



Australian Government

Department of Health and Ageing
Therapeutic Goods Administration

THERAPEUTIC GOODS ACT 1989

Section 10

THERAPEUTIC GOODS ORDER NO. 83

Standards for human musculoskeletal tissue

I, Jenny Hefford, delegate of the Minister for Health and Ageing for the purposes of section 10 of the *Therapeutic Goods Act 1989* (the Act) and acting under that section, having consulted with the Therapeutic Goods Committee in accordance with subsection 10(4) of the Act, **HEREBY:**

DETERMINE that the matters specified in this Order shall constitute a standard for biologicals that are human musculoskeletal tissue.

Dated this 8 day of July 2011

(signed by)

Jenny Hefford

Delegate of the Minister for Health and Ageing

1. Name of Order

This Order may be cited as Therapeutic Goods Order No. 83 Standards for human musculoskeletal tissue.

2. Commencement

This Order commences on 31 May 2012.

3. Purpose of this Order

The purpose of this Order is to specify the minimum technical requirements with which a biological that is a human musculoskeletal tissue must comply.

4. Interpretation

(1) In this Order:

Act means the *Therapeutic Goods Act 1989*.

allogeneic use means the use of a biological that is removed from one person and applied to another.

aseptic technique means the technique that consists of measures used to prevent contamination by micro-organisms.

asystole means the reference time for cardiac death. A documented pronounced time of death is used as asystole when life-saving procedures have been attempted and there were signs of, or documentation of, recent life (e.g. agonal respirations, pulse-less electrical activity). If death was not witnessed, 'asystole' must be determined by reference to the last time that the person was known to be alive. Asystole will be 'cross clamp time' if the tissue donor was also a solid organ donor.

autologous use means the use of a biological that is removed from and applied to the same person.

bioburden has the same meaning as in the Act.

biological has the same meaning as in the Act.

cell(s) means individual cells, or a collection of cells when not bound by any form of connective tissue.

collection means removing a biological or a source of a biological from a donor.

container has the same meaning as in the Act.

critical material means all materials or supplies used in the manufacture of therapeutic goods which could have a direct impact on the quality, safety or function of the final goods.

cryopreserved means suspended in a medium containing a suitable cryoprotectant and cooled according to a method which has been validated to allow maintenance for long periods.

donor means any source, whether living or deceased, of blood, blood components, cells or tissues.

manufacture has the same meaning as in the Act.

microbial means microorganisms including, but not limited to, bacteria, fungi, Mycoplasma and Rickettsia but does not include viruses or prions.

minimal manipulation has the same meaning as in the Regulations.

physical assessment means a clinical inspection of a living or deceased potential donor to determine suitability of the person to be a donor and may include, but is not limited to, assessing the relevance of any abrasion/laceration, bruise/haematoma, fracture, tattoo, piercing, scar, skin lesion, surgical incision or other distinguishing external feature that may be indicative of a behaviour or lifestyle or suggestive of any risk factor in relation to a relevant communicable disease.

processing means any activity involved in the preparation, manipulation, preservation for storage and packaging of a biological.

recipient means a person who receives blood, blood components, cells or tissues by infusion or implantation.

Regulations means the Therapeutic Goods Regulations 1990.

specified microorganism means a microorganism of clinical significance which, if isolated from the tissue, necessitates rejection of the tissue for therapeutic use.

storage means maintaining a substance, material or product under appropriate controlled conditions.

tissue means all constituent parts of the body formed by cells.

trained assessor means a person who is trained in physical assessment and is an employee of, or has a contractual arrangement with, a manufacturer.

transport means the transfer within or between premises of a substance, material or product under appropriate controlled conditions.

5. Application of this Order

- (1) Subject to section 6, the requirements of this Order apply to biologicals that are human musculoskeletal tissue, including muscle, ligament, bone or cartilage, collected from:
 - (a) living human donors for autologous or allogeneic use; or
 - (b) deceased human donors for allogeneic use.

6. Exemptions

- (1) The following biologicals that are human musculoskeletal tissue are exempt from the requirements set out under this Order:
 - (a) human musculoskeletal cells and tissue biopsied for the purpose of an *in vitro* diagnosis and that are not for manufacture and/or reintroduction or transplant to a recipient; and
 - (b) human musculoskeletal tissue that is processed beyond minimal manipulation.

7. General Requirements

- (1) In relation to manufacturing procedures relating to human musculoskeletal tissue, any critical materials used in the collection and manufacture of such tissue must be of a design and quality that will protect the quality and condition of the musculoskeletal tissue.
- (2) Human musculoskeletal tissue from a deceased donor must be collected as soon as possible after asystole and collection must be completed within 36 hours of asystole. Collection must commence:
 - (a) within 24 hours provided the body has been refrigerated below 10°C within 12 hours of asystole; or
 - (b) if the body has not been refrigerated, within 15 hours of asystole.
- (3) A physical assessment of the donor of human musculoskeletal tissue must be conducted by a trained assessor, and must take place within 30 days prior to donation.
- (4) Human musculoskeletal tissue that is to be transported to a manufacturing site must be packaged using an aseptic technique, with at least one moisture impermeable barrier.
- (5) Human musculoskeletal tissue that will not undergo further processing prior to packaging must be sampled at the time of collection for bioburden using a validated sampling technique to collect surface microorganisms. That sample must be tested for bioburden using a validated test method.
- (6) Human musculoskeletal tissue sampled and tested in accordance with subsection 7(5) must:
 - (a) demonstrate no microbial growth; or
 - (b) if microbial growth is demonstrated, be rejected for therapeutic use; or
 - (c) if microbial growth is demonstrated and the results of the testing excludes specified microorganisms, the tissue can be subject to further processing in accordance with subsection 7(7).

- (7) Human musculoskeletal tissue that is subjected to further processing and/or a bioburden reduction process:
- (a) should be sampled at the time of collection or prior to processing for bioburden using a validated sampling technique and tested using a validated method to exclude tissue contaminated with specified microorganisms; and
 - (b) either:
 - (i) must be sampled using a validated sampling technique after processing for bioburden and tested for bioburden using a validated test method and, when tested, must demonstrate no microbial growth; or
 - (ii) must be subjected to a bioburden reduction process that has been validated to render the tissue free from any microbial contamination.
- (8) Musculoskeletal tissue that demonstrates growth of specified microorganisms when tested in accordance with paragraph 7(7)(a), or that demonstrates any microbial growth when tested in accordance with subparagraph 7(7)(b)(i), must not be used for therapeutic use.
- (9) Written specifications for human musculoskeletal tissue must include a list of specified microorganisms, developed using a risk assessment process, listing microorganisms which, if tested and found to be present on sampled tissue specimens of human musculoskeletal tissue, must result in rejection of the musculoskeletal tissue for therapeutic use.
- (10) If the human musculoskeletal tissue has been subjected to a terminal sterilisation process, the sterilisation process must be qualified to ensure that a sterility assurance level of 10^{-6} is achieved for the tissue.
- (11) After processing, human musculoskeletal tissue must be sealed within a sterile container and at least double packaged so as to:
- (a) prevent ingress/egress of material (other than for a gas sterilant if applicable); and
 - (b) ensure that any breach of integrity will be evident.
- (12) Human musculoskeletal tissue must be stored as follows:
- (a) either:
 - (i) at minus 20°C to minus 40°C for no more than 6 months from completion of processing; or
 - (ii) frozen or cryopreserved at less than minus 40°C for no more than 5 years from completion of processing; or
 - (iii) in accordance with conditions and duration specified and justified by validation data or documented evidence from the relevant scientific literature; and
 - (b) when transported, in a manner that ensures that whichever of the conditions set out at (i), (ii) or (iii) applies, is maintained during transport.