- The NetCord-FACT International Standards 3rd Edition does not represent industry best practice. There are significant differences in requirements between 3rd edition and 6th edition that relate to the quality of the CBUs.
- Australia's regulation of HPCs derived from cord blood would remain inconsistent with international practices.

- The cord blood sector in Australia may continue to be divided with some CBBs complying with the requirements of the 6th edition and other CBBs only complying with the requirements of the 3rd edition of the NetCord-FACT International Standards.
- The requirements in the NetCord-FACT International Standards 3rd Edition are not consistent with some of the requirements in TGO88.

Option 2: Remake TGO 75 as a new order specifying the requirements of 6th edition

Under this option the new Order would specify the requirements of the NetCord-FACT International Standards 6th Edition. In addition, the new Order would also include definitions and provisions which clarify the scope of the Order to ensure best regulatory practice and to minimise unnecessary regulatory burden, in the same manner as outlined in Option 1.

Transitional arrangements would be included to allow CBBs to bring their practices in line with the requirements of the new Order. A period of 3-6 months may be afforded to all CBBs to transition to the new requirements and would be determined in consultation with the CBBs. Although compliance with the new requirements is expected after this transition is complete, some standards may require a longer implementation phase. CBBs will be expected to have compliant policies and Standard Operating Procedures in place by the end of the transition date, although it may not have been practical to complete all activities within those procedures.

The new Order would apply to all products from the date it commences, subject to any transitional arrangements. However, for tissue processed before the new Order takes effect, only the new requirements that impact on processes relating to the post-thaw and release of the tissue would apply.

In this scenario, there will be CB units in inventory that met all requirements and standards at the time of collection, but no longer meet release criteria due to changes in these requirements. The expectation of TGA is that the Quality Management (QM) Plan be sufficiently robust to describe the processes used to determine the disposition of such CB units. The QM Plan should include an initial risk assessment related to the quality of the CB unit compared to the necessity or value of keeping the CB unit for its rarity or uniqueness, or for the specific expectations of the family. The CBB must have its own algorithm for this determination. For example, testing donors for communicable diseases using newer test kits improves the safety of the CB unit; CB units tested with older methodologies may still be safe but no longer meet requirements. These judgements must be made by the directors, medical directors, and quality staff of the individual CBB. If it is determined that some or all of the CBUs should be maintained in inventory, there must be a plan to document the decision-making, mitigate risk, and inform the potential user of the CBU of the details of non-conformance. These processes must be detailed in the CBB QM Plan and supporting policies and procedures. You are not required to discard these older CBUs.

The advantages of adopting Option 2 are:

- It represents current industry best practice.
- The proposed additional definitions and provisions which clarify the scope of the new Order would provide greater clarity for the regulation of cells derived from cord blood and ensure best regulatory practice.
- Adoption of the NetCord-FACT International Standards 6th Edition would ensure that Australia's regulation of HPCs derived from cord blood remains internationally consistent.
- It would align the processes in place at all CBBs.

- It provides clearer and less redundant requirements compared to the NetCord-FACT International Standards 3rd Edition.
- It provides detailed requirements that complement those in TGO 88 and cGMP.
- Guidance for the interpretation of the NetCord-FACT International Standards 6th Edition is available and published on the FACT website.
- Banks that have maintained FACT accreditation already have processes in place that comply with the requirements in NetCord-FACT International Standards 6th Edition.

The disadvantages of adopting Option 2 are:

- Minor changes to the TMF dossier structure are required.
- Some CBBs may need to upgrade their practices to meet the additional requirements in the NetCord-FACT International Standards 6th Edition.

Impact of the new order

TGA is seeking your input on the impact of the new Order specifying a standard in relation to HPCs derived from cord blood.

Your views are sought

1. Do you support Option 1 or 2 in the consultation paper, which and why?
2. Would manufacturers and CBBs be able to meet the requirements of NetCord-FACT International Standards 6th Edition? If so, what changes would manufacturers and CBBs need to make? If not, what are the impediments?
3. What financial impact (both costs and savings) would implementing the new requirements in the NetCord-FACT International Standards 6th Edition have? If possible please provide a breakdown of the impacts. This information will be used to quantify the financial impact to all affected stakeholders.
4. What period of time would be needed by CBBs to implement the proposed changes? We note that the FACT imposes a 3 month transition period for compliance with new requirements when an updated edition of the NetCord-FACT International Standards is published. This information will be used to inform any transitional arrangements.
5. If the new requirements in the NetCord-FACT International Standards 6th Edition are implemented, how should they apply to previously collected HPC units? For example, should all units collected before the implementation date be exempt from the new requirements, or should the new requirements be imposed on all HPC units for steps that have not yet been performed, e.g. testing performed prior to release? What problems can you foresee?
6. Is the limited application of the new Order (specifically, HPCs derived from cord blood) appropriate? For example, it is proposed that if HPC units were expanded *ex vivo* (beyond minimal manipulation) prior to use, then the new Order and standard would not apply.
7. Are there any technological developments occurring in this sector that TGA should be aware of that may impact on the design of the new Order?

Attachments

1. *NetCord-FACT International Standards for Cord Blood Collection, Banking, and Release for Administration - Significant Changes from Third Edition to Fourth Edition*
2. *5th Edition NetCord-FACT International Standards for Cord Blood Collection, Banking, and Release for Administration - Summary of Changes*
3. *6th Edition NetCord-FACT International Standards for Cord Blood Collection, Banking, and Release for Administration - Summary of Changes*

Version history

Version	Description of change	Author	Effective date
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