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| Remaking of standards and legislative instruments for human cell and tissue (HCT) products, blood and blood components |
| Consultation paper |
| Version 1.0, May 2021 |

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## Purpose

The Therapeutic Goods Administration (TGA) is seeking feedback on a proposal to remake some of the legislative instruments relating to human cell and tissue (HCT) products (including blood and blood components), which sunset in October 2021.

Most of these legislative instruments are Therapeutic Goods Orders (TGOs) which ensure the quality and safety of HCT products for Australian patients and consumers. They fulfil this purpose by specifying Australian-specific donor screening, labelling and manufacturing requirements for therapeutic goods comprising, derived from or containing HCTs, as well as blood and blood components.

Although all these legislative instruments continue to operate largely effectively and efficiently, it would be beneficial to improve clarity on some requirements as well as create efficiency through increased international harmonisation thus ensuring they continue to be fit for purpose. Accordingly, we are proposing to remake these TGOs and the other legislative instruments under section 10 and section 32A of the *Therapeutic Goods Act 1989* (the Act), respectively.

## Scope

The TGOs relevant to this consultation can be broadly categorised into three groups:

* Product-specific standards:

1. [TGO 83: Standards for human musculoskeletal tissue](http://www.legislation.gov.au/Series/F2011L01489)
2. [TGO 84: Standards for human cardiovascular tissue](http://www.legislation.gov.au/Series/F2011L01490)
3. [TGO 85: Standards for human ocular tissue](http://www.legislation.gov.au/Series/F2011L01491)
4. [TGO 86: Standards for human skin](http://www.legislation.gov.au/Series/F2011L01492)

* Labelling requirements:

1. [TGO 87: General requirements for the labelling of biologicals](http://www.legislation.gov.au/Series/F2011L01493)

* General donor selection and testing requirements:

1. [TGO 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](https://www.legislation.gov.au/Series/F2013L00854)

This consultation will also consider two other legislative instruments:

* [*Therapeutic Goods (Things that are not Biologicals) Determination No. 1 of 2011*](https://www.legislation.gov.au/Details/F2011L00894)
* [*Therapeutic Goods (Things that are Biologicals) Specification 2019*](https://www.legislation.gov.au/Details/F2019L01669)

## Background

TGOs 83-87 commenced in 2011, while TGO 88 commenced in 2013. Legislative instruments are automatically repealed after a fixed period of time (subject to some exceptions) in accordance with the *Legislative Instruments Act 2003*. This automatic repeal is called ‘sunsetting’. TGOs 83-87 are due to sunset in October 2021. Although TGO 88 does not sunset until October 2023, this Order cross-references TGOs 83-87 and so will be reviewed at the same time to provide clarity across these HCT-relevant TGOs.

In accordance with the [sunsetting legislative instruments guidance note](https://www.pmc.gov.au/resource-centre/regulation/sunsetting-legislative-instruments-guidance-note), TGOs 83-88 were assessed as to whether they are operating ‘effectively and efficiently’ when compared to no regulation in force. Preliminary feedback from stakeholders confirmed that the TGOs should be remade to provide continuing clarity on specific requirements needed to maintain quality standards for therapeutic goods comprising, containing or derived from HCT.

An additional HCT-relevant instrument, the [*Therapeutic Goods (Things that are not Biologicals) Determination No. 1 of 2011*](https://www.legislation.gov.au/Details/F2011L00894), also sunsets in October 2021. This instrument will be reviewed to ensure it is fit for purpose and provides clarity in the regulatory pathways for therapeutic goods.

The review of our TGOs and legislative instruments will propose updates to:

* improve clarity on technical requirements
* ensure alignment with international best practice and standards
* bring legislation into alignment with recent amendments, including updates to autologous HCT requirements

The proposed updates should not be interpreted to imply that there are concerns with the general quality of therapeutic goods that comprise, contain, or are derived from HCT currently supplied in Australia.

## Summary of proposed amendments

### 1. Proposed remade TGOs

It is proposed to remake the six TGOs mentioned above into the following three TGOs:

* TGO 87 will be remade as ***Therapeutic Goods (Standard for Biologicals—Labelling Requirements) (TGO 107) Order 2021***. This order will continue to specify labelling, traceability, and accompanying information requirements consistent with current TGO 87 objectives.
* TGO 88 will be remade as ***Therapeutic Goods (Standard for Human Cell and Tissue Products—Donor Screening Requirements) (TGO 108) Order 2021****.* This order will specify donor screening requirements for minimising the risk of infectious disease transmission via therapeutic goods comprising, derived from or containing HCTs. In remaking this Order we propose to separate donor selection requirements from manufacturing, microbial and critical material requirements currently in TGO 88. It is proposed to transfer these requirements to a manufacturing-specific order, TGO 109, so that TGO 108 focuses on donor selection criteria.
* TGOs 83-86, which govern manufacture of product-specific HCTs, will be consolidated into ***Therapeutic Goods (Standard for Biologicals) (TGO 109) Order 2021***. This order will specify manufacturing standards for biologicals, broken up into two major parts. The first part is a standard applicable to all biologicals that consists of the transferred manufacturing requirements from TGO 88. The subsequent parts specify individual manufacturing standards for the existing product-specific standards, TGOs 83-86, and an additional new standard for amnion products.

The following table summarises the remade TGOs:

| Current TGO | New TGO | Scope of new TGO | Summary of changes |
| --- | --- | --- | --- |
| [TGO 87](http://www.legislation.gov.au/Series/F2011L01493) | TGO 107 | all biologicals including faecal microbial transplant (FMT) | (a) allow use of machine-readable codes  (b) additional labelling requirements for Class 3 and 4 biologicals |
| [TGO 88](https://www.legislation.gov.au/Series/F2013L00854) | TGO 108 | (a) all biologicals excluding FMT  (b) blood and blood components | (a) exempt autologous HCT products  (b) exempt directed allogenic HCT products from donor deferral criteria  (c) amend some donor deferral criteria |
| TGO [83](http://www.legislation.gov.au/Series/F2011L01489), [84](http://www.legislation.gov.au/Series/F2011L01490), [85](http://www.legislation.gov.au/Series/F2011L01491), [86](http://www.legislation.gov.au/Series/F2011L01492)  + parts of TGO 88 | TGO 109 | all biologicals excluding FMT | (a) merge TGO 83-86  (b) transfer microbiological and critical materials requirements from TGO 88  (c) extend some general manufacturing requirements to all biologicals |

Copies of the proposed remade TGOs and draft guidance documents are included (Appendices 1-3). The draft TGOs have been reformatted and some requirements clarified. Where an updated requirement is proposed, it is discussed below. The accompanying mapping documents shows the relationship between the current TGOs and proposed remade TGOs (Appendices 1-3).

Throughout the remade TGOs, the term ‘HCT materials’ specifies materials collected for or during their manufacture into biologicals, that is, starting material and intermediates which may include blood or blood components.

In the remade TGO 108, the term ‘HCT product’ specifies the ‘finished product’, which is either a biological, blood or blood component.

### 2. Merging legislative instruments

Because these instruments complement each other, we propose to merge the [*Therapeutic Goods (Things that are not Biologicals) Determination No. 1 of 2011*](https://www.legislation.gov.au/Details/F2011L00894) with the [*Therapeutic Goods (Things that are Biologicals) Specification 2019*](https://www.legislation.gov.au/Details/F2019L01669).

A copy of the proposed new legislative instrument is included (Appendix 4).

## Seeking feedback

We are seeking feedback from stakeholders on the suitability and potential impact of the remade TGOs (107, 108 and 109) and the merged legislative instrument.

## Proposed amendments to TGO 107

TGO 107 supersedes [TGO 87](http://www.legislation.gov.au/Series/F2011L01493) and specifies the labelling requirements for biologicals and HCT materials.

TGO 107 applies to:

* biologicals
* HCT materials

TGO 107 does not apply to autologous HCT regulated with the exemptions specified in the *Therapeutic Goods Regulations 1990* (the Regulations).[[1]](#footnote-1) These amendments were implemented in 2018.

Appendix 1 contains:

* draft TGO 107 legislative standard
* draft TGO 107 guidance document
* clause-based mapping document, which shows how the requirements in TGO 107 arose from TGO 87

### 1. Modernised and more informative labelling

#### Background

There has been considerable evolution in the labelling of biologicals and HCT materials due to the emergence of new technologies and extensive movement of such products across international borders. This has underscored the need for reliable traceability and increased identification.

With the availability of increased sources of information on the internet, there is a growing appetite from patients, consumers and healthcare providers for reliable, evidence-based sources of information regarding the use of therapeutic goods. The proposed changes seek to address this need.

The proposed amendments are not envisaged to change the regulatory impact on affected stakeholders.

#### Proposal

Updates proposed for TGO 107 include:

* the provision of information relating to: (a) incompatibilities and instructions for reporting adverse events; and (b) biochemical, biodynamic or biokinetic properties, and outcomes of clinical trials and preclinical safety studies for Class 3 and 4 biologicals (where applicable)
  + these two proposed new requirements are broadly consistent with TGA labelling requirements for prescription medicines and seek to align important therapeutic goods information and allow the healthcare prescriber, patient or consumer to properly consider the risk-benefit of the biological
  + these proposed new requirements are consistent with recent recommendations in the Council of Europe’s [4th Edition of the Guide to the quality and safety of tissues and cells for human application (2019)](https://www.edqm.eu/en/organs-tissues-and-cells-technical-guides)

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|  | **Question 1: Do you agree mandating additional information for Class 3 and 4 biologicals facilitates safe and effective use of such therapeutic goods?**  **Question 2: If this proposed change affects you, please explain how.** |

* the use of machine-readable codes as an optional alternative to the currently required unique identification number/alphanumeric by which to uniquely identify the donor of HCT materials
  + such an option will ensure the accuracy of records since machine-readable codes avoid the occurrence of manual transcription errors, and the machine output can easily be entered into electronic databases

### 2. Other issues

No other major changes are proposed for TGO 107. We welcome any suggestions and other comments to improve the changes proposed in TGO 107 and its associated guidance.

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|  | **Question 3: Please tell us any other suggestions or comments that you believe will improve the proposed TGO 107 and its associated guidance.** |

## Proposed amendments to TGO 108

TGO 108 largely supersedes [TGO 88](https://www.legislation.gov.au/Series/F2013L00854) and specifies numerous aspects around donor eligibility:

* social and medical history
* physical assessment
* testing
* deferral requirements

TGO 108 applies to:

* biologicals
* HCT materials
* blood
* blood components (including plasma for fractionation)

Appendix 2 contains:

* draft TGO 108 legislative standard
* draft TGO 108 guidance document
* clause-based mapping document, which shows how the requirements in TGO 108 arose from TGO 88

### 1. Exemption for autologous HCT products

#### Background

Following legislative changes in 2018, [TGA increased regulatory oversight for autologous HCT products](https://www.tga.gov.au/autologous-human-cells-and-tissues-products-regulation). The level of regulation of autologous HCT products varies depending on criteria including the level of external governance, clinical oversight, the manufacturing process and the intended use of the product. Thus, autologous HCT products could be either: (a) excluded from regulation, (b) regulated with exemptions, or (c) fully regulated.

TGO 88 currently exempts blood components collected, manufactured and administered by a medical practitioner from its requirements.

#### Proposal

The remade TGO 108 specifies minimum donor screening criteria for minimising infectious disease transmission from donor to recipient. Autologous HCT products have an inherently lower risk of transmitting infectious diseases than those used for allogeneic purposes given they are for use within the same individual, not another individual. Thus, we propose that TGO 108 not apply to autologous HCT products where the collection and administration is under the professional supervision of a medical or dental practitioner.

Although autologous HCT products have a lower risk of transmitting infectious diseases than their allogeneic counterparts, there are nonetheless risks associated with contamination or cross-contamination of such products or other products during manufacture. In order to efficiently and effectively mitigate these risks, we propose the following regulatory requirements:

* in the case of ‘autologous HCT products regulated with exemptions’:[[2]](#footnote-2)
  + These products can only be minimally manipulated, deployed for homologous use, for a single indication in a single clinical procedure, and manufactured and administered under high-level clinical oversight. These criteria clarify the boundaries between clinical practice, which is already regulated to manage such risks, and therapeutic goods regulations. TGA requirements such as adverse event reporting and recalls continue to apply. It is proposed that TGO 107 and TGO 109 will not apply to these products; see proposed amendments to TGO 107 and TGO 109.
* in the case of fully regulated autologous HCT products:
  + To consider this risk, the remade TGO 109 includes a section titled: ‘Diseases and conditions that may compromise biologicals’. This section is reworded from TGO 88 sections 9(13-15) and clarifies that where a risk of contamination or cross-contamination of other products manufactured at the same facility (amongst other factors that may affect the quality, safety or efficacy) is possible, any or all the donor screening requirements specified in TGO 108 can be applied. This is in addition to the general manufacturing requirements which have been transferred from TGO 88 to TGO 109. Further, the requirements of donor traceability from TGO 87 will continue to apply to such products via TGO 107. GMP requirements also apply to these products.

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| Information | GMP requirements continue to apply for autologous HCT products that do not meet the ‘autologous HCT products regulated with exemptions’ criteria. These GMP requirements include measures for the minimisation of contamination or cross-contamination of premises, equipment, and of any other therapeutic goods that are manufactured at the shared facility. Other areas that need to be considered are personnel working in areas where contamination may be an issue (for example, clean areas or areas where infectious materials are handled) – such personnel must be given specific training. For further information, refer:  <https://www.tga.gov.au/manufacturing-biologicals>  <https://www.tga.gov.au/manufacturing-blood-and-blood-components> |

This proposed change is likely to minimise regulatory **impact** on affected sponsors. If the quality and safety of the HCT product is maintained, and compliance with TGO 109 is demonstrated, sponsors of autologous HCT products will no longer require donor screening.

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|  | **Question 4: Do you agree that the specified requirements in the proposed Order related to the following don’t need to be mandated for autologous HCT products when there is medical or dental practitioner oversight for collection and administration?**   * **donor social and medical history** * **donor physical assessment** * **donor deferral and testing requirements.**   **Question 5: If this proposed change affects you, please explain how.**  Note: TGO 109 and GMP requirements, amongst other regulatory requirements, will still apply to autologous HCT products whose manufacture involves more than minimal manipulation. |

### 2. Donor deferral exemption for directed allogeneic HCT products

#### Background

Directed allogeneic HCT products are those manufactured from the HCT material of a donor, and are only for a designated patient with a pre-existing condition. The collection of HCT material and administration of such HCT products are under the professional supervision of dental or medical practitioner.

TGO 88 currently exempts blood components collected, manufactured and administered by a medical practitioner from its requirements.

#### Proposal

The remade TGO 108 specifies minimum donor screening criteria for minimising infectious disease transmission from donor to recipient. There is a risk of transmitting infectious diseases from donor to recipient with HCT products for allogeneic purposes given they are for use in different individuals. However, in the case of directed allogenic HCT products, the donor deferral criteria is a clinical decision based on a risk-benefit assessment for that particular patient. Thus, we propose to exempt directed allogenic HCT products from donor deferral criteria.

This change clarifies the exemption for directed allogeneic HCT products by extending it from blood components to **all HCT products**. The collection of donor social and medical history, physical assessment and testing, and the provision of outcomes to the treating medical or dental practitioner is still required.

There are nonetheless risks associated with contamination or cross-contamination of such products or other products during manufacture. To consider this risk, the remade TGO 109 includes a section titled: ‘Diseases and conditions that may compromise biologicals’. This section is reworded from TGO 88 sections 9(13-15) and clarifies that where a risk of contamination or cross-contamination of other products manufactured at the same facility (amongst other factors that may affect the quality, safety or efficacy) is possible, any or all the donor screening requirements specified in TGO 108 can be applied. This is in addition to the general manufacturing requirements transferred from TGO 88 to TGO 109. Further, the requirements of donor traceability from TGO 87 will continue to apply to such products via TGO 107. GMP requirements also apply to these products.

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| Information | GMP requirements continue to apply for directed allogeneic HCT products. These GMP requirements include measures for the minimisation of contamination or cross-contamination of premises, equipment, and of any other therapeutic goods that are manufactured at the shared facility. Other areas that need to be considered are personnel working in areas where contamination may be an issue (for example, clean areas or areas where infectious materials are handled) – such personnel must be given specific training. For further information, refer:  <https://www.tga.gov.au/manufacturing-biologicals>  <https://www.tga.gov.au/manufacturing-blood-and-blood-components> |

As with the proposed change for autologous HCT products, this change is likely to reduce the regulatory **impact** on affected sponsors.

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|  | **Question 6:**  **Do you agree that donor deferral requirements don’t need to be mandated for directed allogeneic HCT products when there is medical or dental practitioner oversight for collection and administration?**  **Question 7: If this proposed change affects you, please explain how.**  Note: TGO 109 and GMP requirements, amongst other regulatory requirements, will still apply to directed allogeneic HCT products whose manufacture involves more than minimal manipulation. |

### 3. Deferral period for donors with high-risk sexual behaviour

#### Background

TGA recently granted an exemption to Australian Red Cross Lifeblood to reduce the donor deferral period for blood/plasma donors with high-risk sexual behaviours from 12 months to 3 months since the last sexual contact. This exemption was based on a risk analysis and used scientific, clinical and epidemiological data submitted by Lifeblood, and informed by data from other countries. The analysis showed that the majority of the transfusion-transmitted infection risk comes from donors with newly-acquired blood borne infections donating during the so-called ‘window period’. To minimise this risk, a three month donor deferral period is acceptable provided donor testing includes nucleic acid testing (NAT) for HIV-1/2, HBV and HCV.

#### Proposal

It is proposed to extend the exemption for donors with high-risk sexual behaviours from 12 months to 3 months since the last sexual contact to all HCT material, that is, not just blood/plasma. This exemption is provided these donors are screened as per requirements specified in TGO 108, that is, where donor testing includes NAT.

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|  | **Question 8:**  **Do you agree that the deferral period for donors with high-risk sexual risk behaviours can be reduced from 12 months to three months for all HCT donors provided that donor testing is the same as for blood donors and includes NAT?**  **Question 9: If this proposed change affects you, please explain how.** |

### 4. Malaria donor deferral criteria

#### Background

TGO 88 defers donors who have had potential exposure to malaria unless they test negative with a validated immunological test.[[3]](#footnote-3) TGA acknowledges that clearance of malarial parasites from HCT materials could be an alternative to this requirement. Recognising the sensitivity of the malaria parasite to gamma irradiation, HCT material subjected to irradiation with ≥ 25 kGy during manufacture of the HCT product appears sufficient to clear malaria parasites. Similarly, if the HCT product from such a donor will be terminally sterilised, the risk of malaria transmission is likely low.

#### Proposal

We propose that donors who have had potential exposure to malaria may be accepted without any deferral period if the HCT material will, during manufacture, have additional treatments of either:

* a terminal sterilisation process during manufacture of the HCT product, which must be validated to ensure a maximal sterility assurance level of 10-6
* ≥ 25 kGy of gamma irradiation as an additional manufacturing step

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|  | **Question 10: Do you agree that donors who have had potential exposure to malaria may be accepted without any deferral period if the HCT material will, during manufacture, have additional treatments of either:**   1. **a terminal sterilisation process during manufacture of the HCT product, which must be validated to ensure a maximal sterility assurance level of 10-6; or** 2. **≥ 25 kGy of gamma irradiation as an additional manufacturing step?**   **Question 11: If this proposed change affects you, please explain how.** |

### 5. Requirements for cornea only donors

#### Background

TGO 88 requires that donors whose ocular tissue will be released for supply solely for the purpose of corneal transplantation (‘cornea only donors’) only need to be serology tested for HIV-1/2, HCV and HBV (hepatitis B surface antigen [HBsAg]).[[4]](#footnote-4) Consequently, for ‘cornea only donors’, TGO 88 exempts serological testing for HTLV-1/2 and syphilis, and NAT for HIV, HCV and HBV.

These exemptions are inconsistent with international best practice for eye banking establishments. The risk of infectious disease transmission from ‘cornea only donors’ is similar to all other ocular tissue donors. Although the corneal tissue is avascular, neural and immune cells may remain, which poses a risk of viral carriage. Further, corneas may be supplied with a scleral rim, which is vascularised.

#### Proposal

We propose that for ‘cornea only donors’, serological testing for HTLV-1/2 and syphilis is mandated, along with NAT for HIV, HCV and HBV, in order to establish their donor eligibility. A 12-month transition period for these testing requirements is also proposed (see below).

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|  | **Question 12: Do you agree that ‘cornea only donors’ must also be serologically tested for HTLV-1/2 and syphilis, and NAT for HIV, HCV and HBV, in order to establish their donor eligibility?**  **Question 13: If this proposed change affects you, please explain how.** |

### 6. Requirements for plasma for fractionation only donors

#### Background

TGO 88 requires that donors whose HCT material will be used solely for the purpose of plasma for fractionation (‘plasma for fractionation only donors’) only need to be serology tested for HIV-1/2, HCV and HBV (hepatitis B surface antigen [HBsAg]), and NAT for HIV-1/2 and HCV.[[5]](#footnote-5) Consequently, for ‘plasma for fractionation only donors’, TGO 88 exempts NAT for HBV.

This exemption is inconsistent with international best practice. Currently, NAT for HBV DNA is mandated by the US Food and Drug Administration and recommended by World Health Organization where its implementation is likely to shorten the window period of detection and potentially identify HBsAg negative occult infection.

#### Proposal

We propose to remove this exemption such that NAT for HBV is mandated for ‘plasma for fractionation only donors’ to establish their eligibility.

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|  | **Question 14: Do you agree that ‘plasma for fractionation only donors’ must undergo NAT for HBV in order to establish their donor eligibility?**  **Question 15: If this proposed change affects you, please explain how.** |

### 7. Transition period

It is proposed to allow sponsors a 12-month transition period for any proposed change in donor testing requirements, including serological testing for HTLV-1/2 and syphilis; NAT for HIV, HCV and HBV (‘cornea only donors’); and NAT for HBV (‘plasma for fractionation only donors’).

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|  | **Question 16: Do you agree that a 12-month transition period from the commencement date of TGO 108 (30 September 2021) is sufficient to allow sponsors to comply with any change in donor testing requirements (‘cornea only donors’ and ‘plasma for fractionation only donors’)?**  **Question 17: If no, please explain why.** |

### 8. Other issues

No other major changes are proposed for TGO 108. We welcome any suggestions and other comments to improve the changes proposed in TGO 108 and its associated guidance.

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|  | **Question 18: Please tell us any other suggestions or comments that you believe will improve the proposed TGO 108 and its associated guidance.** |

## Proposed amendments to TGO 109

TGO 109 largely supersedes the tissue-specific standards in [TGO 83](http://www.legislation.gov.au/Series/F2011L01489) (musculoskeletal tissue), [TGO 84](http://www.legislation.gov.au/Series/F2011L01490) (cardiovascular tissue), [TGO 85](http://www.legislation.gov.au/Series/F2011L01491) (ocular tissue) and [TGO 86](http://www.legislation.gov.au/Series/F2011L01492) (skin) and specifies general manufacturing requirements for biologicals.

TGO 109 consists of two distinct parts:

* Part 2: applies to all biologicals and includes general requirements from TGO 88 such as critical materials and microbial controls
* Parts 3 to 7: specify requirements for specific tissue types from current TGOs 83-86 and a new standard for amnion products

The intent of the remade TGO 109 is to formalise and clarify requirements to which sponsors already adhere.

TGO 109 applies to:

* biologicals
* HCT materials

TGO 109 does not apply to autologous HCT regulated with exemptions specified in Item 13, Schedule 5A of Therapeutic Goods Regulations 1990. These amendments to the regulations were implemented in 2018.

Appendix 3 contains:

* draft TGO 109 legislative standard
* draft TGO 109 guidance document
* clause-based mapping document, which shows how the requirements in TGO 109 arose from TGOs 83, 84, 85, 86 and 88

### 1. Diseases and conditions that may compromise biologicals

#### Background

While the purpose of TGO 108 is donor screening and the minimisation of transmission of infectious diseases, TGO 109 specifies parameters that affect the quality of the finished product. TGO 88 notes that a biological must not be manufactured from a donor known to have a disease or condition that may compromise the quality, safety or efficacy of the therapeutic good unless criteria for donor acceptance are based on validated data or a medical officer accepts the donor.[[6]](#footnote-6)

#### Proposal

This requirement has been reworded to clarify the intent and transferred from TGO 88 to TGO 109. Sponsors must continue to consider any donor diseases or conditions that may affect the quality, safety or efficacy of the biological. This includes diseases such as infections, malignancies, degenerative neurological disorders, and cardiac conditions. This also includes any donor treatments or medications, along with behavioural risk factors such as excessive alcohol consumption, smoking or illicit drug use. It also includes pregnancy, age limits, or any relevant donor social or medical history.

This section underscores the quality of a HCT material used in manufacture of a biological. Manufacturers must consider any diseases or conditions that affect the final product, irrespective of exemptions in TGO 108.

**Since there is no change to the intent of this existing requirement, this change is unlikely to impact affected sponsors.** Sponsors will continue to demonstrate compliance by including a specified list of diseases or conditions in their dossiers.

### 2. Processing completion timeframes for cardiovascular tissue

#### Background

TGO 84 specifies collection and processing timeframes for cardiovascular tissue[[7]](#footnote-7) but does not mandate the processing completion timeframes. The completion timeframes are critical to ensure the quality and safety of the cardiovascular tissue for its intended use.

#### Proposal

We propose to specify that the processing of human cardiovascular tissue product must be completed within 72 hours of asystole or collection of the tissue. This is consistent with recent recommendations in the Council of Europe’s [4th Edition of the Guide to the quality and safety of tissues and cells for human application (2019)](https://www.edqm.eu/en/organs-tissues-and-cells-technical-guides) which states that entire manufacturing process (completion of cryopreservation) should be completed within 72 hours of asystole. Manufacturing timeframes longer than this should be justified and validated to ensure that the quality and safety of the allograft tissue is not adversely affected.

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|  | **Question 19: Do you agree that completion of processing timeframes should be mandated for human cardiovascular tissue products?**  **Question 20: If yes, do you also agree that processing should be completed within 72 hours of collection unless otherwise validated?** |

### 3. Other issues

No other major changes are proposed for TGO 109. We welcome any suggestions and other comments to improve the changes proposed in TGO 109 and its associated guidance.

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|  | **Question 21: Please tell us any other suggestions or comments that you believe will improve the proposed TGO 109 and its associated guidance.** |

## Merging legislative instruments

For the purposes of clarity and simplicity, we propose to merge the [Therapeutic Goods (Things that are not Biologicals) Determination No. 1 of 2011](https://www.legislation.gov.au/Details/F2011L00894) with the [Therapeutic Goods (Things that are Biologicals) Specification 2019](https://www.legislation.gov.au/Details/F2019L01669). This change involves no substantive changes and is instead simply the drafting of a single legislative instrument that defines whether a material is or is not a biological.

A copy of the proposed new legislative instrument is in Appendix 4.

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|  | **Question 22: Please tell us if you have any comments on the draft legislative instrument.** |

## Providing feedback

TGA is seeking feedback on the suitability and potential regulatory impact that any proposed amendments may have on affected stakeholders. We invite you to provide your feedback by completing our online survey on the [Department of Health’s Consultation Hub](https://consultations.health.gov.au/).

All responses will be published on the TGA website unless you specifically request that your response be kept confidential.

## Commencement date

The commencement date of the new legislative instruments will be 30 September 2021, with publication of the finalised instruments beforehand.

Any transition period will be introduced where necessary and based on the outcomes of our consultation.

## What happens next

Submissions will be reviewed by the TGA and a summary of the submissions will be posted on this website. A decision about remaking the TGOs will be made after submissions have been considered.

Sponsors of existing HCT products will be required to submit a single [notification for included biologicals](https://www.tga.gov.au/book-page/notifications-included-biologicals) to confirm their ongoing compliance after these TGOs are remade.

## Appendices

### Appendix 1: Proposed amendments to TGO 107

* Draft *Therapeutic Goods (Standard for Biologicals—Labelling Requirements) (TGO 107) Order 2021*
* Draft TGO 107 Guidance
* Mapping document, which tracks the requirements specified in TGO 107 from TGO 87

### Appendix 2: Proposed amendments to TGO 108

* Draft *Therapeutic Goods (Standard for Human Cell and Tissue Products—Donor Screening Requirements) (TGO 108) Order 2021*
* Draft TGO 108 Guidance
* Mapping document, which tracks the requirements specified in TGO 108 from TGO 88

### Appendix 3: Proposed amendments to TGO 109

* Draft *Therapeutic Goods (Standard for Biologicals) (TGO 109) Order 2021*
* Draft TGO 109 Guidance
* Mapping document, which tracks the requirements specified in TGO 109 from TGOs 83, 84, 85, 86 and 88

### Appendix 4: Proposed amendments to legislative instruments

* Draft *Therapeutic Goods (Biologicals—Specified Things) Instrument 2021*

Version history

| Version | Description of change | Author | Effective date |
| --- | --- | --- | --- |
| V1.0 | Original publication | Biological Sciences Section, Scientific Evaluation Branch | May 2021 |

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| --- |
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| Reference/Publication # |

1. Schedule 5A, Item 13. [↑](#footnote-ref-1)
2. *Therapeutic Goods Regulations 1990*, Schedule 5A, Item 13. [↑](#footnote-ref-2)
3. Section 9 and Table 1. [↑](#footnote-ref-3)
4. Section 11 and Table 3. [↑](#footnote-ref-4)
5. Section 9 and Table 3. [↑](#footnote-ref-5)
6. Section 9. [↑](#footnote-ref-6)
7. Section 7. [↑](#footnote-ref-7)