Regulation of cell and gene therapies in Australia

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Overview

- Regulatory pathways for Cell and Gene therapy products in Australia
- Available regulatory pathways
- Priority Pathway for Biologicals
- Export-Only Pathway for Biologicals

Biological and Biological Medicines

Biological

- ✓tissue-based products
- ✓cell-based products
- ✓immunotherapy products containing human cells
- ✓autologous human cells and tissue products (including stem cells)
- ✓**gene-modified cell therapies**

Biological Medicines (prescription medicines)

- ✓vaccines (that do not contain viable human cells)
- ✓recombinant products
- ✓plasma derived products (or that contain plasma derived products)
- ✓**gene-therapy vectors alone**

Regulatory Pathways for Gene therapy products

Type of gene therapy	Example	Regulatory pathway	Further information
Ex vivo (gene is delivered to cells outside of the body, which are then transferred back into the body)	CAR-T cells (human cells)	Class 4 biological	Australian regulatory guidelines for biologicals (ARGB)
In vivo (gene is transferred to cells inside the patient's body)	Adeno-associated virus	Prescription medicine	Australian Regulatory Guidelines for Prescription Medicines (ARGPM)

GMP Pathways for Gene therapy products

Product type	Example Regulatory pathway	Further information
Gene therapy vector	GMP clearance pathway (API) MRA pathways available	Manufacturing therapeutic goods
Biological product (human cells and tissues)	GMP certificate for manufacturing site (GMP clearance for Sponsor) This includes sites that conduct donor testing and release testing of biological product	Manufacturing biologicals Australian code of good manufacturing practice for human blood and blood components, human tissues and human cellular therapy products

Pathways and provisions for Cell and Gene Therapy products

Pathway	Biological	Medicine
Standard review pathway	Yes	Yes
Priority review pathway	**Yes***	Yes
Orphan status	No	Yes
Provisional review pathway	No	Yes
Comparable Overseas Regulator (COR)	No	Yes
Export-only pathway	**Consultation complete**	Yes

Priority Pathway for Biologicals

New pathway active November 2022

- New pathway aligned with Priority Pathways for Prescription Medicines and Medical Devices
- Introduction of Priority Pathway for Biologicals was a key recommendation in submissions made to the House of Representative Inquiry (process for approval of new drugs and novel medical technologies in Australia) and from a TGA-commissioned MTPconnect report into regulatory framework for gene, cell and tissue therapies in Australia

- Sponsors must first obtain a Priority Determination for their product
  - Determination applies to one product for one therapeutic indication or intended use
  - Determination fee applies (currently $13,971)
- Once a Priority Determination has been obtained, Sponsors have six months to submit their Priority Inclusion application (evaluation of dossier)

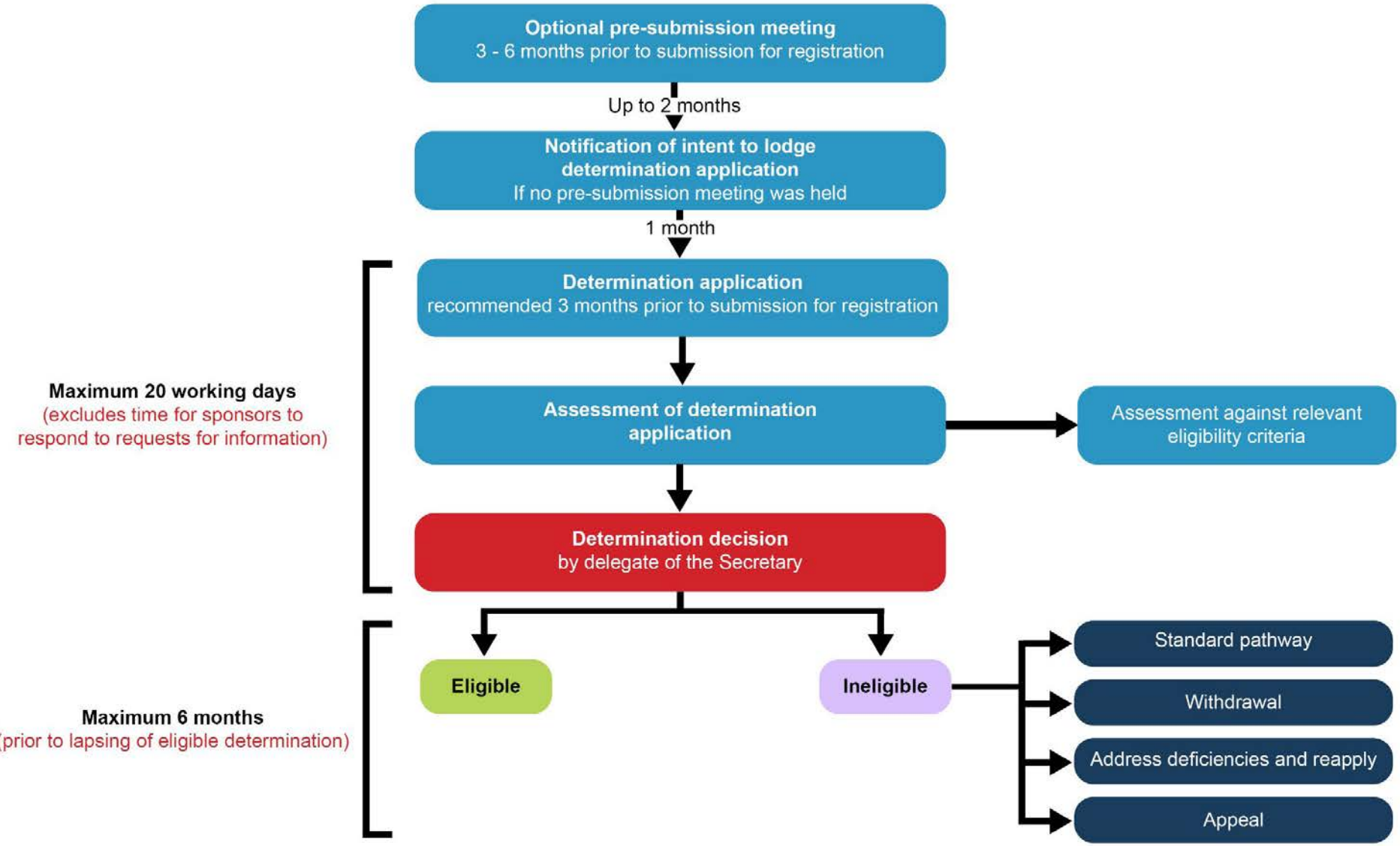
TGA Website:
Priority review pathway for biologicals

Criteria for Priority Determination

Criteria for accepting an application under a priority pathway considered similar pathways followed by the pathways implemented for both prescription medicines and medical devices

- Criterion 1 – New biological or new use
    - the biological is either a new Class 2, 3 or 4 biological for entry in ARTG or an already registered biological with a new intended use / therapeutic indication
- Criterion 2 – Life-threatening disease or seriously debilitating condition
    - the biological is to be used for treatment, prevention or diagnosis of a life threatening or seriously debilitating condition (as described by the TGA)
- Criterion 3 – Fulfils an unmet clinical need or clinically significant improvement over already approved therapeutic goods
    - No therapeutic goods that are intended to treat, prevent or diagnose the condition are entered on or included in the ARTG; or
    - there is substantial evidence demonstrating that the biological provides a clinically significant improvement in the safety or efficacy of the treatment, prevention or diagnosis of the condition compared to therapeutic goods already included in the ARTG
- Criterion 4 – Major therapeutic advantage
    - there is substantial evidence demonstrating that the biological provides a major therapeutic advance

Priority Determination Process



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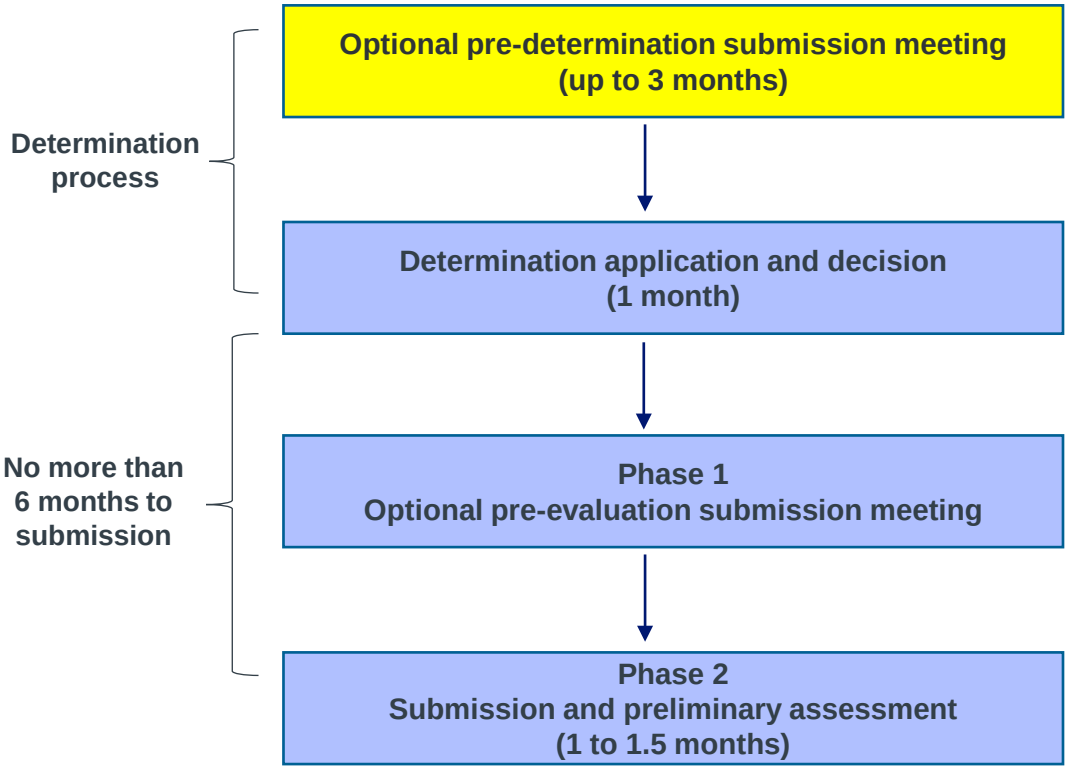
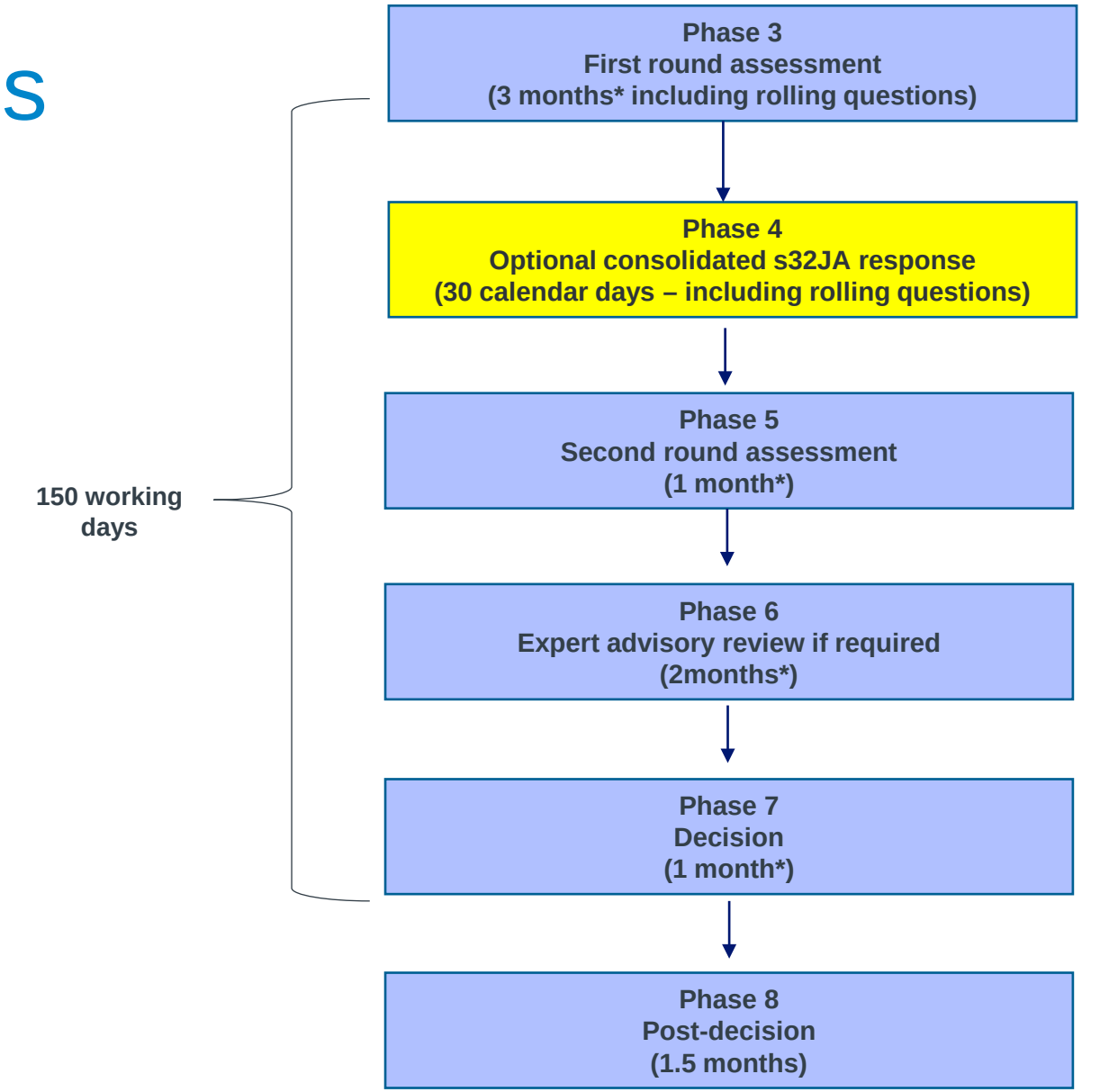
Priority Inclusion Process

- Priority Inclusion Pathway has a target timeframe of 150 working days
  - Compared to 255 WD for Standard Pathway
  - Slightly higher evaluation fees (~5% increase)
  - Dossier requirements for quality/safety/efficacy the same

- Rolling questions during the evaluation phase - if responses obtained by the end of the first round, stop clock will not be applied, and the evaluation can proceed to the next phase.
- Exit criteria – return to Standard Pathway
  - failure to respond to our requests for additional information as part of a formal s32JA request within 30 calendar days
  - identification of significant safety concerns that require further assessment
  - submission of unsolicited or more extensive data than what is required during evaluation (excluding the provision of new safety related data, which you must bring to our attention)
  - you are unlikely to meet the Good Manufacturing Practice (GMP) requirements for inclusion (that is, obtaining either an Australian manufacturing licence or GMP certification by 150 WD).

Priority Inclusion Process





*Timelines are indicative only and may vary on case by case basis

Export only pathway for biologicals

- Therapeutic Goods legislation currently provides a registration pathway for export only medicines and medical devices, however, no such pathway is available for export only biologicals.
- Currently, biologicals manufactured in Australia can be exported but they are not allowed to differ from biologicals included in the ARTG.
    - This means that ‘export only’ biologicals cannot have different indications, release specifications, or labels to the product approved by the TGA
    - This puts extra regulatory burden on the sponsors as importing country may have different requirements
- Public consultation was conducted in Nov-Dec 2021 and respondents showed general support for creation of a dedicated pathway to allow for the export only biologicals that are manufactured in but not supplied in Australia.

Proposed pathway for export only biologicals

- The TGA proposed a dedicated pathway for inclusion of export only biologicals in the ARTG to the Government.
- Objective of this pathway is to :
  - minimise regulatory burden on biologicals that are for export only
  - bring the biologicals framework into alignment with how other export only therapeutic products are regulated by the TGA.
- The introduction of new pathway is to allow for **a new class** of biologicals in the ARTG for the export only biologicals.
    - Export only biologicals will not be subject to pre-market assessment.
      - All manufacturing sites will require GMP certification
      - There is no formal evaluation. However, the Sponsor must certify that they are meeting the requirements of the legislation.
    - there will be a reduced regulatory and financial burden on the sponsors.
    - aligned with the medicines and medical devices pathways
- The proposed policy position has been approved by the Government and necessary amendments are being made to the legislation for making this provision.

Website references

TGA website	www.tga.gov.au
Australian regulatory guidelines for biologicals (ARGB)	https://www.tga.gov.au/publication/australian-regulatory-guidelines-biologicals-argb
Australian Regulatory Guidelines for Prescription Medicines (ARGPM)	https://www.tga.gov.au/publication/australian-regulatory-guidelines-prescription-medicines-argpm
Manufacturing therapeutic goods	https://www.tga.gov.au/manufacturing-therapeutic-goods
Manufacturing biologicals	https://www.tga.gov.au/manufacturing-biologicals
Australian code of good manufacturing practice for human blood and blood components, human tissues and human cellular therapy products	https://www.tga.gov.au/publication/australian-code-good-manufacturing-practice-human-blood-and-blood-components-human-tissues-and-human-cellular-therapy-products
Priority review pathway for biologicals	https://www.tga.gov.au/how-we-regulate/supply-therapeutic-good/supply-biological/application-process-supplying-biological/priority-review-pathway-biologicals

Therapeutic Goods Administration (TGA)

Exhibition booth **No.1**

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Australian Government

Department of Health and Aged Care

Therapeutic Goods Administration