Australian Government

Department of Health and Ageing

THERAPEUTIC GOODS ACT 1989
Section 10

THERAPEUTIC GOODS ORDER NO. XX - *Standards for banked human ocular tissue*

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

DETERMINE that the matters specified in this Order shall constitute a standard for banked human ocular tissue.

Dated this ….. day of ……. 2010

Rohan Hammett
Delegate of the Minister for Health and Ageing

1. Name of Order

This Order may be cited as Therapeutic Goods Order No. XX Standards for banked human ocular tissue.

2. Commencement

This Order commences on the day after the day it is registered on the Federal Register of Legislative Instruments.

3. Introduction

This Order specifies the minimum technical requirements for the safety and quality assurance for a biological that is a banked human ocular tissue.

4. Interpretation

(1) For the purpose of this Order, the term "must" means that the Order is to be complied with at all times.

(2) In this Order:

allogeneic means material for administration to an individual that is obtained, or derived, from a genetically different individual;

aseptic technique means the measures used to prevent contamination by microorganisms;

banked means maintenance, under appropriate controlled conditions, in an inventory, of a finished product that has been determined suitable for supply;

biological means:

(1) Subject to subsection (3), a biological is a thing that:

(a) either:

(i) comprises, contains or is derived from human cells or human tissues; or

(ii) is specified under subsection (2); and

(b) is represented in any way to be , or that is, whether because of the way in which it is presented or for any other reason, likely to be taken to be:

(i) for use in the treatment or prevention of a disease, ailment, defect or injury affecting persons; or

(ii) for use in making a medical diagnosis of the condition of persons; or

(iii) for use in influencing, inhibiting or modifying a physiological process in persons; or

(iv) for use in testing the susceptibility of persons to a disease or ailment; or
(v) for use in the replacement or modification of parts of the anatomy in persons.

(2) The Secretary may, by legislative instrument, specify things for the purposes of subparagraph (1)(a)(ii).

(3) the Secretary may, by legislative instrument, determine that a specified thing is not a biological for the purposes of the Act.;

clean collection environment means an area or facility, such as a mortuary or equivalent facility with the following conditions:
(a) air-conditioning to regulate temperature, humidity and particulates required for maintenance of tissue quality; and
(b) control measures to limit access to qualified and operational persons; and
(c) sufficient space to perform the tissue recovery and avoid cross contamination; and
(d) work surfaces able to be adequately cleaned prior to commencing retrieval; and
(e) records confirming current pest control measures.;

container has the same meaning as in "container" in subsection 3(1) of the *Therapeutic Goods Act 1989* (the Act), as amended from time to time. Container, in relation to therapeutic goods, means the vessel, bottle, tube, ampoule, syringe, vial, sachet, strip pack, blister pack, wrapper, cover or other similar article that immediately covers the goods, but does not include an article intended for ingestion.;

critical material means all components, materials or supplies which could have a direct impact on the quality of the end product;

cryopreserved means suspended in a validated medium containing a suitable cryoprotectant and cooled according to a validated method that allows maintenance for long periods;

donor means every source, whether living or deceased, of blood, cells or tissues;

primary pack has the same meaning as in "primary pack" in subsection 3(1) of the Act, as amended from time to time. Primary pack, in relation to therapeutic goods, means the complete pack in which the goods, or the goods and their container, are to be supplied to consumers.;

storage means maintaining a substance, material or product under appropriate controlled conditions until supply;

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

5. Application

(1) This Order applies to banked biologicals that are human ocular tissue, including the eye globe, cornea or sclera, retrieved from

(a) living human donor(s) intended for allogeneic use; or

(b) deceased human donor(s) intended for allogeneic use.

(2) This Order specifies requirements for biological and other therapeutic goods that are critical materials used in the manufacture of biologicals in subsection 5(1).

(3) This Order does not apply to

(a) human ocular tissue that is manufactured so that its physical (disregarding shape or size) or biological characteristics are altered or is otherwise highly manipulated; or

(b) amniotic membrane that may be used for therapeutic ocular procedures.

6. Exemptions

Biologicals exempt from this Order:

(1) banked human ocular tissue that is a biological and to which an exemption from compliance with this Order has been granted by the Secretary in accordance with section 14 and 14A of the Act.

(2) ocular cells and tissue samples biopsied for the purpose of an *in vitro* diagnosis and not for manufacture and/or reintroduction or transplant to a recipient.

7. General requirements

(1) Each manufacturer releasing banked tissue for supply in Australia must have a formally established comprehensive quality system that is fully documented and meets the requirements of the *Therapeutic Goods Act* 1989.

(2) Banked human ocular tissue must comply with Therapeutic Goods Order No. XX *Standards for minimising infectious disease transmission via therapeutic goods that are human blood and blood components, human tissues and human cellular therapies.*

(3) A biological must not be manufactured from ocular tissues obtained from a donor who is known to have a disease or condition compromising the quality and safety of the tissue including

(a) Ocular/intraocular infection-active inflammation giving rise to clinically diagnosed endophthalmitis at the time of death;

(b) Malignant tumours of the eye, e.g. retinoblastoma, melanoma, adenocarcinoma.

(4) The minimum donor age to donate ocular tissue for a banked biological for allogeneic use is two (2) years old. Each tissue establishment must have a documented policy regarding the upper age limit for donation.

(5) Collection of ocular tissues from a deceased donor must take place in, at minimum, a clean collection environment such as a mortuary or equivalent facility, using aseptic technique. For a living donor the ocular tissue must be retrieved in an operating theatre.

(6) The collection of tissue from a deceased person must occur as soon as possible and no more than 24 hours after death. Time intervals between death and enucleation and preservation and/or corneal excision must be recorded.

(7) Critical materials, media, containers and closures employed in the manufacture of banked ocular tissue must be of a design, composition, quality and safety to protect the quality and safety of the biological at the various stages during manufacture and transport.

(8) The critical processing zone for processing and handling of ocular tissue in the tissue establishment's laboratory is a Class II Biosafety cabinet.

(9) Ocular tissue

(a) is preserved as:
  (i) a globe (whole eye) in a moist chamber system at 0°C to 10°C for no more than 48 hours;
  (ii) excised cornea in a corneal storage medium under refrigeration at 0°C to 10°C for no more than 14 days;
  (iii) excised cornea maintained in culture medium at 28°C to 37°C for no more than 30 days;
  (iv) excised cornea maintained in a cryopreservation medium between minus 75°C to minus 196°C for up to 2 years;
  (v) sclera in accordance with conditions and duration specified for the chosen preservation medium;

(b) described in subsection 7(9)(a)(i),(ii), or (iii) may be banked for an extended period of time under the specified conditions, but that period must be less than the maximum documented storage period respective to the medium used and only if authorised by the Medical Director of the facility and with the agreement of the transplanting surgeon.

(c) that is excised corneas, preserved according to subsections 7(9)(a)(iii), then a subsequent exposure to transport medium at 28°C to 37°C must not exceed 5 days.

(10) Ocular tissue must be sealed within a sterile container and packaged and sealed so as to

(a) prevent ingress/egress of material other than for a gas sterilant (if applicable);

(b) ensure any breach of integrity will be evident.

(11) Labelling of ocular tissue must comply with Schedule 1.

8. Evaluation and testing of ocular tissue

(1) Corneas must be evaluated by one or more of the following methods. Observations and results obtained from the following examinations and evaluations must be recorded.

(a) Gross examination and evaluation: When *in situ* excision of the corneoscleral button is performed, an initial gross examination of the corneal-scleral segment must be conducted with the aid of a pen light or slit lamp to assess tissue clarity, epithelial defects, foreign objects, contamination and scleral colour, e.g. jaundice.

(b) Slit-lamp examination and evaluation undertaken in any of the following circumstances:

(i) the cornea must be examined for epithelial and stromal pathology, and in particular endothelial disease, with particular attention to the epithelium, stroma and endothelium such as, but not limited to, scars, oedema, significant arcus, striae, epithelial defects, guttata, polymegathism, pleomorphism, infiltrates or foreign bodies.

(ii) enucleated whole globes must be examined in the laboratory prior to distribution and/or corneal excision.

(iii) after excision of a cornea to be stored hypothermically, the corneoscleral button must be evaluated by slit-lamp biomicroscopy, to detect any damage to the corneal endothelium or surgical detachment of Descemet's membrane.

(iv) slit-lamp examination of cornea stored in culture media at 28°C to 37°C is recommended to identify gross defects.

(c) Endothelial cell examination and evaluation: Endothelial cell morphology and density must be evaluated by specular microscopy or quantitative light microscopy.

(2) The scleral shell must be visually examined for gross defects before banking and distribution.

(3) Bioburden on ocular tissue that is preserved according to subsection 7(9)(a)(iii) and/or its storage medium must be determined prior to release or transfer to transport medium.

(a) Unless the visual evidence of growth results in discard of the biological, a report of positive microbial culture must include an estimate of the total viable count and the organism(s) identified to at least the genus level; and

(b) results of the microbial tests must be reported to the transplanting surgeon.

(4) Bioburden on ocular tissue that is preserved in accordance with subsection 7(9)(a)(iv) and (v) must be determined and meet specification documented for the clinical application of the tissue prior to its release by the manufacturer.

Schedule 1 Labelling

(1) The container and primary pack in which each final biological product that is ocular tissue is packaged and banked, and for release to the transplant unit must be labelled with at least the following:

(a) name and address of the supplying tissue establishment;

(b) tissue identification code;

(c) type of tissue;

(d) type of preservation media.

(2) The exterior of the transport container must clearly display:

(a) the name, address, telephone number of the Eye Bank supplying the tissue;

(b) the name, address, telephone number of the Transplant Unit to which the tissue is dispatched;

(c) the type of tissue;

(d) storage conditions and expiry date;

(e) any special handling instructions;

(f) biohazard label and a statement including that the biological could transmit infectious agents.

(3) Documentation to accompany tissue to Transplant Unit must include, at minimum, tissue specific details and product information relating to tissue processing and handling as follows:

(a) donor screening information

(b) tissue establishment, donor and tissue information
- (i) name of Eye Bank;
- (ii) address and telephone number of Eye Bank; and may include email address/web address;
- (iii) unique tissue identification number;
- (iv) type of preservation medium;
- (v) age of donor;
- (vi) death and preservation dates and times, and/or death-to-preservation interval and storage interval;
- (vii) results confirming mandatory serological test were non-reactive;
- (viii) results of microbiological tests performed in accordance with subsections 8(3) and (4).

(c)

(i) the recommended temperature for maintaining specific type of tissue (cornea, sclera, whole globe) and the preservation method, with emphasis being given to prohibited conditions after arrival at the transplant unit.

(ii) the surgeon should check for integrity of the seal and immediately report to the Eye Bank any evidence of possible breach.

(iii) for corneas:- that colour change of storage medium outside a specified range may indicate an unacceptable change in pH, in which case the tissue should not be used and be reported immediately to the Eye Bank.

(iv) if microbiological tests were not performed by the Eye Bank for ocular tissue (that is, that preserved according to subsection 7(8)(a)(i) and (ii), a statement to that effect must be included. Microbiological testing is required for tissue preserved as described in subsection 7(8)(a)(iii),(iv) and (v), as specified in subsections 8(3) and (4).

(v) advice to the receiving surgeon that the ocular tissues are delivered with no absolute guarantee of safety or efficacy, or fitness for a particular purpose, and that the receiving surgeon is ultimately responsible for judging if the ocular tissue is suitable for a particular use.