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

SUBMITTING ORGANISATION: Australian Red Cross Blood Service

Reference	Issue	Comment
Pg 3	Definitions: Distinction between blood products and blood components.	Definition of "Blood Products" (referred to in Table 1) should be included, specifically to distinguish the difference between "Blood", "Blood Components" and "Blood Products". The definition of "blood component" includes "plasma for fractionation" and could theoretically include plasma derivatives, however the reference to "blood products" in Table 1 confuses the definition. The best solution is to include "blood product" as a specific term for plasma derivatives.
Pg 4, (c)	Prion disease, risk of	The wording for risk of iatrogenic transmissible spongiform encephalopathies differs slightly from the current wording in Therapeutic Goods Order 81 (TGO81), which refers to "blood and blood **products**". The new wording refers to "blood and blood **components**", which according to the definition on page 3 would exclude fractionated products. It is the view of the Blood Service, on the basis of the evidence available to us that fractionated product should be included in the iatrogenic risk statement, as per TGO81, but that this restriction should be limited to processed plasma products provided prior to 31 December 2001. The 31 December 2001 date limitation takes into account the change in practices whereby UK plasma ceased to be used for fractionation, and all potentially affected product would have expired. The following revision to the wording is requested: *Iatrogenic, which includes donors who received a blood transfusion or blood products in or from England, Wales, Scotland, Northern Ireland, the Channel Islands, the Isle of Man and the Falkland Islands from 1 January 1980 onwards, unless the only blood products received were processed plasma products and they were given after 31 December 2001.*

		Also refer previous comment regarding the need for a definition of "blood products" ***Impact:*** If suggested wording not adopted there is potential for an increase in risk of transfusion transmitted infection (based on the evidence currently available to the Blood Service). The impact of this requirement depends on the clarification of the definitions of blood components/products" (refer previous comment above). The definition of "blood component" includes "plasma for fractionation" and could theoretically include plasma derivatives, however the reference to "blood products" in Table 1 confuses the definition.
Pg 6, 8. (b)	Requirements in relation to the medical and social history of prospective donors**.**	Although it is noted that the requirements in the order are minimum standards and that more stringent requirements may be applied, the Blood Service does not believe it is appropriate to interview prospective blood donors 7 days prior to, or 30 days post collection, as risk may have been incurred in the intervening period.
Pg 7, Part 3 **8. (4) (a)** **Table 1:**	Minimum medical and social criteria required to determine donor risk of exposure to infections disease and ineligibility period.	The period of ineligibility prior to donation outlined in Table 1 does not apply to autologous donors. The Blood Service has commented previously that acceptance of autologous blood donors without the donor ineligibility periods that apply to homologous blood donors could potentially introduce risk to the Blood Service where both autologous and homologous donations are collected and processed. The inclusion of the requirements for adequate segregation of autologous units is however noted as a positive improvement to the document. The current Blood Service eligibility criteria for autologous donations are more stringent than those proposed in the new standard. ***Impact :*** • If autologous donors are permitted to donate without the donor eligibility periods applicable for homologous donors, there will be increased risk to staff required to handle these positive or potentially positive units. • Impact on improving the quarantine and storage facilities for such units (if collected).

		Increased risk to the blood supply by having positive units released for autologous transfusion – potential for mix ups during shipment, or at hospitals. • Potential risk of autologous donor backlash if deferred on basis of more stringent Blood Service criteria.
Pg 8, Table 1 (d)	Injection of drug for non-medical reasons	Request revision of the wording as it is currently restricted only to injection of drugs by the donor, and would not identify a donor who had been injected by another individual. The following wording (from the current approved Donor Declaration applicable to all blood donors) is suggested: *Ever "used drugs" by injection or been injected, **even once**, with drugs not prescribed by a doctor or dentist"*
Pg 8, Table 1 (e)	Recipient of human derived clotting factors	Recipients of human derived clotting factors that are not in accordance with the Order are permanently ineligible. Recipients of clotting factors that conform to the requirements would therefore be considered eligible. **Impact :** Difficulty in distinguishing the difference between eligible and ineligible products (would be date dependent and would be reliant upon donor memory). Potential for confusion in donor assessment.
Pg 8, Table 1 (g)	Recipient of human pituitary derived growth hormone	The permanent ineligibility status for recipients of human pituitary derived growth hormone should be limited to receipt of the hormone prior to 1986 (as practices changed post this date to mitigate the risk)
Pg 8, Table 1 (i)	Recipient of allogeneic blood, blood components or blood products	Recipients of allogeneic blood, blood components or **blood products** that are not in accordance with the Order are ineligible for 12 months. Issue 1: Definition of "blood products" is required in this context of a 12 month ineligibility period because the assumption is that "blood products" are plasma derivatives (as blood and blood components are listed separately). However, recipients of blood products (eg clotting factor) would also be subject to category (e) of Table 1, which requires permanently ineligibility.

		Issue 2: Recipients of blood, blood components or blood products that conform to the requirements of the Order would therefore be considered eligible immediately. The Blood Service currently applies an ineligibility period to these donors ***Impact:*** • Difficulty in distinguishing the difference between eligible and ineligible products and potential for confusion in donor assessment. • Potential for increased risk profile of blood components than that in place currently
Pg 8, Table 1 (m)	A donor who has lived in a malarial area within the first five years of life	Donors who have lived in a malarial area within the first 5 years of life are ineligible for 3 years from last visit, or 4 months if malarial testing is negative. Plasma collected from such individuals should be considered suitable as plasma for fractionation, yet this requirement is not included in the exemptions for plasma for fractionation listed on Page 8 (5). It is requested that section (m) is added to the list of exemptions recorded on page 8 in PART 3 – Specific requirements, 8. (5). The stated ineligibility period for donors living in malarial areas is inconsistent with the malaria strategy previously agreed with TGA and inconsistent with the requirements contained in the currently mandated COE 14th edition. The TGA and Blood Service made a joint submission to the Council of Europe to change the malaria deferral strategy several years ago. The submission was successful and the revised wording from that submission appears on page 68 of the 14th edition. The revised strategy was subsequently implemented, on approval by TGA, into Blood Service practice. This strategy requires that donors who have **spent a cumulative period of 6 months in malaria endemic area(s) at any time during their life** may be accepted as a blood donor if the result of a validated immunological test for antibodies to the malaria parasite, taken at least 4 months after the last visit to a malaria area is negative. It is requested that the donor ineligibility statement be amended to reflect the above 6 month

		cumulative period at any time during the donor's life. ***Impact***: • Loss of considerable product (plasma for fractionation) if Table 1 (m) entry is not included in the exemption statement in section (5) on page 8. ie, permitting the plasma collected from donors who have lived in a malarial area within the first 5 years of life to be used exclusively for plasma for fractionation. • Modification to the Blood donor Questionnaire and modification to the Blood Donor Guidelines will be required to capture the information pertaining to the first 5 years of life if the ineligibility statement is not revised as suggested.
Pg 8 **Table 1 (o)**	Format An asymptomatic visitor to endemic malarial areas.	Suggest revision of wording to be consistent with the wording of (m) and (n), ie "Ineligible for 6 months after leaving the endemic area. *This may be reduced to 4 months if* an immunologic or molecular genomic test is negative at donation."
Pg 8 **Table 1 (m), (n), (o), (p)**	Molecular genomic test for Malaria	Remove the reference to a "molecular genomic test" for malaria because a negative test result in a molecular genomic test would not necessarily accredit the donation due to the low likelihood that the test sample would contain actual malaria parasitic DNA . Accreditation of the donor status via testing should be limited to Immunologic testing.
Pg 8 (5)	Testing and deferral requirements of Table 1	The requirements of Table 1 not required to be met when the donation is to be used exclusively for plasma for fractionation should include (m) and should NOT include (q).
Pg 9, Table 2	Vaccines with sera of animal origin	Further clarification of this type of vaccine is requested, as it is unclear which vaccines may fall within this category. Provision of an example would also be of assistance.
Pg 10, 9, (2) (a)	Blood sampling…no more than 7 days prior to or 7 days after collection…	Although it is noted that the requirements in the order are minimum standards and that more stringent requirements may be applied, the Blood service does not believe it is appropriate to sample blood donors up to 7 days prior to their donation as risk activity may occur in the intervening period. For blood donation, the sample which is used to perform the mandatory screening testing should be collected AT the time of the blood donation. The option for a blood sample for donor testing to be collected 7 days prior to blood donation is inconsistent with the requirement for the timing of collection of a sample for testing archive (refer

		page 11, 9. (8)), which must be taken "at time of collection…"
Pg 10, 9 (4)	Format	Format of item Parts (a) and (b) relate to initial sentence. Part (c) should be a stand-alone sentence. E.g. The results of such testing must be evaluated prior to release……
Pg 11, **9, (8),**	Sample archive Expiry date- clarification	*Requirement for dedicated samples of serum or plasma to be archived at or below minus 25 degrees C ... for retesting up to, at minimum, 2 years after the expiry date of products or as set out in product specific orders for the purposes of section 10 of the Act.* The Blood Service does not currently have a sample archive in place, and this is a pre-existing gap of which TGA are informed. The Blood Service is in the process of closing this gap. Request clarification of the term "products" as it appears in the requirement for retention of samples for 2 years post expiry. Although the term "blood product" is often used to refer to fractionated product, it is the Blood Service understanding that in this context, the "product" is the blood component (ie plasma intended for fractionation) and is not the finished (fractionated) product. ***Impact*** **:** Significant financial and operational impact would result if the term "product" is extended to include finished (fractionated) product, particularly in regard to the duration of sample retention. ie 2 years post expiry of the manufactured product could potentially require a 10 year archive duration if fractionated product is included in the scope of the requirement.
Pg 11, 9 (9) Requirement to test archived sample if screening protocols change during the life of a product	Re-testing using archived sample	Where screening protocols change during the life of a product in storage, the donor's archived sample MUST be retested (based on risk and in consultation with regulator). ***Impact*** Direct costs of retesting archive on introduction of new screening protocol could be considerable. These costs would need to be incorporated into the risk-benefit analysis and considered in consultation with the regulator.
Pg 11, 10, (2)	Physical assessment	Physical assessment of the donor must be conducted. The Blood Service has commented previously that for healthy blood donors, a physical

		examination of tattoos, piercings, scars etc would be viewed as an unnecessary intrusion and likely to deter donors. The amendments made to this requirement from the previous draft are a positive improvement, however the Blood Service would like to see further refinement to ensure that healthy blood donors are not unnecessarily subjected to physical examination as part of the mandatory criteria for routine blood donation. Suggest replacement of existing requirement with the following; *"Assessment of the suitability of the donor, which may include a physical assessment , where appropriate must be conducted by a trained assessor and, must take place…"*
Pg 14, 11, (3), (a)	transport conditions of human blood and blood components	Transport temperature requirement of 2 degrees C to 8 degrees C is more restrictive than the Council of Europe Guidelines (2-10 degrees C) . It is our understanding that for blood components, the Council of Europe Guide to the Preparation Use and Quality Assurance of Blood Components would be designated as the product specific Standard and would therefore take precedence over this requirement. The 72 hour limit in transport duration is inconsistent with the BP requirements for plasma for fractionation. ***Impact*:** Significant impact if 2-8^{o}C must be met, as transport would require re-validation and possible change in shippers.
Pg 14, 11, (5)	Bioburden specifications	It is unclear which of the stated bioburden release specifications (a or b or c) would be required to apply for blood and blood components. ***Impact:*** It is the position of the Blood Service that (c) would be the applicable criteria for blood components, however if (a) or (b) apply then there will be considerable cost and resource impact on the Blood Service to implement these requirements.

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

Any perceived impacts on the Blood Service in implementing the requirements of the proposed standard for minimising infectious disease transmission have been noted in the body of the table above, and recorded against the specific requirement/clause.

The requirements of most concern are:

- Transport conditions of blood and blood components required to be maintained between 2-8C (page 14, 11 (3), (a), as this is restriction of the current temperature range permitted under the Council of Europe Guidelines.

- Requirements for sample archive – in relation to the duration of archive applicable to " products". Pg 11, 9, (8). Impact is contingent on definition of the term "product"

- Prion disease – The Blood Service is concerned that there will be an increased potential for transmission of vCJD given the putative case attributable to UK factor VIII concentrate, and believes that the wording must be revised to include "blood products" and not just blood components, given the AHMAC decision of 2003.

- Product Release Bioburden Specifications - Significant operational and cost implications if Blood Service required to implement additional bioburden surveillance, control or testing beyond the level of monitoring conducted currently in accordance with Council of Europe requirements, and approved arrangements with the TGA.

- The introduction of less stringent donor assessment criteria than those currently in place at the Blood Service, would be likely to introduce risk – eg conducting the donor interview 7 days prior to blood donation, or collection and processing of autologous blood from donors known to be infected with hepatitis C, HIV, HTLV1/HTLV2. It is recognised that the aim of the document is to describe the minimum standards across the industry and that an individual organisation may apply more stringent criteria. However, this leaves the onus on the individual organisations and may result in variable application of risk reduction strategies. It is therefore suggested that clauses which are unable to be applied equally across all sectors of the industry, should be addressed separately (either within the document marked as applicable to that the relevant sector only, or addressed within the product specific standards).

- Prior to implementation it would be beneficial to understand how this therapeutic goods order will transition into force; either alongside or in conjunction with the existing TGOs which define the component specific standards (eg TGO81) .

Standards for human cardiovascular tissue

SUBMITTING ORGANISATION: Australian Red Cross Blood Service

Reference	Issue	Comment
		Nil comment

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

Nil

Other general comments:

Standards for human musculoskeletal tissue

SUBMITTING ORGANISATION: Australian Red Cross Blood Service

Reference	Issue	Comment
		Nil Comment

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

Nil

Other general comments:

Standards for human ocular tissue

SUBMITTING ORGANISATION: Australian Red Cross Blood Service

Reference	Issue	Comment
		Nil comment

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

Nil

Other general comments:

Standards for human skin

SUBMITTING ORGANISATION: Australian Red Cross Blood Service

Reference	Issue	Comment
		Nil comment

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

Nil

Other general comments:

General requirements for the labelling of biologicals

SUBMITTING ORGANISATION: Australian Red Cross Blood Service

The labelling standards only apply to biologicals defined under the biologicals framework, and it is understood that at the time of implementation of the biologicals framework, blood and blood components will not be included. The following comments are therefore provided as potential impact should the framework extend to blood components at a later date.

Reference	Issue	Comment
Pg 4 , (3) (c) and (d)		Requires the date and time of collection to be recorded on the container. For blood components, the collection date is recorded on the container but not the time. This information is contained in a linked donor record. There should be facility within the labelling standards to permit information such as this to be captured in an adjunct record unique to that donation/component. Similarly the standard requires that the collection facility is recorded on the container. For Blood Components, the name of the organisation (Australian Red Cross Blood Service) is recorded on the label however the specific facility at which the unit was collected is not recorded on the container. It is recorded on the donation record and enables complete traceability. With hundreds of blood collection facilities across the country, it is not feasible to individually record the facility name on the blood component. Additionally, many of the blood components are collected at one facility, then transported and processed at a different facility. It has been a long standing agreement with TGA that the name of the individual collection facility is not required on the component label, but that this information must be recorded and be completely traceable.. It is suggested that there should be scope within the labelling standards to permit the collection (and manufacturing facility information where appropriate) to be either recorded on the label or captured in records linked uniquely to the individual component, in such a way as to enable complete traceability.

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

Other general comments: