Submission on TGA consultation: Proposed standards for human blood and blood components, human tissues and human cellular therapy products

Organisation: [redacted]

Thank you for providing your comments using the template below.

- Rows may be added or deleted as required. Tables may be left blank or deleted if no comments are to be made on other documents.
- 'Reference' indicates the specific section/ subsection/ paragraph where relevant, e.g. In the infectious disease Order, 8(1)(b) would be used to reference requirements for donor interview timeframe in Part 3, Section 8, Subsection (1), paragraph (b).
- 'Issue' invites a short statement to summarise the comment.
- 'Comments' may include a position including justification or an alternative position.
- Additional general comments are also invited on the impact of these standards, as indicated below each table.

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

[redacted]

Reference	Issue	Comment
4(2) Prion disease, risk of	Countries listed do not include all BSE countries	Countries listed are not all countries with BSE risk
8(2)	Interview	There is no time limit in the USA for when this interview can occur. A 7-day time limit presents an unreasonable and unnecessary burden.
8(4) Table 1	Periods of ineligibility prior to donation do not agree with USA	(c) In the USA it is not possible to accept a donor known to be infected with HBV, even if they are HBsAg negative persons who are demonstrated to be immune. We recommend you remove this exception. (d) In the USA, a donor is ineligible if they have injected any drug for a non-medical reason in the past 5 years. Because of the incubation period associated with diseases transmitted by drug injection, it is not necessary to make donors ineligible if they have done so more than 5 years ago. (e) In the USA, a donor is ineligible if they are a recipient of human derived clotting factors within the past 5 years. Because of the incubation period associated with diseases transmitted by human derived clotting factors, it is not necessary to make donors ineligible if they received them more than 5 years ago. (g) This is no longer a deferral in the USA. It has been determined there is no risk associated with receiving human pituitary derived growth hormone. (m) AATB states persons who are known to have malaria or to be at risk for malaria & FDA does not address malaria

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8(11)	Age requirements	[redacted] has advanced past the arbitrary use of age as an indicator for tissue acceptability. For tissues requiring mechanical strength, for example, tissues from multiple donors are tested after being subjected to [redacted] processing to verify sufficient biomechanical strength is retained. For some tissues in which age may affect its utility (e.g., osteoinductivity of demineralized bone matrix), quality tests are performed with tissue from each donor.
9(8)	Archive samples	It is possible to archive only if a sample is available. Recommend changing the wording to "Dedicate samples... must be archived, if available, at or below minus 25°C..."
11(2)(a)	Tissue collections	The USA requirement is tissue excision shall commence within 24 hours of asystole if refrigerated or cooled (i.e., without specifying a temperature range). Recommend changing the wording to "...provided the body has been refrigerated or cooled within 12 hours of asystole; or"
11(3)	Temperature	AATB refrigerated temperature range is defined as 1-10°C, not 2-8°C. Recommend changing the temperature range to "1°C to 10°C".
11(4)	Validated Temp	Storage conditions ... validated by the manufacturer. Not all tissue banks in the USA will have this information, and most go by the AATB temperature requirements. Differences between temperature ranges listed in product specific Orders and those listed in AATB Standards may preclude import of those tissues from the USA. Recommend changing storage condition temperature ranges in product specific Orders to match those developed by the AATB. The AATB standards have a long history of use in the USA.

What is the perceived impact, if any, of implementing these requirements in your organisation?

[redacted] accredited by the American Association of Tissue Banks (AATB). The American Association of Tissue Banks (AATB) is a professional, non-profit, scientific and educational organization. It is the only national tissue banking organization in the United States, and its membership totals more than 100 accredited tissue banks and 1,000 individual members. These banks recover tissue from more than 30,000 donors and distribute in excess of two million allografts for more than one million tissue transplants performed annually in the U.S. The overwhelming majority of the human tissue distributed for these transplants comes from AATB-accredited tissue banks. AATB issues standards, and inspects tissue banks for compliance with these standards.

Differences between the TGA Orders and AATB standards may preclude distribution of tissue originating in the USA from being distributed to Australia. To avoid an unnecessary shortage of tissue available in Australia, we strongly recommend TGA consider harmonizing the Orders with AATB standards.

Standards for human musculoskeletal tissue

[redacted]

Reference	Issue	Comment
7(2)(a)	Maintaining tissue at or below 8° C prior to and during shipment.	We currently require tissue to be shipped at 10° C or below in accordance with the State of New York regulation (section 52-5.5(c)) and AATB standards (12th Edition, section D5.800). Tissue shipped at 10°C or below prior to and during shipment is safe; tissue does not need to be maintained at or below 8°C prior to and during shipment.
7(4)	Bioburden reduction	This requirement appears to presume that it is not possible (under the constraints of minimal manipulation) to develop and validate a bioburden reduction process to eliminate microorganisms of clinical significance. [redacted] is a chemical flushing and washing process that was developed to render allograft tissue sterile,[1] and [redacted] is validated to sterilize tissue.[2] Because the objective of a bioburden reduction process is to reduce or eliminate microorganisms of clinical significance, the Standard should allow for the possibility of validating a bioburden reduction process to reproducibly reduce or eliminate microorganisms of clinical significance. With a validated sterilization process, the need for sampling for bioburden determination *after* the bioburden reduction process is eliminated. In this scenario, the requirement to sample musculoskeletal tissue for bioburden determination (as required in 7(2)(b)) is sufficient to screen incoming tissue bioburden to detect the presence of microorganisms which fall outside the validated sterilization process.

1 [redacted]

2 [redacted]

7(8)(b)	Storage conditions	"frozen and cryopreserved at less than minus 40°C for no more than 5 years" Cryopreservation of musculoskeletal tissue for storage at less that minus 40°C is not necessary. Although "cryopreserved" is not defined in this Order, it is defined in the "Standards for minimising infectious disease transmission..." as "suspended in a validated medium containing a suitable cryoprotectant and cooled according to a validated method that allows maintenance for long periods." Because cellular viability is not necessary for safe and effective use of transplanted musculoskeletal tissue, it can be stored without a cryoprotectant at less than minus 40°C for up to 5 years. [redacted] and other AATB-accredited tissue banks have a long history of distribution of musculoskeletal tissue which has been frozen at less than minus 40°C without a cryoprotectant with a shelf life of 5 years. For this reason, AATB standards indicate that "Processed frozen or Cryopreserved musculoskeletal tissues shall be stored at temperatures of – 40°C or colder." Recommendation: modify the text of 7(8)(b) to read "frozen ~~and~~ or cryopreserved at less than minus 40°C for no more than 5 years"
7(8)(d)	Storage temperatures must be maintained during transport.	Some tissues processed by [redacted] are stored at room temperature (e.g., following lyophilization). Tissues labelled for storage at ambient temperatures may experience higher or lower temperatures during transport. [redacted] experience is that tissues stored at room temperature are not harmed by the temporary increases or decreases associated with transport.

What is the perceived impact, if any, of implementing these requirements in your organisation?

Section 6.1(c) describes musculoskeletal tissue that has been freeze dried or demineralised as altered beyond minimally manipulated tissue, and therefore exempted from this standard. As a result, many of [redacted] products will most likely not be made available for distribution to Australia due to the regulatory submission burden associated with Class 4 registrations. Furthermore, a Class 4 designation for freeze dried or

demineralised musculoskeletal tissue may prevent other U.S. tissue banks from pursuing registration in Australia. Lastly, the FDA definition of "minimally manipulated" is not consistent with the TGA definition.

Standards for human ocular tissue

[redacted]

What is the perceived impact, if any, of implementing these requirements in your organisation?

It is not clear from section 6.1(c) whether ocular tissue that has been dehydrated is considered to be altered beyond minimally manipulated, and therefore exempted from this standard. [redacted] processes ocular tissue using the proprietary [redacted] process, and has a history of safe use of this tissue. If, however, dehydration of ocular tissue is considered as processing beyond minimal manipulation, many of [redacted] products will most likely not be made available for distribution to Australia due to the regulatory submission burden associated with Class 4 registrations. Furthermore, a Class 4 designation for dehydrated tissue may prevent other U.S. tissue banks from pursuing registration in Australia. Lastly, the FDA definition of "minimally manipulated" is not consistent with the TGA definition.

Standards for human skin

[redacted]

Reference	Issue	Comment
7(2)(a)	Maintaining tissue at or below 8° C prior to and during shipment.	We currently require tissue to be shipped at 10° C or below in accordance with the State of New York regulation (section 52-5.5(c)) and AATB standards (12th Edition, section D5.800). Tissue shipped at 10°C or below prior to and during shipment is safe; tissue does not need to be maintained at or below 8°C prior to and during shipment.
7(10)(d)	Storage temperatures must be maintained during transport.	Some tissues processed by [redacted] are stored at room temperature (e.g., following lyophilization). Tissues labelled for storage at ambient temperatures may experience higher or lower temperatures during transport. [redacted] experience is that tissues stored at room temperature are not harmed by the temporary increases or decreases associated with transport.

What is the perceived impact, if any, of implementing these requirements in your organisation?

It is not clear from section 6.1(c) whether dermis that has been dehydrated is considered to be altered beyond minimally manipulated, and therefore exempted from this standard. [redacted] processes dermis using the proprietary [redacted] process, and has a history of safe use of this tissue. If, however, dehydration of dermis is considered as processing beyond minimal manipulation, [redacted] dermis tissue will most likely not be made available for distribution to Australia due to the regulatory submission burden associated with Class 4 registrations. Furthermore, a Class 4 designation for dehydrated tissue may prevent other U.S. tissue banks from pursuing registration in Australia. Lastly, the FDA definition of "minimally manipulated" is not consistent with the TGA definition.