Draft AUSTRALIAN CODE OF GOOD MANUFACTURING PRACTICE HUMAN BLOOD AND BLOOD COMPONENTS, HUMAN TISSUES AND HUMAN CELLULAR THERAPIES

PAGE	CLAUSE	COMMENTS
2	Product Standards	*"Manufacturers will be required to develop Technical Standards Files for product groups to demonstrate Standards are met."* Product Standards templates that are specifically for each class of tissues and cells is required instead of the blood template.
2	103	*Management should define objectives pertaining to the quality, safety, efficacy, and applicable regulatory and legal requirements. Procedures should be available to detail how these objectives are to be met.* Having to demonstrate efficacy is a concern if TGA will require this to be similar to that for a pharmaceutical. As achieving and maintaining quality, safety, efficacy and regulatory and legal requirements are the fundamental reasons for all of a bank's procedures why make a statement requiring procedures for meeting objectives? Suggest deleting.
5	104	Reference to meeting the requirements of Good Laboratory Practice leaves the door open for us having to process to medicinal standards where it may not be relevant. Suggest replacing "Therapeutic products" with "human blood products, tissues and cellular therapies" and either quoting the relevant sections of GLP or preferably state the actual requirements for each product class. This would sit better within the relevant Standard for each tissue type.
6	104 5th •	*Quality Assurance should ensure that "ALL necessary controls on intermediate products, and any other in-process controls & validations are carried out"* Who defines 'all' and 'necessary"; need a definition for 'intermediate products'. Doesn't "in process controls and validations are carried out' cover the intent of this point?
7	113	*Regular periodic quality reviews of all products should be conducted with the objective of verifying the consistency of processes and the appropriateness of current specifications for both starting material and finished product.* Does 'starting materials' mean tissues? Clear distinction is required between 'starting material', 'material' 'product' and 'tissues'.
7	113 6th •	Is this need for stability data only for freeze dried or material that has undergone higher levels of processing?
7	113 8th •	*A review of adequacy of any other previous product, process or equipment corrective actions* How far back into the past is intended for these reviews? Suggest deleting.
7	115	This clause precisely covers clauses 108, 112, 113, etc and can replace them if the references to management are removed and "The records of these reviews should be reported to management" is added.

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10	207	*The Quality nominee generally has the following responsibilities:* • *to approve or reject, as appropriate, materials and therapeutic products;* IF "approve or reject, as appropriate, materials and therapeutic products" relates to release of product, then both the Quality nominee and the Production nominee should share responsibility for this activity. This statement needs to be clarified to minimise the potential for misinterpretation. *Quality nominee is responsible for ensuring maintenance of the quality department premises.* 'Premises' may not be the appropriate term, depending on definition. Is this referring to QC lab rather than the QA office? I suggest replacing with *"…of the Quality Control facility and equipment".*
10	209	Why say Quality Control instead of Quality?
12& 13	300 & 306	Definition of what constitutes 'premises' as opposed to 'facility' is required as many banks are sited within a hospital or similar. If 'premises' encompasses the whole building then formal qualification may not be relevant or achievable. Suggest replacing premises with facility.
14	305	*Storage areas ……monitored environmental conditions (eg temperature, light, humidity).* To avoid implementing expensive monitoring procedures & equipment for conditions that are not required by the materials' manufacturers I suggest replacing *'under monitored environmental conditions*' with a new sentence *'For critical materials, records should demonstrate that manufacturer stipulated storage conditions are being met.'* (e.g. *temperature, light, humidity).*
13	307	As this section is about the production facility, can it be assumed that this refers to donor interviews that are only conducted at the bank? Does this only refer to in-person interviews or are phone conversations with donors included?
14	314	*Storage areas should provide adequate space, suitable lighting, and be arranged and equipped to allow dry, clean and orderly placement of stored material under monitored environmental conditions (eg temperature, light, humidity)* Who determines "adequate space" and "suitable lighting"? Who decides what environmental conditions are required and hence controlled? When the manufacturer does not identify any temperature, light and humidity requirements and the bank likewise, then this clause still requires these to be monitored. Suggest adding 'as required' to this clause.

PAGE	CLAUSE	COMMENTS
14	315 and 317	*317 Storage facilities should be secured to ensure that quarantined or released product cannot be tampered with or removed by unauthorised persons. Product storage facilities should not be used for any other purpose.* In this clause, is 'storage facilities' synonymous with storage equipment? If it is not and means the room or building then the last sentence should be deleted. Suggest combining with 315 and deleting second sentence of 317. As long as the storage facility (i.e. not equipment) is properly controlled and segregated, there is no reason why it can't be used for other purposes e.g. storage of materials. Suggest "Storage areas/facilities should provide for suitable and effective segregation of quarantined, rejected and released material, and should be secured to ensure that quarantined or released product cannot be tampered with or removed by unauthorised persons".
15	325	Rephrase: Defective equipment should be labelled as defective and removed from the processing area, if possible.
15	327	Delete. Part of Australian Std – does not need to be in Code.
15	328 2nd •	Dot point 2 is appropriate only for fixed site equipment (eg. fridges; freezers), not during transport. This should be stipulated. Suggest "for fixed site equipment (eg. fridges; freezers) there should be an alarm to indicate when a temperature control system has failed. The system should permit resetting only by authorised personnel, and should be checked at regular defined intervals.
15	330	Why would the expiry date of cleaning agents be written into cleaning procedures? For all materials the requirement should be that expiry dates are written on the items and procedures or policy require that expired materials not be used and be disposed of. If this is meant for cleaning agents that are made up by the bank and the cleaning procedure does not require disposal of cleaning solutions at the completion of cleaning, then this needs to be clarified. Suggest replacing "premises" with "facilities and replacing the final point with 'Document dilution to be used and length of use once diluted'.
17	336	Delete "premises".
18	411, 412, 413	Shouldn't these be under Section 10 'Computers' or are they not in section 10 because section 10 is not intended for this use of computers?

PAGE	CLAUSE	COMMENTS
19, 20	503, 504, 510	Define “assessed”. If a “critical” material/solution is supplied by an approved supplier who fulfils the QC specifications listed in 503, and conducts the testing requirements listed in Schedule 6, page 19 of the Infectious Diseases TGO (Selection & evaluation of critical materials), and provides documentation of all assessment outcomes, then the manufacturer should not have to physically re-assess the material “to ensure they meet approved specifications”. The incoming material/solution should be quarantined until it and the documentation is checked against required specifications. The reason for using an “approved”, GMP-licensed supplier is to ensure that the required QC and screening tests have already been conducted on the material/solution in accordance with regulatory requirements prior to its use by the manufacturer. Where all of these are met, the potential for the material to adversely effect the quality of the product if it is not re-assessed by the manufacturer should be an acceptable risk.
20	512	Section 5 is about materials. Due to previous misunderstandings regarding when requirements for materials do or do not apply to product and vice versa, the inclusion of 512 in this section will suggest that ‘materials’ can also be read as ‘products’ in the preceding sections. 512 would fit much better in section 9 *Product Release*. Refer to comment for clause page 30 Product Release. By using the term *Quality Control Department* it is assumed that all banks have such a department. As many do not, I suggest deleting *by the Quality Control Department.* Critical assessment of products returned from the customer should be able to be done by any authorised staff and against a written procedure with QA approval.
21	Section 6	Are subcontractors the same as contractors? This needs to be very clearly defined in the Glossary.
22	Section 7	Hazard Alerts should be identified in this section. For tissue allografts hazard alerts are far more likely to be required than recalls. This aspect of the tissue banking industry has been ignored for too long by TGA. Accurate and appropriate addressing by TGA is required.
23	801 & 802	These statements are unnecessary as they are covered in Section 2 (Personnel & Training; 210 & 212), Section 4 (Documentation; 401) and Tissue Specific Standards. Why are *materials* included here when section 5 is about materials and these requirements are stated there?

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23	806	*For Tissue Collections, there should be a documented procedure for defining the medical assessment requirements for live and deceased donors, including the acceptable timeframe for assessment, if not able to be done on the day of donation. For a live donor, the donor selection records, including consent and medical history, signed by the donor should be witnessed and signed by an authorised person.* Should read: "documented procedure that defines the medical assessment requirements for live and deceased donors etc. For a live donor, the donor selection records, including consent and medical history, signed by the donor should be witnessed and signed by an authorised person. Donor selection records usually contain more information than that provided by the donor. Screening test results are part of these records and these are always obtained post donation. "Medical history" does mean the doctor's medical history records and donors' do not sign these. This should be reworded as follows; *For a live donor, the donor consent and medical and social history* ***documentation*** *that has been collected from the donor, should be signed by the donor and witnessed and signed by an authorised person.*
24	807	This needs re-wording as follows; 'For a deceased tissue donor, there should be a statement signifying that medical records have been assessed and the donor has been found acceptable, by a nominated authorised person.'
25	819	*819. Collection documentation records should include:* • *The donor identity* • *The date, time and place of the procedure* • *The identity of the person(s) performing the procurement* • *For Cellular Therapies; the Cells retrieved, Donor and cell selection information* • *For Tissues; The tissue(s) retrieved, Donor and Tissue selection information, Details of the physical examination of the donor prior to collection* *Collection documentation records* – why say *documentation?* In the last dot point (*Donor and Tissue selection information) Tissue* is not relevant and should be omitted. *Details of the physical examination* is not relevant to live donors, only cadaveric donors. Suggest "*For Tissues; The tissue(s) retrieved, Donor selection information. For cadaveric donors, details of the physical examination of the donor prior to collection should also be recorded"*.
26	827	"Work in process" needs to be defined.
28	900	Need to define and state requirements for exceptional release. Who has the responsibility / authority –treating physician accepting product?
28	903	We have not been able to identify this requirement in the Act or the Regulations. Suggest quoting the applicable reference.

PAGE	CLAUSE	COMMENTS
29	906, 907, 909 & 910	These all sound like we are responsible for ensuring that labs meet their TGA license requirements. Since TGA require us to use TGA licensed labs, surely then it is TGA's responsibility to ensure that TGA licensed labs operate to their TGA licence requirements. The Infectious Disease Transmission Standard clauses 6,7,8,9,10,12 similarly require banks to ensure labs meet TGA license requirements. Is 909 about banks auditing their testing laboratories? If it is then this is covered in 601, (assuming TGA mean subcontracted to = contracting).
29	912	The Infectious Disease Transmission Standard clause 10 specifies serum archiving requirements and does not allow the risk assessment that this clause does. However if this clause is about more than serology samples, then it needs to say so e.g. define 'donor test samples'.
30	915	It may be that because of the typos, the intent is not clear. Clause 914 specifies meeting documented, defined and regulatory requirements for release. Where a product does not meet release criteria and is failed clauses 105 and 107 specify the required actions. This clause could have relevance for releasing product that does not meet all specified release criteria.
30	Product release	This section is meant to be about releasing product, but most of the requirements are about products not being suitable for release. Clauses 916 and 918 are about products that cannot be released and are in fact failed and disposed of. A separate section titled Non-conforming Product or Product Failure would be more appropriate
31	1000	*Where a computerised system is implemented* should be expanded to identify the purpose or function of the computerised system. Why would this section be applicable to a computerised system that has nothing to do with product quality and safety or data security and integrity? Clause 1001 is an appropriate definition for the computer systems to which this section should apply. Refer comments for clauses 411,412,413.
Page 34	Glossary	Many definitions need to be added as indicated. Materials Starting materials – should not include tissues / donations At PBTB we use the following to distinguish between different stages for tissues from donation to release. Hence the following; Tissue : The items that make up the donation e.g. femoral head, humerus, Achilles tendon etc; tissues are processed into allografts (synonymous with product) Product: Processed tissues and released tissues (may or may not have been processed); products are distributed and implanted. premises facility