Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

Clinical Trial Approval (CTA) Scheme

Targeted consultation with HRECs

Version 1.0, April 2024

Contents

Overview

Clinical trials conducted in Australia are subject to various regulatory controls to ensure the safety of participants. The Clinical Trial Notification (CTN) scheme and the Clinical Trial Approval (CTA) scheme allow clinical trials sponsors to import and/or supply 'unapproved' therapeutic goods in Australia for use in a clinical trial.

The CTN scheme is a notification process where the Australian sponsor must notify the Therapeutic Goods Administration (TGA) of the intent to supply an 'unapproved' therapeutic good in a clinical trial. This must take place before use of the good(s) commences. For more information on CTNs visit the TGA website.

The CTA scheme involves an application to the TGA for approval to supply an 'unapproved' therapeutic good(s) in a clinical trial. This involves the evaluation of scientific data about the therapeutic good(s) (quality, preclinical and early clinical safety data) and a decision to approve supply of the unapproved good(s) by the TGA prior to the start of a trial. The approving Human Research Ethics Committee (HREC) is responsible for the review and approval of the trial protocol, along with the ongoing monitoring of the trial. Further information can be found in the Clinical Trials Handbook.

The CTA scheme is only mandatory for Class 4 biologicals (except where evidence from previous clinical use supports the use of the biological, or a national regulatory body with comparable regulatory requirements has approved a clinical trial for an equivalent indication outside Australia). The CTA is optional for all other clinical trials using 'unapproved' therapeutic goods. The sponsor can decide, in consultation with the approving HREC, whether to submit a CTA or a CTN.

The TGA has evaluated fewer than 10 CTAs since the scheme started. However, use of the CTA pathway has increased recently. Stakeholders have called for improved communication about the CTA pathway. We committed to undertake a review of the CTA process and timelines in response to the MTP Connect report on the Cell, Gene and Tissue Regulatory Framework in Australia. We need your input to inform the review and options for the CTA scheme.

Why your views matter

We want to better understand the HREC review process and your views on barriers and opportunities for engaging with the TGA through the CTA process.

Your feedback will give us insights into the different functions, responsibilities and processes of HRECs and will inform our priorities as we work to improve our processes and guidance for the CTA scheme.

Please complete the responses online via the TGA consultation hub. At the end of the consultation, you will have an opportunity to upload supporting documentation to support your response e.g., process maps.

Please contact us at clinical.trials@tga.gov.au if you have any issues responding to this consultation.

Give us your views

Online survey

Privacy and your personal information

The TGA invites you to share your views on the Clinical Trial Approval (CTA) Scheme – targeted consultation with HRECs.

Your personal information is protected by law, including the Privacy Act 1988 (Privacy Act) and the Australian Privacy Principles, and is being collected by the TGA, via Citizen Space, for the purposes of conducting a consultation process in relation to the Clinical Trial Approval Scheme – targeted consultation with HRECs. The TGA will collect your personal information at the time that you provide a submission, unless you choose to make a submission anonymously, and you are not reasonably identifiable from the information provided in your submission.

The TGA will collect your personal information in this survey to:

- contact you if we need to clarify or seek more information about issues raised in your feedback
- seek your feedback about how the consultation was run.

The TGA will not publish the responses of this consultation.

You should not include information in your submission about another individual who is identified, or reasonably identifiable. If you need to include information about another individual in your submission, you will need to inform that individual of the contents of this notice, and obtain their consent to the Department collecting their personal information.

You can get more information about the way in which the Australian Government Department of Health and Aged Care (the Department) will manage your personal information, including our privacy policy, at https://www.health.gov.au/resources/publications/privacy-policy. You can obtain a copy of the Department's privacy policy by contacting the Department using the contact details set out below. The Department's privacy policy contains information about:

- how you may access the personal information the Department holds about you and how you can seek correction of it; and
- how you may complain about a breach of
  - the APPs; or
  - a registered APP code that binds the Department; and
  - how the Department will deal with such a complaint.

You can contact the Department by telephone on (02) 6289 1555 or freecall 1800 020 103 or by using the online enquiries form at http://www.health.gov.au.

Most questions in this consultation are optional. Questions that you must respond to are marked as 'required'.

About you

This is a targeted consultation for HRECs to share their feedback with the TGA on the CTA process. To ensure we can fully utilise your feedback, please share some details about yourself.

Question 1. What is your name?

Question 2. Please provide your email address if you consent to us contacting you with consultation updates (separate to receiving a copy of your submission). Email:

Question 3. Are you responding on behalf of your HREC/organisation or as an individual? (required)

Question 4. Which HREC/organisation are you affiliated with? (required)

Question 5. What is your role? E.g., member & category/chair/management/administration/ principal investigator/health professional/other (please specify) (required)

Current CTA process

The current process is summarised below. The TGA currently provides this information to individual sponsors where required as it is not published on the TGA website.

1. Pre-submission meetings

Once we receive confirmation that a sponsor is planning to submit a CTA, the TGA encourages all sponsors to request a pre-submission meeting.

In the pre-submission meetings, the TGA:

- ✓ provides advice to clarify any questions the applicant has relating to existing studies or the proposed data package for a CTA application
- ✓ provides advice on the CTA application process
- ✘ does **not** address issues that require evaluation of data
- ✘ does **not** generally give advice on developing a data package or the number of studies required to support a CTA application

2. Submission of the CTA application

The sponsor submits a paper-based form and accompanying dossier to the TGA. The TGA undertakes a preliminary assessment to ensure that the data is sufficient to begin evaluation and then the invoice is charged. Once the fee has been paid, the evaluation begins.

3. TGA evaluation process

Evaluations are performed by multiple specialist evaluation areas across TGA to assess the quality and safety of the therapeutic good(s) proposed to be used in the trial. Evaluation reports with recommendations are submitted to the decision maker for consideration. The sponsor is informed of the decision whether to approve or not in a formal decision letter. More information on what is assessed by the TGA is detailed later in this document.

There is a target timeframe of **50 days** from payment of the invoice to decision – this is not legislated. We set internal target times that allow 40 days for 2 rounds of evaluation and 10 days for administrative processes. These timeframes have been difficult to meet, in part due to the complexity of these novel products and the inconsistent quality of dossier submissions.

4. HREC review and approval

Following TGA approval or in parallel with TGA evaluation, the sponsor contacts their chosen HREC to complete reviews of the scientific and ethical details of the trial proposal. Trials can commence once both TGA and HREC approval has been received.

5. Commencement of the trial

Sponsors use a paper-based form to notify the TGA when a trial commences at each site supplying the therapeutic good(s) under the CTA exemption. There is no fee for this notification.

6. Completion of the trial

Sponsors use a paper-based form to notify the TGA of the completion of the trial supplying the therapeutic good(s) under the CTA exemption at all sites. There is no fee for this notification.

7. Safety reporting

Safety reporting requirements are detailed in the NHMRC Guidance: Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods (NHMRC Guidance).

The NHMRC Guidance outlines the responsibilities of trial sponsors, investigators, HRECs and institutions (referred to as the 'approving authority' in this Guidance); however, it is the trial sponsor that is responsible for reporting to the TGA. The NHMRC Guidance also outlines the trial sponsor's safety reporting responsibilities for clinical trials conducted under the CTN and CTA schemes. Safety reporting timelines can be found in the Australian Clinical Trial Handbook.

Question 6. Has your HREC reviewed a clinical trial that requires a TGA CTA, or do you expect to in the next 12 months? (required)

a. **Have experience reviewing a trial requiring a CTA**

b. **Expect to review a trial requiring a CTA in the next 12 months**

c. **Do not have experience reviewing a trial requiring a CTA**

d. **Do not expect to review a trial requiring a CTA in the next 12 months**

Question 7. How does your HREC approach discussions with the sponsor if the HREC recommend the CTA pathway? What factors does your HREC consider when recommending the CTA pathway?

Question 8. What is your HREC's target timeline for considering ethics approval for a trial? Does this differ if a trial will be submitted to TGA as a CTA?

Question 9. Please provide any feedback you have on the TGA's CTA process. For example, where there may be opportunities to streamline and better align with HREC processes.

The TGA's role in evaluating CTAs

Both the CTN and CTA schemes provide for the lawful importation and/or supply of 'unapproved' therapeutic goods in Australia for use solely for experimental purposes in humans.

The focus of the CTA scheme is to evaluate the quality and safety of the (generally novel or first-in-class) 'unapproved' therapeutic good(s) for supply at Australian trial sites. Trials submitted under a CTA may involve one or multiple 'unapproved' therapeutic goods.

During the CTA evaluation process, the TGA evaluates the following:

Medicines and biologicals

1. Quality of the therapeutic good(s), including

   a. Manufacturing process, including process validation
   b. Proposed specifications, including release and stability
   c. Transportation

2. Safety of the therapeutic good(s)
   a. Non-clinical safety studies
   b. Clinical assessment of publications and data supplied as part of the CTA dossier
   c. Adventitious agent safety (if materials are of human or animal origin)
   d. Microbiological safety/sterility
   e. Container integrity
   f. Endotoxin risks
3. Compliance with applicable *Therapeutic Goods Orders*, international guidelines and TGA adopted international guidelines such as EMEA/CHMP/SWP/28367/07
4. Labelling (including traceability)

Medical devices

The TGA has never received an application for a medical device CTA. We would apply similar principles to the evaluation of a medical device CTA as those applying to medicines and biologicals.

What the TGA does not evaluate

As part of the CTA evaluation and decision making, the TGA does not assess:

- ethical considerations of the trial
- accreditation of the clinical trial sites
- the currency or suitability of Good Manufacturing Principles (GMP) licences/clearances for clinical trials
- compliance with the ICH Guideline for Good Clinical Practice (medicines and biologicals)
- compliance with the ISO 14155:2020 Clinical investigation of medical devices for human subjects — Good clinical practice (medical devices)
- compliance with the National Statement on Ethical Conduct in Human Research 2023

Under the CTN and CTA schemes the use of therapeutic goods in the trial must be in accordance with the applicable GCP guidelines, the National Statement and the protocol approved by the HREC responsible for monitoring the conduct of the trial. It is the sponsor's responsibility to ensure that all relevant GMP licences are obtained and updated (unless the exemption for initial experimental studies applies). The trial sponsor must also comply with the requirements of any other Commonwealth and/or state and territory legislation in relation to clinical trials and the supply of therapeutic goods.

Compliance with the above will not be assessed during the CTA evaluation, but may be assessed by the TGA as part of the Good Clinical Practice (GCP) Inspection Program. Under the GCP Inspection Program, the TGA can investigate

trial sites to assure that the rights, safety and well-being of clinical trial participants are protected and that the trial data generated is credible.

The decision to approve the supply of unapproved therapeutic goods under the CTA scheme

The decision on whether or not to approve the supply of unapproved therapeutic goods under the CTA scheme is made by a senior medical officer of the TGA, who is a delegate of the Secretary of the Department of Health and Aged Care.

The decision maker considers the TGA evaluation reports, the trial's usage guidelines (which include the trial protocol, investigator's brochure, literature references and PI/IFU/pharmacy guidelines where applicable) and plans for shipment and storage at trial sites. Additional supporting documents may be requested, such as statistical analysis plans, patient information/education packages and further safety reports, especially when referred to in the submitted data package.

Variations

If a sponsor wishes to change the therapeutic good(s) or any aspect of the clinical trial that was evaluated in the original CTA submission, a variation requiring additional evaluation by the TGA may be required. These variations are assessed to ensure that the quality and safety of the good(s), or the overall risk-benefit profile of the trial, will not be inadvertently altered by the variation.

Any changes that were not evaluated in the original submission or are predicted to have no effect on the therapeutic good or safety of the trial will not be assessed by the TGA. The TGA advises the sponsor to ensure that these changes are communicated to and approved by the HREC before commencement.

Question 10. Does the scope of the TGA's evaluation of clinical trials under the CTA scheme align with your HREC's expectations? If not, please describe the differences.

Question 11. If your HREC has had experience reviewing (or intends to review) a trial requiring a CTA in the next 12 months, are any aspects of the trial documentation you review duplicative of what the TGA reviews?

The HREC's role in approving and monitoring clinical trials

The National Health and Medical Research Council (NHMRC) registers Human Research Ethics Committees (HRECs). The NHMRC's webpage on HRECs lists approximately 200 HRECs in research organisations across Australia that have been registered or certified with the NHMRC.

The National Statement on Ethical Conduct in Human Research 2023 (National Statement) is a human research ethics guideline developed in fulfillment of the requirements of the *National Health and Medical Research Council Act 1992.*

Human Research Ethics Committees (HRECs) play a central role in the scientific and ethical review and oversight of clinical trials.

- HRECs review research proposals involving human participants to ensure that they are ethically acceptable and have been developed in accordance with relevant standards and guidelines.
- HRECs are responsible for review and approval of the trial protocol under both the CTN and CTA schemes.
- HRECs are responsible for establishing what information should be provided in support of an application for ethics approval and reviewing the application. The HREC should request any additional information that it believes is necessary to undertake review of the proposed research.

The TGA understands that each HREC has its own requirements and processes for assessing and approving clinical trials.

Question 12. To help us better understand HREC approval process, please provide the key steps and timeframes of your HREC's review and approval process.

Question 13. Does the process change if your HREC is reviewing an application that requires a TGA CTA? Do you require TGA CTA approval prior to commencing your review?

Question 14. Does your HREC require sponsors to provide the information required for HREC review and assessment in a specific format? If yes, what is the format?

Collaboration and education

We are dedicated to continuously improving our collaboration with key stakeholders and welcome the opportunity to hear your feedback on how we can work together effectively.

Question 15. Do you engage with the TGA regularly?

a. **If yes, what is your experience of engaging with the TGA?**

b. **If no, are there any obstacles for your HREC to engage with the TGA?**

Question 16. Do you see any opportunities for improved collaboration between the TGA and the HRECs on CTAs? For example, ways to make the process more efficient or improve information sharing.

Education on Good Clinical Practice (GCP) for clinical trials

We want to better understand the areas of educational need within the clinical trials sector to inform the development of educational tools and activities. The TGA's Good Clinical Practice (GCP) Inspection Program focuses on education and building awareness within the clinical trials sector to improve compliance, in addition to inspecting individual clinical trial sites. Your feedback will help us deliver targeted education to increase awareness of GCP obligations that apply to local clinical trials regulated under the CTN and CTA scheme.

Question 17. What GCP education providers or resources does your HREC currently use?

Question 18. What topics related to the TGA's expectations on compliance with the ICH GCP E6 (medicines and biologicals) and ISO14155 (medical devices) would you like to receive more guidance on?

Conclusion and feedback

Your feedback will be used to inform the CTA review and options to improve this pathway.

Please contact us at clinical.trials@tga.gov.au if you have any questions on this consultation.

Attach any supporting documents below.

Question 19. Are you willing to discuss your responses further with the TGA?

a. **Yes**
b. **No**

Attach any supporting documents.

Please make sure your file is under 25MB

Version history

Version	Description of change	Author	Effective date
V1.0	Original HREC Consultation	Risk Management Section	April 2024

Therapeutic Goods Administration

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