



Australia and New Zealand Corneal Society  
*The Royal Australian and New Zealand College of  
Ophthalmologists.*

27 January 2011

**Joint Submission to Therapeutic Goods Administration Consultation on the Proposed TGOs for 1) Standards for minimising infectious disease transmission and 2) Standards for banked human ocular tissue**

Please find attached a joint submission from The Eye Bank Association of Australian and New Zealand and the Australian and New Zealand Corneal Society (the special interest group on cornea and eye banking of the Royal Australian and New Zealand College of Ophthalmologists).

Both associations represent the highest level of professional expertise in relation to eye donation, eye banking and corneal transplantation in Australia and New Zealand.

The high standards that have been developed and applied by these organisations are based on many years of accumulated experience, research, risk assessment and the application of world's-best practice. The result is an enviable record of quality, safety, efficiency and transplantation success that is unmatched in any other field of human donation or transplantation. Our two Associations are uniquely placed to comment and advise on codes of practice and infectious disease risk in relation to ocular tissue, and have also published internationally recognised Medical and Quality Standards for Eye Donation and Eye Tissue Banking.

We recognise and are pleased with the importance that the TGA placed on our comments regarding Draft 1 of these TGO's, and appreciate the willingness to incorporate our suggestions during the framing of the relevant standards. Both of the new drafts demonstrate a significant amount of rework over the previous versions, and the Ocular Standards TGO in particular now approaches that that of a good workable set of Standards for Banked Ocular Tissue.

However we wish to restate that eye donation, eye banking and corneal transplantation should be regarded in a separate category from blood and other tissues. This recognises the unique properties of the cornea and the specific risks to the patient of transplantation. These issues and risks are distinct, separate and significantly different from all other tissues covered under the new Biologicals Framework.

The attached comments embodies advice that allows for a workable, rational, and efficient set of standards while still retaining the highest principles of safety and quality that are clinically significant to ocular tissue transplantation. We believe all these comments need to be incorporated into any future documents to ensure that Australia develops a practical and responsible regulatory approach to ocular tissue donation and transplantation.

Yours sincerely,

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## Therapeutic Goods Order

- Standards for minimising infectious disease transmission via therapeutic goods that are human blood and blood components, human tissues and human cellular therapy products

### COMMENT AND JOINT SUBMISSION FROM:

EYE BANK ASSOCIATION OF AUSTRALIA AND NEW ZEALAND and AUSTRALIAN AND NEW ZEALAND CORNEAL SOCIETY OF THE ROYAL COLLEGE OF AUSTRALIAN AND NEW ZEALAND OPHTHALMOLOGISTS

## General Comments

This second draft of the Therapeutic Goods Order remains an ambitious document that attempts to include all blood and tissues under the one set of infectious disease standards. It continues to be complicated, inconsistent and in some instances inaccurate because of its aim in applying the same universal standards to all tissue types. This not appropriate because different tissues have different risk profiles.

The risk profile for ocular tissues have been reviewed over many years by the international ophthalmic community, incorporated into Eye Donation Standards, and this continues to provide the best specialist opinion regarding infectious disease transmission via ocular tissue. The application of exclusionary criteria that are not applicable for ocular tissue places unreasonable restrictions on the provision of transplantable corneas and other ocular tissue and thus inappropriately reduces the access to and benefits of this type of transplantation. As per our previous consultation on draft 1 of this document we believe **that for clarity, accuracy, workability and responsiveness to a constantly changing operating environment and changing standards, this Therapeutic Goods Order should be discarded, and its standards incorporated appropriately into the Therapeutic Goods Order that is specific to the product group.**

Notwithstanding these comments and suggestions, the following are specific comments and corrections necessary to allow this document to accurately represent those standards that apply to ocular tissue. They highlight the problems of trying to apply Standards that do not apply to ocular tissues.

## Specific Comments on Parts and Clauses.

### Part 1 – Introduction

#### 4. Interpretation

The draft TGO states:

*“prion disease, risk of means having been exposed to the putative causative agent(s) of any one of the family of pathogenic transmissible spongiform encephalopathies through the following means:*

*(a) genetic (familial), or*

*(b) environmental, which includes donors who have lived in or visited England, Scotland, Wales, Northern Ireland or the Isle of Man for a cumulative period of six months or more, between 1st January 1980 and 31st December 1996 inclusive, or*

*(c) iatrogenic, which includes donors who have received a transfusion or injection of blood or blood components while in England, Scotland, Wales, Northern Ireland or the Isle of Man from 1st January 1980 onwards”*

Suggested change and reason(s):

The definition of environmental and iatrogenic risks in the TGO only addresses exposure to the putative causative agent(s) of variant CJD, and *not* any other form of prion disease. This needs to be addressed so that appropriate risk factors are included and non-significant risk factors are excluded.

Thus,

**1) the exclusions as listed in the TGO for ocular tissue to address vCJD are not warranted on the basis of a risk versus benefit analysis and should be removed as ocular tissue donor criteria. See Hogan et.al.<sup>1</sup>, Hirst et al.<sup>2</sup> and Chu<sup>3</sup>.**

**2) Risk factors for other forms of *prion* disease which have a higher risk profile should be included as they currently are in the professional standards. See Hogan et.al.<sup>1</sup> and EBAANZ Medical Standards<sup>4</sup>.**

5. Application of this Order

The Draft TGO states:

*“(1) Subject to section 6, the requirements of this Order apply to human blood and blood components, human tissues and human cellular therapy products that are collected from (a) a living human donor and intended for autologous use; or (b) a living human donor and intended for allogeneic use; or (c) a deceased human donor and intended for allogeneic use.”*

Suggested addition and reason(s):

The intent of the Biologicals Framework is that *“that registered medical practitioners will be exempted where they take a biological from their patient and return the biological unmodified to the same patient during the same clinical procedure”*. Presently this intent is not clear in the wording of “5. Application of this order” or in “section 6. Exemptions”.

Although one could interpret that “6. Exemptions” are intended to include a medical practitioner single surgical procedure it is still not clear and should be directly stated.

**“Registered medical practitioners will be exempted where they take a biological from their patient and return the biological unmodified to the same patient during the same clinical procedure”**, should be stated under in this, and other applicable TGOs.

### Part 3 – Specific Requirements

8. Requirements in relation to the medical and social history of the donor.

(1) & (2)

The TGO states:

*“(1) Blood, blood components, cells or tissues must be collected from a living donor with whom a Medical and Social History interview has been conducted and recorded. The interview that is required must be in accordance with the following:*

*(a) The interview must be conducted by a trained interviewer and should be at a face-to-face interview with the donor or guardian/next-of- kin.*

*(b) The interview must occur no more than 7 days prior to or 30 days after collection, and must occur prior to release of product from quarantine, unless otherwise specified in product-specific Orders under section 10 of the Act.*

*(2) An interview, where possible, with the next-of-kin/guardian or other knowledgeable historian of a deceased donor and/or examination of the medical documentation to obtain and record the*

*medical and social history of the donor must take place and be recorded at the time of, or no more than 7 days prior to or following collection.”*

Suggested change and reason(s):

Sub-titles are required for each of the two sections for clarity – (1) referring to living donors and (2) referring to deceased donors. This is required for reasons of clarity.

(3)

The TGO states:

*“Donor medical and social history criteria as set out in column 1 of Table 1 must be reviewed and responses at interview evaluated using these criteria.”*

Suggested change and reason(s):

This is currently ambiguous. The intent is - that donor medical and social history needs to be evaluated, including those responses given at interview if appropriate – but this is not clear. Medical and social history information for cadaveric donation will be derived from a number of sources that will vary for each individual case.

A simpler clause would be to **omit the words “and responses at interview” to “Donor medical and social history criteria as set out in column 1 of Table 1 must be reviewed and evaluated using these criteria”**

**General comments on Section 8, Table 1**

The time periods of ineligibility listed within the Table are inconsistent and seem not to relate to risk assessment, virology testing window periods, current industry standards or harmonisation with international standards.

There also needs to be some rewording of some criteria for clarification and a balance in regard to emphasis on certain conditions with regard to risk and consequence (e.g. malaria). The authors of the TGO have also confused ineligibility for living donation (especially those of blood) with those of ineligibility for cadaveric donation (e.g. a recent febrile illness - a person with the flu or a cold, would be ineligible for blood donation but certainly not for cadaveric eye donation).

In addition, there are clauses where the authors have confused those questions asked during the medical and lifestyle interview with exclusion criteria. The question asked initially at interview is often a broad question that is then used to elicit further information upon which a decision can be made i.e. the interview question itself is not an exclusion criteria (e.g. the interview question *ever* used I.V. drugs being applied to mean a permanent ineligibility to donate).

Table 1 (d)

The TGO states:

(d) A donor who has ever injected any drug for a non-medical reason	Permanently ineligible
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Suggested change and reason(s):

**The ineligibility should be 12 months.** It appears that the Draft has confused the interview question with the period of ineligibility. The question is whether a person has ever used drugs, and a “yes” is then questioned further to determine when, where, how and the

likelihood of drug use still occurring. For example, a single use 30 years ago should not make the donor ineligible but a long history of drug use may be considered for ineligibility.

Table 1 (e)

The TGO states:

(e) A recipient of (i) human derived clotting factors that are not in accordance with the requirements of this Order (ii) viable animal cells or tissues	Permanently ineligible
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Suggested change and reason(s):

The criteria should be re-worded to:

**If not in accordance with this Order, recipient of (i) human derived clotting factors (ii) viable animal cells or tissues**

**The ineligibility should be 12 months.**

Without this change a recipient of an animal cell or tissue (e.g. a porcine heart valve) which had been provided in accordance with this order, would be permanently ineligible to donate. If provided in accordance with this order the risk is no greater than that of a recipient of human derived clotting factors.

Table 1 (h) and (i)

The TGO states:

(h) A deceased donor who has been a recipient of allogeneic organ(s), cells, or tissue that are not in accordance with the requirements of this Order	Permanently ineligible
(i) A recipient of allogeneic blood, blood components or blood products, organs, cells or tissues that are not in accordance with the requirements of this Order	Ineligible for 12 months unless (f) or (g) apply, then permanently ineligible

Suggested change and reason(s):

**The ineligibility for both (h) and (i) should be 12 months unless (f) or (g) apply, then permanently ineligible.**

There is no reason for a discrepancy between a deceased donor and a living donor. Death *per se* does not increase the risk for transmission of disease (especially for eye donation).

Table 1 (l)

The TGO states:

(l) A donor with an unexplained fever or infectious illness	Ineligible for at least 2 weeks following the date of full recovery
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Suggested change and reason(s):

**This should be deleted or specifically not apply to eye donors.** The authors have confused the question at medical and lifestyle interview with the ineligibility criteria. As written this would exclude anyone with the flu or a common cold from cadaveric donation. The interview question is designed to determine if there could be some more insidious and contra-indicated disease process occurring such as HIV infection. A positive answer to the question “did the donor have any unexplained fever or infectious illness?” is not an exclusion in itself.

Table 1 (m), (n), (o), (p)

The TGO states:

(m) A donor who has lived in a malarial area within the first five years of life	Ineligible for 3 years from last visit to any endemic area provided the person remains free of symptoms; this may be reduced to 4 months if an immunologic or molecular genomic test is negative at donation
(n) A donor with a history of malaria	Ineligible for 3 years from last visit to any endemic area provided the person remains free of symptoms; this may be reduced to 4 months if an immunologic or molecular genomic test is negative at donation
(o) An asymptomatic visitor to endemic malarial areas	Ineligible for 6 months after leaving the endemic area unless an immunologic or molecular genomic test is negative
(p) A donor with a history of undiagnosed febrile illness during or within 6 months of a visit to a malarial endemic area	Ineligible for 3 years following resolution of symptoms; this may be reduced to 4 months if an immunologic or molecular genomic test is negative.

Suggested change and reason(s):

**These should be deleted or specifically not apply to eye donors.**

Transmission of malaria by corneal transplantation is highly unlikely because of the vector of transmission (erythrocytes), and there is no evidence of this ever having occurred. While an eye donor is likely to be rejected if active infection with malaria was established, the requirement to screen for malaria based on risk factors of travel and time, without confirmation of actual infection, is not warranted on the basis of risk.

Table 1 (q)

The TGO states:

(q) A donor with exposure to risk of acquiring a blood borne transmissible infection (i) Mucosal splash with blood (ii) Needle stick injury (iii) Tattoo (iv) Body piercing (v) Acupuncture unless performed using sterile single use needles	Ineligible for 6 months from the time of exposure, or for 4 months provided NAT test for HCV is negative.
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Suggested change and reason(s):

**Ineligibility should be increased to 12 months or the ineligibility criteria applied to all sources of risk of blood borne infections.**

The increase in ineligibility would be consistent with risk of blood borne infections acquired by any other means. If ineligibility is for six months and 4 months for a NAT HCV result, the same criteria should be applied to all other ineligibility for risk of acquiring a blood borne transmissible infection.

Table 1 (s)

The TGO states:

(s) A donor with exposure to particular epidemiological situations (e.g. disease outbreaks)	Deferral consistent with the epidemiological situation and these deferrals should be notified to the Head of the Office of Scientific Evaluation of the Therapeutic Goods Administration.
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Suggested change and reason(s):

**“Exposure to particular epidemiological situations” – This should be deleted or refined.**

This requirement is far too generalist to be of any practical use. Who determines the epidemiological situation? Who decides if it is relevant to the tissue donation e.g. a flu outbreak for eye donation is irrelevant to the risk of donation for corneal transplantation.

Table 2

The TGO states:

Vaccine Composition	Period of donor ineligibility prior to donation
Live attenuated bacteria or viruses, except smallpox	4 weeks
Smallpox	8 weeks
Sera of animal origin	12 weeks
Unknown	12 months

Comments and reason(s):

**“Sera of animal origin” is not well defined. This requires some better qualifying or descriptive guidelines. Why is the period for “vaccines unknown” 12 months?**

## Section 9: Requirements in relation to donor blood sampling, test kits, test protocols and test management

Part (3)

The TGO states:

*“(3) Blood sampling for testing of a deceased donor must take place no later than 24 hours after asystole. A pre-mortem blood sample taken up to 7 days prior to collection of the product may be used if available and suitable.”*

Comments, suggested change and reason(s):

Why is there a 24 hour restriction on blood sampling? If it relates to validation of the blood test in regards to sample viability then the sampling time should be that defined by the test validation. For eye donation NAT testing (which has tighter requirement for the blood specimen samples) is not required, and a sample taken more than 24 hours after death is still valid for serological testing. In Europe where normothermic storage of corneas is widespread it is not uncommon for more than 24 hours to have passed before blood sampling and retrieval of eyes is performed. Indeed, some countries such as Denmark restrict access to coronial donors until after 24 hours has elapsed<sup>5</sup>. A restriction of 24 hours unreasonably restricts access to this valuable donor pool for eye tissues.



**This requirement needs to be rewritten both for 1) clarification of the reasons for the restriction and 2) to ensure that samples taken after 24 hours are still considered suitable for mandatory testing for Eye Donors.**

## **Section 10: Requirements in relation to donor physical assessment and testing**

(2)(b)

The TGO states:

*“A physical assessment of the donor must be conducted by a trained assessor, and must take place*

*(a) for a living donor at the time of donation, unless specified in the product specific Order;*

*(b) for a deceased donor, prior to cell or tissue collection and no later than 24 hours after asystole;*

*(c) the cells and tissues of a deceased donor whose cause of death is unknown must be deemed unacceptable unless autopsy provides sufficient information to conclude that death has not been caused by a transmissible disease or any other condition that would be a contraindication or preclude transplantation of the cells or tissue from that donor”.*

Suggested change and reason(s):

Under part (b) - It is unclear why 24 hours restriction should apply, and it does not seem to be related to risk. Because of *rigour mortis* physical assessment may sometimes be more appropriate *after* 24 hours.

**The reference to 24 hours in (b) should be deleted or specifically exclude eye donors from this requirement.**

(3)(c) and also Table 3

The TGO uses:

“Cornea” or “corneal donor”.

Suggested change and reason(s):

**The word “cornea” in both (3)(c) and Table 3 needs to be changed to “ocular tissue” or “eye tissue”.** This is consistent with what is donated and removes ambiguity.

## **Section 11 Requirements in relation to microbial control**

### **General Comments**

The requirement for microbial control varies between product i.e. It is product-specific. Those aspects of microbial control that may be appropriate for one tissue (e.g. bioburden in relation to bone processing) are not appropriate for another tissue (e.g. non-sterile transplant of non-sterile cornea).

In addition, microbial control is not a standard for minimising infectious disease transmission and thus should not be included in an infectious diseases TGO.

**This section should be removed, rewritten to be product-specific, and the appropriate re-write placed in the Product-specific Therapeutic Goods Order.**

Notwithstanding these comments and suggestions, the following are specific comments and corrections necessary to allow this Section to accurately represent those standards that apply



to ocular tissue. Again, they highlight the problems of trying to apply Standards that may apply to other tissues or blood but that *do not apply to ocular tissues*.

Part 11(2)

The TGO uses:

*“(2) Human cells and tissues from a deceased donor must be collected  
(a) as soon as possible after asystole and take place within 24 hours of asystole provided the body has been refrigerated at 2°C to 8°C within 12 hours of asystole; or  
(b) if the body has not been refrigerated, within 15 hours of asystole death.”*

Suggested change and reason(s):

There is no evidence that refrigeration within these parameters significantly reduces the safety or efficacy of eye tissue. In addition, collection beyond 24 hours, if there is an assessment of endothelial viability and microbial contamination such as in normothermic storage of corneas, is acceptable. See European Eye Banking Association (reference 5)

**This clause (2) must exclude ocular tissue.**

Part 11(5)

The TGO uses:

*“The product release bioburden specifications must include:  
(a) the absence of microorganisms; or  
(b) the absence of specified microorganisms of clinical significance; or  
(c) the surveillance and control measures for minimisation of microbial contamination of the product during collection and manufacture; or  
(d) the respective product specific Order where requirements are specified; and  
(e) when the product is subject to terminal sterilisation or when the product is labelled as sterile, Annex 1 of the Code of GMP for Medicinal Products applies.”*

Suggested change and reason(s):

**Ocular tissue is not subject to bioburden testing and therefore this section must exclude ocular tissue.**

## **Section 12: Requirements in relation to substances used in collection and manufacture**

### **General Comments**

This section relates to Good Manufacturing Practice *not* “minimising infectious disease transmission” and therefore should be removed from this TGO and incorporated into the relevant cGMP using terminology and language that is consistent with the cGMP.

Notwithstanding these comments and suggestions, the following are specific comments and corrections necessary to allow this Section to accurately represent those standards that apply to ocular tissue. Again, they highlight the problems of trying to apply Standards that may apply to other tissues or blood, but that *do not apply to ocular tissues*.

Part 12(2)(a)

The TGO uses:

*“Critical materials used in the manufacture of human blood and blood components, human tissues and human cellular therapy products that are:*

*(a) solutions, which contact the human cells or tissue during collection, processing, storage or transport, other than the antimicrobial agents used in a cell or tissue cleaning process validated by the manufacturer, must be: (i) manufactured under an approved quality management system and be supplied as a sterile solution; or (ii) tested for and satisfy sterility requirements in accordance with an approved pharmacopoeial test for sterility; or (iii) if required by the Act, approved for an equivalent purpose and entered on the Register”*

**Suggested change and reason(s):**

Any standard or requirement must (i) significantly reduce risk, (ii) add value (iii) be enabling. The requirement to “*test for and satisfy sterility requirements in accordance with an approved pharmacopoeial test for sterility*” provides none of these principles in regard to normothermically stored corneas. While the solutions used for normothermic storage are put through a sterilisation process, its purpose is to reduce the likelihood of microbial contamination which would otherwise grow and multiply in a nutrient enriched environment. The corneas placed in storage are not sterile, yet microbial contamination testing during normothermic storage ensures that any clinically significant degree of contamination is detected and the corneas not used for transplant surgery. Therefore it is not necessary to demonstrate sterility at the level required by this standard. *Demonstration* of sterility to the levels required by the TGO 1) adds no value, 2) does not reduce risk, 3) is costly and inefficient (and could reduce the efficacy) of this process.

To ensure the continued viability of normothermic storage of corneas, **solutions used in this process must be excluded from the requirement to demonstrate sterility .**

**Part 12(2)(c)**

*This Part references specific external documents that are likely to be updated with new versions or addition with time. We appreciate the difficulty that TGA Standards have in incorporating external documents and referencing up-to-date revisions/editions of these documents.*

**Therefore, there needs to be a mechanism (policy) on how the most up-to-date and relevant documents can be readily incorporated as required.** This is necessary to ensure that the TGA standards do not lag behind changes in practice, many of which may be changes to address risk reduction as new risks are identified or emerge.

## References

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<sup>1</sup> Hogan RN, Heck E and Cavenagh HD. Risk of prion disease transmission from ocular donor tissue transplantation. *Cornea* 18: 2-11, 1999.

<sup>2</sup> Hirst LW, Pascual C, Madden P, Whitby M, McLaws M-L. Potential Effect of Excluding Variant Creutzfeldt-Jakob Disease on the Eye Donor Pool in Australia. *Cornea* 27: 773-775, 2008.

<sup>3</sup> Chu W. The past twenty five years in Eye Banking. *Cornea* 19: 754-65, 2000.

<sup>4</sup> Eye bank Association of Australia and New Zealand. Medical Standards for Eye Donation and Ocular Tissue Banking. Ed 2. April 2009. <http://www.ebaanz.org>

<sup>5</sup> European Eye Bank Association: c/o Fondazione Banca degli Occhi del Veneto, via Felisati 109, Venezia Mestre 30174, Italy. <http://www.europeaneyebanks.org>



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We recognise and are pleased with the importance that the TGA placed on our comments regarding Draft 1 of these TGO's, and appreciate the willingness to incorporate our suggestions during the framing of the relevant standards. Both of the new drafts demonstrate a significant amount of rework over the previous versions, and the Ocular Standards TGO in particular now approaches that that of a good workable set of Standards for Banked Ocular Tissue.

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The attached comments embodies advice that allows for a workable, rational, and efficient set of standards while still retaining the highest principles of safety and quality that are clinically significant to ocular tissue transplantation. We believe all these comments need to be incorporated into any future documents to ensure that Australia develops a practical and responsible regulatory approach to ocular tissue donation and transplantation.

Yours sincerely,

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## **Therapeutic Goods Order - Standards for banked human ocular tissue.**

**COMMENT AND JOINT SUBMISSION FROM:  
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AUSTRALIAN AND NEW ZEALAND CORNEAL SOCIETY OF  
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### **General Comments**

This Therapeutic Goods Order relates to standards that must embody current, recognised and acceptable best-practice for ocular tissue, and standards that should also be achievable *in practice*. Many of the standards listed within this draft are based on those approved by the Eye Banking Association of Australia and New Zealand (EBAANZ) and verified by its associated Societies and Colleges, and it is gratifying to now see part of these Standards referenced in this document. We believe that this draft now approaches that of a good workable set of Standards for Banked Ocular Tissue.

We do however consider that there are several important issues that still need to be addressed

- The strict application of absolutes to a living biological system
  - There needs to be recognition of the many different variables that will affect decision making in a clinical environment. Greater flexibility is required in regard to some time limits and approaches, as long as it can be demonstrated that the tissue is suitable for transplant for each individual patient case. (this is discussed further in the specific points listed below). In most cases this can be rectified by the use of the work “should” rather than “must”.
- The Standards need to be up-to-date and be directly responsive to a continually changing environment.
  - Currently there is no provision or process to ensure that the Standards are reviewed in a timely manner, yet cGMP would seem to dictate a minimum review cycle. EBAANZ reviews its Standards on at least an Annual basis and also reviews new issues and circumstances as they occur. This ensures that the Standards can 1) address risk reduction as new risks are identified or emerge and, 2) reflect the best practice and efficiencies to improve patient benefit. We consider that this TGA document requires review at least annually.
- *Restating our comments on the First Draft of this document* this second draft also needs to incorporate the elements of the draft ‘Therapeutic Goods Order - Standards for minimising infectious disease transmission’ that would apply to ocular tissue.
  - In attempting to cover all blood and tissues (cadaveric and non-cadaveric) the Infectious Disease Order contains many exemptions and conditions. For clarity, accuracy, workability and responsiveness to a constantly changing operating environment and changing standards, the standards for minimising infectious disease transmission that relate to ocular tissue should be appropriately incorporated into the Therapeutic Goods Order for banked human ocular tissue.

Notwithstanding these comments and suggestions, the following are specific comments and corrections necessary to allow this document to accurately represent those standards that apply to ocular tissue.

## Part 7 General Requirements

### Section (2)

The draft TGO states: *“Collection of ocular tissue from a deceased donor must occur no more than 24 hours after asystole and the time intervals between death, enucleation, preservation and/or corneal excision must be recorded”*

Warm ischaemic damage to the corneal endothelium will occur soon after death and progress as time passes. There are many variables that will impact on the dynamics and significance of this damage such as age of the donor, ambient temperature and the circulatory physiological status of the donor prior to death. The degree of warm ischaemic damage is one factor that determines whether or not the cornea is viable upon retrieval and also whether it will remain viable after a period of storage.

There are two ways in addressing this issue to ensure that quality of the cornea is maintained in a state suitable for transplantation. The first approach is to create a benchmark that is conservative enough to exclude those corneas that may have been subject to significant warm ischaemic damage. This is the approach when functional viability testing of the cornea is not possible, as is the case with hypothermic storage. It is also the approach that this draft standard has taken.

The alternative approach is to not impose time limits on retrieval but to perform viability testing on the cornea. This is the approach used with normothermic corneal storage. Any time limits placed on retrieval in these instances are internal benchmarks used by the Eye Bank to improve efficiency e.g. to go beyond 24 hours means that the discard rate of corneas (once viability tested) will be higher than those under 24 hours. In Europe where normothermic storage of corneas is widespread it is not unusual for Eye Banks to accept eye donation beyond 48 hours and even out to 72 hours. Indeed, in some countries it is *unusual* for eye donation to occur inside of 24 hours<sup>1</sup>.

*Thus: Section (2) needs to be re-written to accommodate this normal, acceptable and safe practice. Replacing the word “must” with “should” provides a good practice standard without imposing unreasonable absolutes. Viability could still be demonstrated if the time was exceeded. Otherwise the European Standard could be incorporated - “It is recommended that corneal preservation occurs as soon as possible after death. All time intervals for each donor (death to enucleation and preservation) shall be recorded”.*

### Section (3)

The draft TGO states: *“Ocular tissue must be stored as follows:.....(a), (b), (c)...”*

This section, like (2) above, relates to maintaining the viability of the cornea during storage for a particular transplant purpose and using a particular storage technique.

The draft standard pre-supposes that these are the only techniques and parameters available or likely to be available within the period of review of the standards. However, other temperatures and time frames are already suitable for Optisol storage (for example) – the manufacturers have published data to show that 48 hours at room temperature provides good storage<sup>2</sup>. Cycles of cooling and warming a hypothermically stored cornea to enable specular microscopy viewing of the endothelium has also been shown to have no adverse effects on

the cornea<sup>3</sup> and could be considered an important element in determining the likely efficacy of the cornea for transplantation. Strict application of the current TGO standard would prohibit this safe practice.

*Thus: Section (3) needs to be altered to ensure that current acceptable, safe, and sometimes necessary practices are not prohibited. In addition, a change is necessary to ensure that the application of future technologies (that may provide greater efficiencies with less risk) is not prevented. Replacing the word “must” with “should” provides a good practice standard without imposing unreasonable restrictions on practice – as long as validity testing showed the practice to be acceptable.*

#### Section (9)

The draft TGO states: *“If terminal sterilisation is performed on the ocular tissue.....”*

This section does not apply to ocular tissue and could be removed. It implies that corneas can remain viable if sterilised. They cannot.

#### Part 8 Examination and evaluation of ocular tissue

##### Section (1)

We appreciate the difficulty that TGA Standards have in incorporating external documents and referencing up-to-date revisions/editions of these documents.

Therefore, there needs to be a mechanism (policy) on how the most up-to-date and relevant documents can be readily incorporated as required. This is necessary to ensure that the TGA standards do not lag behind changes in practice, many of which may be changes to address risk reduction as new risks are identified or emerge.

#### References

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<sup>1</sup> European Eye Bank Association: c/o Fondazione Banca degli Occhi del Veneto, via Felisati 109, Venezia Mestre 30174, Italy. <http://www.europeaneyebanks.org>

<sup>2</sup> Linstrom RL, Kaufman HE, Skelnik DL et.al. Am J Ophthalmol 114:345 (1992)

<sup>3</sup> Oak SS, Laing RA, Chiba HM, Tsubata K. Invest Ophthalmol Vis Sci 30:1585-87 (1989)