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Chair
c/- Lions Eye Donation Service
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RE: Consultation: Proposed medical device classification for human cells, tissues and organs storage solutions and IVF media.

Thank you for the opportunity to provide comment to the Consultation: Proposed medical device classification for human cells, tissues and organs storage solutions and IVF media.

The Eye Bank Association of Australia and New Zealand (EBAANZ) is the peak body for eye donation and eye banking in Australia and New Zealand. Our membership includes world experts on low temperature biology, cryobiology, organ preservation and especially corneal preservation, and corneal donation and transplantation, and thus we are well placed to provide informed expert comment to this Consultation.

Our comments are largely restricted to the new classification for IVF media and medical devices that are substances used for storing human cells, tissues and organs to Class III. We refer particularly to organ and corneal storage (preservation) solutions.

- **We acknowledge the justification for aligning IVF media with the EU MD Class III classification**. The embryo is placed in a culture medium (*nutritive liquid*) and is allowed to **grow** for some days. IVF *culture media* are designed to mimic the composition of oviduct and uterine fluids to closely simulate the natural environment of the **developing** embryo. As such the quality of IVF culture media may have an impact on pre and post-implantation development and possibly the future health of the child. Such impacts and risks appear to justify classification of IVF devices as high-risk.
- **The categorisation of Organ and Corneal Storage (Preservation) solutions with IVF media is not scientifically- or risk-based and it is <u>not</u> appropriate.** The purpose, use, mechanism of action and functionality of organ and corneal preservation solutions markedly differs from those solutions used in IVF. Organ and corneal preservation solutions are primarily designed to support cell volume homeostasis during ischaemia and/or hypothermia. Hypothermia itself is applied to preserve the cells. Any added substrates are designed to secondarily support the reactivation of cell energy production upon transplantation (and subsequent rewarming and oxygenation of the tissue)[1],[2]. *Corneal and organ preservation solutions do not support growth, division, development or expansion of cells. They are not intended to modify the normal biological or chemical composition of the organ, cornea, tissues or cells.* In the context of their use in preservation of organ and corneal viability prior to transplantation **these solutions are low-risk.**

[1] Guibert EE, Petrenko AY, Balaban CL et.al. Organ Preservation: Current Concepts and New Strategies for the Next Decade. *Trans Med Hemother.* 2011: 38(2): 125-142

[2] Pels and Pollock. Storage of donor cornea for penetrating and lamellar transplantation. In Corneal Disease Eds. T Reinhard and F. Larkin. Springer 2013 pp. 91-106.

- **The EU re-categorisation of corneal preservation solutions as Class III is within the context of less regulatory oversight of corneal donation and transplantation than is legislated within Australia.** The TGA already has adequate regulatory oversight of the composition, quality and use of corneal preservation solutions through the cGMP of Blood and Tissue and the ARTG listing of Corneas for transplantation. It does not require additional regulatory requirements.

Impacts and unintended consequences regarding the proposed reclassification of corneal and organ preservation solutions

- **The ability to perform corneal transplants in Australia would be placed at risk**. The supply of corneal preservation media in Australia is already fragile. Only <u>one</u> commercially manufactured solution is available – OptisolGS. It has been on Australian market unaltered since 1991 and was "grandfathered" when TGA regulations were first introduced. There have been no adverse reactions or outcomes related to its use. The Australian market for this solution is small and unprofitable and a reclassification to high-risk, and the increased regulatory requirements and costs involved, would risk this product being withdrawn from the Australian market. *This would **halve** the corneal transplantation rate in Australia.*
- **The entry of normothermic corneal preservation media in the Australian market would be further discouraged.** There are no commercially available normothermic corneal preservation solutions available to Australia. The reasons are two-fold 1). The Australian market is small for the European manufacturers of these solutions and the manufacturers are discouraged by the Australian regulatory environment. 2). Solution viability and necessary transport logistics from Europe to Australia make it an expensive and unprofitable endeavour. Classification of these solutions to "high-risk" would make it even more likely that Australia would be unable to source these solutions now and into the future.
- **Normothermic corneal preservation solutions manufactured "in-house" under TGA cGMP for Blood and Tissues could be placed at risk. This would threaten the viability and sustainability of corneal transplantation in Australia.** More than half of all corneal transplants in Australia are processed through *normothermic preservation solutions.* All are manufactured "in-house" under the TGA cGMP for Blood and Tissues and considered in-process solutions. As such their use is also regulated through product dossiers and ARTG Product listing. These "in-house" solutions are necessarily compounded from components unavailable through ARTG listed products. It is important that any reclassification or amendments to cell, tissue and organ storage (preservation) solutions do not adversely affect the ability of such "in-house" manufacture. Any affect, unintended or otherwise would place at jeopardy more than half of all corneal transplantation in Australia.

Our considered and expert advice is:

- Corneal and organ preservation solutions are low-risk devices.
- Corneal and organ preservation solutions that do not modify the normal biological or chemical composition of the organ, cornea, tissues or cells should not be classified as Class III devices.
- The current approach of the TGA towards corneal and organ preservation solutions should remain unchanged. However, if it is determined that reclassification is required it is more appropriate to place these solutions (devices) in the EU Class I category as they present *less risk* than "non-invasive devices intended for modifying the biological or chemical composition of human tissue or cells….." which are considered Class IIa.

- Regulatory oversight of corneal preservation solutions, their use and their efficacy are already covered under the Biologicals provisions of the TGA, and do not require inappropriate duplication in the devices section.

Thank you for this opportunity and best regards,

Yours sincerely,

Dr Graeme A Pollock OAM
Chair