



**Australian Government**

**Department of Health and Ageing**  
Therapeutic Goods Administration

***THERAPEUTIC GOODS ACT 1989***  
**Section 10**

***Therapeutic Goods Order No. 88 - Standards for donor selection, testing and minimising infectious disease transmission via therapeutic goods that are human blood and blood components, human tissues and human cellular therapy products***

I, John Skerritt, delegate of the Minister for Health for the purposes of section 10 of the *Therapeutic Goods Act 1989* (the Act) and acting under that section, having consulted with the Therapeutic Goods Committee in accordance with subsection 10(4) of that Act, HEREBY:

DETERMINE that the matters specified in this Order shall constitute a standard for therapeutic goods that are human blood and blood components, human tissues and human cellular therapy products, being a standard directed at minimising the risk that these therapeutic goods will transmit infectious diseases. This standard sets out the processes that include the following activities:

- (a) donor selection;
- (b) donor testing; and
- (c) blood, blood component, cells and tissue collection and manufacture

to minimise infectious disease transmission via therapeutic goods that are human blood and blood components, human tissues and human cellular therapy products.

Dated this 20<sup>th</sup> day of May 2013

(Signed by)

John Skerritt  
Delegate of the Minister for Health

# PART 1 - INTRODUCTION

## 1. Name of Order

This Order may be cited as *Therapeutic Goods Order No. 88 Standards for donor selection, testing, and minimising infectious disease transmission via therapeutic goods that are human blood and blood components, human tissues and human cellular therapy products*.

## 2. Commencement

- (1) This Order commences on 31 May 2013.

## 3. Transition

- (1) Human blood and blood components, human tissues and human cellular therapy products that are collected from a donor, or that are subjected to any other manufacture, on or after 31 May 2014 must comply with all relevant requirements of this Order from 31 May 2014.
- (2) Human blood and blood components, human tissues and human cellular therapy products that are both:
  - (i) collected from a donor or subjected to any other manufacture; and
  - (ii) released for supply;before 31 May 2014 (including before 31 May 2013), will be exempt from the requirements of this Order.

Note 1: Nothing in (2) is intended to prevent a person from complying with this Order in relation to human blood or a human blood component or human tissues or a human cellular therapy product to which (2) applies before the date of compliance, if they wish to do so.

Note 2: However, if a person elects to do so, that collection or other manufacture must also comply with the *Australian Code of Good Manufacturing Practice for human blood and blood components, human tissues and human cellular therapy products (2013)*, unless the goods or the manufacturer of those goods are exempt from the operation of Part 3-3 of the Act under either of Schedule 7 or Schedule 8 to the Therapeutic Goods Regulation 1990 (the Regulations).

Note 3: Alternatively, a person may, in relation to human blood or a human blood component or human tissues or a human cellular therapy product to which (2) applies, comply with the *Australian Code of Good Manufacturing Practice for blood and tissues (August 2000)* in relation to such goods before the 31 May 2014 (i.e. rather than complying with both this Order and the *Australian Code of Good Manufacturing Practice for human blood and blood components, human tissues and human cellular therapy products (2013)*, unless the goods or the manufacturer of those goods are exempt from the operation of Part 3-3 of the Act under either of Schedule 7 or Schedule 8 of the Regulations.

- (3) Human blood and blood components, human tissues and human cellular therapy products that are collected from a donor before 31 May 2014 (including before 31 May 2013), and that are released for supply on or after 31 May 2014, must comply with the testing requirements set out in subsections 11(3), 11(4) and 11(5) of this Order.
- (4) Subsection 3(3) does not apply where the sponsor or manufacturer of human blood or a human blood component or human tissues or a human cellular therapy product determines, based on a risk analysis, that it is not possible to comply with the testing requirements mentioned in subsection (3), and where the TGA has agreed to that approach.

#### 4. Purpose of this Order

The purpose of this Order is to specify the minimum technical requirements, particularly in relation to donor selection, donor testing, and the collection and manufacture of therapeutic goods that are human blood, blood components, human tissues and human cellular therapy products, with which these products must comply to minimise the risk that these products may transmit infectious diseases.

#### 5. Interpretation

(1) In this Order:

*Act* means the *Therapeutic Goods Act 1989*.

*allogeneic use* means the use of blood, blood components, tissues or cellular therapy products that are removed from one person and applied to another person.

*antimicrobial* means the ability of a substance to kill or inhibit growth of microorganisms.

*aseptic technique* means the technique that consists of measures used to prevent contamination by microorganisms.

*asystole* means the reference time for cardiac death. A documented pronounced time of death is used as asystole when life-saving procedures have been attempted and there were signs of, or documentation of, recent life (e.g. agonal respirations, pulse-less electrical activity). If death was not witnessed, ‘asystole’ must be determined by reference to the last time that the person was known to be alive. Asystole will be ‘cross clamp time’ if the tissue donor was also a solid organ donor.

*autologous use* means the use of blood, blood components, tissues or cellular therapy products that are removed from and applied to the same person.

*bioburden* has the same meaning as in the Act.

*blood* means whole blood collected from a single human donor and processed either for transfusion or further manufacturing.

*blood components* means components of blood (red cells, white cells, platelets, plasma) that can be prepared by centrifugation, filtration and freezing, but not including haematopoietic progenitor cells.

*blood donation centre* means a site licensed under Part 3-3 of the Act for the collection of blood, blood components or haematopoietic progenitor cells.

*cell(s)* means individual cells or a collection of cells when not bound by any form of connective tissue.

*collection* means removing human blood, blood components, cells, or tissue from a donor.

**cornea only donors** means persons who donate ocular tissue that will be released for the specific purpose of corneal transplantation.

**critical material** means all materials or supplies used in the manufacture of therapeutic goods which could have a direct impact on the quality, safety or function of the final goods.

**cryopreserved** means suspended in a medium containing a suitable cryoprotectant and cooled according to a method which has been validated to allow maintenance for long periods.

**default standard** has the same meaning as in the Act.

**domino donor** means a person who by receiving an organ transplant donates the removed organ or tissue for allogeneic use.

**donor** means any source, whether living or deceased, of blood, blood components, cells or tissues.

**extrinsic microbial contamination** means contamination of blood, blood components, tissues or cellular therapy products caused by compromised processing.

**haematopoietic progenitor cells** means cells that are primitive multipotent cells capable of self-renewal as well as differentiation and maturation into all haematopoietic lineages.

**HBsAg** means Hepatitis B surface antigen.

**HBV** means Hepatitis B virus.

**HCV** means Hepatitis C virus.

**HIV** means Human Immunodeficiency Virus.

**HPC** means haematopoietic progenitor cells.

**HPC-A** means haematopoietic progenitor cells- apheresis.

**HPC-C** means haematopoietic progenitor cells-cord.

**HPC-M** means haematopoietic progenitor cells-marrow.

**HTLV-1** means Human T-Lymphotropic Viruses type 1.

**HTLV-2** means Human T-Lymphotropic Viruses type 2.

**intrinsic microbial contamination** means contamination of the blood, blood components, tissues or cellular therapy products with microorganisms already present in the starting material.

**knowledgeable historian** means a person who is knowledgeable about the donor's medical and social history, if the donor is deceased or unable to participate in an interview. A

knowledgeable historian may be a person who is, or persons who are, able to provide relevant information about a donor's medical and social history, and may include the donor's next of kin or the nearest available relative, a member of the donor's household, another person with a relationship with the donor (e.g. carer, friend, partner), or the donor's treating physician.

**manufacture** has the same meaning as in the Act.

**microbial** means microorganisms including, but not limited to, bacteria, fungi, Mycoplasma and Rickettsia, but does not include viruses or prions.

**NAT** means Nucleic acid Amplification Technique.

**physical assessment** means a clinical inspection of a living or deceased potential donor to determine suitability of the person to be a donor and may include, but is not limited to, assessing 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 or lifestyle, or suggestive of any risk factor in relation to a relevant communicable disease.

**processing** means any activity involved in preparation, manipulation, preservation for storage, and packaging of a blood, blood component, tissue or cell therapy product.

**QC** means quality control.

**quarantine** means the status of starting or packaging materials, intermediate, bulk or finished products isolated physically or by other effective means whilst awaiting a decision on their release or refusal.

**recipient** means a person who receives blood, blood components, cells or tissues by infusion or implantation.

**Register** has the same meaning as in the Act.

*Note "Register"* under the Act means the Australian Register of Therapeutic Goods maintained under section 9A.

**risk of prion disease** means where a donor has been exposed to the putative causative agent(s) of any one of the family of pathogenic transmissible spongiform encephalopathies through the following means:

- (a) genetic (familial), or
- (b) environmental, which includes 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<sup>st</sup> January 1980 and 31<sup>st</sup> December 1996 inclusive, or
- (c) iatrogenic, which includes 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 at any time since 1<sup>st</sup> January 1980 onwards

***specified microorganism*** means a microorganism of clinical significance which, if isolated from the blood, blood components, cells or tissues, necessitates rejection of the product for therapeutic use.

***storage*** means maintaining a substance, material or product under appropriate controlled conditions.

***tissue*** means all constituent parts of the body formed by cells.

***transport*** means the transfer within or between premises of a substance, material or product under appropriate controlled conditions.

***trained interviewer*** means a person who is trained in interviewing skills and is an employee of, or who has a contractual arrangement with, a person engaged in the collection or manufacture of human blood and blood components, human tissues and human cellular therapy products.

***trained assessor*** means a person who is trained in the physical assessment of donors or potential donors of human blood and blood components, human tissues or human cellular therapy products and who is an employee of, or has a contractual arrangement with, a person engaged in the collection or manufacture of human blood and blood components, human tissues or human cellular therapy products.

***TSE*** means transmissible spongiform encephalopathy.

## **6. Application of this Order**

- (1) Subject to section 7, the requirements of this Order apply to human blood and blood components, human tissues and human cellular therapy products (which, for the purposes of this entire Order, includes haematopoietic progenitor cells) that are collected from:
  - (a) living human donors for autologous or allogeneic use; or
  - (b) deceased human donors for allogeneic use.

## **7. Exemptions**

The requirements of this Order do not apply to the following:

- (1) fresh viable human organs, or parts of human organs and associated cells and tissue for direct donor to host transplantation;
- (2) biopsied cell or tissue samples taken for in vitro diagnosis and that are not for manufacture and/or reintroduction or transplant to a recipient;
- (3) human blood, blood components and haematopoietic progenitor cells that are:
  - (a) collected by a medical practitioner, registered under a law of a State or Territory, or a person under the professional supervision of such a practitioner, in the course of medical treatment and for the purposes of diagnosis of, and testing for, a medical condition; or
  - (b) manufactured by a medical practitioner, registered under a law of a State or Territory, or a person under the professional supervision of such a practitioner, for therapeutic application to a particular patient under the practitioner's care; or
  - (c) manufactured by a blood donation centre for a medical practitioner who is registered under a law of a State or Territory, for therapeutic application to a particular patient under the practitioner's care.

## **PART 2 – GENERAL REQUIREMENTS**

### **8. General requirements for human blood and blood components, human tissues and human cellular therapy products**

- (1) In relation to the collection and manufacture of human blood, blood components, human tissues or human cellular therapy products, a person collecting or manufacturing such products must have procedures in place approved by the TGA that demonstrate:
  - (a) steps taken to mitigate the risk of infectious disease transmission during collection and manufacture; and
  - (b) processes for notifying persons/organisations of a donor test result that is positive for, or reactive to, an infectious disease; and
  - (c) criteria for acceptance and release of human blood and blood components, human tissue and human cellular therapy products based on microbial specifications.
- (2) In all cases, procedures in place as required by subsection 8(1) must be followed.

## **PART 3 – SPECIFIC REQUIREMENTS**

### **9. Requirements in relation to the medical and social history of prospective donors**

- (1) In the case of a living donor, the blood, blood components, cells or tissues must only be collected from a living donor with whom an interview to obtain the donor's medical and social history has been conducted and recorded in accordance with the following requirements:
  - (a) The interview must be conducted with the donor or guardian/next of kin by a trained interviewer and should be a face-to-face interview.
  - (b) The interview must be conducted no more than 30 days prior to or 30 days after collection of the blood, blood components, cells or tissues, and must occur prior to any release of the relevant product from quarantine, unless otherwise specified in another, current Therapeutic Goods Order made under section 10 of the Act that applies to the relevant product.
- (2) In the case of a deceased donor, the medical and social history of the donor must be obtained and recorded no more than 7 days prior to, or following, collection, in the following manner:
  - (a) by interview with a knowledgeable historian and examination of the donor documentation to obtain and record the medical and social history of the donor; or
  - (b) if such an interview is not possible, the donor documentation must be examined for sufficient evidence to determine donor acceptability.
- (3) Donor medical and social history criteria, as required to be obtained by each of subsection 9(1) and 9(2), must be reviewed and evaluated using the minimum donor medical and social history criteria set out in column 1 of Table 1 below.
- (4) A donor of a blood, blood components, cells or tissues for allogeneic use who meets any of the criteria listed in column 1 of Table 1 is subject to the corresponding period of ineligibility prior to donation, as set out in column 2 of Table 1 below.
- (5) For a donor of blood, blood components, cells or tissues for autologous use, the manufacturer and sponsor must determine which, if any, of the medical and social history criteria listed in column 1 of Table 1 will apply, based on a risk assessment considering the nature and intended use of the product.
- (6) The testing and deferral period requirements of items (a) (iii), (b) (iii), (l), (n), (o), (p) and (q) of Table 1 are not required to be met when the donation is to be used exclusively for plasma for fractionation.
- (7) The testing and deferral period requirements of items (n), (o), (p) and (q) of Table 1 are not required to be met when the donation is to be used exclusively for ocular tissue.
- (8) When the criteria for donor medical and social history criteria change during the life of any human blood, blood component, tissue or human cellular therapy product that has been taken from the donor and that has been placed in storage, reassessment of the donor against the new medical and social history criteria should be undertaken prior to release of the product. The requirement for reassessment must be determined by the sponsor and manufacturer based on risk, and after consultation with the TGA.



- (9) To address the possible vertical transmission of infectious agents in infant donors of less than 18 months old, or up to 6 months beyond breast feeding, whichever is the greater time, the birth mother must also be evaluated for high risk behaviour against the criteria set out in items (a) to (e), and (j), (k), (l), (p) and (r) of Table 1. If the birth mother meets any of those criteria, ineligibility periods set out in column 2 of Table 1 for those criteria in respect of the birth mother must be observed in relation to the child donor.
- (10) In addition to the requirements in subsections 9(3) and (4), a potential donor of human blood or blood component or human tissue or human cellular therapy products for allogeneic use who was vaccinated with a live vaccine is ineligible to donate if the minimum donor ineligibility period has not been met as set out in Table 2.
- (11) The requirements relating to donor ineligibility in Table 2 will not apply when the blood or blood components are to be used exclusively for the purpose of plasma for fractionation.
- (12) The donor ineligibility periods set out in Column 2 of Table 2 will not apply to a potential donor of human blood or blood component or human tissue or human cellular therapy products for allogeneic use if the donor has been vaccinated with a killed bacterial vaccine, subunit vaccine, or inactivated virus and the donor is not covered by any of the criteria in column 1 of Table 2.
- (13) Human blood or a blood component, or human tissue or human cellular therapy product, must not be manufactured from a donor who is known to have a disease or condition, including those that are a consequence of donor treatment, that may compromise the quality, safety or efficacy of the blood, blood component, cells or tissue for the intended therapeutic purpose, unless:
  - (a) criteria for donor acceptance and periods of donor ineligibility that are based on data validated by the sponsor or manufacturer, or documented evidence obtained from scientific literature review, which supports the quality, safety, and efficacy of the product for its intended therapeutic purpose, are applied for donors with the specified disease or condition; or
  - (b) where the condition has not been specifically identified in the donor acceptance and deferral criteria, and where individual donors are subject to review and subsequent acceptance by the sponsor or manufacturer's medical officer. The rationale for such acceptance must be recorded.
- (14) A human blood or blood component or human tissue or human cellular therapy product must not be manufactured from blood, blood components, cells or tissues collected from a donor if the age of the donor could compromise the safety and efficacy of the human blood or blood component or human tissue or human cellular therapy product.
- (15) There must be criteria for upper and lower age limits for donors of blood or blood components, cells or tissues and these must be documented and supported by validation data or evidence which demonstrates that the intended therapeutic application for the donated human blood or blood component, or human tissue or human cellular therapy product is justified and appropriate.

**Table 1: Minimum medical and social criteria required to determine donor risk of exposure to infectious disease and ineligibility periods**

<b>Column 1: Donor medical and social history criteria</b>	<b>Column 2: Period of ineligibility, and related testing and notification requirements, prior to donation</b> <i>(donors of products for allogeneic use only)</i>
(a) A donor known to be infected with (i) HCV; (ii) HIV; (iii) HTLV-1/HTLV-2.	Permanently ineligible.
(b) A donor suspected to be infected with (i) HCV; (ii) HIV; (iii) HTLV-1/HTLV-2.	Ineligible until an uninfected state can be established.
(c) A donor known to be, or suspected of being, infected with HBV.	Permanently ineligible except HBsAg negative persons who are demonstrated to be immune or demonstrated to have never been exposed.  For HBsAg negative persons who are demonstrated to be immune or never exposed, no ineligibility period applies provided the NAT test for HBV is negative.
(d) A donor who has ever injected, or been injected with, any drug for a non-medical reason.	Ineligible for 5 years from last injection.
(e) A recipient of viable non-human animal cells or tissues.	Permanently ineligible.
(f) A donor with a risk of prion disease	Permanently ineligible.
(g) A recipient of human pituitary derived hormone	Permanently ineligible.
(h) A donor with exposure to the following risks of acquiring a blood borne transmissible infection: (i) mucosal splash with blood; (ii) needle stick injury; (iii) tattoo; (iv) body piercing; (v) acupuncture unless performed using sterile single use needles.	Ineligible for 6 months from the time of exposure, or for 4 months provided NAT test for HCV is negative.  For living donors who will be retested at 180 days in accordance with paragraph 11(4)(c), no ineligibility period applies.
(i) A deceased donor who, within 12 months prior to asystole, has been a recipient of allogeneic organ(s), cells, or tissue that are not in accordance with the requirements of this Order.	Ineligible.

<b>Column 1: Donor medical and social history criteria</b>	<b>Column 2: Period of ineligibility, and related testing and notification requirements, prior to donation</b> <i>(donors of products for allogeneic use only)</i>
(j) A recipient of allogeneic blood, blood components or human derived clotting factors, organs, cells or tissues that are not in accordance with the requirements of this Order.	Ineligible for 6 months from the time of exposure, or for 4 months provided NAT test for HCV is negative.
(k) A donor whose sexual practices put them at increased risk of acquiring infectious diseases that can be transmitted by blood, cells or tissues.	Ineligible for 12 months from last contact.
(l) An inmate of a prison.	Ineligible for 12 months from date of release (when imprisoned for a consecutive period of 72 hours or more).
(m) A donor with an unexplained fever or unexplained infectious illness.	Ineligible for at least 2 weeks following the date of full recovery.
(n) A donor who has lived in a malaria endemic area for a continuous period of 6 months or more at any time in life.	Accepted if a validated immunological test, taken at least 4 months after the last visit to a malaria endemic area, is negative.  Permanently ineligible if the immunological test is positive or not performed.
(o) A donor with a history of malaria.	Deferred until asymptomatic and off treatment. Accepted if a validated immunological test, taken at least 4 months since cessation of treatment/last symptoms is negative.  If the test is positive donor must be deferred and may be re-evaluated after 3 years.  Permanently ineligible if the immunological test is not performed.
(p) All other persons who have visited a malaria endemic area.	Accepted if a validated immunological test, taken at least 4 months after the last visit to a malaria endemic area, is negative.  If the test is positive the donor must be deferred and may be re-evaluated after 3 years.  If the test is not performed the donor may be accepted 12 months after last return from a malaria area.
(q) A donor who reports an undiagnosed febrile illness consistent with malaria during or within 6 months of a visit to a malarial endemic area.	Accepted if a validated immunological test, taken at least 4 months since cessation of treatment/last symptoms, is negative.  If the test is positive the donor must be deferred and may be re-evaluated after 3 years.  If the test is not performed the donor must be deferred for 3 years.

<b>Column 1: Donor medical and social history criteria</b>	<b>Column 2: Period of ineligibility, and related testing and notification requirements, prior to donation</b> <i>(donors of products for allogeneic use only)</i>
(r) A donor with active infection of the cells or tissue to be collected, or active infection of other cells or tissues that are indicative of an infection that would render the target cells or tissues unsuitable for manufacture.	Ineligible until a disease free state can be established.
(s) A donor with exposure to particular epidemiological situations.	Deferral consistent with the epidemiological situation. Deferral procedures and parameters for particular epidemiological situations should be informed to the Head of the Office of Scientific Evaluation of the TGA.

**Table 2: Ineligibility period for allogeneic use for potential donors who have received a vaccine**

<b>Vaccine Composition</b>	<b>Period of donor ineligibility prior to donation</b>
Live attenuated bacteria or viruses, except smallpox	4 weeks
Smallpox	8 weeks
Sera of animal origin	12 weeks
Unknown	12 months

## **10. Requirements in relation to donor blood sampling, test kits, test protocols and test management**

- (1) To determine the infectious disease status of persons who are potential donors of human blood or blood components, human tissues or human cellular therapy products, samples of the person's blood must be collected using aseptic procedures, and those samples must be tested in accordance with this section for the purpose of infectious disease screening.
- (2) In the case of a living donor, blood sampling for testing must take place:
  - (a) no more than 7 days prior to, or 7 days after, collection of the blood, blood components, cells or tissues; or
  - (b) as required in another, current Therapeutic Goods Order made under section 10 of the Act that applies to the relevant product.
- (3) In the case of a deceased donor, blood sampling for testing must be within the timeframe specified by the test method. The testing methodology must have been validated for cadaveric samples to include the relevant time period of sample collection following asystole. A blood sample taken up to 7 days prior to collection of the product may be used.
- (4) For the manufacture of human blood and blood components, human tissue and human cellular therapy products, testing of the donor blood samples must be performed:
  - (a) as soon as practicable after collection of the blood sample for testing; or
  - (b) as required in another, current Therapeutic Goods Order made under section 10 of the Act that applies to the relevant product.
- (5) The testing of blood samples from donors must take into account any factors which may cause plasma dilution sufficient to alter serology test results. Where a pre-infusion sample is unavailable for infectious disease testing and plasma dilution is suspected, then an algorithm must be applied to assess the degree of dilution. Plasma dilution must be less than 50% unless the use of samples with greater than 50% dilution is validated by the sponsor or manufacturer.
- (6) The test kits/methodologies used for screening infectious diseases that are performed in accordance with subsection 11(3) tests must be:
  - (a) the most appropriate technology/ methodology for the sample being tested; and
  - (b) approved by the relevant regulatory authority in the country in which the testing is performed; and
  - (c) performed in a facility approved by the same authority to perform such testing; and
  - (d) considered acceptable by the TGA.
- (7) The test kit/methodologies used for the testing of donor blood samples must be recorded in procedures and/ or the service agreement with the contracted testing laboratory.
- (8) The results of the tests performed in accordance with subsection 10(4) must be evaluated prior to release of the product. If the results of the tests are not available, the product must be placed in quarantine until the results become available and are evaluated.

- (9) Samples of serum or plasma taken from deceased or living donors, except when the donation is to be used exclusively for plasma for fractionation, must be:
  - (a) taken in accordance with subsections 10(2) or 10(3), or be samples taken from living donors at a minimum of 180 days after collection if samples are collected in accordance with paragraph 11(4)(c); and
  - (b) archived, unless otherwise justified, at or below minus 25°C (unless other conditions of storage are validated by the sponsor or manufacturer in relation to a different temperature, or as recommended by the test kit manufacturers); and
  - (c) retained for a minimum of 2 years after the expiry date of the products unless otherwise required in another, current Therapeutic Goods Order made under section 10 of the Act that applies to the relevant product.
- (10) When the testing requirements mentioned in subsections 11(3), 11(4) or 11(5) change while a product is in storage, where possible the donor's archived sample must be retested with the new screening test protocol prior to release of the product. The requirement to retest is to be determined by the sponsor or manufacturer based on a risk assessment, and after consultation with the TGA.
- (11) Records on individual donors of the tests performed, test modifications, test results, analyses and any anomalies in the test results must be maintained.

## **11. Requirements in relation to donor physical assessment and testing**

- (1) All potential donors of human blood or blood components, human tissues or human cellular therapy products must be evaluated in accordance with this section before any such products are collected from that donor. Each potential donor of human blood or blood components, human tissues or human cellular therapy products must be assessed and tested for evidence of infectious diseases in accordance with the relevant and applicable donor groups.
- (2) A physical assessment of the potential donor must be conducted by a trained assessor, and must take place:
  - (a) in the case of a living donor, at the time of collection, unless otherwise specified in another, current Therapeutic Goods Order made under section 10 of the Act that applies to the relevant product;
  - (b) in the case of a deceased donor, prior to cell or tissue collection;
  - (c) in the case of a deceased donor whose cause of death is unknown, the cells and tissues must be deemed unacceptable, and the person must no longer be considered a potential donor, unless autopsy provides sufficient information to conclude that death has not been caused by a transmissible disease or any other condition that would be a contraindication to transplantation of the human tissues or human cellular therapy product from that donor.
- (3) Blood samples from all potential donors of human blood, blood components, cells and tissues must be tested in accordance with the requirements set out in Table 3.
  - (a) in Table 3, a “✓” sign indicates that the test must be performed.
    - i. For all donors except autologous donors, a test indicated in Table 3 with a “✓” sign must demonstrate that the samples tested are non-reactive.

- ii. For autologous donors, a test indicated with a “✓” sign in Table 3 must be performed and if the test demonstrates that the samples tested are reactive then subsection 11(6) applies.
  - (b) The HPC-C testing requirements set out in Table 3 apply only to the birth mother and do not apply to the respective donor infant.
  - (c) The requirements in the “deceased donors” column of Table 3 includes testing to be performed on blood samples of deceased donors for the donation of any tissue, other than cornea only donors.
- (4) In addition to the requirements set out in subsection 10(3), blood samples from all potential donors must be tested in accordance with and must comply with the following requirements:
- (a) all donor samples collected in accordance with subsection 10(2) or 10(3) must be tested by serology, and
  - (b) NAT testing for HIV, HCV and HBV must be performed on samples collected in accordance with subsection 10(2) or 10(3); or
  - (c) where products can be stored for more than 180 days without impairing the fitness of the product for use in a recipient, the donor must be repeat sampled after 180 days post collection and tested by serology for HIV, HCV and HBV, unless NAT testing was performed at the time of collection.
  - (d) To address the possible vertical transmission of infectious agents in infant donors of less than 18 months old, or up to 6 months beyond breast feeding, whichever is the greater time, the birth mother must also be screened and tested in accordance with Section 10 and paragraphs (a) to (c) above.
- (5) The requirements to test for HBV by NAT in paragraph 11(4)(b) and (4)(c) do not apply when the donation is used exclusively for the purpose of plasma for fractionation.
- (6) In cases where human blood or blood components, human tissue or human cellular therapy products are manufactured for autologous use from a donor with repeatedly reactive mandatory screening tests as set out in Table 3:
- (a) segregation and quarantine must be applied to that human blood or blood component, human tissue or human cellular therapy product, and cross-contamination is to be avoided; and
  - (b) if requested, records must be made available to the Head of the Office of Scientific Evaluation of the TGA to demonstrate the rationale for the use of the product.

**Table 3: Donor testing requirements**

Donor group		Deceased donors	Cornea only donors	Living donors										
				Allogeneic use						Autologous use				
				Blood / components	Plasma for fractionation	HPC-A HPC-M	HPC-C	Domino donor	Other	Blood/ components	HPC-A HPC-M	HPC-C	Other	
<b>Testing requirement</b>														
Serology test Initial sample	anti HIV-1 anti HIV-2	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	anti HCV	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	HBsAg	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	HTLV-1/2 (antibodies)	✓		✓		✓	✓	✓	✓	✓	✓	✓	✓	✓
	syphilis	✓		✓		✓	✓	✓	✓	✓	✓	✓	✓	✓
<b>AND</b>														
NAT Initial sample	HIV	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	HCV	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	HBV	✓		✓		✓	✓	✓	✓	✓	✓	✓	✓	✓
<b>OR</b>	<b>OR</b>			<b>OR</b>		<b>OR</b>	<b>OR</b>	<b>OR</b>	<b>OR</b>	<b>OR</b>	<b>OR</b>	<b>OR</b>	<b>OR</b>	<b>OR</b>
Serology ≥180 day sample	anti HIV-1 anti HIV-2			✓		✓	✓	✓	✓	✓	✓	✓	✓	✓
	anti HCV			✓		✓	✓	✓	✓	✓	✓	✓	✓	✓
	HBsAg			✓		✓	✓	✓	✓	✓	✓	✓	✓	✓



## **12. Requirements in relation to microbial control**

- (1) A strategy for the minimisation of intrinsic and extrinsic microbial contamination in a product must be established based on a risk assessment considering the nature and therapeutic use of the product.
- (2) Human cells and tissues from a deceased donor that are proposed to be used in a recipient must be collected:
  - (a) as soon as possible after asystole and be completed within 24 hours of asystole provided the body has been refrigerated at less than 10°C within 12 hours of asystole; or
  - (b) if the body has not been refrigerated, within 15 hours of asystole death; or
  - (c) as set in another, current Therapeutic Goods Order made under section 10 of the Act that applies to the relevant product.
- (3) The transport and storage conditions of the blood, blood components, cells or tissues after collection but prior to processing (other than plasma for fractionation) must be no more than 72 hours in duration, and temperature must be maintained at less than 10°C, unless otherwise validated by the sponsor manufacturer, or otherwise specified in another, current Therapeutic Goods Order made under section 10 of the Act that applies to the relevant product.
- (4) The transport and storage conditions of the human blood and blood components, human tissues and human cellular therapy products after processing must be determined and validated by the sponsor or manufacturer of the product including, at minimum, the temperature and duration of storage and transport, unless otherwise specified in another, current Therapeutic Goods Order made under section 10 of the Act which applies to the relevant product.
- (5) Human blood, blood components, human tissues or human cellular therapy products must meet the following bioburden specifications:
  - (a) the absence of microorganisms; or
  - (b) the absence of specified microorganisms; or
  - (c) the surveillance and control measures for minimisation of microbial contamination of the product during collection and manufacture; or
  - (d) requirements specified in another, current Therapeutic Goods Order made under section 10 of the Act which applies to the relevant product; or
  - (e) qualification of the sterilisation process to ensure that a sterility assurance level of  $10^{-6}$  is achieved for the specific blood, blood component, tissue or cellular therapy product, where the product has been subjected to a terminal sterilisation process.

## **13. Requirements in relation to critical materials used in collection and manufacture**

- (1) In relation to manufacturing procedures relating to human blood and blood components, human tissues and human cellular therapy products, critical materials used in those manufacturing procedures must be selected and evaluated to ensure

that they are not contaminated with or likely to introduce bacteria or other infectious agents.

- (2) In relation to critical materials used in the manufacture of human blood and blood components, human tissues and human cellular therapy products, the following requirements apply:
- (a) in the case of critical materials that are solutions, which contact the human cells or tissue during collection, processing, storage or transport (other than the antimicrobial agents used in a cell or tissue cleaning process validated by the sponsor or manufacturer) such solutions must be:
    - (i) manufactured under an approved quality management system and supplied as a sterile solution; or
    - (ii) tested for and found to satisfy sterility requirements in accordance with a test for sterility specified in a current default standard or Therapeutic Goods Order made under section 10 of the Act which applies to that specific product.
  - (b) in the case of critical materials that are antimicrobial agents used in a cell or tissue cleaning process validated by the sponsor or manufacturer that are not supplied sterile, such materials should be passed through a 0.22µm filter prior to use in the manufacture of human blood or blood components, human tissues or human cellular therapy products;
  - (c) in the case of critical materials containing any components of human or animal origin (other than the starting materials of blood, cells or tissue) such materials must have been sourced, tested (if methodology is available) and assessed as presenting a minimal risk of transmitting infectious disease agents in accordance with the requirements set out in the following documents:
    - (i) *TGA approach to minimising the risk of exposure to Transmissible Spongiform Encephalopathies (TSEs) through therapeutic goods*, published by the TGA at < <http://www.tga.gov.au/industry/tse-approach.htm> >; and
    - (ii) the EMEA guidance document titled *Note for Guidance on Virus Validation Studies: The design, contribution and interpretation of studies validating the inactivation and removal of viruses Feb 1996*, published by the EMEA at <<http://www.emea.europa.eu/pdfs/human/bwp/026895en.pdf>>;
  - (d) in the case of critical materials that are not required to be in the Register, or that are the subject of an approval or authorisation in relation to the requirement to be included in the Register, the following information must be documented:
    - (i) screening tests performed; and
    - (ii) QC specifications, e.g. criteria and limits for the tests performed; and
    - (iii) storage conditions; or
  - (e) if the information specified in (d)(i) to (iii) is not available from the sponsor or manufacturer of the material, the material must be assessed by the manufacturer of the human blood or blood component, human tissue or human cellular therapy product.