THERAPEUTIC GOODS ORDER NO. XX - *Standards for minimising infectious disease transmission via therapeutic goods that are human blood and blood components, human tissues and human cellular therapies*	
Reviewer: CTTWA (RPH-Heart Valve Bank & Cellular Therapies)	Date 09/02/2010

Clause Ref.	Page Ref.	Comment
4. Interpretation	Page 2	***allogeneic*** means material for administration to an individual that is obtained, or derived, from a genetically different individual; Does not include provisions for identical twin, **Recommend wording:** derived "from an individual other than the recipient"
4. Interpretation	Page 3	***banked*** means maintenance, under appropriate controlled conditions, in an inventory, of a finished product that has been determined suitable for supply; Current wording does not include cells/tissues "banked" prior to release. **Recommend wording:** "in an inventory, of any tissue/cellular in-process material through to a finished product that has been determined suitable for supply".
Interpretation	Page 3	***bioburden*** means the quantity and characteristics of microorganisms present in the goods or to which the goods may be exposed in a manufacturing environment; **Clarification/ definition** "goods". Does this refer to product or materials or both?
4. Interpretation	Page 3	***donor*** means every source, whether living or deceased, of blood, cells or tissues; Should clarify that the source is "human". **Recommend wording:** means every "human" source…
Interpretation	Page 4	***physical examination*** means a clinical based inspection of a living or deceased potential donor to determine suitability of the person to be a donor and includes at minimum the relevance of any abrasion/laceration, bruise/haematoma, fracture, tattoo, piercing, scars, skin lesion, surgical incision or other distinguishing external feature that may be indicative of a behaviour, lifestyle or disease. **Clarification/ definition:** This definition is too prescriptive and difficult to achieve for live donors (eg. blood donors; femoral head donors etc..). Minimum requirements should apply only to deceased potential donors. **Recommend wording: *physical examination*** means a clinical based inspection of a living or deceased potential donor to determine suitability of the person to be a donor, and for cadaveric donors should include at a minimum….. ……
4. Interpretation	Page 4	***tissue*** means all constituent parts of the body formed by cells. should state exclusion of organs, hair, nails etc as these are also defined as tissue under this order. **Recommend wording:** …formed by cells "excluding organs, hair, nails etc.."
6. Exemptions	Page 5	Human blood and blood components, human tissues and human cellular therapies exempt from the requirements of this Order: (1) vascularised organs and associated tissue for direct organ transplant Need to cover autologous tissue used in the same procedure eg osteochondral grafts. **Recommend wording:** vascularised organs and associated tissue for direct organ/tissue transplant

Schedule 2 (1a)	Page 9	The manufacturer must have the following policies in place. (1) The manufacturer must demonstrate that steps are taken to mitigate the risk of infectious disease transmission either during collection, manufacture or via the finished product. The policy (or policies) must address the process for selection of suitable donors and include: (a) eligibility requirements for donors who have resided/travelled outside Australia; and **Clarification/definition:** "Policy" vs "Procedure". (a) how does this apply to autologous donors? 1(a) should be an exclusion for autologous donors in Table 1 in addition to 1(b). **Recommend inclusion:** Policy/procedure for "exceptional release".
Schedule 2 (4)	Page 9	(4). 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. **Recommend inclusion:** Policy/procedure for "exceptional release"
Schedule 3 (3)	Page 10	(3) An interview, where possible, with the next-of-kin/guardian of a deceased donor and/or examination of the medical record to obtain and document the medical and social history of the donor must take place and be documented at the time of, or no more than 7 days prior to the donation. Typographical error – an interview or examination of records etc.. 7 days prior to the donation is not feasible for a deceased donor. **Recommend wording**: and be documented at the time of, or no more than 7 days after the donation.
Schedule 3 – Table 2 (c)	Page 11	(c) Needle stick injury, or contact of non-intact skin or mucous membrane with blood or body fluid – period of ineligibility – 6 months where the injury or contact is thought to be at high risk … Why is a needle stick injury considered to be potentially safer than a tattoo or body piercing? The period of ineligibility for allogeneic donors should be 6 months without exception. **Recommend deletion:** where the injury or contact is thought to be at high risk
Schedule 3 – Table 2 (d-g)	Page 11	(d) Inmate of a prison 12 months from date of release (e) Sex worker, or received money for sex 12 months from last contact (f) Male to male sexual relationship 12 months from last contact (g) A sexual relationship with a person known to 12 months from last contact The ineligibility period for allogeneic use should be standardised to 6 months which covers the window period for all mandatory infectious agents. 12 months is listed for these donor groups only because this is the exclusion period required by law in NSW. **Recommend wording:** 6 months from date of release/last contact unless applicable State or Territory law states otherwise.
Schedule 3 – Table 2 (s)	Page 12	(s) Being a recipient of allogeneic organ(s), or cells, or deceased donor tissue allograft. The risk from a tissue allograft would be the same if the donor was deceased or living. Permanent exclusion for allogeneic cell or tissue donors seems somewhat extreme given the screening requirements for these donors. **Recommend wording:** "Being a recipient of allogeneic organs(s), tissue(s) or cells. Ineligibility period for allogeneic organs: permanent Ineligibility period for allogeneic cells or tissue: 10 years
Schedule 3 (5a) Table 3. title	Page 12	(5) A potential donor of allogeneic tissues or cells who received (a) live vaccine is ineligible to donate tissues if… **Table 3: Ineligibility period for potential tissue donors who have received a live vaccine** Statement (5) covers tissues & cells, but (a) and Table 3 identifies only potential **tissue** donors – does this mean that these donors can donate

		cells? **Recommend wording:** (a) …. Live vaccine is ineligible to donate tissues or cells if…. Table 3: Ineligibility period for potential tissue or cell donors who have received….
Schedule 4 – (3)	Page 14	(3). Blood sampling of a deceased donor must take place prior to cell or tissue collection and no later than 24 hours after death, if a pre-mortem blood sample is not available. This suggests that a pre-mortem blood sample (regardless of when it was collected) has to be used if it is available which has the potential to delay testing if the post-mortem sample is suitable. **Recommend wording:** "Blood sampling of a deceased donor must take place prior to cell or tissue collection and no later than 24 hours after death. A pre-mortem blood sample collected up to seven (7) days prior to donation may be used if available.
Schedule 4 – (6a)	Page 14	(6). The test kits/methodologies used for the mandatory tests for screening must (a) be current technology; and Sometimes "current" technology is not the most appropriate (eg. NAT vs 180 day retesting). **Recommend wording:** (a) "be the most appropriate technology /methodology" for the sample being tested.
Schedule 6 – (6, 7 & 8)	Page 14 & 15	(6) The test kits/methodologies used for the mandatory tests for screening must (b) have regulatory approval for the intended use; and (c) be used in accordance with the approved methodology (i.e. in accordance with the test kit instructions); and (d) be validated for the purpose for which it is to be used. In the case of any changes to test methodology, these must also be formally validated and documented. (7) The test kits used in evaluation of donor samples must be documented. (8) Screening and confirmatory microbiological and virological tests must be performed in laboratories using appropriately validated testing techniques as regulatory requirements specify. Manufacturers should only be required to ensure the test kits/methodologies used for the mandatory tests for screening and confirmatory testing have regulatory approval for the intended used (a). They should not be required to ensure these laboratories meet the requirements of their license (6 c & d; 7 & 8). That is the responsibility of the licensing body. If the licensing body does not approve of the testing being conducted, the deficiency should be applied to the testing laboratory to address, not the manufacturer. **Recommend wording:** (6) The test kits/methodologies used for the mandatory screening and confirmatory microbiological and virological tests must: (a) be the most appropriate technology/methodology for the sample being tested; and (b) have regulatory approval for the intended use. (7) The test kits used in evaluation of donor samples must be documented in procedures and/or the service agreement with the contracted testing laboratory. (8) Delete
Schedule 4 – (9 & 10)	Page 15	(9) Samples of donor serum/plasma must be archived under optimal conditions to ensure sample availability for retesting or additional testing up to, at minimum, the time of transfusion or implantation of human blood and blood components, human tissues or human cellular therapies. (10) Dedicated samples of the serum from deceased or living donors taken at time of donation, and also the samples taken from live donors at 180 days post-donation, must be archived at or below minus 25°C unless the conditions of archive are validated at a different temperature (or as recommended by the test kit manufacturers) for the period from sample collection to a minimum of 2 years after the expiry date of the human blood and blood components, human tissues or

		human cellular therapies. These two clauses seem to be saying the same thing but have potentially conflicting time frames (eg. time of transfusion or implantation vs 2 years after the expiry date). **Recommend deletion** clause (9) and **Recommend wording** clause (10): Dedicated samples of the serum from deceased or living donors taken at time of donation, and also the samples taken from live donors at 180 days post-donation, must be archived at or below minus 25°C (unless the conditions of archive are validated at a different temperature or as recommended by the test kit manufacturers) to ensure sample availability for retesting or additional testing up to, at minimum, 2 years after the expiry date of the human blood and blood components, human tissues or human cellular therapies. In the previous Code, archive or retention samples had to be stored at -15°C or below (839) – the requirement is now -25°C. Does this mean that all samples currently archived at the higher temperature are no longer valid?
Schedule 4 (11)	Page 15	(11) Where screening protocols change during the life of a product in storage, where possible and practicable the donor's archived serum/plasma must be retested. The statement "and practicable" is open to broad interpretation. and requires clarification. **Recommend wording:** "Where screening protocols change during the life of a product in storage, where possible and practicable, as determined by the manufacturer based on risk, the donor's archived serum/plasma must be retested.
Schedule 5 (1)	Page 16	(1) Each donor of human blood and blood components, human tissues or human cellular therapies must be tested and examined for evidence of infectious diseases in accordance with the relevant and applicable donor groups. Assessment of donor blood samples and the physical examination of the donor are key determinants of donor acceptability or rejection. Donors of human blood and blood components, human tissues and human cellular therapies must be evaluated as follows: The minimum requirements for a physical examination as defined in the draft is only appropriate for deceased donors . **Recommend wording**: Assessment of donor blood samples and the clinical based inspection of donors are key determinants of donor acceptance or rejection.
Schedule 5 (1c)	Page 16	(c) A physical examination must be conducted by a competent person to ascertain the suitability of a donor to donate cells or tissues and must take place, **Recommend wording**: A clinical based inspection of the donor must be conducted by a competent person to ascertain… **Clarification/ definition:** "competent person".
Schedule 5 (5)	Page 17	(5) For blood and blood components, human tissues and human cellular therapies required to be manufactured in a facility with an approved quality system, the bioburden of the cell or tissue specimens must be determined and the results recorded. Specifications for the human blood and blood components, human tissues or human cellular therapy must be in accordance with (a) those set in the respective product specific Orders, or (b) those set based on established and clinically acceptable numbers and types of organisms for the indication of use and should include (i) a limit for Total Viable Count (aerobic and anaerobic microorganisms); and (ii) absence of specified microorganisms of clinical significance. Bioburden as the "quantity and characteristics of microorganisms present in the goods or to which the goods may be exposed in a manufacturing environment". This clause needs to allow for bioburden testing systems where results are recorded as "growth/no growth" rather than a number or cell count (i.e. quantity). **Recommend wording:** (b) those set based on "growth/no growth" outcomes or established and clinically acceptable numbers and

		types of organisms for the indication of use and should include (i) a limit for growth/no growth outcomes (eg. subculturing of positive cultures) (ii) a limit for Total Viable Count (aerobic and anaerobic microorganisms); and (iii) absence of specified microorganisms of clinical significance.
Table 4.	Page 18	Donor Testing Requirements: Living Donors – Allogeneic Use Do the requirements for plasma equate to serum? **Inclusion:** Plasma/serum Living Donors – Autologous Use Autologous plasma/serum products are not included in this section of the Table. **Inclusion**: Plasma/serum
Schedule 6 (1 & 2)	Page 19	(1) Critical materials employed in the processing of human blood, blood components, human tissues or human cellular therapies must be selected and evaluated to ensure they are not contaminated with or likely to introduce pathogenic bacteria or other infectious agents to the human blood, blood components, human tissues or cellular therapy. (2) For products which must be manufactured in a facility with an approved quality system: (a) solutions must be (i) manufactured under an approved quality management systems and be supplied as a sterile solution OR (ii) tested for & 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 ARTG **Identification:** Relevant Section of the Act to which (iii) applies. **Clarification: .** Requirement for critical solutions (i.e. those coming into direct contact with the product) to be listed or registered on the ARTG. 2(b) materials must have been sourced, tested & assessed as presenting minimal risk of transmitting infectious disease agents. IF the *product* is not required to be on the ARTG, the recorded information must include at a minimum: (iv) screening tests performed (v) QC specifications (vi) Storage conditions The term “product” needs to be replaced by “materials”. **Clarification:** Requirement for critical materials (i.e. those coming into direct contact with the product) to be listed or registered on the ARTG.