

The Australian Clinical Trial Framework for Cell and Gene Therapy

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Session Overview

Key regulatory considerations for cell
and gene therapies in clinical trials

Supplying 'unapproved' therapeutic goods in clinical trials

Supply exemptions by the TGA are required

Goods that are not registered on the ARTG or are being used outside of their registration parameters must have a supply exemption in place.



Clinical Trial Notification (CTN) Scheme

Summary

- Notification pathway
- TGA does not evaluate any data relating to clinical trials at the time of submission.
- All material relating to the proposed trial, including the trial protocol is submitted directly to the Human Research Ethics Committee (HREC) for review and approval.
- Supply of goods cannot commence without valid notification and fee paid.
- Vast majority of trials conducted under this scheme.
- Target timeframe for acknowledgement: 5-7 working days



Clinical Trial Approval (CTA) Scheme

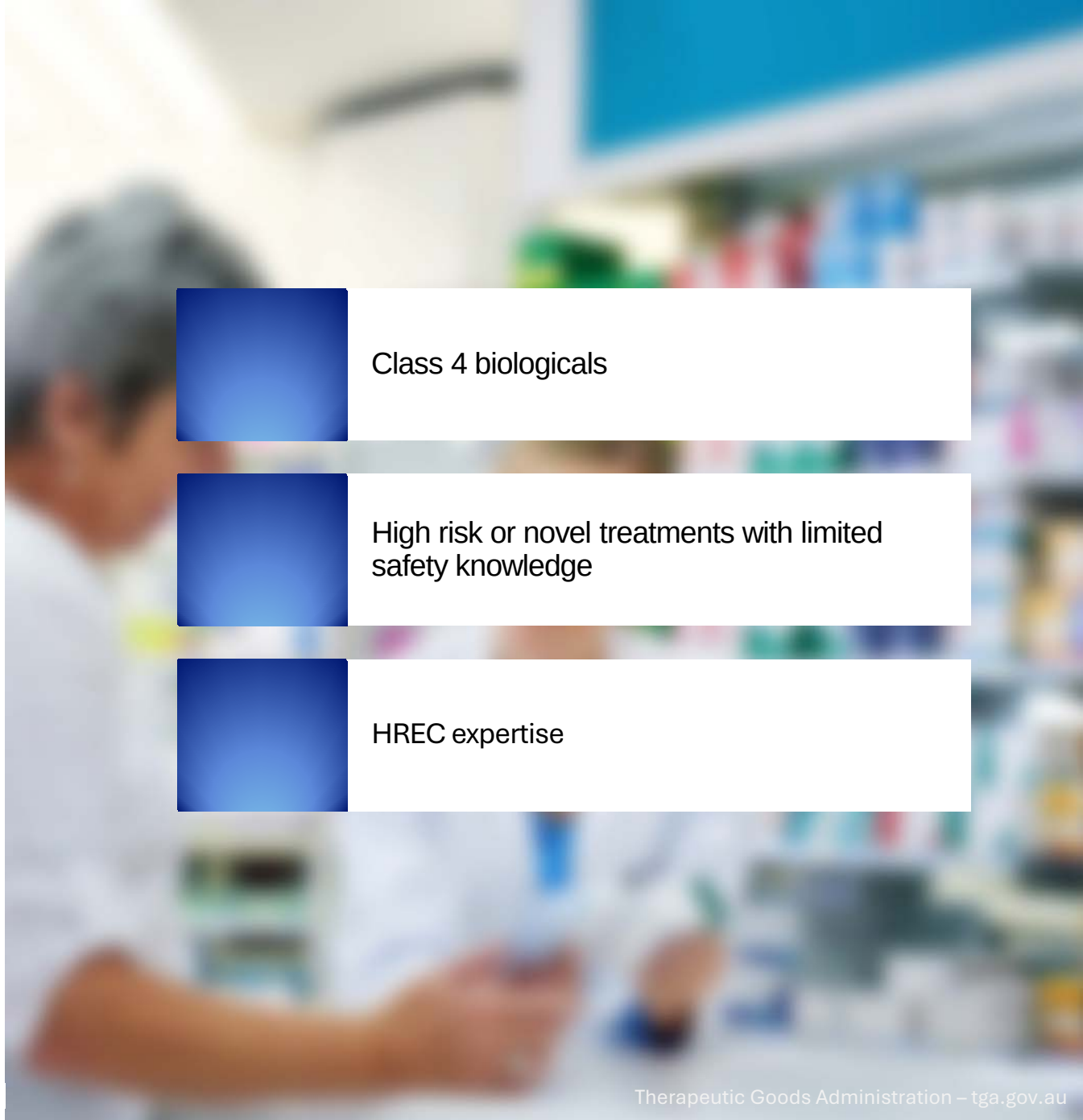
Summary

- Evaluation pathway
- Generally designed for complex therapies (required for certain class 4 biologicals)
- Supply of goods cannot commence without HREC and TGA approval.
 - Our primary responsibility is to review the safety of the product
 - HREC is responsible for considering the scientific and ethical issues of the proposed trial protocol
- Small number of trials conducted under this scheme.
- Target timeframe for evaluation: 50 working days



Major considerations

Supply exemptions for cell and gene therapies



Class 4 biologicals

High risk or novel treatments with limited safety knowledge

HREC expertise

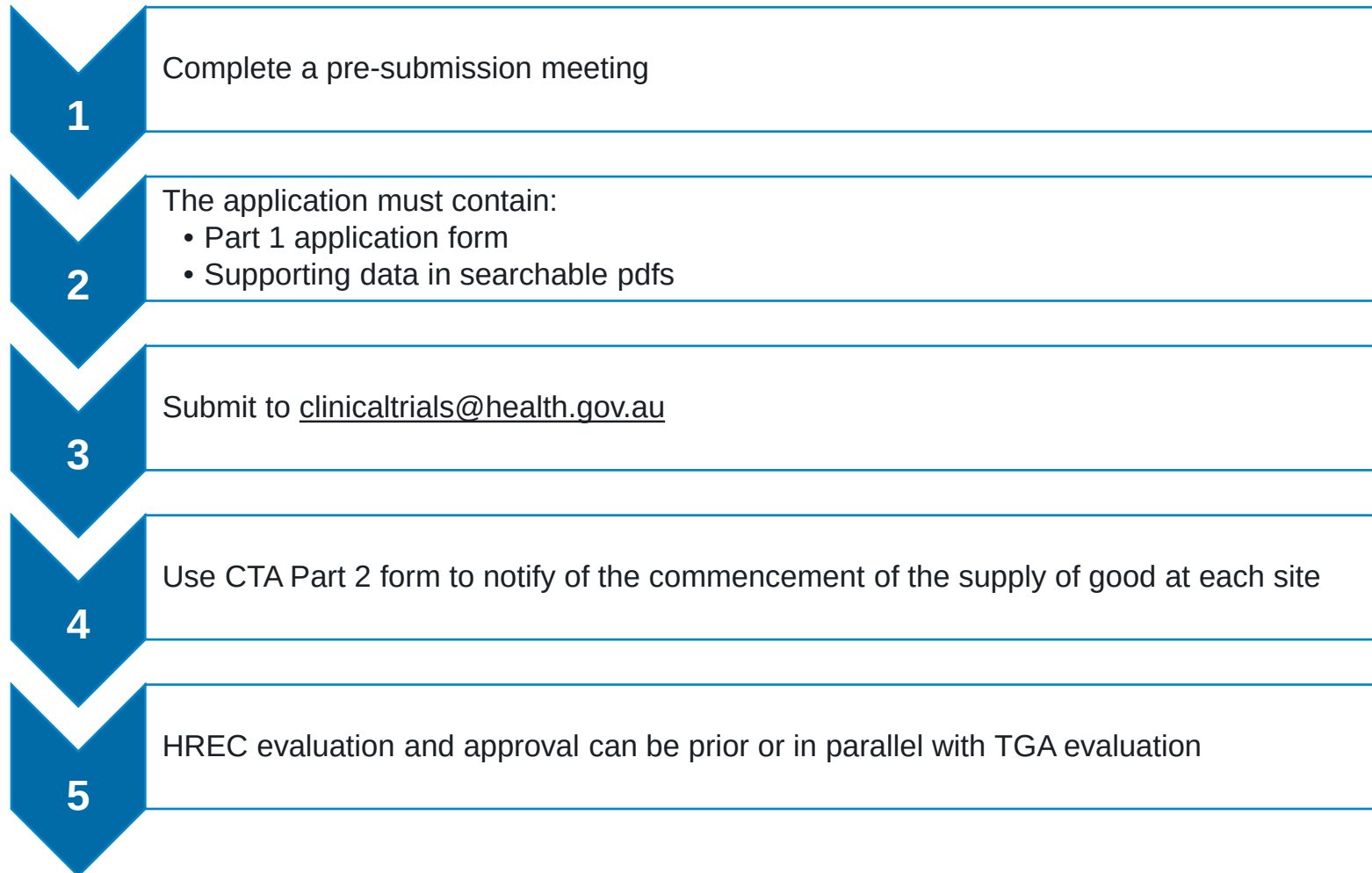
CTA Scheme

More information about our approval scheme

- Typical CTA process
- Revised guidance coming soon
- Dossier requirements



Typical CTA Process



Coming soon...

- Updated forms
- Clear CTA application dossier guidance



Review of the Clinical Trial Approval (CTA) Scheme

We are currently in the process of reviewing the Clinical Trial Approval (CTA) Scheme.

Last updated: 1 September 2024

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On this page

[Updates on the CTA review](#)

[Background and resources for the current CTA scheme](#)

[Resources](#)

[Overview of the usual CTA process](#)

[Variations](#)

The TGA committed to undertake a review of the CTA process in response to the [MTP Connect report on the Cell, Gene and Tissue Regulatory Framework in Australia](#). Stakeholders have called for improved communication about the CTA pathway.

This page will be updated as the review of the CTA scheme progresses. We encourage any stakeholder seeking more information on the CTA process to contact us at clinical.trials@health.gov.au.

Clinical trials

How we regulate Australian clinical trials that use unapproved therapeutic goods

Clinical Trial Notification (CTN) scheme

Roles and responsibilities for clinical trial safety reporting of significant safety issues and urgent safety measures

Investigator's brochures for medical device clinical trials

Good Clinical Practice (GCP) Inspection Program

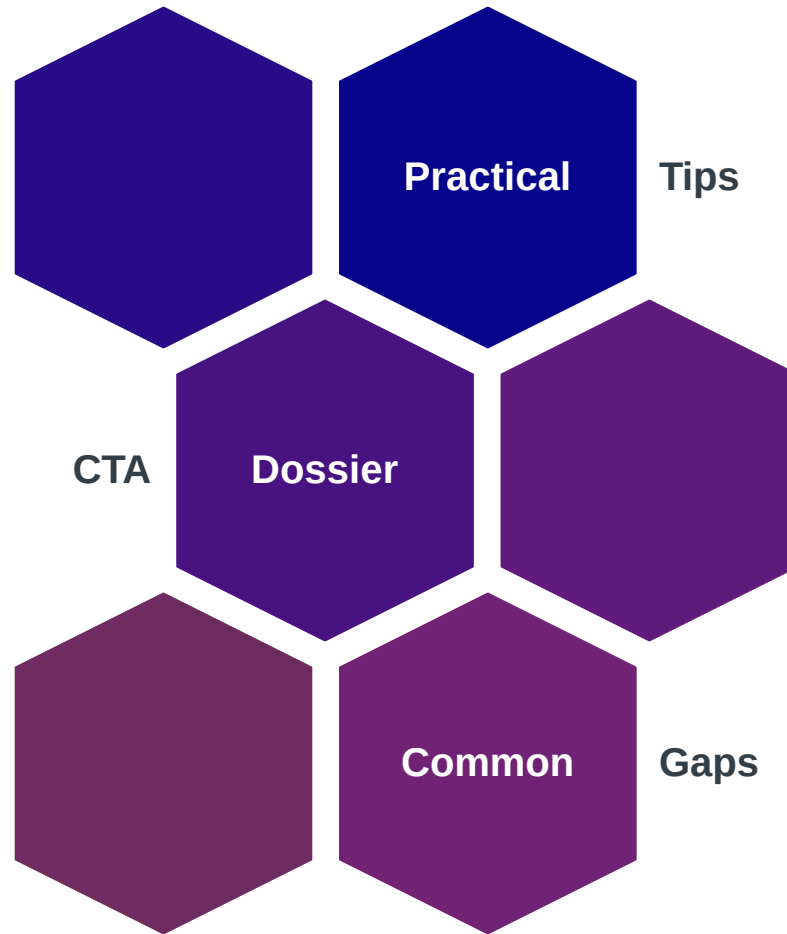
Australian clinical trial reforms

CTA dossier requirements*

1. Administrative and trial information
2. Quality and manufacturing information
3. Non-clinical information
4. Clinical information
5. Risk Management Plan (biologicals)

*data requirements may change between workshop and publication





Practical tips and common gaps



Microbiological controls



Scientific first principles and reference to available guidance



Data extrapolation



Pre-submission meeting

Microbiology evaluation

- Omission of microbiological monitoring
- Lack of reference to recognised/adopted standards



Scientific first principles and reference to available guidance

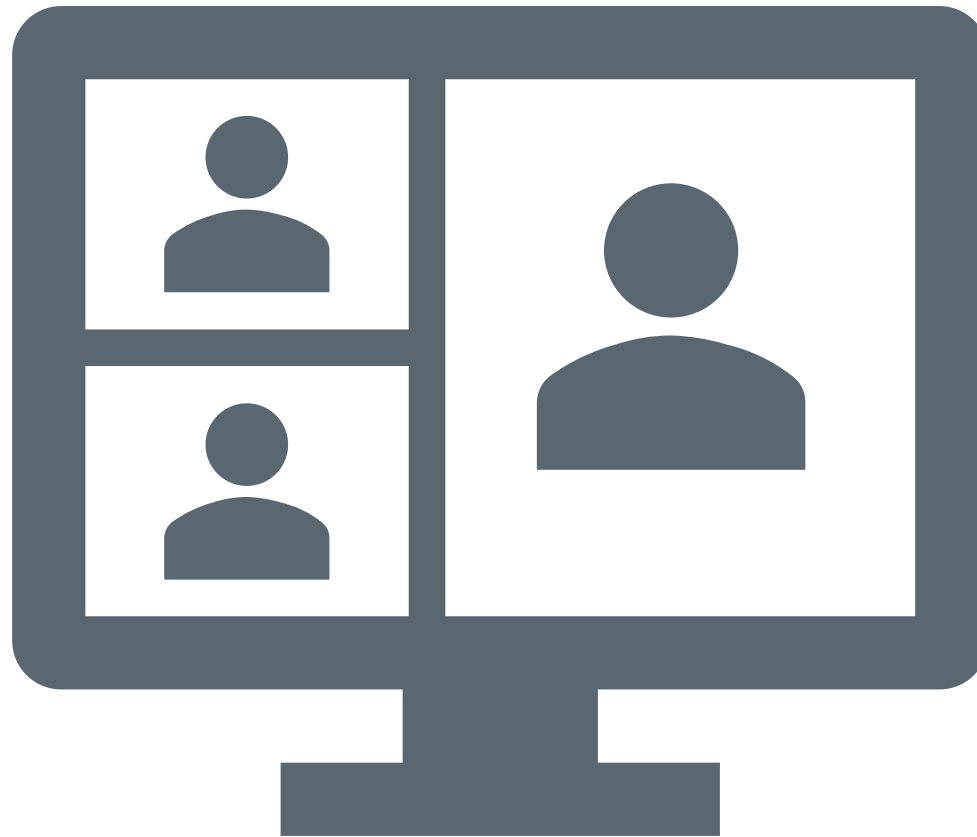
- Does the mechanism of action include a scientifically defensible rationale?
- Where possible refer to available guidance on cell therapies, for example:
 - EMEA/CHMP/410869/2006 – Guideline on Human Cell-Based Medicinal Products (TGA Adopted)
 - EMEA/CHMP/CPWP/83508/2009 – Guideline on Xenogeneic Cell-Based Medicinal Products (TGA Adopted)
 - EMA/CAT/22473/2025 - Guideline on Quality, Non-Clinical and Clinical Requirements for Investigational advanced therapy medicinal products in clinical trials (NOT Adopted)
 - EMA/CAT/571134/2009 - Reflection Paper on Stem Cell-Based Medicinal Products (NOT Adopted)
 - FDA Guidance for Industry - Considerations for the Development of Chimeric Antigen Receptor (CAR) T Cell Products (NOT Adopted)
 - FDA Guidance for Industry - Preclinical Assessment of Investigational Cellular and Gene Therapy Products (NOT Adopted)
 - EMA/CAT/GTWP/671639/2008 Rev. 1 - Guideline on quality, non-clinical and clinical aspects of medicinal products containing genetically modified cells (pending)

Non-clinical extrapolation

- Is sufficient data/discussion included to extrapolate safety for a first in human trial?
- Where possible, avoid generalised extrapolations/comparisons that are of limited predictive value in terms of efficacy or safety.



CTA pre-submission meeting



Information about [presubmission meeting](#) on our website

Other supply exemptions

When should other supply exemptions be considered?

- Special Access Scheme (SAS)
- Authorised Prescriber (AP) Pathway

Special Access Scheme (SAS) – three possible pathways

Allows access to unapproved therapeutic goods for an individual patient on a case-by-case basis

- **Category A**

- Notification pathway accessed by a medical practitioner for a patient who is *“seriously ill with a condition from which death is reasonably likely to occur within a matter of months, or from which premature death is reasonably likely to occur in the absence of early treatment.”*

- **Category B**

- Application pathway that can be accessed by a health practitioner for a patient that does not fit the Category A definition and where the unapproved therapeutic good is not authorised for supply under the Category C pathway. An approval letter from the TGA is required before the product can be supplied to the patient.

- **Category C**

- Notification pathway that allows specified health practitioners to supply unapproved therapeutic goods from a list of products deemed to have an established history of use. This list is reviewed and updated annually.

Authorised Prescriber (AP) Scheme

- Allows an authorised medical practitioner to prescribe and supply an unapproved therapeutic good (or class of goods) to a class of patients with a particular medical condition.
- No need for individual notifications or approvals for each patient (as is required via SAS).
- May be suitable where a prescriber intends to treat multiple patient in their care.
- Designed for ongoing clinical management of a define patient group, not for investigational use.
- 6 monthly reporting requirements (number of patients treated only).

Established history of use pathway

- 12B(1B) – Unapproved therapeutic goods with an established history of use for the indication listed
- 12B(1C) – Unapproved medicinal cannabis products/indications with an established history of use

Standard pathway (HREC pathway)

- All other unapproved therapeutic goods (including medicinal cannabis)
- Requires HREC approval of Specialist college letter of endorsement

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