# Therapeutic Goods Order -DRAFT – Standards for minimising infectious disease transmission via therapeutic goods that are human blood and blood components, human tissues and human cellular therapies

**Schedule 2**

*(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*
*(b) for manufacturers of allogeneic blood and blood components, human tissues and human cells required to be manufactured in a facility with an approved quality system, an informed risk/benefit analysis regarding donors who have resided/travelled outside Australia and at minimum, be consistent with the policy applied to donors of blood for blood components:*
*(i) must not be manufactured from donors who have lived in or visited England, Scotland, Wales, Northern Ireland or the Isle of Man for a cumulative period of six months or more, between 1 January 1980 and 31 December 1996 inclusive; and*
*(ii) must not be manufactured from donors who have received a transfusion or injection of blood or blood components while in England, Scotland, Wales, Northern Ireland or the Isle of Man from 1 January 1980 onwards.*

Will this require exceptional release for all donors who have lived in the UK? This clause appears to exclude the use of allogeneic donors who have (i) resided in the UK for more than 6 months between 1980 and 1996, or (ii) have received a blood transfusion or blood components in the UK after 1980. If this is an example where collection of such a donor would require authorisation from the TGA via the "exceptional release" mechanism for release of product, what would be the mechanism for application for authorisation and what time frame would be expected in obtaining authorisation.

**Schedule 3,**
**Table 2 (l)**

| | **Donor medical and social history criteria** | **Period of ineligibility prior to donation for** |
|---|---|---|
| | | **Allogeneic use** |
| **(l)** | *Known, suspected or at risk of being infected with hepatitis B* | *Ineligible until*<br>*(i) disease resolved (donor immunised or HepBsAb≥100 IU/L) or*<br>*(ii) as prescribed for the risk factors (a) to (h) above* |

Where a donor is known, suspected or at risk of being infected with Hepatitis B – the donor is ineligible until the disease is resolved (donor immunized or HepBsAb $\geq$ 100 IU/L). Regarding the value of HepBsAb $\geq$ 100 IU/L. In Hepatitis B Virus Reactivation literature for HPC transplants the cutoff value referred to is commonly $\geq$10 IU/L – see example reference Hepatitis B Virus Reactivation following Allogeneic HSCT, Hammond et al, Biol Blood Marrow Transplant 15: 1049-1059). Can you clarify why the value $\geq$100 IU/L is specified/mandated?

Submitted by XXXXXX XXXXXX XXXXXX on behalf of XXXXXX, XXXXXX XXXXXX
Date: 12/02/2010

Schedule 4

*(8) Screening and confirmatory microbiological and virological tests must be performed in laboratories using appropriately validated testing techniques as regulatory requirements specify.*

Can TGA clarify which regulatory body's requirements will be specified as a standard for confirmatory microbiological and virological testing.?

*(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.*

We request clarification of the paragraphs in relation to HPC. They seem to be contradictory and as no samples are required on the day of collection for HPCs is it possible that 10 is redundant. For HPC product expiry is contentious. Is the product considered to expire at the time of recipient death?

These clauses require storage of donor serum/plasma to facilitate retesting or additional testing at the time of cell infusion (clause 9) and a sample of serum for a minimum of 2 years after the product expiry date (clause 10). Can the TGA clarify the reason that the type of specimen sample required to be stored in clauses 9 & 10 is different. What is the anticipated intent of clauses 9 & 10.

*(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 with the new screening test protocol prior to release of human blood and blood components, human tissue or human cellular therapy products.*
Retrospective testing – will all product currently held require re-testing for HTLV II and upon issue of these codes for Hepatitis B Core antibody. HPC products can be held for up to 20 years – there are sure to be numerous changes in the protocols for screening tests during this time.

**Schedule 5**

*(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:*

*(a) The donor testing must include, at minimum, serological tests and, unless justified otherwise (e.g. donor sampling and testing at ≥180 days after the initial blood sample is taken, or time restrictions due to tissue lability), tests using Nucleic Acid Amplification Technology (NAAT1), where available, for the infectious diseases/infectious disease markers as indicated in Table 4 of this Schedule.*

The clause mandates the use of NAAT for HIV, HCV and (when approved HBV), for all autologous and allogeneic HPC donors. How and when will the requirement to commence routine HBV NAAT testing be communicated to the therapeutic goods manufacturers and what will be required for product in inventory ie. will HBV NAAT testing need to be performed prior to release.

Submitted by XXXXXX XXXXXX XXXXXX on behalf of XXXXXX, XXXXXX XXXXXX
Date: 12/02/2010

**Schedule 5**

*(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*

Clarification is required. Obviously total absence of microorganisms is safest. Where are the microorganisms specified for clinical significance.

Submitted by XXXXXX XXXXXX XXXXXX on behalf of XXXXXX, XXXXXX XXXXXX
Date: 12/02/2010