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| ARGB Appendix 12 - Guidance on TGO 108: Standard for Human Cell or Tissue Products – Donor Screening Requirements |
| Australian Regulatory Guidelines for Biologicals (ARGB) |
| Version 1.0, May 2021 |

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## About this guidance

As prepared by the Therapeutic Goods Administration (TGA), this guidance describes the requirements for [manufacturers](https://www.tga.gov.au/manufacturing-therapeutic-goods) and [sponsors](https://www.tga.gov.au/role-sponsor) of biologicals and human cell or tissue (HCT) products set out in the Therapeutic Goods (Standard for Human Cell and Tissue Products – Donor Screening Requirements) (TGO 108) Order 2021.

Generally, [TGOs](https://www.tga.gov.au/therapeutic-goods-orders) are standards that determine the consistency of product quality, including label quality. TGO 108 specifies requirements around the minimisation of transmission of communicable diseases through the use of therapeutic goods comprising, derived or containing HCT, specifically with regard to donor:

* medical and social history requirements
* testing requirements for blood and other samples
* physical assessment requirements
* deferral criteria

As a provider of such therapeutic goods, you must comply with requirements that contribute to their quality and safety, and that mitigate infectious disease risks.

TGO 108 replaces:

* [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 (TGO 88)](https://www.legislation.gov.au/Details/F2013L00854)

TGO 88 is due to ‘sunset’ on 1 October 2023. Sunsetting is the process whereby legislative instruments undergo automatic repeal after 10 years following their registration.

TGA updated TGO 88 at the same time as numerous other TGOs which sunsetted on 1 October 2021 because all these TGOs were inter-related and cross-referenced each other:

* [Therapeutic Goods Order No. 83 - Standards for human musculoskeletal tissue (TGO 83)](http://www.legislation.gov.au/Series/F2011L01489)
* [Therapeutic Goods Order No. 84 - Standards for human cardiovascular tissue (TGO 84)](http://www.legislation.gov.au/Series/F2011L01490)
* [Therapeutic Goods Order No. 85 - Standards for human ocular tissue (TGO 85)](http://www.legislation.gov.au/Series/F2011L01491)
* [Therapeutic Goods Order No. 86 - Standards for human skin (TGO 86)](http://www.legislation.gov.au/Series/F2011L01492)

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| This information is provided for guidance only and has been developed on the basis of current knowledge of the subject matter.  It should not be relied on to address every aspect of the relevant legislation. You should seek your own independent legal advice to ensure that all of the legislative requirements are met.  For clarification of a particular requirement, contact [TGA’s Biological Science Section (BSS)](https://www.tga.gov.au/biologicals-0#contacts). |

## About TGO 108

TGO 108 specifies the minimum criteria for donor selection to minimise the risk of infectious disease transmission through the use of therapeutic goods comprising, derived from, or containing HCT. This guidance provides an interpretation of how the various requirements can be met.

Additional or higher requirements may be included at a sponsor’s discretion or may be required by a product-specific order or [default standard](https://www.tga.gov.au/pharmacopoeias). Further testing as clinically relevant for specific products or patient populations may also be necessary, for example, Cytomegalovirus testing where recipients are children or immunocompromised.

TGO 108 **applies to**:

* biologicals (encompassing starting materials and finished therapeutic goods) comprising, derived from, or containing HCTs.
* all human donors of one or more of the following that are collected from a donor for use in the manufacture of an HCT product:
  + human blood and blood components including:
* red cells
* white cells
* platelets and
* plasma (including plasma for fractionation)
  + human cells (including haematopoietic progenitor cells)

TGO 108 **does not apply to** biologicals that are:

* not intended for therapeutic use, that is, blood or tissue samples for infectious disease or bioburden testing
* [Excluded from TGA regulation](https://www.tga.gov.au/what-regulated-biological#excluded)
* [Faecal Microbiota Transplant (FMT) products](https://www.tga.gov.au/publication/faecal-microbiota-transplant-fmt-product-regulation)[[1]](#footnote-1)
* [Autologous HCT products](https://www.tga.gov.au/autologous-human-cells-and-tissues-products-regulation)

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| Although [autologous HCT products](https://www.tga.gov.au/autologous-human-cells-and-tissues-products-regulation) are exempt from TGO 108, any or all of the requirements specified in TGO 108 could be required for demonstrating compliance to TGO 109. |

If you are unsure whether TGO 108 applies to a specific biological, please contact [bloodandtissues@health.gov.au](mailto:bloodandtissues@health.gov.au) for clarification.

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| TGA accepts that alternative approaches may be suitable to satisfy the requirements of TGO 108 for specific product types, provided there is appropriate justification. Where alternative approaches are used, these must be validated by the manufacturer.  The justification and supporting validation information is subject to TGA review and approval. It must be provided in the data supporting the application for product approval or in an application for a variation, post approval. Subject to approval, and requirements in the standard, sponsor may still be required to obtain consent prior to import, supply or export therapeutic goods that do not comply with a standard applicable to the goods (see section 14 the [*Therapeutic Goods Act 1989*](https://www.legislation.gov.au/Series/C2004A03952)). |

### Commencement of TGO 108

TGO 108 commences on 30 September 2021. Prior to this date, this TGO applied:

* [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 (TGO 88)](https://www.legislation.gov.au/Details/F2013L00854)

### Review of TGO 108

TGO 108 will be reviewed regularly as changes in legislation, emerging technology, and best practice occur. Sponsors and manufacturers are encouraged to discuss with TGA any proposed changes in practice or evolving technologies that may affect, or be affected by, the requirements of TGO 108.

### Part 1 – Preliminary

#### Section 4 – Definitions

The definitions provided within TGO 108 are specific to this TGO and are not intended to apply outside of TGO 108.

Where possible, definitions included in TGA’s [Acronyms & glossary](https://www.tga.gov.au/acronyms-glossary) page are derived from current TGA legislation, international regulatory documents, or current industry guidance documents. Where a suitable definition has not been identified by those means, TGA has developed a definition that is informed by equivalent terms used in the aforementioned documents, expert committees, or through public consultation.

Further clarification of some definitions, specific to TGO 108, are provided below.

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| ***allogeneic use***, in relation to an HCT product, means administration to, or application in the treatment of, a person other than the person from whom the HCT materials used in the manufacture of the product were collected. |

This definition intends to capture all non-self-transplantation or transfusion, and includes syngeneic use (for example, between identical twins).

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| ***asystole***, in relation to a donor of HCT materials, means the reference time for cardiac arrest, which is determined as follows:   1. the documented pronounced time of death; or 2. if death is not witnessed – the last time the donor was known to be alive; or 3. the tissue donor is also a solid organ donor – the cross clamp time. |

This definition includes cross-clamp time, which for organ donors refers to the time that the aorta is cross clamped by a surgical team. 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 (for example, agonal respirations, pulse-less electrical activity).The time of certification of circulatory death would also be considered appropriate if the tissue donor is also a solid organ donor.

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| ***HCT materials*** means one or more of the following that are collected from a donor for use in the manufacture of an HCT product:   1. human cells (including haematopoietic progenitor cells); 2. human tissues; 3. blood; 4. blood components (including plasma). |

HCT materials applies to collected material and at any stage during processing for manufacture of HCT product.

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| ***specified microorganism*** – see [Acronyms & glossary](https://www.tga.gov.au/acronyms-glossary) |

A sponsor should develop a list of specified microorganisms of clinical significance, which, if isolated, require rejection of the product for clinical use. This process should be based on a risk assessment and consider the category of tissue, the method of processing and the nature and type of microorganisms that might be present. The definition does not mandate a requirement to test for rickettsia or mycoplasma, but these may be considered significant organisms for particular HCT materials.

### Part 2 – Requirements

Part 2 specifies the minimum standards for samples and test methods used for infectious disease testing for determining donor suitability.

#### Section 8 – General requirements

##### Subsections 8(1) to 8(3) – Manufacture

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| **8 General requirements**   1. An HCT product must be manufactured in accordance with procedures that mitigate the risk of infectious disease transmission. 2. An HCT product must not be released for supply, unless the applicable screening procedures and requirements specified in this instrument are satisfied. 3. Acceptance criteria based on microbial specifications must be applied to HCT materials used in the manufacture of an HCT product. |

All manufacturers must ensure that the design and construction of the manufacturing facility is suitable to the type of processing conducted, with separation of areas for minimising mix-ups and contamination.

If the manufacture of an HCT product takes place in a hospital, the facility and procedures should be designed and developed in a way that takes account the principles of GMP.

Where a facility holds a TGA manufacturing licence, compliance with the requirements outlined in this subsection are achieved through complying with the requirements of the [Australian Code of GMP](https://www.tga.gov.au/publication/australian-code-good-manufacturing-practice-human-blood-and-blood-components-human-tissues-and-human-cellular-therapy-products).

Guidance is available to assist facilities on how the Australian Code of GMP applies to the manufacture of HCT products.

Note that all HCT products and materials must be segregated from the mainstream inventory until the HCT product has been determined to be compliant with all necessary requirements or release criteria, for example, where infectious disease test results may not be complete. This is especially relevant for products stored in an inventory (or banked) with other products for potentially long periods of time as these products pose a risk of transmission to other products through physical contact, and a risk to the public from unintentional release and use. Quarantine procedures are assessable under the current Good Manufacturing Practice (cGMP) requirements. Quarantine practices should be determined based on risk; however, the conditions of quarantine should be consistent with storage conditions, wherever possible.

##### Subsection 8(4) – Blood sample testing timeframe

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| **8 General requirements**   1. Blood samples of a donor of HCT materials must be tested: 2. as soon as practicable after the blood sample is taken; or 3. in accordance with the timeframe specified by the manufacturer of the IVD medical device or the in-house IVD medical device that is used for testing the sample; or 4. where testing is conducted outside of Australia – within a timeframe that is validated by the testing laboratory. |

Timeframes for sample testing should be in accordance with requirements of validated test kits. The testing methodology must have been validated for cadaveric samples to include the relevant time period of sample collection following asystole.

##### Subsection 8(5) – Blood sample testing using IVDs

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| **8 General requirements**   1. Blood samples must be tested using IVD medical devices or in-house IVD medical devices that: 2. use the most appropriate methodology available that is validated for testing the samples (including cadaveric samples); and 3. where testing is conducted in Australia – are either included in the Register or exempt from the requirement to be included in the Register, or are the subject of an approval or authority under the Act; and 4. where testing is conducted outside of Australia – are: 5. approved by a relevant regulatory authority in the country in which the testing is conducted; and 6. used in a facility that has been approved for such testing by a relevant regulatory authority in the country in which the testing is conducted; and 7. considered acceptable by the Therapeutic Goods Administration. |

Each in vitro diagnostic (IVD) medical device or in-house IVD medical device used for the mandatory donor screening tests and confirmatory tests (if these support final product release) should be validated for the purpose for which it is to be used (intended use) and used in accordance with the test kit instructions. Where test methods are used beyond the test kit instructions (for example, use on cadaveric samples), validation to support the extended use must be demonstrated.

###### Methodology of testing kits

The most appropriate methodology shall be determined and justified by the sponsor. The infectious diseases test screening protocol could be an ‘in-house’ test or a commercial kit and may be conducted by the sponsor or a contract laboratory. The sponsor should also consider utilising new test methods, such as more sensitive assays, as they become available.

In addition, when testing a sample of cadaveric blood, the screening test must be specifically approved for use on cadaveric specimens or validated for this purpose by the testing laboratory.

###### Approval of test kits

If the test kit and methodology has current approval by the relevant regulatory authority in the country where the testing is performed, the evidence of this approval should be provided.

Where test methods are used beyond the level approved by the local regulatory approval, for example, use on cadaveric samples, validation to support the extended use must be demonstrated.

A well-characterised assay already established for blood donors may be used for testing cadaveric specimens. Alternative methods to characterise a cadaveric assay may be acceptable to TGA and the supporting validation data should be provided for review with the application.

###### Testing facility

All facilities performing donor testing must be approved by the regulatory authority in the country where the testing is performed. For domestic facilities, a TGA licence will be required; for overseas testing facilities, the sponsor must hold a TGA clearance demonstrating compliance with GMP requirements. Where confirmatory testing is utilised to decide suitability of a donor, the facility’s GMP must include this purpose.

###### Acceptance of testing kits

Sponsors are encouraged to contact TGA’s Biological Science Section (BSS) as to the acceptability of test kits.

Test kits used in Australia for donor screening should meet the requirements of the IVD regulatory framework. Testing facilities in Australia would also need a GMP licence from TGA.

For test kits used overseas, sponsors are encouraged to contact TGA’s Biological Science Section (BSS) as to kit acceptability.

##### Subsection 8(6) – Blood sample testing by laboratories

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| **8 General requirements**   1. Where the testing of a blood sample is conducted by a laboratory that is not under the direct control of the manufacturer of the relevant HCT product: 2. the testing must be conducted under a contract between the manufacturer and the laboratory; and 3. the contract mentioned in paragraph (a) must clearly set out the responsibilities of the manufacturer and the laboratory, and include arrangements to ensure that information relating to matters in this section and any other relevant details relating to the IVD medical devices or in‑house IVD medical devices used for such testing can be obtained from the laboratory. |

When external laboratories are used for testing of blood samples, a contract must be in place to stipulate the responsibilities of the manufacturer. The contract should clearly outline what tests the laboratory will do, the IVDs that they will use and the record keeping or reporting structure that should be in place. The testing laboratory is also responsible for notifying the manufacturer of any changes to IVDs and this should be clear in the contract. The contract should be submitted to TGA with the dossier.

This clause is also stipulated in the dossier requirements.

##### Subsections 8(7) and 8(8) – Plasma dilution

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| **8 General requirements**   1. The testing of blood samples must take into account all factors that may cause plasma dilution. 2. Where plasma dilution is suspected at a level sufficient to alter the test results in relation to a blood sample, and a pre-infusion sample is unavailable for testing, then: 3. an algorithm must be applied to assess the extent of plasma dilution; and 4. the extent of plasma dilution must be less than 50 per cent, unless use of samples with more than 50 per cent plasma dilution is validated by the manufacturer of the IVD medical devices or in-house IVD medical devices used for testing the sample. |

The results of infectious disease testing may be affected where a potential donor may have recently received an intravenous treatment, for example infusion of blood components, colloids or crystalloids. For infectious disease test screening protocols, it is recommended that a complete haemodilution assessment be undertaken on all living and deceased donors. Plasma dilution algorithms may be used to calculate appropriate amounts.

If the infusion or transfusion volume for the donor totals more than 2000 mL, it is considered essential that a haemodilution assessment be performed if:

* an infusion or transfusion of blood or colloids was received within 48 hours preceding collection of the sample or within 48 hours preceding death, whichever occurred earlier
* an infusion of crystalloids was received within one hour preceding collection of the sample, or within one hour preceding death, whichever occurred earlier
* a combination of blood, crystalloids or colloids was received within the applicable timeframes

It is also considered essential that an assessment be performed where there have been any infusions or transfusions that might affect test results in a child of less than 12 years of age. The time frames are as defined above.

The date and time of sample collection should be recorded.

An appropriate algorithm must be used to evaluate that plasma dilution and show that it is not sufficient to affect the test results. The plasma dilution factor should be less than 50 per cent, that is, if greater than 50 per cent dilution has occurred, then the post-transfusion/infusion specimen should not be used.

When performing the algorithm:

* consider volumes of medications administered with IV fluids
* if the volume administered is unknown, consider the worst-case scenario that all was given

##### Subsections 8(9) and 8(10) – Record keeping

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| **8 General requirements**   1. Records must be maintained in relation to the following: 2. the tests performed in relation to blood samples and the results of those tests; and 3. the IVD medical device or in-house IVD medical device used for testing the samples; and 4. any test modifications; and 5. any evaluations of, or anomalies in, test results. 6. Procedures must be implemented for notifying a donor of HCT materials, a relevant health practitioner, a relevant hospital and any other relevant organisation, of a test result in relation to the donor that is indicative of a disease or carrier state. |

The retention of records is required by TGO 108 and is consistent with the requirements of the cGMP. The period of retention must take into account jurisdictional or hospital policies. The application should specify and justify record retention periods and include consideration of product risk, shelf life of product, and timeframe for which the product is expected to have a therapeutic or physiological function in the recipient. Records can be kept in paper or electronic form and must be available to GMP inspectors. A documented process must be in place to demonstrate that donor test results that are indicative of an infectious disease or carrier state are reported back to that donor, where necessary.

#### Section 9 – Medical and social history of donors

Section 9 specifies the minimum standards for assessing the suitability of a donor. The medical and social history is the first tier of risk minimisation in terms of infectious disease transmission since high risk donors can be identified before donation, or, where allowed, after donation but before introduction of the therapeutic good into the mainstream inventory of the manufacturing facility.

##### Subsections 9(1) and 9(2) – Donor interviews

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| **9 Medical and social history of donors**  **Living donors**   1. A medical and social history in relation to a living donor of HCT materials, covering the ineligibility criteria for donor selection specified in Schedule 1 and any other relevant matters, must be obtained by interview. 2. The interview must be: 3. conducted by an interviewer who is: 4. appropriately qualified and trained; and 5. an employee of, or under a contract with, a person engaged in the collection of HCT materials or the manufacture of the HCT product; and 6. held face-to-face (to the extent that it is possible in the circumstances) with the donor or the donor’s guardian or next of kin; and 7. conducted within 30 days before or 30 days after the collection of the HCT materials; and 8. documented. |

For living donors, a face-to-face interview is preferred, but it is recognised that this may not be possible within the specified timeframe. Where a face-to-face interview is not conducted, the alternative process should be described.

Obtaining preliminary information without a trained interviewer prior to interview may be acceptable, but confirmation of information/currency of donor history must be in the presence of a trained interviewer (as defined) within 30 days before or 30 days after the collection and must be completed before HCT product is released from quarantine. To ensure the relevance of the information collected, the timeframes around when the donor interview is performed should be as close to the collection date as feasible.

##### Subsection 9(3) – Deceased donor: medical and social history

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| **9 Medical and social history of donors**  **Deceased donors**   1. A medical and social history in relation to a deceased donor of HCT materials, covering the ineligibility criteria for donor selection specified in Schedule 1 and any other relevant matters, must be obtained and documented within 7 days before or 7 days after the collection of the HCT materials, by: 2. both: 3. an interview with a person who is sufficiently informed about the donor’s medical and social history; and 4. an examination of relevant documentation in relation to the donor; or 5. where the interview mentioned in subparagraph (3)(a)(i) is not possible—an examination of the donor documentation to ensure there is sufficient evidence to determine the acceptability of the donor’s medical and social history.   Example: A person who is sufficiently informed about a deceased donor’s medical and social history may include the donor’s treating physician, next of kin or closest available relative, a member of the donor’s household, or a person with a relationship with the donor, such as a carer, friend or partner. |

For deceased donors, it is recognised that the next of kin (knowledgeable historian) may not be available for interview within the required timeframe and therefore donor documentation may provide the necessary evidence to obtain the donor history within the specified timeframe.

##### Subsection 9(4) – Donors of HCT materials for plasma fractionation: medical and social history

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| **9 Medical and social history of donors**  **Donors of HCT materials used exclusively for plasma fractionation**   1. The periods of ineligibility specified in column 3 of items 2, 4, 13, 16 to 19, and 23 to 26 of the table in Schedule 1 do not apply in relation to a donor of HCT materials that are exclusively for plasma fractionation. |

This subsection provides specific exemption from certain donor history criteria and deferrals for plasma for fractionation.

‘Plasma for fractionation’ is defined in European Pharmacopoeia (Ph. Eur.) monograph 0853 as the liquid part of human blood remaining after the separation of the cellular elements from blood collected and is intended for the manufacture of plasma-derived products.

##### Subsection 9(5) – Ocular donors: medical and social history

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| **9 Medical and social history of donors**  **Donors of HCT materials that are human ocular tissue only**   1. The periods of ineligibility specified in column 3 of items 16 to 19 of the table in Schedule 1 do not apply in relation to a donor of HCT materials that are human ocular tissue only. |

This subsection provides specific exemption from certain donor history criteria and deferrals for donors of ocular tissue.

##### Subsection 9(6) – Change in circumstances of donor

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| **9 Medical and social history of donors**  **Change of circumstance of donor**   1. Where the circumstances of a donor of HCT materials used in the manufacture of an HCT product change in relation to the ineligibility criteria for donor selection specified in Schedule 1, the relevant aspects of the medical and social history of the donor must be reviewed by the manufacturer of the HCT product with respect to those changes, before the HCT product is released for supply. |

A change in circumstances for a donor of HCT may include detection of a latent condition after donation or previous travel to an area that has since been found to have an outbreak of a disease (for example, malaria, Dengue fever, COVID-19). In these instances, donor eligibility should be reviewed prior to release of the HCT product.

##### Subsections 9(7) and 9(8) – Screening requirements

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| **9 Medical and social history of donors**  **Screening requirements**   1. An HCT product must not be released for supply, unless the medical and social history of a donor is reviewed and evaluated in accordance with this section. 2. Where a donor meets any of the medical and social history criteria specified in column 2 of an item of the table in Schedule 1, the donor must be subjected to the period of ineligibility specified in column 3 of that item in relation to the collection of HCT materials from the donor for use in the manufacture of HCT products. |

Where possible and practicable these criteria and deferral periods are harmonised with international criteria.

##### Subsections 9(9) to 9(12) – Vertical transmission risk

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| **9 Medical and social history of donors**  **Screening in relation to donors less than 18 months old**   1. If the donor is less than 18 months old, a medical and social history in relation to the donor’s birth mother, covering the ineligibility criteria for donor selection specified in column 2 of items 1 to 7, 11 to 13, 17 and 20 of the table in Schedule 1 must be obtained. 2. Where the donor’s birth mother meets the medical and social history criteria specified in column 2 of item 1 to 7, 11 to 13, 17 or 20 of the table in Schedule 1, then the donor must be subjected to the period of ineligibility specified in column 3 of that item, in relation to the collection of HCT materials from the donor.   **Screening in relation to donors who have consumed breast milk**   1. If the donor has consumed breast milk from a person (the ***relevant person***) within the previous six months, a medical and social history in relation to the relevant person, covering the ineligibility criteria for donor selection specified in column 2 of the items 1 to 7, 11 to 13, 17 and 20 of the table in Schedule 1 must be obtained. 2. Where the relevant person meets the medical and social history criteria specified in column 2 of item 1 to 7, 11 to 13, 17 or 20 of the table in Schedule 1, then the donor must be subjected to the period of ineligibility specified in column 3 of that item, in relation to the collection of HCT materials from the donor. |

This subsection provides specific criteria that apply to the mothers of infant donors or the relevant persons, in order to reduce the risk of vertical transmission of disease via placenta or lactation. This clause also applies to any person who has donated milk to the HCT material donor.

##### Subsection 9(13) – Directed allogeneic donation

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| **9 Medical and social history of donors**  **HCT products that are manufactured for directed allogeneic use**   1. Subsections (8), (10) and (12) do not apply in relation to HCT products that are manufactured for directed allogeneic use where the medical or dental practitioner who is responsible for the administration to, or application in the treatment of, the designated patient is provided the complete medical and social history of the donor of the HCT materials, including (where applicable) the medical and social history of the donor’s birth mother or the relevant person. |

In certain circumstances, subsections (8), (10) and (12) do not apply to HCT products that are manufactured for directed allogeneic use.

#### Section 10 – Blood samples – taking and testing

Section 10 specifies the minimum standards for samples and test methods used for infectious disease testing. Quality of the samples and validation of the methods used in donor testing is critical for determining donor suitability.

##### Subsections 10(1) to 10(4) – Living donor blood sampling

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| **10 Blood samples – taking and testing**   1. Blood samples must be: 2. taken from a donor of HCT materials; and 3. tested for the purpose of donor screening. 4. Blood samples must be taken using aseptic procedures.   **Blood samples – living donors of HCT materials other than materials used exclusively for plasma fractionation**   1. Subject to subsections (4) and (5), blood samples of a living donor of HCT materials must: 2. be taken within 7 days before, or 7 days after, the collection of the HCT materials from the donor; and 3. undergo both NAT and serology testing in accordance subsection (7). 4. Where an HCT product is able to be stored for more than 180 days without compromising the quality, safety or efficacy of the product, blood samples of a living donor of the HCT materials used in the manufacture of the product may instead: 5. be taken: 6. within 7 days before, or 7 days after, the collection of the HCT materials from the donor; and 7. at least 180 days after the collection of the HCT materials from the donor; and 8. undergo serology testing in accordance with subsections (8) and (9). |

The 7-day window for living donors represents the nominal timeframe to collect samples to accurately reflect the donor infectious disease status. It may be appropriate for manufacturers to apply more stringent timeframes to some cell or tissue types, such as fresh blood.

##### Subsection 10(5) – Blood sampling for plasma fractionation

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| **10 Blood samples – taking and testing**  **Blood samples – living donors of HCT materials used exclusively for plasma fractionation**   1. Blood samples of a living donor of HCT materials that are used exclusively for plasma fractionation must: 2. be taken within 7 days before, or 7 days after, the collection of the HCT materials from the donor; and 3. undergo both NAT and serology testing in accordance subsection (10). |

Donors of HCT materials that are going to be used for plasma fractionation only are not required to undergo testing for HTLV or syphilis. All other tests as specified in subsection 10(10) must be non-reactive.

The term ‘non-reactive’ is intended to include other terminology for the same test result such as ‘negative’ and ‘not detected’.

The decision as to which test results lead to a ‘reactive’ or ‘non-reactive’ test should be justified. In addition, the role of any confirmatory testing in the determination of meeting this requirement should also be justified.

##### Subsection 10(6) – Deceased donor blood sampling

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| **10 Blood samples – taking and testing**  **Blood samples – deceased donors of HCT materials**   1. Blood samples of a deceased donor of HCT materials must: 2. be taken: 3. in accordance with subsection 8(4); or 4. within 7 days before the collection of the HCT materials; and 5. undergo NAT and serology testing in accordance with subsection (7). |

The quality of the cadaveric blood sample must be suitable to allow infectious disease testing to be performed. Instructions for use provided with a test method may define the appropriate time frame for collection of the blood sample prior to testing, or the appropriate time frame should be validated.

##### Subsections 10(7) to 10(9) – Living and deceased donor infectious disease testing

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| **10 Blood samples – taking and testing**  **Testing – living and deceased donors of HCT materials**   1. The following testing must be conducted in relation to blood samples taken in accordance with paragraphs (3)(a) or (6)(a): 2. serology testing for HIV-1, HIV-2, HCV, HBsAg, HTLV-1, HTLV-2, and syphilis (*Treponema pallidum*); and 3. NAT for HIV-1, HIV-2, HBV, and HCV. 4. The following testing must be conducted in relation to blood samples taken in accordance with subparagraph (4)(a)(i): 5. serology testing for HIV-1, HIV-2, HCV, HBsAg, HTLV-1, HTLV-2, and syphilis (*Treponema pallidum*). 6. The following testing must be conducted in relation to blood samples taken in accordance with subparagraph (4)(a)(ii): 7. serology testing for HIV-1, HIV-2, HCV, and HBsAg. |

The policy for determining the individual infectious disease status based on test results must be documented, for example, HBV testing algorithms required to interpret the status of the donor (whether NAT positive/serology negative result or NAT negative/serology positive result).

If the test result for syphilis is reactive by a non-specific test, there are two options:

* discard product

OR

* perform a specific confirmatory test to rule out the positive result from the non-specific test (non-specific [reaginic] syphilis tests are prone to false positive results)

Initial serology and, where applicable, NAT on the sample collected at the time of donation must be undertaken during the timeframe specified.

There are two main infectious diseases testing options:

* for HCT, the mandatory requirements for initial sample serology as well as its initial sample NAT for HIV, HCV and HBV can be performed

OR

* for HCT that can be stored for over 180 days, initial sample serology is mandatory, and the donor must be sampled and tested by serology again more than 180 days after HCT collection

If serology testing is not able to be done after 180 days (as described above), it may be possible to justify retrospective testing of the initial donor sample by NAT in combination with the initial sample serology. However, the validity/suitability of using donor samples that may have been held in longer-term storage prior to undertaking NAT on the initial sample should be demonstrated under such circumstances.

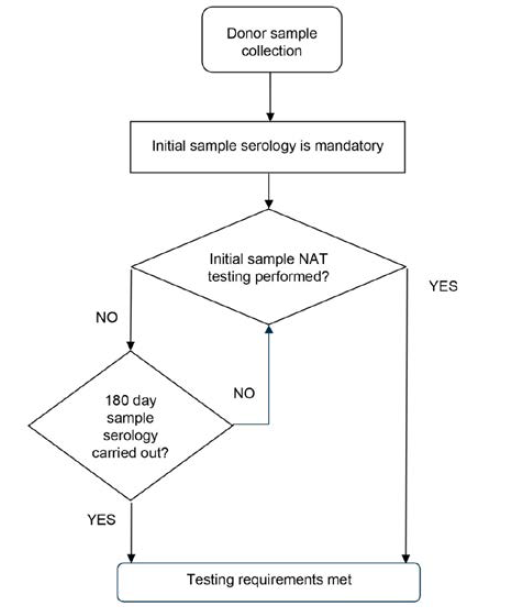
Initial donor sampling by NAT minimises the window period of infection, and as such, product from a donor that has not had a sample tested by NAT must not be released until 180 day serology testing is performed.

Information on the timeframe between collection and sampling should be included in the application and may be subject to GMP inspection.

The requirement to perform NAT is to significantly shorten the window period for detection of HIV, HBV and HCV infections.

Figure 1 provides a summary of these requirements.

Figure 1: The requirements of donor blood sample testing.



##### Subsection 10(10) – Infectious disease testing for plasma fractionation

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| **10 Blood samples – taking and testing**  **Testing – living donors of HCT materials used exclusively for plasma fractionation**   1. The following testing must be conducted in relation to blood samples taken in accordance with paragraph (5)(a): 2. serology testing for HIV-1, HIV-2, HCV, and HBsAg; and 3. NAT for HIV-1, HIV-2, HBV and HCV. |

This clause stipulates the testing that must be conducted on donors of HCT material who had samples taken in accordance with subsection 10(5).

Donors of HCT materials for plasma fractionation must be non-reactive to the tests stipulated.

Donors of HCT materials for plasma fractionation do not require testing for syphilis and HTLV-1/HTLV-2.

##### Subsections 10(11) and 10(12) – Infectious disease testing for donors less than 18 months old

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| **10 Blood samples – taking and testing**  **Testing in relation to donors less than 18 months old**   1. If a donor of HCT materials is less than 18 months old, then the donor’s birth mother must be subjected to the same testing requirements that are applicable to the donor, as set out in subsections (1) to (10). 2. In the case of a donor of the HCT materials that are HPC(CB) only, the applicable testing requirements in this section apply only in relation to the donor’s birth mother.   Note: An infant donor of HPC(CB) only is not required to be tested in accordance with this section. |

Where a donor is less than 18 months old, the birth mother must be subjected to the same sampling and testing as the infant donor. The sampling and testing requirements are dependent on the state of the donor (living or deceased) and the HCT products that are being manufactured, that is, if the donor’s HCT material is being used for plasma fractionation, then the testing requirements set out under subsection 10(10) apply to the birth mother and the infant donor.

Where the HCT material is haematopoietic progenitor cell cord blood [HPC(CB)], the infant is not required to undergo testing; however, the birth mother must be tested. The tests required are again dependent on the state of the infant donor and the HCT product being produced.

##### Subsection 10(13) – Infectious disease testing for donors who have consumed breast milk

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| **10 Blood samples – taking and testing**  **Testing in relation to donors who have consumed breast milk**   1. If a donor has consumed breast milk from a person (the ***relevant person***) within the previous six months, then the relevant person must be subjected to the same testing requirements that are applicable to the donor, as set out in subsection (1) to (10). |

Where a HCT donor has consumed breast milk from a person in the previous six months, the person who provided the breast milk must also undergo the same sampling and testing as the HCT donor.

The sampling and testing requirements are dependent on the state of the HCT donor (living or deceased) and the HCT products being manufactured, that is, if the donor’s HCT material is being used for plasma fractionation, then the testing requirements set out under subsection 10(10) would apply to the donor and the provider of the breast milk.

In this clause, the relevant person is the one who donated the breast milk.

##### Subsections 10(14) to 10(16) – Assessment of testing results

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| **10 Blood samples – taking and testing**  **Assessment of testing results**   1. An HCT product must be placed in quarantine, and must not be released for supply, until the results of the testing mentioned in subsections (1) to (13) are assessed. 2. If the testing of a blood sample demonstrates a reactive result, then the relevant HCT product must not be released for supply. 3. Subsection (15) does not apply to an HCT product that is manufactured for directed allogeneic use where the medical or dental practitioner who is responsible for the administration to, or application in the treatment of, the designated patient is notified about the testing results. |

While awaiting the test results for samples taken and tested in accordance with subsections 10(1)-10(10), HCT products must be placed into quarantine. No products can be released until all test results are assessed and the donor/relevant persons are shown to be non-reactive/negative. If a blood sample is shown to be reactive to any of the tests conducted, the product must not be released.

Where a product is for directed allogeneic use and shown to be reactive to any of the tests conducted, the product may still be released if a medical or dental practitioner is responsible for the administration/application of the product, provided the designated recipient has been notified of the results.

##### Subsections 10(17) to 10(18) – Archiving of serum of plasma of blood samples

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| **10 Blood samples – taking and testing**  **Serum or plasma of blood samples**   1. The serum or plasma of a blood sample taken from a donor of HCT materials in accordance with subsection (3), (4) or (6) must be: 2. archived at or below minus 25°C, or in accordance with conditions that are validated or recommended by the manufacturer of the IVD medical device or in‑house IVD medical device used for testing the samples; and 3. retained for a minimum of two years after the expiry date of the relevant HCT product, or for a period that is validated on the basis of validated data or documented evidence from relevant scientific literature. 4. If: 5. an HCT product has not been released for supply; and 6. following the testing of a blood sample in relation to the product, a protocol or methodology for the testing changes;   then, the archived serum or plasma of the blood sample must be tested in accordance with the new protocol or methodology before the product is released for supply, unless the testing is not required on the basis of a risk assessment. |

A donor blood sample (plasma or serum) must be archived for two years after the expiry date of the product, unless otherwise justified or validated. Circumstances that could be considered as justification for a failure to archive or maintain a sample may include:

* low sample volume
* breakage and loss
* the sample is used up by relevant testing

This requirement is in place to allow a manufacturer the ability to conduct reviews of the infectious disease status of donors, or conduct additional tests if donor selection and deferral criteria change during product storage.

Failure to store a sample or loss of sample is a ‘non-conformance’ and should follow internal non-conformance procedures. This may be subject to review during GMP inspection.

If there are changes to donor deferral during product storage (which may be for several years after the completion of processing), the archived donor blood sample may need to be re-tested based on these changes.

Before the release of the product, the suitability of the donor (based on donor deferral criteria at the time of product release) should be reviewed to ensure the donor meets all current requirements.

During the storage of the product, there may be changes to mandatory donor infectious disease testing requirements, either introduced by the manufacturer or mandated by TGA. This may include the requirement to test for additional infectious diseases in the event of a disease outbreak. In these situations, it may be required to reassess the donor before the release of product derived from their collected starting material. This must be done using archived serum or plasma, stored according to TGO 108.

The requirement to retest the donor will be based on a risk assessment conducted by the manufacturer or sponsor taking into account the nature of the risk to the recipient. TGA should be consulted if changes to donor deferral criteria will be introduced.

#### Section 11 – Physical assessment

Section 11 specifies the requirements for the physical assessment of donors and the minimum donor infectious disease testing requirements.

In addition to the medical and social history of the donor, assessment of donor blood samples and the physical assessment of the donor are further key determinants of donor acceptability. Assessment and testing of donors are critical tiers of risk mitigation as they may be indicative of a behaviour or lifestyle of infectious disease transmission.

##### Subsection 11(1) – Potential donor testing for infectious diseases

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| **11 Physical assessment**   1. A physical assessment must be conducted in relation to a donor of HCT materials as follows: 2. in the case of a living donor (other than a living donor of human musculoskeletal tissue only)—at the time of the collection of the HCT materials; or 3. in the case of a living donor of human musculoskeletal tissue only—within 30 days before or 30 days after the collection of the tissue; or 4. in the case of a deceased donor—before the collection of the HCT materials. |

This subsection specifies when physical assessments must be conducted.

##### Subsection 11(2) – Donor physical assessments

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| **11 Physical assessment**   1. A physical assessment must: 2. include a clinical inspection of any physical features or characteristics of a donor (such as an abrasion, laceration, bruise, haematoma, fracture, tattoo, piercing, scar, skin lesion, or surgical incision) that may indicate that the donor poses a risk of infectious disease transmission; and 3. be conducted by a person who is: 4. appropriately qualified and trained; and 5. an employee of, or under a contract with, a person engaged in the collection of HCT materials or the manufacture of HCT products; and 6. demonstrate that the donor does not pose a risk of infectious disease transmission. |

The requirements for [physical assessment](https://www.tga.gov.au/acronyms-glossary#id_8953) of a potential donor of HCT must be determined by each individual collection facility according to a risk assessment for the tissue(s) or cells to be collected. The exact nature of this assessment is not prescribed, but it is emphasised that the assessment must be sufficient to ‘determine suitability of the person to be a donor’. The requirements will be influenced by the type of product and by the constraints of the clinical requirements of different patient (recipient) groups.

The time periods during which donor physical assessment should occur were specified to allow for the assessment to take place at a convenient time prior to surgical procedures, but be sufficiently current to allow determination of acceptability of the collection.

The physical assessment process must be appropriately documented. Requirements for performing and documenting the physical assessment must be specified in the dossier submitted by the sponsor to TGA for evaluation and approval. Some provisions for post-collection assessment have been made in product-specific orders.

The term ‘trained assessor’, or ‘trained interviewer’, denotes a person who has undergone training in the specific assessment and consent procedures required by the manufacturer and who has a formal relationship with the manufacturer for this purpose. The requirement for a trained assessor implies that the person undertaking the assessment has an adequate level of training and clinical skills appropriate to the particular assessment being undertaken, and fully understands the requirements for donor evaluation to determine suitability. The assessor need not be a staff member of the manufacturer as long as adequate training has been confirmed.

In addition, there is no prescriptive description as to what entails ‘training’, but it is required that the manufacturer ensures that the person performing the assessment has an appropriate level of expertise and is familiar with the manufacturers requirements for donor acceptance. The process for training must be documented in the dossier.

### Schedule 1 – Ineligibility criteria for donor selection

Schedule 1 of TGO 108 describes the medical and social history that must be collected, and the potential periods of ineligibility that must be applied to a proposed donor.

Ensure you familiarise yourself with **all items listed in schedule 1** and the associated requirements.

#### Items 1 to 5 – Known infection or potential exposure to certain viruses

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|  | **Item**  1 | **Medical and social history criteria**  a person who is infected with:  (a) HCV;  (b) HIV-1; or  (c) HIV-2 | **Period of ineligibility**  permanently ineligible |
|  | **Item**  2 | **Medical and social history criteria**  a person who is infected with:  (a) HTLV-1; or  (b) HTLV-2 | **Period of ineligibility**  permanently ineligible |
|  | **Item**  3 | **Medical and social history criteria**  a person who has potentially been exposed to:  (a) HCV;  (b) HIV-1; or  (c) HIV-2 | **Period of ineligibility**  ineligible until it has been demonstrated that the person is not infected |
|  | **Item**  4 | **Medical and social history criteria**  a person who has potentially been exposed to:  (a) HTLV-1; or  (b) HTLV-2 | **Period of ineligibility**  ineligible until it has been demonstrated that the person is not infected |
|  | **Item**  5 | **Medical and social history criteria**  a person who has potentially been exposed to HBV | **Period of ineligibility**  ineligible until it has been demonstrated that the person is:  (a) immune from HBV infection; or  (b) not infected with HBV, as confirmed by NAT |

The ability to allow donors to be accepted after a period of ineligibility is dependent on an uninfected state of the donor being demonstrated.

For HCV, an uninfected state can be established if an individual had undergone successful anti-viral treatment, and the individual has been shown to be HCV negative by polymerase chain reaction (PCR) over a period of time.

For HBV, if a patient previously infected with HBV is Hepatitis B surface antibody positive (with or without core antibody positivity), but negative for both Hepatitis B surface antigen and HBV DNA, then they may be re-eligible to donate. Demonstration of exposure versus immunity to HBV must be determined by a testing algorithm that is informed from evidence in scientific literature or other reliable sources, as above. For example, donors suspected of being infected with HBV who are HBsAg negative are considered ‘immune’ if both of the following apply:

* they have an antibody titre to HBsAg at a level greater than or equal to 10 IU/L (or 10 mIU/mL)

AND

* HBV NAT is negative

Donors suspected of being infected with HBV, who are HBsAg negative, are considered to be ‘not exposed’ if they test negative for antibodies to HBsAg and test negative by HBV NAT. For HBsAg negative persons who are demonstrated to be immune or never exposed, no ineligibility period applies.

Table 1 shows a summary of donor deferral criteria according to known or suspected HBV infections.

Table 1: Summary of donor deferral criteria according to known or suspected HBV infections

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| Deferral criterion | How to determine infection status | Deferral outcome |
| If known to have HBV infection | Positive HBsAg test | Ineligible |
| If suspected of having an HBV infection | Symptoms of infection or close contact with infected person established at interview but negative HBsAg test and cannot establish immunity status | Ineligible |
| If suspected of having an HBV infection | Negative HBsAg test  AND  Positive anti-HBc test  AND  Positive anti-HBs test  **AND**  Negative NAT | Immune due to natural infection previously, so no deferral required if negative NAT result confirms no current infection |
| If suspected of having an HBV infection | Negative HBsAg test  And  Negative anti-HBc test  And  Positive anti-HBs test | Immune due to hepatitis B vaccination, and so no deferral required if NAT result confirms no current infection |

#### Item 6 – Injected with drugs for a non-medical reason

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|  | **Item**  6 | **Medical and social history criteria**  a person who has received an injection of any substance in connection with a use that is not a therapeutic use or cosmetic use | **Period of ineligibility**  ineligible for at least 5 years from the last injection |

‘Non-medical reason’ refers to procedures such as recreational drug use or cosmetic use or any procedure that is not undertaken by a registered healthcare provider in Australia.

This deferral criterion is not intended to apply to individuals who have participated in medically-supervised, registered clinical trials.

#### Item 7 – Recipients of viable, non-human cells or tissues

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|  | **Item**  7 | **Medical and social history criteria**  a person who has been a recipient of viable animal cells or tissues | **Period of ineligibility**  permanently ineligible |

For recipients of viable, non-human animal cells or tissue products, there is a risk of xenogeneic infections. Donors receiving such transplants should not be accepted.

#### Item 8 – At risk of prion disease

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|  | **Item**  8 | **Medical and social history criteria**  a person who is at risk of prion disease because the person has been, or potentially been, exposed to the putative causative agent of one of the family of pathogenic transmissible spongiform encephalopathies, including:  (a) genetic (familial) exposure;  (b) environmental exposure, including living in or visiting England, Scotland, Wales, Northern Ireland or the Isle of Man for a cumulative period of 6 months or more, at any time between 1 January 1980 and 31 December 1996; or  (c) iatrogenic exposure, including receiving a transfusion or injection of blood or blood components while in England, Scotland, Wales, Northern Ireland or the Isle of Man at any time on or after 1 January 1980 | **Period of ineligibility**  permanently ineligible |

Permanent deferral of a donor may need to be considered due to risk of prion disease where:

* patients have symptoms of progressive neurological disease consistent with prion disease

AND

* activities that could iatrogenically transfer prion disease have occurred

#### Item 9 – Recipients of human pituitary derived hormone

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|  | **Item**  9 | **Medical and social history criteria**  a person who has been a recipient of human pituitary-derived hormone | **Period of ineligibility**  permanently ineligible |

Human derived pituitary hormone is currently not available in Australia. Synthetically derived products are currently used. This permanent ineligibility **does not** apply to proposed donors that have received **synthetically** derived product.

#### Item 10 – At risk of acquiring a blood borne infection

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|  | **Item**  10 | **Medical and social history criteria**  a person who has been exposed to any of the following risks of acquiring a blood borne transmissible infection:  (a) mucosal splash with blood or other bodily fluids;  (b) needle stick injury;  (c) tattoo;  (d) body piercing (including earring); or  (e) acupuncture or dry-needling, unless performed using sterile, single-use needles | **Period of ineligibility**  (a) where the person tests negative for HCV using NAT – ineligible for at least 4 months from exposure; or  (b) in all other circumstances – ineligible for at least 6 months from exposure |

A donor with exposure to the risk of acquiring a transmissible blood borne infection such as HIV, HBV and HCV must be deferred for:

* a period that allows determination of disease development

AND

* they subsequently test negative for HIV, HBV and HCV after this period of time

#### Item 11 – Allogeneic products

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|  | **Item**  11 | **Medical and social history criteria**  a person who has been a recipient of allogeneic blood, blood components, human derived clotting factors, organs, cells or tissues that did not conform with this instrument | **Period of ineligibility**  (a) where the person tests negative for HCV using NAT – ineligible for at least 4 months from receiving the allogeneic blood, blood components, human derived clotting factors, organs, cells or tissues  (b) in all other circumstances – ineligible for at least 6 months from receiving the allogeneic blood, blood components, human derived clotting factors, organs, cells or tissues |

If a proposed donor has received allogeneic HCT materials or an allogeneic organ that did not conform with TGO 108, the sponsor must ensure that the product the donor received is compliant with TGO 108.

This may take the form of a statement describing the international standard with which the product was compliant and confirming equivalence to TGO 108. Where any of these products is not in accordance with the requirements of TGO 108, the proposed donor is ineligible from 6 months after receiving them.

#### Item 12 – At increased risk due to sexual practices

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|  | **Item**  12 | **Medical and social history criteria**  a person who has engaged in sexual activity that puts the person at an increased risk of acquiring infectious diseases that could be transmitted through blood, cells or tissues | **Period of ineligibility**  ineligible for at least 3 months from the last sexual contact |

Sexual practices that are considered to increase the risk of acquiring infectious diseases that can be transmitted through blood, cells or tissues include, but are not limited to:

* sexual activity with a sex-worker
* sexual activity with someone who uses intravenous drugs
* having a partner who lives or lived in a high HIV-risk country
* for male donors, sexual activity with a male partner
* for female donors, sexual activity with a male partner who also has sex with men

The donor information that informs this deferral should be determined based on risk as relevant to the nature of the product and its use.

#### Item 13 – Prison inmate for 72 or more consecutive hours

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|  | **Item**  13 | **Medical and social history criteria**  a person who has been imprisoned for a consecutive period of 72 hours or longer | **Period of ineligibility**  ineligible for 12 months from the date of release from prison |

There is a known relationship between imprisonment, drug use, sexually transmitted and blood-borne virus infections such as hepatitis B and C.

#### Item 14 – Active infection, fever or infectious disease

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|  | **Item**  14 | **Medical and social history criteria**  a person who has an active infection, fever or infectious illness | **Period of ineligibility**  ineligible for at least 2 weeks from the date of full recovery |

Clinical judgement should be used to determine the relevance of the infection, fever or illness to the suitability of the donor.

Determination of a disease-free state should be established before a proposed donor can be allowed to donate. This may include an algorithm and testing or specified parameters to demonstrate that an infection has cleared.

#### Item 15 – Travel to specific regions

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|  | **Item**  15 | **Medical and social history criteria**  a person who has travelled to another country or region within Australia with exposure to particular epidemiological situations | **Period of ineligibility**  ineligible for a period of time based on a risk assessment using the most up-to-date epidemiological data |

This deferral is intentionally broad to encompass unforeseen infectious disease risks such as an epidemic, pandemic, or other emerging or re-emerging infectious disease outbreak. It is the responsibility of the sponsor to demonstrate that a process is in place to satisfactorily monitor, assess and action epidemiological situations relevant to their products.

In the case of the COVID-19 disease pandemic, which began to spread globally in 2020, a manufacturer will need to monitor advice on the risk of infection to the safety of their product and consider how to manage the risk through deferral of donors (and potentially testing).

For travel-based deferrals, a documented procedure must be in place to record the countries where crucial infectious diseases are endemic or where there is an outbreak. The deferral may be based on a country of travel, or where an agent is endemic to a local area within that country. WHO publishes a list of countries where specific diseases such as malaria, Zika virus, Dengue fever, Ebola virus disease, West Nile Virus (WNV) are present.

Management of this requirement should be achieved through a policy for monitoring for outbreaks and notification by e-mail to TGA’s Biological Science Section (BSS) if interim measures are put in place. If there is a serious outbreak, but the risk to HCT products is considered to be minimal, you should notify TGA’s Biological Science Section (BSS) that no action is needed at this time.

#### Items 16 to 18 – Risk of malaria

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|  | **Item**  16 | **Medical and social history criteria**  a person who has lived in a malaria endemic region for a continuous period of 6 months or more at any time | **Period of ineligibility**  (a) ineligible until an immunological test that is performed at least 4 months after the person’s return from the malaria endemic region (an ***immunological test***) demonstrates a negative result; or  (b) in all other circumstances, including where the immunological test demonstrates a positive result – permanently ineligible |
|  | **Item**  17 | **Medical and social history criteria**  a person (other than a person mentioned in item 16) who has visited a malaria endemic region | **Period of ineligibility**  (a) ineligible until an immunological test that is performed at least 4 months after the person’s return from the malaria endemic region (an ***immunological test***) demonstrates a negative result; or  (b) if an immunological test demonstrates a positive result –ineligible for 3 years from the time of the test result; or  (c) in all other circumstances – ineligible for 12 months from the person’s return from the malaria endemic region |
|  | **Item**  18 | **Medical and social history criteria**  a person who has or has had malaria | **Period of ineligibility**  (a) ineligible until an immunological test that is performed at least 4 months after the later of the cessation of treatment or the person’s last symptoms (an ***immunological*** ***test***) demonstrates a negative result; or  (b) if an immunological test demonstrates a positive result – ineligible for 3 years from the time of the test result; or  (c) in all other circumstances – permanently ineligible |

Endemic areas for malaria are published online by WHO and the Centers for Disease Control and Prevention. The definition of endemic region may be at the country level, or it may be possible to justify more specifically local areas within any one particular country.

The concept of having ‘visited’ a malaria endemic region is to be applied as consistent with WHO guidelines. In the case of malaria, visitation includes any situation where the donor has been potentially exposed to the external environment. For example, it would not include a stop-over in an airport terminal where the individual did not leave the terminal, but would include if the donor were to travel to another location (including another terminal) in a bus or private taxi. Malarial prophylaxis does not affect the malaria exclusion periods.

#### Item 19 – Undiagnosed febrile illness consistent with malaria

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|  | **Item**  19 | **Medical and social history criteria**  a person who has or has had an undiagnosed febrile illness, with symptoms consistent with malaria during, or within 6 months of return from, a visit to a malaria endemic region | **Period of ineligibility**  (a) ineligible until an immunological test that is performed at least 4 months after the later of the cessation of treatment or the person’s last symptoms (an ***immunological*** ***test***) demonstrates a negative result; or  (b) if an immunological test demonstrates a positive result – ineligible for 3 years from the time of the test result; or  (c) in all other circumstances – ineligible for 3 years from the later of the cessation of treatment or the person’s last symptoms |

The decision to apply this deferral criterion must be based on clinical judgement as to whether the febrile illness is consistent with malaria.

#### Item 20 – Active infection

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|  | **Item**  20 | **Medical and social history criteria**  a person with an active infection that would render HCT materials collected from that person unsuitable for use in the manufacture of HCT products | **Period of ineligibility**  ineligible until it has been demonstrated that the person no longer has the infection |

A list of infections that are relevant to the product and warrant deferral should be established. Determination of a disease free state should include an algorithm and at minimum the essential assays or parameters to demonstrate that an infection has cleared or will render the target cells or tissue unsuitable for manufacture.

#### Items 21 and 22 – Deceased donors

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|  | **Item**  21 | **Medical and social history criteria**  a deceased person who, within 12 months prior to asystole, has been a recipient of allogeneic HCT materials or an allogeneic organ that did not conform with this instrument | **Period of ineligibility**  permanently ineligible |
|  | **Item**  22 | **Medical and social history criteria**  a deceased person whose cause of death is unknown | **Period of ineligibility**  ineligible until a post-mortem examination of the person provides sufficient information to conclude that the person’s death was not caused by a transmissible disease |

If a deceased donor who, within 12 months prior to asystole, has received allogeneic HCT materials or an allogeneic organ that did not conform with TGO 108, the sponsor must ensure that the product the donor received is compliant with TGO 108. This may take the form of a statement describing the international standard with which the product was compliant and confirming equivalence to TGO 108. Where any of these products is not in accordance with the requirements of TGO 108, the deceased donor is permanently ineligible.

A post-mortem is required for a deceased donor whose cause of death is unknown, to ensure their death was not caused by a transmissible disease, before they are allowed to donate.

#### Items 23 to 26 – Risk of transmission of vaccination strain

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|  | **Item**  23 | **Medical and social history criteria**  a person who has been vaccinated with a live vaccine that contains attenuated bacteria or viruses, other than a vaccine mentioned in item 24 | **Period of ineligibility**  ineligible for 4 weeks |
|  | **Item**  24 | **Medical and social history criteria**  a person who has been vaccinated with a live vaccine against smallpox | **Period of ineligibility**  ineligible for 8 weeks |
|  | **Item**  25 | **Medical and social history criteria**  a person who has been vaccinated with a live vaccine that contains sera of animal origin | **Period of ineligibility**  ineligible for 12 weeks |
|  | **Item**  26 | **Medical and social history criteria**  a person who has been vaccinated with an unknown vaccine | **Period of ineligibility**  ineligible for 12 months |

A proposed donor who has been vaccinated with a live vaccine, where there is a risk of transmission of the vaccine strain, must be deferred.

The length of deferral should be based on knowledge of the length of persistence of the vaccine agent, testing of the proposed donor, or based on the assessment of the risk to use of blood, cells or tissues for transplantation.

## Version history

| Version | Description of change | Author | Effective date |
| --- | --- | --- | --- |
| V1.0 | Original publication  Replaces:  ARGB Appendix 4 – Guidance on TGO 88 | Biological Science Section, Scientific Evaluation Branch | May 2021 |

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| Reference/Publication # |

1. The relevant TGO that governs FMT products is the [Therapeutic Goods (Standard for Faecal Microbiota Transplant Products) (TGO 105) Order 2020](https://www.legislation.gov.au/Details/F2020L01011/). [↑](#footnote-ref-1)