



Therapeutic Goods (Standards for Biologicals— General and Specific Requirements) (TGO 109) Order 2021

I, John Skerritt, as delegate of the Minister for Health and Aged Care, make the following order.

Dated 24 September 2021

Adjunct Professor John Skerritt
Deputy Secretary
Health Products Regulation Group
Department of Health

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Part 1—Preliminary

1 Name

- (1) This instrument is the *Therapeutic Goods (Standards for Biologicals—General and Specific Requirements) (TGO 109) Order 2021*.
- (2) This instrument may also be cited as TGO 109.

2 Commencement

- (1) Each provision of this instrument specified in column 1 of the table commences, or is taken to have commenced, in accordance with column 2 of the table. Any other statement in column 2 has effect according to its terms.

| Commencement information | | |
|---------------------------------|--------------------|-------------------|
| Column 1 | Column 2 | Column 3 |
| Provisions | Commencement | Date/Details |
| 1. The whole of this instrument | 30 September 2021. | 30 September 2021 |

Note: This table relates only to the provisions of this instrument as originally made. It will not be amended to deal with any later amendments of this instrument.

- (2) Any information in column 3 of the table is not part of this instrument. Information may be inserted in this column, or information in it may be edited, in any published version of this instrument.

3 Authority

This instrument is made under section 10 of the *Therapeutic Goods Act 1989*.

4 Definitions

Note: A number of expressions used in this instrument are defined in subsection 3(1) of the Act, including the following:

- (a) bioburden;
- (b) biological;
- (c) container;
- (d) manufacture;
- (e) manufacturing site;
- (f) standard;
- (g) supply.

In this instrument:

Act means the *Therapeutic Goods Act 1989*.

allogeneic use, in relation to a biological that comprises, contains or is derived from HCT materials, means administration to, or application in the treatment of,

a person other than the person from whom the HCT materials used in the manufacture of the biological were collected.

asystole, in relation to a donor of HCT materials, means the reference time for cardiac death, being:

- (a) the documented pronounced time of death; or
- (b) if death is not witnessed—the last time the donor was known to be alive; or
- (c) if the donor of the HCT materials is also a solid organ donor—the cross clamp time.

autologous use, in relation to a biological that comprises, contains or is derived from HCT materials, means administration to, or application in the treatment of, the person from whom the HCT materials used in the manufacture of the biological were collected.

critical materials means all the materials, other than HCT materials, used in the manufacture of a biological that may directly affect the quality, safety or efficacy of the biological.

cryopreservation, in relation to a biological, means suspension in a medium containing a suitable cryoprotectant and cooling according to a method that has been validated to allow maintenance for long periods.

Note: Other grammatical forms of the word **cryopreservation** (such as **cryopreserved**) have a corresponding meaning (see section 18A of the *Acts Interpretation Act 1901*).

EBAANZ Standards for Eye Donation and Eye Tissue Banking means the document titled *EBAANZ Medical and Quality Standards for Eye Donation and Eye Tissue Banking* (Edition 2, April 2009) published by the Eye Bank Association of Australia and New Zealand (EBAANZ), as in force or existing at the commencement of this instrument.

Note: The document is published on the Eye Bank Association of Australia and New Zealand (EBAANZ) website at <http://www.ebaanz.org/>.

faecal microbiota transplant product has the same meaning as in the Regulations.

Guidance on Virus Validation Studies means the document titled *Note for guidance on virus validation studies: the design, contribution and interpretation of studies validating the inactivation and removal of viruses* (February 1996) published by the European Medicines Agency, as in force or existing at the commencement of this instrument.

Note: The document is published on the European Medicines Agency website at www.ema.europa.eu/en.

HCT materials means one or more of the following materials:

- (a) human cells;
- (b) human tissues;

that are collected for use in the manufacture of a biological and are:

- (c) materials intended to comprise, or be contained in, the biological; or

(d) materials from which the biological is intended to be derived.

Note: Human cells and human tissues include human musculoskeletal tissue, human cardiovascular tissue, human ocular tissue, human skin, and human amnion.

human amnion product means a biological that comprises, contains or is derived from human amnion.

human cardiovascular tissue product means a biological that comprises, contains or is derived from human cardiovascular tissue, including aortic, pulmonary, mitral or tricuspid heart valves or any part of such valves, conduit or greater vessel graft, peripheral vascular tissue graft, or pericardial graft.

human ocular tissue product means a biological that comprises, contains or is derived from human ocular tissue, including the eye globe, cornea or sclera.

human musculoskeletal tissue product means a biological that comprises, contains or is derived from human musculoskeletal tissue, including bone, cartilage, fascia lata, ligament, muscle, and tendon.

human skin product means a biological that comprises, contains or is derived from human skin.

microorganism or **microbe** includes a bacterium, fungus, mycoplasma and rickettsia, but does not include a virus or prion.

Note: Other grammatical forms of the words **microorganism** and **microbe** have a corresponding meaning (see section 18A of the *Acts Interpretation Act 1901*).

Example: **Microbe** and **microbial** have corresponding meanings.

minimal manipulation has the same meaning as in the Regulations.

processing, in relation to HCT materials, means any activity involved in the preparation, manipulation, preservation for storage and packaging of the materials.

Regulations means the *Therapeutic Goods Regulations 1990*.

skin means the outer integument or covering of the body, consisting of the dermis and the epidermis and resting on subcutaneous tissue.

specified microorganism means a microorganism of clinical significance that, if detected, necessitates rejection of HCT materials or a biological.

TGA Approach to TSE means the document titled *Transmissible Spongiform Encephalopathies (TSE): TGA approach to minimising the risk of exposure* (Version 2.0, April 2014) published by the Therapeutic Goods Administration, as in force or existing from time to time.

Note: The TGA Approach to TSE is published on the Therapeutic Goods Administration website at www.tga.gov.au.

transportation means the transfer of a substance, material or product, within or between premises including manufacturing sites, under appropriate controlled conditions.

5 Standards

- (1) The matters specified in Part 2 constitute a standard for all biologicals.
- (2) The matters specified in Part 3 constitute a standard for human musculoskeletal tissue products that are subjected to only minimal manipulation.
- (3) The matters specified in Part 4 constitute a standard for human cardiovascular tissue products that are subjected to only minimal manipulation and are manufactured for allogeneic use only.
- (4) The matters specified in Part 5 constitute a standard for human ocular tissue products that are subjected to only minimal manipulation and are manufactured for allogeneic use only.
- (5) The matters specified in Part 6 constitute a standard for human skin products that are subjected to only minimal manipulation.
- (6) The matters specified in Part 7 constitute a standard for human amnion products that are subjected to only minimal manipulation.

Note 1: Part 2 constitutes a general standard that applies to all biologicals, whether or not the biological is also subject to a standard specified in Part 3, 4, 5, 6 or 7.

Note 2: Parts 3 to 7 constitute specific standards that apply to certain human musculoskeletal tissue products, human cardiovascular tissue products, human ocular tissue products, human skin products, and human amnion products, respectively.

Example: Human musculoskeletal tissue products to which Part 3 applies must comply with both Parts 2 and 3.

6 Application

- (1) Subject to subsection (2), this instrument applies to biologicals.
- (2) This instrument does not apply to biologicals that are:
 - (a) faecal microbiota transplant products; or
 - (b) mentioned in item 13 of Schedule 5A to the Regulations, subject to compliance with the condition specified in that item; or
 - (c) samples of HCT materials that are:
 - (i) biopsied for in vitro diagnostic examination; and
 - (ii) not for further manufacture, or reintroduction or transplant to a person.

7 Transitional arrangements

- (1) In this section:

former instruments means the:

- (a) Therapeutic Goods Order No. 83 Standards for human musculoskeletal tissue, as in force immediately before the commencement of the repeal instrument; and

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- (b) *Therapeutic Goods Order No. 84 Standards for human cardiovascular tissue*, as in force immediately before the commencement of the repeal instrument; and
 - (c) *Therapeutic Goods Order No. 85 Standards for human ocular tissue*, as in force immediately before the commencement of the repeal instrument; and
 - (d) *Therapeutic Goods Order No. 86 Standards for human skin*, as in force immediately before the commencement of the repeal instrument.

former provisions means the following provisions of the *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*, as in force immediately before the commencement of the repeal instrument:

- (a) subsection 9(13); and
- (b) subsection 9(14); and
- (c) subsection 9(15); and
- (d) section 12; and
- (e) section 13.

repeal instrument means the *Therapeutic Goods (Standards for Biologicals) Repeal Instrument 2021*.

transition period means the period beginning on 30 September 2021 and ending on 30 September 2022.

- (2) Despite the repeal of the former instruments and former provisions by the repeal instrument, the former instruments and former provisions continue to apply for the duration of the transition period, such that the standards for biologicals constituted by the former instruments and former provisions may be conformed with as an alternative to the standards for biologicals constituted by this instrument.

Part 2—Standard for all biologicals

8 What this Part is about

This Part specifies general requirements that must be met in the manufacture of all biologicals, including requirements relating to the HCT materials used in the manufacture of those biologicals.

Unless otherwise specified, the requirements in this Part apply to all biologicals, including a biological that is subject to a specific standard in Parts 3 to 7 of this instrument.

9 Diseases and conditions that may compromise biologicals

A biological must not be manufactured using HCT materials collected from a donor who is known to have a disease or condition that may compromise the quality, safety or efficacy of the biological, unless:

- (a) criteria for donor selection and periods of donor ineligibility, based on validated data or documented evidence from relevant scientific literature, are applied that support and justify the quality, safety and efficacy of the biological, and the application of the criteria is documented; or
- (b) in any case where it is not possible to comply with paragraph (a)—a registered medical practitioner acting for or on behalf of the manufacturer or the sponsor has agreed to, and documented the rationale for, the use of the HCT materials in the manufacture of the biological.

10 Critical materials

- (1) The critical materials used in the manufacture of a biological must:
 - (a) not be contaminated with, or be likely to introduce, microorganisms or other infectious disease agents; and
 - (b) not adversely affect the quality, safety or efficacy of the biological; and
 - (c) where the critical materials are solutions that come into contact with HCT materials or biologicals (other than critical materials mentioned in paragraph (d))—be manufactured under an approved quality management system and either:
 - (i) be supplied as a sterile solution; or
 - (ii) satisfy sterility requirements specified in an applicable standard; and
 - (d) where the critical materials are non-sterile antimicrobial agents used in a bioburden reduction process for HCT materials—be passed through a 0.22µm filter prior to use in the bioburden reduction process; and
 - (e) where the critical materials are of human or animal origin (other than HCT materials)—meet the requirements set out in:
 - (i) the TGA Approach to TSE; and
 - (ii) the Guidance on Virus Validation Studies.

Critical materials not included in the Register

- (2) The following information in relation to critical materials that are not included in the Register must be available and documented:
 - (a) screening tests performed and quality control specifications, including criteria and limits for tests; and
 - (b) storage conditions.

11 Microbial contamination control strategy

A risk-based microbial contamination control strategy, which considers the nature of HCT materials and biologicals, must:

- (a) be implemented to minimise intrinsic and extrinsic microbial contamination of HCT materials and biologicals; and
- (b) specify storage, handling and transportation requirements (including in relation to temperature and duration) for the HCT materials and biologicals.

12 Samples for bioburden testing

- (1) Samples must be taken for bioburden testing.
- (2) Samples must be:
 - (a) taken using a validated sampling technique; and
 - (b) tested using a validated test method.

Note: Subsections (1) and (2) apply in relation to all biologicals, other than human ocular tissue products to which Part 5 applies.

- (3) This section does not apply in relation to human ocular tissue products to which Part 5 applies.

Note: Part 5 specifies bioburden testing requirements in relation to human ocular tissue products that are subjected to only minimal manipulation and are manufactured for allogeneic use only. However, subsections (1) and (2) apply in relation to all other human ocular tissue products.

13 Bioburden testing requirements

- (1) Written specifications for HCT materials and biologicals must include specified microorganisms determined on the basis of a risk assessment.
- (2) Samples must demonstrate that HCT materials are free from contamination with specified microorganisms.
- (3) Samples must demonstrate that biologicals are:
 - (a) free from microbial contamination; or
 - (b) if, on the basis of a risk assessment, it is not necessary for the biological to be free from microbial contamination—free from contamination with specified microorganisms.
- (4) This section does not apply in relation to:

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- (a) human cardiovascular tissue products to which Part 4 applies; and
 - (b) human ocular tissue products to which Part 5 applies.

Note 1: Part 4 provides that human cardiovascular tissue products that are subjected to only minimal manipulation and are manufactured for allogeneic use only, and human cardiovascular tissue used in the manufacture of those products, must be free from microbial contamination. However, this section applies in relation to all other human cardiovascular tissue products.

Note 2: Part 5 specifies bioburden testing requirements in relation to human ocular tissue products that are subjected to only minimal manipulation and are manufactured for allogeneic use only. However, this section applies in relation to all other human ocular tissue products.

(5) Subsection (3) does not apply in relation to:

- (a) human musculoskeletal tissue products to which Part 3 applies; and
- (b) human skin products to which Part 6 applies.

Note 1: Part 3 provides that human musculoskeletal tissue products that are subjected to only minimal manipulation must be free from microbial contamination, and human musculoskeletal tissue used in the manufacture of those products must be free from contamination with specified microorganisms. However, subsection (3) applies in relation to all other human musculoskeletal tissue products.

Note 2: Part 6 provides that human skin products that are subjected to only minimal manipulation and human skin used in the manufacture of those products must be free from contamination with specified microorganisms. However, subsection (3) applies in relation to all other human skin products.

14 Sterilisation

The sterilisation process for a biological that is terminally sterilised must be validated to ensure a maximal sterility assurance level of 10^{-6} .

15 Collection from deceased donors

(1) HCT materials must be collected from a deceased donor as soon as possible after asystole, and collection must be completed:

- (a) if the body has been refrigerated below 10°C within 12 hours of asystole—not later than 24 hours after asystole; or
- (b) if paragraph (a) does not apply—not later than 15 hours after asystole.

(2) This section does not apply in relation to:

- (a) human musculoskeletal tissue products to which Part 3 applies; and
- (b) human ocular tissue products to which Part 5 applies; and
- (c) human amnion products to which Part 7 applies.

Note 1: Part 3 provides requirements in relation to the collection of human musculoskeletal tissue used in the manufacture of human musculoskeletal tissue products that are subjected to only minimal manipulation. However, this section applies in relation to all other human musculoskeletal tissue products.

Note 2: Part 5 provides requirements in relation to the collection of human ocular tissue used in the manufacture of human ocular tissue products that are subjected to only minimal manipulation and are manufactured for allogeneic use only. However, this section applies in relation to all other human ocular tissue products.

Note 3: Part 7 provides requirements in relation to the collection of human amnion used in the manufacture of human amnion products that are subjected to only minimal manipulation. However, this section applies in relation to all other human amnion products.

16 Storage and transportation

HCT materials

- (1) Immediately following collection and prior to processing, HCT materials must be:
 - (a) stored as follows:
 - (i) at less than 10°C for not longer than 72 hours; or
 - (ii) as otherwise validated by the manufacturer to prevent microbial proliferation and to ensure the quality, safety and efficacy of the biological manufactured using the HCT materials; and
 - (b) transported in a manner that ensures the relevant storage conditions specified in paragraph (a) are maintained during transportation.
- (2) Subsection (1) does not apply in relation to:
 - (a) human cardiovascular tissue products to which Part 4 applies; and
 - (b) human skin products to which Part 6 applies; and
 - (c) human amnion products to which Part 7 applies.

Note 1: Part 4 provides storage and transportation requirements in relation to cardiovascular tissue used in the manufacture of cardiovascular tissue products that are subjected to only minimal manipulation and are manufactured for allogeneic use only. However, subsection (1) applies in relation to all other human cardiovascular tissue products.

Note 2: Part 6 provides storage and transportation requirements in relation to human skin used in the manufacture of human skin products that are subjected to only minimal manipulation. However, subsection (1) applies in relation to all other human skin products.

Note 3: Part 7 provides storage and transportation requirements in relation to human amnion used in the manufacture of human amnion products that are subjected to only minimal manipulation. However, subsection (1) applies in relation to all other human amnion products.

- (3) HCT materials that are collected and transported for use in the manufacture of a biological must be packaged using aseptic technique and with at least one moisture impermeable barrier.

Biologicals

- (4) Biologicals must be stored and transported under conditions that are validated, including justified time and temperature specifications, to ensure the quality and safety of the biologicals.
- (5) Subsection (4) does not apply in relation to:
 - (a) human musculoskeletal tissue products to which Part 3 applies; and
 - (b) human cardiovascular tissue products to which Part 4 applies; and
 - (c) human ocular tissue products to which Part 5 applies; and

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- (d) human skin products to which Part 6 applies; and
 - (e) human amnion products to which Part 7 applies.

Note 1: Part 3 provides storage and transportation requirements in relation to human musculoskeletal tissue products that are subjected to only minimal manipulation. However, subsection (4) applies in relation to all other human musculoskeletal tissue products.

Note 2: Part 4 provides storage and transportation requirements in relation to human cardiovascular tissue products that are subjected to only minimal manipulation and are manufactured for allogeneic use only. However, subsection (4) applies in relation to all other human cardiovascular tissue products.

Note 3: Part 5 provides storage and transportation requirements in relation to human ocular tissue products that are subjected to only minimal manipulation and are manufactured for allogeneic use only. However, subsection (4) applies in relation to all other human ocular tissue products.

Note 4: Part 6 provides storage and transportation requirements in relation to human skin products that are subjected to only minimal manipulation. However, subsection (4) applies in relation to all other human skin products.

Note 5: Part 7 provides storage and transportation requirements in relation to human amnion products that are subjected to only minimal manipulation. However, subsection (4) applies in relation to all other human amnion products.

- (6) A biological that is returned to its manufacturer cannot be released for supply unless:
 - (a) the biological was at all times stored and transported in accordance with applicable storage and transportation requirements in relation to the biological; and
 - (b) the labelling and packaging of the biological has not been compromised.

17 Containers of biologicals

- (1) A biological must be sealed within a sterile container and must be at least double packaged so as to:
 - (a) prevent ingress or egress of all materials; and
 - (b) ensure that any breach of integrity of the container and packaging is evident.
- (2) This section does not apply in relation to human ocular tissue products to which Part 5 applies.

Note: Part 5 provides requirements in relation to containers of human ocular tissue products that are subjected to only minimal manipulation and are manufactured for allogeneic use only. However, this section applies in relation to all other human ocular tissue products.

Part 3—Standard for human musculoskeletal tissue products

18 What this Part is about

This Part specifies requirements that must be met in the manufacture of human musculoskeletal tissue products that have been subjected to only minimal manipulation, including requirements relating to human musculoskeletal tissue that is collected for use in the manufacture of those products.

Unless otherwise specified, a biological to which this Part applies must meet the general requirements in Part 2 in addition to the specific requirements in this Part.

19 Application of this Part

This Part applies in relation to human musculoskeletal tissue products that have been subjected to only minimal manipulation.

20 Collection from deceased donors

- (1) The collection of human musculoskeletal tissue from a deceased donor must commence as soon as possible after asystole and:
 - (a) if the body has been refrigerated below 10°C within 12 hours after asystole—not later than 24 hours after asystole; or
 - (b) if paragraph (a) does not apply—not later than 15 hours after asystole.
- (2) The collection of human musculoskeletal tissue from a deceased donor must be completed within 36 hours after asystole.

21 Bioburden testing

Tissue not subjected to processing

- (1) Human musculoskeletal tissue that is not subjected to processing prior to packaging must be sampled at the time of collection for bioburden testing.
- (2) Human musculoskeletal tissue sampled in accordance with subsection (1) must be tested for bioburden and:
 - (a) demonstrate no microbial contamination; or
 - (b) be rejected for therapeutic use if microbial contamination is demonstrated; or
 - (c) be subjected to further processing in accordance with subsection (3) if microbial contamination is demonstrated with microorganisms other than specified microorganisms.

Tissue subjected to processing

- (3) Human musculoskeletal tissue that is subjected to processing prior to packaging (including, for example, a bioburden reduction process) must be:
- (a) sampled for bioburden testing at the time of collection or prior to the processing to exclude tissue contaminated with specified microorganisms; and
 - (b) either:
 - (i) sampled for bioburden testing after the processing and must demonstrate no microbial contamination; or
 - (ii) subjected to a bioburden reduction process that has been validated to render the tissue free from any microbial contamination.
- (4) Human musculoskeletal tissue that demonstrates:
- (a) contamination with specified microorganisms when tested in accordance with paragraph 21(3)(a); or
 - (b) any microbial contamination when tested in accordance with subparagraph 21(3)(b)(i);
- must be rejected for therapeutic use.

22 Demineralised products

The residual calcium of human musculoskeletal tissue products that are demineralised must not exceed 8% w/w.

23 Freeze-dried products

The residual moisture content of human musculoskeletal tissue products that are freeze-dried must not exceed 6% w/w.

24 Storage and transportation

Human musculoskeletal tissue products must be:

- (a) stored as follows:
 - (i) at minus 20°C to minus 40°C for not more than 6 months after the collection of the human musculoskeletal tissue; or
 - (ii) frozen or cryopreserved at less than minus 40°C for not more than 5 years after the collection of the human musculoskeletal tissue; or
 - (iii) if the products are freeze-dried—at room temperature for not more than 5 years after the collection of the human musculoskeletal tissue; or
 - (iv) in accordance with conditions that are validated on the basis of validated data or documented evidence from relevant scientific literature, including justified time and temperature specifications, to ensure the quality, safety and efficacy of the products; and
- (b) transported in a manner that ensures the relevant storage conditions specified in paragraph (a) are maintained during transportation.

Part 4—Standard for human cardiovascular tissue products

25 What this Part is about

This Part specifies requirements that must be met in the manufacture of human cardiovascular tissue products that have been subjected to only minimal manipulation and are manufactured for allogeneic use only, including requirements relating to human cardiovascular tissue that is collected for use in the manufacture of those products.

Unless otherwise specified, a biological to which this Part applies must meet the general requirements in Part 2 in addition to the specific requirements in this Part.

26 Application of this Part

This Part applies in relation to human cardiovascular tissue products that:

- (a) have been subjected to only minimal manipulation; and
- (b) are manufactured for allogeneic use only.

27 Tissue not subjected to a bioburden reduction process

- (1) Human cardiovascular tissue that is not subjected to a bioburden reduction process must be collected, subjected to any processing prior to packaging, sampled for bioburden testing, packaged in an operating theatre, transported to a manufacturing site, and cryopreserved.
- (2) The cryopreservation of human cardiovascular tissue mentioned in subsection (1) must commence:
 - (a) in the case of a deceased donor—within 48 hours of asystole; or
 - (b) in the case of a living donor—within 48 hours of collection.
- (3) Human cardiovascular tissue that is sampled in accordance with subsection (1) must be tested for bioburden and, following that testing, must:
 - (a) demonstrate no microbial contamination; or
 - (b) be rejected for therapeutic use if microbial contamination is demonstrated.

28 Tissue subjected to a bioburden reduction process

- (1) Human cardiovascular tissue that is subjected to a bioburden reduction process must be processed and treated with antimicrobial agents in accordance with subsections (2) and (3).
- (2) The processing and treatment with antimicrobial agents must commence:
 - (a) in the case of a deceased donor—within 36 hours of asystole; or
 - (b) in the case of a living donor—within 36 hours of collection.

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- (3) The human cardiovascular tissue must be exposed, between dissection of the tissue from its surrounding tissue and the time of its cryopreservation, to conditions of antimicrobial treatment at:
 - (a) 34°C to 39°C for 6 to 12 hours; or
 - (b) 2°C to 8°C for 18 to 24 hours.
 - (4) Following the bioburden reduction process and before the addition of cryopreservative, human cardiovascular tissue must be sampled, and tested for bioburden and, following testing, must:
 - (a) demonstrate no microbial contamination; or
 - (b) be rejected for therapeutic use if microbial contamination is demonstrated.
 - (5) Human cardiovascular tissue that is subjected to a bioburden reduction process must be cryopreserved:
 - (a) within 72 hours of asystole; or
 - (b) within a longer timeframe that is validated by the manufacturer to prevent microbial proliferation and to ensure the quality, safety and efficacy of the human cardiovascular product manufactured using the tissue.

29 Heart valves

Human cardiovascular tissue that is a heart valve must be a competent valve prior to cryopreservation.

30 Storage and transportation

Human cardiovascular tissue

- (1) Immediately following collection and prior to processing in accordance with either section 27 or 28, human cardiovascular tissue must be:
 - (a) stored as follows:
 - (i) at a temperature between 0°C to 10°C; or
 - (ii) as otherwise validated by the manufacturer to prevent microbial proliferation and to ensure the quality, safety and efficacy of the human cardiovascular tissue product manufactured using the tissue; and
 - (b) transported in a manner that ensures the relevant storage conditions specified in paragraph (a) are maintained during transportation.

Human cardiovascular tissue products

- (2) Human cardiovascular tissue products that are cryopreserved must be stored as follows:
 - (a) at or below minus 100°C for not more than 5 years after collection of the human cardiovascular tissue; or
 - (b) in accordance with conditions that are validated on the basis of validated data or documented evidence from relevant scientific literature, including justified time and temperature specifications, to ensure the quality, safety and efficacy of the products.

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- (3) Human cardiovascular tissue products that are cryopreserved must be transported in a manner that ensures the relevant storage conditions specified in subsection (2) are maintained during transportation.

Part 5—Standard for human ocular tissue products

31 What this Part is about

This Part specifies requirements that must be met in the manufacture of human ocular tissue products that have been subjected to only minimal manipulation and are manufactured for allogeneic use only, including requirements relating to human ocular tissue that is collected for use in the manufacture of those products.

Unless otherwise specified, a biological to which this Part applies must meet the general requirements in Part 2 in addition to the specific requirements in this Part.

32 Application of this Part

This Part applies in relation to human ocular tissue products that:

- (a) have been subjected to only minimal manipulation; and
- (b) are manufactured for allogeneic use only.

33 Collection

- (1) Collection of human ocular tissue from a deceased donor must be completed not later than 48 hours after asystole, and the time intervals between asystole, enucleation, preservation and corneal excision must be documented.
- (2) A human ocular tissue product that is manufactured using human ocular tissue collected between 24 and 48 hours after asystole must not be released for supply unless:
 - (a) a medical practitioner acting for, or on behalf of, the manufacturer or the sponsor has evaluated the quality, safety and efficacy of the product; and
 - (b) the medical practitioner who is responsible for the administration to, or application in the treatment of, the recipient of the product has been notified that the collection occurred between 24 and 48 hours after asystole; and
 - (c) the medical practitioners mentioned in paragraphs (a) and (b) are registered in a State or internal territory.

34 Storage and transportation

Human ocular tissue products must be stored as follows:

- (a) in the case of an eye globe—in a moist chamber system at 0°C to 10°C for not more than 48 hours after collection of the eye globe; or
- (b) in the case of excised cornea—either:
 - (i) in a corneal storage medium at 0°C to 10°C for not more than 14 days after collection of the cornea; or

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- (ii) in a storage medium at 28°C to 37°C for not more than 30 days after collection of the cornea; or
 - (iii) in a cryopreservation medium between minus 75°C to minus 196°C for not more than 2 years after the collection of the cornea; or
 - (c) in the case of sclera—maintained in at least 75% v/v ethanol solution for not more than 1 year after collection of the sclera; or
 - (d) in accordance with conditions that are validated on the basis of validated data or documented evidence from relevant scientific literature, including justified time and temperature specifications, to ensure the quality, safety and efficacy of the products.

35 Excised cornea—testing of storage medium etc.

- (1) Where excised cornea is stored in accordance with subparagraph 34(b)(ii), then:
 - (a) the storage medium must be tested for microbial contamination using a validated test method prior to transfer of the tissue to a transport medium; and
 - (b) subsequent exposure to the transport medium at a temperature validated to maintain tissue quality must not exceed 5 days.
- (2) If testing of the storage medium in accordance with paragraph (1)(a) demonstrates evidence of microbial contamination, then:
 - (a) where the excised cornea has not been released for supply—the excised cornea must be rejected for therapeutic use; or
 - (b) where the excised cornea has been released for supply—the results of the microbial tests must be reported to the medical practitioner who is responsible for the administration to, or application in the treatment of, the recipient of the product in accordance with the documented procedures of the manufacturer.

36 Containers

A human ocular tissue product must be sealed within a sterile container and must be packaged so as to:

- (a) prevent ingress or egress of all materials; and
- (b) ensure that any breach of integrity of the container and packaging is evident.

37 Examination and evaluation

Examination and evaluation of human ocular tissue must be in accordance with the requirements set out in section 10 of the EBAANZ Standards for Eye Donation and Eye Tissue Banking.

Part 6—Standard for human skin products

38 What this Part is about

This Part specifies requirements that must be met in the manufacture of human skin products that have been subjected to only minimal manipulation, including requirements relating to human skin that is collected for use in the manufacture of those products.

Unless otherwise specified, a biological to which this Part applies must meet the general requirements in Part 2 in addition to the specific requirements in this Part.

39 Application of this Part

This Part applies in relation to human skin products that have been subjected to only minimal manipulation.

40 Processing etc.

- (1) Human skin must be sampled for bioburden testing following collection and prior to being packaged.
- (2) Processing of human skin must commence:
 - (a) within 24 hours of collection; or
 - (b) within a longer timeframe that is validated by the manufacturer to prevent microbial proliferation and to ensure the quality, safety and efficacy of the human skin product manufactured using the human skin.

41 Bioburden testing

- (1) Human skin sampled in accordance with subsection 40(1) must be tested for bioburden and, following that testing, must:
 - (a) demonstrate no microbial contamination with specified microorganisms; or
 - (b) be rejected for therapeutic use if microbial contamination with specified microorganisms is demonstrated.
- (2) If bioburden testing in accordance with subsection (1) demonstrates microbial contamination with microorganisms other than specified microorganisms, then the results of the testing must be reported by the manufacturer of the human skin product to the medical practitioner who is responsible for the administration to, or application in the treatment of, the recipient of the product.

42 Freeze-dried products

The residual moisture content of human skin products that are freeze-dried must be less than 5%.

43 Storage and transportation

Human skin

- (1) Immediately following collection and prior to processing, human skin must be:
 - (a) stored as follows:
 - (i) at less than 10°C in a suitable storage medium; or
 - (ii) as otherwise validated by the manufacturer to prevent microbial proliferation and to ensure the quality, safety and efficacy of the human skin product manufactured using the human skin; and
 - (b) transported in a manner that ensures the relevant storage conditions specified in paragraph (a) are maintained during transportation.

Human skin products

- (2) Human skin products must be stored as follows:
 - (a) at less than minus 40°C for not more than 5 years after collection of the human skin; or
 - (b) at 2°C to 8°C for not more than 14 days after collection of the human skin; or
 - (c) if stored in greater than 75% glycerol solution—at 2°C to 8°C for not more than 2 years after the collection of the human skin; or
 - (d) in accordance with conditions that are validated on the basis of validated data or documented evidence from relevant scientific literature, including justified time and temperature specifications, to ensure the quality, safety and efficacy of the products.
- (3) Human skin products must be transported in a manner that ensures the relevant storage conditions specified in subsection (2) are maintained during transportation.

Part 7—Standard for human amnion products

44 What this Part is about

This Part specifies requirements that must be met in the manufacture of human amnion products that have been subjected to only minimal manipulation, including requirements relating to human amnion that is collected for use in the manufacture of those products.

Unless otherwise specified, a biological to which this Part applies must meet the general requirements in Part 2 in addition to the specific requirements in this Part.

45 Application of this Part

This Part applies in relation to human amnion products that have been subjected to only minimal manipulation.

46 Collection etc.

- (1) Human amnion used in the manufacture of human amnion products must be collected as soon as possible after caesarean section or vaginal delivery.
- (2) Processing of the human amnion must commence:
 - (a) within 24 hours of collection; or
 - (b) within a longer timeframe that is validated by the manufacturer to prevent microbial proliferation and to ensure the quality, safety and efficacy of the human amnion product manufactured using the human amnion.

47 Terminal sterilisation

Human amnion products manufactured using human amnion collected following vaginal delivery must be terminally sterilised in accordance with section 14.

48 Dehydrated or freeze-dried products

The residual moisture content of human amnion products that are dehydrated or freeze-dried must be less than 15%.

49 Storage and transportation

Human amnion

- (1) Immediately following collection and prior to processing, a human amnion must be:
 - (a) stored at less than 10°C in a suitable storage medium, or as otherwise validated by the manufacturer to prevent microbial proliferation and to ensure the quality and safety of the human amnion; and

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- (b) transported in a manner that ensures the relevant storage conditions specified in paragraph (a) are maintained during transportation.

Human amnion products

- (2) Human amnion products must be stored as follows:
 - (a) if the products are cryopreserved—at less than minus 80°C for not more than 2 years after collection of the human amnion; or
 - (b) if the products are dehydrated or freeze-dried—at room temperature for not more than 5 years after collection of the human amnion; or
 - (c) in accordance with conditions that are validated on the basis of validated data or documented evidence from relevant scientific literature, including justified time and temperature specifications, to ensure the quality, safety and efficacy of the products.
- (3) Human amnion products must be transported in a manner that ensures the relevant storage conditions specified in subsection (2) are maintained during transportation.