



Australian Government

Department of Health and Ageing

***THERAPEUTIC GOODS ACT 1989***

**Section 10**

***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***

I, Rohan Hammett, delegate of the Minister for Health and Ageing for the purposes of the exercise of the Minister's powers under section 10 of the *Therapeutic Goods Act 1989* 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 donor selection, donor testing, and cell and tissue management to minimise infectious disease transmission via therapeutic goods that are human blood and blood components, human tissues and human cellular therapies.

Dated this ..... day of ..... 2010

Rohan Hammett  
Delegate of the Minister for Health and Ageing

## 1. Name of Order

This Order may be cited as *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*.

## 2. Commencement

This Order commences on the day after the day it is registered on the Federal Register of Legislative Instruments.

## 3. Introduction

This Order sets particular requirements for minimising the risk of infectious disease transmission via human blood and blood components, human tissues and human cellular therapies. It specifies the minimum general requirements for donor selection, donor testing and cell and tissue management as related to infectious agents during the retrieval and processing for all human blood and blood components, human tissues and human cellular therapies.

For regulatory purposes it will be necessary to reference current product specific Orders, where they apply, which establish additional criteria for retrieval, production and release of a particular human blood and blood component, human tissue or human cellular therapy product or product type.

## 4. Interpretation

- (1) For the purpose of this Order, the term “must” means that the Order is to be complied with at all times. The term “should” indicates that an activity that is strongly recommended or advised, but for which a justified effective alternative can be considered.
- (2) In this Order:

***allogeneic*** means material for administration to an individual that is obtained, or derived, from a genetically different individual;

***antiseptic*** has the same meaning as in ‘antiseptic’ in Part 1, Regulation 2 of the Therapeutic Goods Regulations 1990, as amended from time to time. Antiseptic means a substance:

- (a) that is recommended by its manufacturer for:
  - (i) dermal application; or
  - (ii) application to the mucous membranes of a person or an animal:
    - (A) to kill microorganisms; or
    - (B) to prevent the growth of microorganisms to a level that causes or may cause clinical infection; and
- (b) that is not represented to be suitable for internal use.

***ARTG*** means Australian Register of Therapeutic Goods;

**autologous** means material that is obtained, or derived from, an individual for administration to the same individual;

**banked** means maintenance, under appropriate controlled conditions, in an inventory, of a finished product that has been determined suitable for supply;

**bioburden** means the quantity and characteristics of microorganisms present in the goods or to which the goods may be exposed in a manufacturing environment;

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

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

**cell** means individual cells or a collection of cells when not bound by any form of connective tissue;

**cord blood** means blood collected from human placental and umbilical cord blood vessels;

**critical material** means all components, materials or supplies which could have a direct impact on the quality of the end product;

**disinfectant** has the same meaning as in ‘disinfectant’ in Part 1, Regulation 2 of the Therapeutic Goods Regulations 1990, as amended from time to time. Disinfectant means a substance:

- (a) that is recommended by its manufacturer for application to an inanimate object to kill microorganisms; and
- (b) that is not represented by the manufacturer to be suitable for internal use;

**domino donor** means a living person from whom a diseased organ is removed and replaced with a healthy organ, and healthy parts of the diseased organ are salvaged and processed to produce banked tissue e.g. in a heart transplant the heart valve from the diseased heart, if healthy and structurally sound, may be processed and banked for future use;

**donor** means every source, whether living or deceased, of human blood, human cells or human tissues;

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

**HBcAb** means Hepatitis B core antibody;

**HBsAb** means Hepatitis B surface antibody;

**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;

**manufacture** has the same meaning as in ‘manufacture’ in subsection 3(1) of the *Therapeutic Goods Act 1989* (the Act), as amended from time to time;

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

**petechiae** (pl.) means non-raised round, purplish red spots caused by intradermal or submucosal haemorrhage as opposed to ecchymoses (rounded or irregular patch);

**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.

**pre-mortem blood sample** means a blood sample collected from a heart beating donor;

**prion disease- risk of** means having been exposed to the putative causative agent(s) of any one of the family of pathogenic transmissible spongiform encephalopathies through genetic (familial), environmental\* or iatrogenic\*\* means, i.e. lived in or consumed or undergone treatment with potentially contaminated product, e.g. beef products (e.g. bovine insulin), blood transfusion or tissue transplantation, in a high risk country.

*Criteria used in Australia that define “risk of prion disease” include donors who have*

*\* a) 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;*

*\*\*b) received a transfusion or injection of blood or blood components while in England, Scotland, Wales, Northern Ireland or the Isle of Man from 1<sup>st</sup> January 1980 onwards.*

**processing** means any operation involved in preparation, manipulation, preservation for storage and packaging;

**QC** means quality control;

**specified microorganism** means a microorganism which, if isolated from the tissue, necessitates discard of the tissue;

**storage** means maintaining a substance, material or product under appropriate controlled conditions until supply;

**TGA** means Therapeutic Goods Administration

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

*TSE* means transmissible spongiform encephalopathy.

## **5. Application**

- (1) Subject to section 6, this order applies to human blood and blood components, human tissues and human cellular therapies that are retrieved from
  - (a) a living human donor and intended for autologous use; or
  - (b) living human donor(s) and intended for allogeneic use; or
  - (c) deceased human donor(s) and intended for allogeneic use.
- (2) This Order does not apply to a human derived product declared not to be a therapeutic good in an Order made under section 7 of the Act.

## **6. Exemptions**

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
- (2) blood and blood component samples and biopsied cell or tissue samples taken for *in vitro* diagnosis and not for manufacture and/or reintroduction or transplant to a recipient
- (3) a product in relation to which an exemption from compliance with this Order has been granted by the Secretary in accordance with section 14 and 14A of the Act

## **7. General requirements for human blood and blood components, human tissues and human cellular therapies**

- (1) The manufacturer must comply with the provisions as set out in Table 1 of Schedule 1 for human blood and blood components, human tissue or human cellular therapy products manufactured from a specified donor group.
- (2) Products must also comply with any additional requirements contained in other relevant Orders.

## Schedule 1

### PRODUCT REQUIREMENTS

**Table 1: Schedule 2 to 6 requirements for products manufactured from a particular donor group**

Donor Groups	Intended use	Product or starting material	Compliance with requirements set out in Schedule 2	Compliance with requirements set out in Schedule 3	Compliance with requirements set out in Schedule 4	Compliance with requirements set out in Schedule 5	Compliance with requirements set out in Schedule 6
<sup>a</sup> 1. Deceased donor	Allogeneic	Any tissue other than cornea or skin	All requirements	All requirements except clause (2)	All requirements except clause (2) and paragraph (4)(b)	All requirements except subparagraph (1)(b)(ii) and clauses (2) and (3)	All requirements
2. Deceased cornea donor	Allogeneic	Cornea preserved at ≤10°C	All requirements except clause (4)	All requirements except clause (2)	All requirements except clause (2) and paragraph (4)(b)	All requirements except subparagraph (1)(b)(ii) and clauses (2) to (5)	All requirements
	Allogeneic	Cornea preserved at >10°C	All requirements	All requirements except clause (2)	All requirements except clause (2) and paragraph (4)(b)	All requirements except subparagraph (1)(b)(ii) and clauses (2) and (3)	All requirements
3. Deceased skin donor	Allogeneic	Skin	All requirements	All requirements except clause (2)	All requirements except clause (2) and paragraph (4)(b)	All requirements except subparagraph (1)(b)(ii), clauses (2) and (3) and paragraph (5)(b)	All requirements

Schedule 1 (continued)

Donor Groups	Intended use	Product or starting material	Compliance with requirements set out in Schedule 2	Compliance with requirements set out in Schedule 3	Compliance with requirements set out in Schedule 4	Compliance with requirements set out in Schedule 5	Compliance with requirements set out in Schedule 6
4. Living donor	Allogeneic	<sup>b</sup> Blood and blood components	All requirements	All requirements except paragraphs (2)(b),(c),and (d) and clauses (3) and (4)	All requirements except paragraphs (2)(b),(c) and (d), clause (3) and paragraph (4)(b)	All requirements except subparagraphs (1)(b)(ii) and (1)(c)(iii), paragraph (1)(d) and clauses (2) and (3)	All requirements
	Allogeneic	Plasma only	All requirements	All requirements except paragraphs (2)(b),(c),and (d) and clauses (3) and (4)	All requirements except paragraphs (2)(b),(c),(d), clause (3) and paragraph (4)(b)	All requirements except subparagraphs (1)(b)(ii) and (1)(c)(iii), paragraph (1)(d) and clauses (2) and (3)	All requirements
	Allogeneic	HPC-A HPC-M	All requirements	All requirements except paragraphs (2)(a)(c)(d) and clause (3)	All requirements except paragraphs (2)(a),(b),(c) and clause (3)	All requirements except subparagraphs (1)(b)(ii) and (1)(c)(iii), paragraph (1)(d), and clauses (2) and (3)	All requirements
	Allogeneic	HPC-C	All requirements	All requirements except paragraph (2)(a) and (b) and clause (3)	All requirements except paragraphs (2)(a),(b) and(d) clause (3) and paragraph (4)(b)	All requirements except subparagraph (1)(c)(iii), paragraph 1(d) and clause (3)	All requirements
	Allogeneic	Heart valve - Domino donor only	All requirements	All requirements except paragraphs (2)(b),(c) and (d) and clause (3)	All requirements except paragraphs (2)(c) and (d), clause (3) and paragraph(4)(b)	All requirements except subparagraphs (1)(b)(ii) and (1)(c)(iii), paragraph (1)(d), and clauses (2) and (3)	All requirements
	Allogeneic	<sup>c</sup> Other products	All requirements	All requirements except clause (3)	All requirements except paragraphs (2)(c) and (d), clause (3) and paragraph (4)(b)	All requirements except subparagraphs (1)(b)(ii) and , (1)(c)(iii), paragraph (1)(d) and clause (3)	All requirements

Donor Groups	Intended use	Product or starting material	Compliance with requirements set out in Schedule 2	Compliance with requirements set out in Schedule 3	Compliance with requirements set out in Schedule 4	Compliance with requirements set out in Schedule 5	Compliance with requirements set out in Schedule 6
	<b>Autologous</b>	<sup>d</sup> <b>Blood</b>	All requirements except paragraph (1)(b)	All requirements except paragraphs (2)(b),(c), and(d) and clauses (3),(4) and (5)	All requirements except: paragraphs (2)(b), (c) and (d), clause (3) and paragraph (4)(b)	All requirements except subparagraphs (1)(b)(ii), and (1)(c)(iii), paragraph (1)(d) and clause (2)	All requirements
	<b>Autologous</b>	<b>HPC-A HPC-M</b>	All requirements except paragraph (1)(b)	All requirements except paragraphs (2)(a),(c), and (d) and clauses (3) and (5)	All requirements except: paragraphs (2)(a),(b), (c) and clause (3)	All requirements except subparagraphs (1)(b)(ii) and (1)(c)(iii), paragraph (1)(d) and clause (2)	All requirements
	<b>Autologous</b>	<b>HPC-C</b>	All requirements except paragraph (1)(b)	All requirements except paragraphs (2)(a) and (b) and clauses (3) and (5)	All requirements except paragraphs (2)(a),(b), and (d), clause (3) and paragraph(4)(b)	All requirements except subparagraph (1)(c)(iii) and (1)(d)	All requirements
	<b>Autologous</b>	<sup>c</sup> <b>Other products</b>	All requirements except paragraph (1)(b)	All requirements except clauses (3) and (5)	All requirements except paragraphs (2)(c) and(d), clause (3) and paragraph (4)(b)	All requirements except subparagraph (1)(c)(iii) and paragraph, (1)(d)	All requirements

<sup>a</sup> deceased donors for the donation of tissues or cells, other than cornea or skin

<sup>b</sup> human blood and blood components for allogeneic transfusion **mean** human blood and blood components that are not

(i) 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

(ii) 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 patient under the practitioner's care; or

(iii) 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;

<sup>c</sup> these are products manufactured for either autologous or allogeneic use from a living donor that are within the scope of the Order but are not blood/blood components<sup>b</sup>, plasma, HPC-A, HPC-M, HPC-C, heart valve – domino donor only, and blood<sup>d</sup>

<sup>d</sup> blood refers to the blood manufactured by a medical practitioner or donation centre for a patient in the practitioner's care as described in (ii) and (iii) above



## Schedule 2

### POLICY

This Schedule sets out the requirements for the manufacturer to have a documented and implemented policy (or policies) in relation to the mitigation of the risk for disease transmission during collection, manufacture or the finished product, and to ensure conformity with applicable Commonwealth, State and Territory laws relating to the collection and manufacture of blood, cells and tissues, notification of donor test results, and the acceptance and release of manufactured products.

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
  - (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.
- (2) The manufacturer must conform with the applicable Commonwealth, State or Territory law regarding consent for donation of blood, cells and tissues. Human blood and blood components, human tissues and human cellular therapies must only be manufactured from blood, cells and tissues collected from donors in accordance with the applicable law.
- (3) The manufacturer must have policies in place with regard to donor testing notification process and how person/organisations must be notified of a positive test result relating to an infectious disease.
- (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.

### Schedule 3

#### MEDICAL & SOCIAL HISTORY

This Schedule sets out the requirements relating to the collection, recording and assessment of medical and social history of prospective donors or donors of human blood and blood components, human tissues and cellular therapies.

- (1) The minimum donor medical and social history criteria to be reviewed and responses documented for all donors of human blood and blood components, human tissues and human cellular therapies are set out in Table 2.
- (2) Human blood and blood components, human tissues or human cells must not be collected from a living donor unless the Medical and Social History interview has been conducted by a qualified interviewer at a face-to-face interview with the donor or guardian/next-of-kin.
  - (a) The interview must occur as close as possible to, but at no more than 7 days prior to donation, unless (b) or (c) or (d) applies, and the history must be documented at that time.
  - (b) Where the interview of a donor is in relation to donation of HPC-A or HPC-M then the medical and social history of a donor must take place, or re-confirmation given if previously interviewed, within 30 days before collection of the peripheral blood or bone marrow.
  - (c) If a maternal donor in relation to a donation of cord blood has been interviewed earlier during pregnancy, a confirmation of the currency of the medical and social history must be provided in writing by the donor, if possible, at the time of donation, or no later than 14 days after donation.
  - (d) For cells and tissues, if repeat serological testing will be performed on donor blood samples collected at a minimum of 180 days after the initial sampling in accordance with Schedule 5 Item 2 (a) then the interview must occur within 90 days prior to donation and currency of the history confirmed in writing by the donor within 7 days prior to donation.
- (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.

**Table 2: Minimum medical and social criteria required to define a donor's risk of recent exposure to infectious disease**

Donor medical and social history criteria	Period of ineligibility prior to donation for	
	Allogeneic use	Autologous use
(a) Tattoo or body piercing	6 months	Nil
(b) Acupuncture	6 months unless the acupuncture in that period was performed by a licensed practitioner using sterile non-reused needles or equipment	Nil

Donor medical and social history criteria	Period of ineligibility prior to donation for	
	Allogeneic use	Autologous use
	then nil exclusion period	
(c) Needle stick injury, or contact of non-intact skin or mucous membrane with blood or body fluid	6 months where the injury or contact is thought to be at high risk of carrying hepatitis C, hepatitis B or HIV	Nil
(d) Inmate of a prison	12 months from date of release (when imprisoned for a consecutive period of 72 hours or more)	Nil
(e) Sex worker, or received money for sex	12 months from last contact	Nil
(f) Male to male sexual relationship	12 months from last contact	Nil
(g) A sexual relationship with a person known to <ul style="list-style-type: none"> <li>• have hepatitis C</li> <li>• have HIV</li> <li>• be a sex worker</li> <li>• have male to male sex</li> </ul>	12 months from last contact	Nil
(h) Ever injected any drug for a non-medical reason	Permanent	Nil
(i) A recipient of <ul style="list-style-type: none"> <li>• human derived clotting factors</li> <li>• viable animal cells or tissues</li> </ul>	Permanent	Nil
(j) Known to be infected with <ul style="list-style-type: none"> <li>• hepatitis C</li> <li>• HIV</li> <li>• HTLV 1/HTLV 2</li> </ul>	Ineligible	Nil
(k) Suspected to be infected with <ul style="list-style-type: none"> <li>• hepatitis C</li> <li>• HIV</li> <li>• HTLV 1/HTLV 2</li> </ul>	Ineligible until a disease free state can be established.	
(l) Known, suspected or at risk of being infected with hepatitis B	Ineligible until <ul style="list-style-type: none"> <li>(i) disease resolved (donor immunised or HepBsAb<math>\geq</math>100 IU/L) or</li> <li>(ii) as prescribed for the risk factors (a) to (h) above</li> </ul>	Nil
(m) Physical evidence of sepsis such as unexplained generalised rash/generalised petechiae	Ineligible until a disease free state can be established	Nil
(n) Active infection of the cells and tissue to be retrieved, active infection of other cells and tissues that are indicative of infection that render the target cells and tissues unsuitable for manufacture	Ineligible until a disease free state can be established	Nil
(o) Active infection of tuberculosis	Ineligible until a disease free state can be established	Nil

Donor medical and social history criteria	Period of ineligibility prior to donation for	
	Allogeneic use	Autologous use
(p) Typhus	Ineligible until a disease free state can be established	Nil
(q) Risk of prion disease	Permanent	Nil
(r) Being a recipient of human pituitary derived growth hormone	Permanent	Nil
(s) Being a recipient of allogeneic organ(s) or cells, or deceased donor tissue allograft	Permanent	Nil
(t) Being a recipient of allogeneic blood, blood components or blood products that do not meet the requirements of this Order	12 months unless (q) or (r) apply, then permanent	Nil
(u) Being a recipient of live vaccine(s) or Hepatitis B vaccine	Ineligible for the periods specified in (5)	Nil

- (4) 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 greater time, the birth mother must also be evaluated for high risk behaviour according to criteria (a) to (l) of Table 2 of this Schedule and ineligibility observed as prescribed for the donor.
- (5) A potential donor of allogeneic tissues or cells who received
- (a) live vaccine is ineligible to donate tissues if the minimum donor exclusion period has not been exceeded as set out in Table 3.

**Table 3: Ineligibility period for potential tissue donors who have received a live vaccine**

Vaccines/Antisera Administered	Vaccine Composition	Donor Exclusion Period
(i) Rotavirus	Live attenuated bacteria or viruses	4 weeks
(ii) Oral Polio		
(iii) BCG		
(iv) Measles		
(v) Mumps		
(vi) Rubella		
(vii) Yellow fever		
(viii) Typhoid fever		
(ix) Cholera		
(x) Varicella		
(xi) Small pox		8 weeks
(xii) Antisera/Antivenins	Sera of animal origin	12 weeks
(xiii) Unlicensed vaccine	Unknown	12 months

- (b) any of the following vaccines is not required to be deferred provided the donor is well:
- (i) Cholera and typhoid vaccines with killed bacteria
- (ii) Capsular polysaccharide typhoid fever vaccine

- (iii) Vaccines with inactivated viruses
- (iv) Toxoids
- (v) Diphtheria and tetanus
- (vi) Hepatitis A and Hepatitis B if no exposures have occurred.
- (vii) Rabies, tick-borne encephalitis (where exposure has occurred a one year deferral post exposure is required)
- (viii) Meningococcal
- (ix) Subunit vaccines e.g. cervical cancer vaccine

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## Schedule 4

### SAMPLING, TEST KITS, TEST PROTOCOLS AND TEST MANAGEMENT

This Schedule sets out the requirements to be complied with by the manufacturer in relation to sampling, test kits to be used, test protocols to be applied and test management to be used to determine the infectious disease status of potential donors of human blood and blood components, human tissues and human cellular therapies.

- (1) In order to determine the infectious disease status of persons who are potential donors of human blood and blood components, human tissues and human cellular therapies, testing must be performed on aseptically collected samples of the donor's blood for the purpose of infectious disease screening.
- (2) Blood sampling of a living donor must take place,
  - (a) on the day of blood, cell or tissue collection; or
  - (b) if not possible for cells and tissue, as close as practicable prior to the time of cell or tissue collection, but no more than 7 days; or
  - (c) in the case of a mother of the infant donor(s) of cord blood, within 7 days (before or after) the cord blood collection; or
  - (d) within 30 days before collection of peripheral blood or bone marrow for manufacture of HPC-A or HPC-M
- (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.
- (4) For manufacture of blood, blood components, tissue and cellular therapies, testing of the samples for infectious diseases must normally be performed
  - (a) as soon as practicable; or
  - (b) within 30 days before collection of peripheral blood or bone marrow for therapeutic goods that are HPC-A and HPC-M, respectively.
- (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. When a potential donor has lost blood and has recently received donated blood, blood components, colloids or crystalloids, blood testing may not be valid due to dilution of the sample. Where a pre-transfusion sample is unavailable for infectious disease testing, an algorithm must be applied to assess the degree of dilution. A plasma dilution factor must be less than 50%, i.e. must not exceed the donor's own plasma volume.
- (6) The test kits/methodologies used for the mandatory tests for screening must
  - (a) be current technology; and
  - (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.
  - (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.
  - (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.
  - (12) Documentation of the tests performed, test modifications, analyses and any anomalies required to be appended to the donor record in addition to the test results.
  - (13) Results of all tests, including indeterminate or initial reactive test results, and examinations performed must be documented in the donor record.

## Schedule 5

### DONOR TESTING AND EXAMINATION

This Schedule sets out the requirements in relation to donor testing and examination.

- (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  $\geq 180$  days after the initial blood sample is taken, or time restrictions due to tissue lability), tests using Nucleic Acid Amplification Technology (NAAT<sup>1</sup>), where available, for the infectious diseases/infectious disease markers as indicated in Table 4 of this Schedule.
  - (b) 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,
    - (i) the birth mother must also be screened and tested in accordance with Schedules 4 and 5(1)(a);
    - (ii) for cord blood, each cord unit must be tested according to Table 4 prior to release. Units for allogeneic transfusion must be negative when tested.
  - (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,
    - (i) on the day of blood, cell or tissue collection; or
    - (ii) if not possible for cells and tissue, as close as practicable prior to the time of cell or tissue collection, i.e. generally within 5 days and no more than 7 days; or
    - (iii) for a deceased donor, prior to cell or tissue collection and no later than 24 hours after death;
  - (d) The cells and tissues of a deceased donor whose cause of death is unknown must be deemed unacceptable, 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 or preclude transplantation of the cells or tissue from that donor.
- (2) Where cells and tissues can be stored for long periods without impairing fitness for use, repeat sampling and serological or NAAT testing of the living donor

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<sup>1</sup> NAAT and serological tests used for screening blood from a deceased donor blood must have been validated for post mortem samples.



- (a) for HIV, HBV and HCV must be performed at a minimum of 180 days after collection of the donation sample, to provide assurance that the initial sample was not collected during the window period for infection.
  - (b) and the donor of a rare cell or tissue type is not available for the repeat 180 day sampling, the initial donor sample must be tested by NAAT for HIV, HCV and HBV (when available).
- (3) In cases where a human blood and blood component, human tissue or human cellular therapy is manufactured from a donor with repeatedly reactive mandatory screening tests, with the intended purpose of reintroduction into that donor
- (a) segregation and quarantine must be applied to that human blood and blood component, human tissue or human cellular therapy and cross-contamination is to be avoided; and
  - (b) records must be available to demonstrate the rationale for the use of the product. Authority for the release of this product must also be documented.
- (4) Examination for microbiological contamination of donor cell or tissue specimens must be performed using a validated method.
- (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.

**Table 4: Donor testing requirements**

ID testing		Deceased donors <sup>a</sup>	Cornea only donors	Living donors <sup>b</sup>										HPC-C units Release tests	
				Allogeneic use <sup>b</sup>						Autologous use				Allogeneic	Autologous
				Blood / components	Plasma only	HPC-A HPC-M	HPC-C	Domino donor	Other	Blood	HPC-A HPC-M	HPC-C <sup>b</sup>	Other		
Serology Initial sample	anti HIV-1 anti HIV-2	√ X	√ X	√ X	√ X	√ X	√ X	√ X	√ X	√	√	√	√	√ X	√
	anti HCV	√ X	√ X	√ X	√ X	√ X	√ X	√ X	√ X	√	√	√	√	√ X	√
	HBsAg	√ X	√ X	√ X	√ X	√ X	√ X	√ X	√ X	√	√	√	√	√ X	√
	HBcAb <sup>2</sup>	√ X		√ X		√ X	√ X <sup>c</sup>	√ X	√ X	√	√	√ <sup>c</sup>	√	√ X	√
	HTLV1/2 (antibodies)	√ X		√ X		√ X	√ X	√ X	√ X	√	√	√	√	√ X	√
	syphilis <sup>3</sup>	√ X		√ X		√ X	√ X <sup>d</sup>	√ X	√ X	√	√	√ <sup>d</sup>	√	√ X	√
NAAT Initial sample	HIV	√ X		√ X	√ X	√ X		√ X	√ X <sup>e</sup>	√	√		√		
	HCV	√ X		√ X	√ X	√ X		√ X	√ X <sup>e</sup>	√	√		√		
	HBV (when approved)	√ X		√ X	√ X	√ X		√ X	√ X <sup>e</sup>	√	√		√		
Serology/NAAT ≥180 sample	anti HIV-1 anti HIV-2						√ X		√ X <sup>e</sup>			√			
	anti HCV						√ X		√ X <sup>e</sup>			√			
	HBsAg						√ X		√ X <sup>e</sup>			√			
	HBcAb						√ X		√ X <sup>e</sup>			√			

√ X indicates that the test **must** be performed and the test **must** demonstrate that the samples tested are non-reactive

√ indicates that the test **must** be performed and if the test demonstrates that the samples tested are reactive then Schedule 5(3) applies

<sup>a</sup> includes testing to be performed on blood samples of deceased donors for the donation of any tissue other than cornea

<sup>b</sup> additional testing provisions as specified in Schedule 5(2) apply to some living donors of cells and tissues to be used for allogeneic use and to the maternal donor of cord blood

<sup>c</sup> for a HPC-C unit, the maternal sample may be acceptable if reactive for HBcAb provided it satisfies the criteria given in <sup>2</sup> or if hepatitis B antigen negative when tested by DNA testing (NAAT)

<sup>d</sup> if a maternal sample is syphilis screen positive but tests negative using a specific confirmatory test the sample may be considered acceptable.

<sup>e</sup> (2) of this Schedule applies

<sup>2</sup> A HBcAb reactive sample is acceptable only if HBsAb when tested is ≥100 IU/L, or a specified recipient is known to be immune to HBV.

<sup>3</sup> Non-specific (reaginic) syphilis tests are prone to false positive results. Therefore specific syphilis testing must be conducted on tissue donors, where it is required.

## Schedule 6

### SUBSTANCES USED IN PRODUCTION

This Schedule sets out the requirements in relation to the selection and evaluation of any critical materials employed during the manufacture (collection, processing, storage or transport) of human blood and blood components, human tissues or human cellular therapies.

- (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) Where blood, cells and tissues are required to be manufactured in a facility with an approved quality system, critical materials used in manufacture that are
  - (a) solutions, other than the disinfectant/antiseptic<sup>4</sup> solutions used in a validated tissue cleaning process, which contact the human cells or tissue during collection, processing, storage or transport must be
    - (i) manufactured under an approved quality management system and be supplied as a sterile solution; or
    - (ii) tested for and 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.
  - (b) material, other than the starting materials of blood, cells or tissue, containing any components of human or animal origin, must have been sourced, tested (if methodology is available) and assessed as presenting a minimal risk of transmitting infectious disease agents [refer TGA<sup>5</sup> and EMEA<sup>6</sup> Guidelines]. If the product is not required to be on the ARTG, the recorded information must include at minimum<sup>7</sup>:
    - (i) Screening tests performed;
    - (ii) QC specifications, e.g. criteria and limits for the tests performed;
    - (iii) Storage conditions

<sup>4</sup> Antibiotic/antimicrobial solutions should be sterile. If they are not supplied sterile by the solution manufacturer, they should be sterilised by filtration through a 0.22µm filter prior to use and aseptically dispensed at time of use to prevent further contamination of the tissue.

<sup>5</sup> TGA approach to minimising the risk of exposure to Transmissible Spongiform Encephalopathies (TSEs) through medicines and medical devices <<http://www.tga.gov.au/docs/html/tsepolicy.htm>>

<sup>6</sup> EMEA [Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products \(EMEA/410/01 rev 2, October 2003 \(pdf,181kb\)](#)

<<http://www.emea.europa.eu/pdfs/human/bwp/TSE%20NFG%20410-rev2.pdf>>

EMEA CPMP) Note for Guidance on Virus Validation Studies: The design, contribution and interpretation of studies validating the inactivation and removal of viruses Feb 1996

<<http://www.emea.europa.eu/pdfs/human/bwp/026895en.pdf>>

<sup>7</sup> If this information is not available from the manufacturer of the material, the material will need to be assessed by the manufacturer of the human blood and blood component, human tissue or cellular therapy.