ERA Comment to TGA consultation on

"Standard for minimising infectious disease transmission via therapeutic goods that are human blood and blood components, human tissues and human cellular therapies."

ERA Consulting (ERA) has a number of comments on the aforementioned standard as follows:

A. Section 4 Interpretation Page 2

ERA suggests the following revision, to change:

*"**allogeneic** means material for administration to an individual that is obtained, or derived, from a genetically different individual" (Underline added)*

to the following:

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

Reason: It is acknowledged that allogeneic means genetically different in the broader scientific arena, but in this context we do not believe it to be the most appropriate usage. Under the draft definition, tissue from one identical twin would not be considered allogeneic. Depending on the circumstances surrounding shared life experiences and exposures, an allogeneic approach to otherwise identical twins might be more consistent with the intended regulatory scheme.

Also, future therapies involving technologies such as therapeutic cloning (allogeneic mitochondria with self-DNA, for example) could blur the line between genetically different and genetically similar material, possibly causing confusion between the allogeneic and autologous designations when such a definition is based on genetic difference.

B. Schedule 2, Policy, (4) Page 9

ERA suggests the following revision, to change:

"The manufacturer must have policies in place for the acceptance and release of each human blood and blood component, human tissue or human cellular therapy product based on the microbial specifications."

to the following:

"The manufacturer must have policies in place for the acceptance and release of each human blood and blood component, human tissue or human cellular therapy product based on the microbial specifications and/or microbial control measures."

Reason: Some tissue/cell therapy products have a relatively short shelf-life and must be released for administration to patients before the results of compendial sterility/bioburden tests are known. Microbial safety for these products is generally assured, on a case-by-case basis, through validated aseptic processing, full results of in-process controls, and rapid microbial/sterility testing methods, as available and appropriate.

An example of such a product is a cell-based therapy, authorised in the USA, where the product is released to the patient before the results of the final sterility test are known.

The change in the draft wording is sought to explicitly acknowledge development of products where it is not possible to use traditional compendial microbial specifications for product release.

C. Schedule 4, (12), page 15

ERA suggests the following revision, to change:

"*Documentation of the tests performed, test modifications, analyses and any anomalies required to be appended to the donor record in addition to the test results.*"

to the following:

"Documentation of the tests performed, test modifications, analyses and any anomalies are required to be appended to the donor record in addition to the test results."

Reason: Clarity.

D. Schedule 5 (2), Page 16

ERA Comment: Repeat donor testing can pose a significant challenge for development of therapies manufactured from donated human tissues, especially in Australia where donors are not paid. Often a tissue must undergo significant manipulation such as dissociation and expansion in culture before it can be stored for significant periods of time. If repeat testing is required then the manufacturer of such a cell therapy faces the significant risk that the donor will not return for the repeat testing, possibly forcing the manufacturer to discard product manufactured from that donation.

In Europe repeat donor testing is not required if NAAT testing for HIV, HBV and HCV is performed on the initial donor sample (Directive 2004/23/EC, AnnexII, (2.6)). Also, repeat donor testing is not required in the USA (Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products, FDA 2007).

The implementation of a requirement for repeat testing would place Australia out of step with Europe and the USA in terms of regulatory stringency on this point. This could possibly lead to Australian patients being denied access to important cell therapies that have been manufactured to fulfil European/USA requirements.

We would propose harmonising the Australian regulation with the European regulations, that is repeat donor testing is not required if the NAAT tests for HIV, HBV and HCV are performed on the initial donor sample, and that the testing otherwise meets the appropriate standards. These standards could be described.