



**HUMAN RESEARCH  
ETHICS COMMITTEES AND THE  
THERAPEUTIC GOODS LEGISLATION**

**THE TGA IS A DIVISION OF THE COMMONWEALTH DEPARTMENT  
OF HEALTH AND AGED CARE**

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## **These guidelines**

The aim of this document is to outline to Human Research Ethics Committees (HRECs) the role and responsibilities required of them under the Therapeutic Goods legislation.

It describes the role of HRECs in relation to the supply of unapproved therapeutic goods in connection with the operation of the Clinical Trial Notification Scheme, the Clinical Trial Exemption Scheme, the Special Access Scheme, and in the approval of Authorised Prescribers. Each of these mechanisms for supply of unapproved therapeutic goods is discussed briefly within the document. Members of HRECs wishing to obtain an in-depth understanding of the regulation and supply of unapproved therapeutic goods via these mechanisms should consult the following TGA publications:

- *Access to Unapproved Therapeutic Goods – the Special Access Scheme*
- *Access to Unapproved Therapeutic Goods - Clinical Trials in Australia*
- *Access to Unapproved Therapeutic Goods - Authorised Prescribers*
- *Access to Unapproved Therapeutic Goods – Personal Importation*

The TGA has also developed a publication *Access to Unapproved Therapeutic Goods in Australia* that is a consolidation of all the documents in the series.

## **Abbreviations and Acronyms**

AHEC	Australian Health Ethics Committee
ARTG	Australian Register of Therapeutic Goods
CPMP	Committee for Medicinal Products
CTN	Clinical Trial Notification (Scheme)
CTX	Clinical Trial Exemption (Scheme)
DSEB	Drug Safety and Evaluation Branch, TGA
HREC	Human Research Ethics Committee
NHMRC	National Health and Medical Research Council
ICH	International Conference on Harmonisation on Technical Requirements for Registration of Pharmaceuticals for Human Use.
Good Clinical Practice	ICH Guideline for Good Clinical Practice (document CPMP/ICH/135/95)
the National Statement	National Statement on Ethical Conduct in Research Involving Humans
SAS	Special Access Scheme
the Act	Therapeutic Goods Act 1989
TGA	Therapeutic Goods Administration
the Regulations	Therapeutic Goods Regulations 1989

## **Acknowledgments**

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## 1. INTRODUCTION

The *Therapeutic Goods Act, 1989* establishes a uniform, national system of regulatory controls to ensure the quality, safety, efficacy and timely availability of therapeutic goods for human use. Responsibility for the regulatory controls lies with the Therapeutic Goods Administration (TGA) as the national regulatory authority for therapeutic goods.

The TGA controls the supply of therapeutic goods through three main processes:

- the pre-market evaluation and approval of products intended for supply in Australia;
- the licensing of manufacturers; and
- post market surveillance.

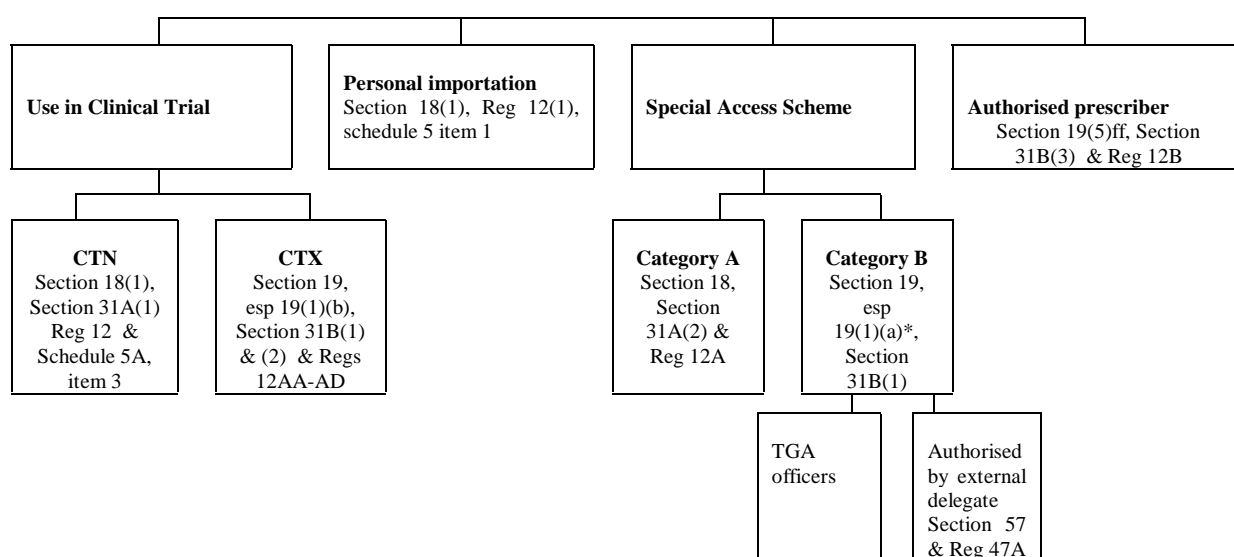
Under the Act, therapeutic goods for human use that are imported, manufactured in Australia, supplied by a corporation, supplied interstate or to the Commonwealth, or exported must be included in the Australian Register of Therapeutic Goods (ARTG) unless specifically exempted.

Items which are exempt from entry on the ARTG are set out in Schedule 5 (Regulation 12(1)), Schedule 5A (Regulation 12(1A)) and Regulation 12A. These exemptions allow individuals to gain limited access to unapproved therapeutic goods through the following mechanisms:

- the Special Access Scheme (categories A and B);
- clinical trials (CTN and CTX schemes);
- authorised prescribers; and
- importation for personal use.

The figure below provides a graphic representation of these mechanisms and the sections of the Act and Regulations relevant to their operation.

*Figure* Access to unapproved therapeutic goods



\* Section 19 (1)(a) allows supply for Category A and Category B patients but, in practice, category A cases are dealt with under section 18 and regulation 12A.

Human Research Ethics Committees play an important role in the regulation of the supply of unapproved goods under the Act in connection with the operation of clinical trials (both the CTN and CTX Schemes), the Special Access Scheme and approval of Authorised Prescribers.

The full text of relevant sections of the legislation can be found in **Appendix 1**.

The full legislation can be found at the following website:

<http://www.health.gov.au/tga/docs/html/legis.htm>

*It is important to appreciate that unapproved therapeutic goods have undergone little or no evaluation of quality, safety or efficacy by the Therapeutic Goods Administration. Accordingly, use of all such goods carries with it some risks that have not been defined in the Australian context. As such, use of these products is considered to be experimental and should be guided by the principles and practices as outlined in the National Statement on Ethical Conduct in Research Involving Humans. It is in relation to this issue, that HRECs are relied upon because of their developed expertise in assessing risks and precautions in research involving humans.*

## 2. CLINICAL TRIALS

Clinical trials of unapproved therapeutic goods can be conducted in Australia under either the Clinical Trial Notification (CTN) Scheme or the Clinical Trial Exemption (CTX) Scheme. These two schemes, described below, have quite separate legislative bases.

Notification under the CTN scheme or application under the CTX scheme is required for:

- any medicine or device not entered on the ARTG, including any new formulation of an existing product or any new route of administration; or
- the use of a registered medicine or device beyond the conditions of its marketing approval, including new indications extending the use of the product to a new population group and the extension of doses or duration of treatments outside the approved range.

The choice of which scheme (CTN or CTX) to follow lies firstly with the sponsor and then with the HREC. Studies in which medicines and medical devices that are already included on the ARTG and are used within their approved indications and doses do not need to be subject to CTN or CTX requirements. However where they constitute research they will still need to be approved by an HREC.

### **Clinical Trial Notification (CTN) Scheme**

#### Legal Basis

The legal basis for the CTN scheme is found in the general powers of Section 18, then Regulation 12 then Schedule 5A Item 3 (including Regulation 12AD).

Section 18 permits the regulations to exempt goods from the Act. Regulation 12 states that goods specified in Schedule 5A are exempt provided that conditions set out in that schedule are met. Schedule 5A item 3 exempts goods used in experimentation in humans provided that certain conditions are met. These conditions are:

- the sponsor notifies the TGA using the approved CTN form and paying the appropriate fee
- the trial must be approved by the sponsor of the goods and the sponsor of the trial (if not the sponsor of the goods) having regard for the advice of the HREC which reviewed the protocol and is assuming responsibility for the monitoring of the trial.
- the terms of approval of the sponsor or the body or organisation conducting the trial for the sponsor must be no less restrictive than terms advised by the HREC.
- the TGA must not:
  - have become aware that to start or continue the trial is not in the public interest
  - have directed that the trial not start or be stopped.
- The sponsor has not received advice from the HREC that is inconsistent with continuation of the trial.
- The conditions set out in regulation 12AD must be complied with.
  - Regulation 12AD sets out that use of therapeutic goods must be in accordance with Good Clinical Practice, the protocol approved by the HREC and the National Statement.
  - Regulation 12AD also requires that the trial must cease if the ethics committee inform the principal investigator that the use is inconsistent with the protocol

they have approved or any other condition to which approval for use was given.

### Procedure for CTN

Under the CTN scheme, all material relating to the proposed trial, including the trial protocol is submitted directly to the HREC by the researcher at the request of the sponsor. The TGA does not review any data relating to the clinical trial and the HREC is responsible to ensure that there is an assessment of the scientific validity of the trial design and the safety and efficacy of the medicine or device as well as the ethical acceptability of the trial process.

The TGA 'Notification of Intent to Conduct a Clinical Trial' form (the CTN Form) is submitted by the investigator on behalf of the sponsor to the HREC and to the Approving Authority. Once the sponsor, the principal investigator, the Chairman of the HREC and the person responsible from the institution or site where the trial will be conducted (called the Approving Authority) have signed the CTN Form, it is submitted by the sponsor of the trial to the TGA along with the appropriate notification fee.

The Therapeutic Goods Regulations require that the notification be in a form approved by the Secretary of the Department of Health and Aged Care. Sponsors must use the current CTN form (located at **Appendix 2**). Use of old (out-of-date) CTN forms will invalidate the notification.

### **Clinical Trial Exemption (CTX) Scheme**

#### Legal Basis

The legal basis for the CTX is found in sections 19(1)(b) and the following subsections 19(1A), 19(2)(b), 19(3), (4) and (4A), then regulations 12AA to 12AD.

Under subsection 19(1)(b) of the Act, the TGA may give approval for the import, export, or supply in Australia of goods used solely for experimental purposes in humans and which are not included in the ARTG. This provision enables access by sponsors, including medical practitioners to use otherwise unapproved drugs in clinical trials conducted under the CTX Scheme.

Subsection 19(1A) allows TGA to set conditions on the approval of a CTX application. These conditions are set out in the regulations (see below).

Subsection 19(2)(b) requires that the CTX application must be in writing, contain the information required by the TGA and the application must be accompanied by the appropriate fee. Subsection 19(3) allows for fees to be charged.

Subsection 19(4) provides that the CTX application must be evaluated and notice given of the approval within 28 days of the decision being made and if refused reasons for the decision must be given.

Subsection 19(4A) provides for conditions to be specified in the regulations which may relate to the preconditions on the use of the goods, principles to be followed in the use of the goods,

the monitoring of the use and results of the use of the goods and the circumstances in which use of the goods must cease.

Regulations 12AA to 12AD set out the conditions which may be applied to be CTX trial.

Regulation 12AA provides that the TGA may require the following information to be provided:

- the names of members of the HREC that approved the proposed clinical trial and is assuming responsibility for monitoring the conduct of the trial
- the name of, and contact details for, the principal investigator for each trial.
- the name of the person which will be in charge of the trial site or each site if more than one.
- information about whether or not any conditions specified by the HREC have been met.

Regulation 12AB requires the sponsor and the principal investigator to provide written assurances to the TGA before the trial commences:

- that that trial will be conducted according to GCP
- that any requests for information about the conduct of the trial will be complied with.
- that they will allow a TGA auditor (authorised person) to do the things mentioned in regulation 12AC.

Regulation 12AC outlines the powers of a TGA auditor in relation to a trial site.

Regulation 12AD sets out that use of therapeutic goods approved under CTX must be in accordance with Good Clinical Practice, the protocol approved by the HREC and the National Statement. It also requires that the trial must cease if the ethics committee inform the principal investigator that the use is inconsistent with the protocol they have approved or any other condition to which approval for use was given.

### Procedure for CTX

A sponsor cannot commence a CTX trial until:

- written advice has been received from the TGA regarding the CTX application; and
- approval for the conduct of the trial has been obtained from an ethics committee and the institution at which the trial will be conducted.

An application for a CTX trial must be in the form required by TGA.

The CTX application comprises summary information about the product, including the overseas status of the drug, proposed guidelines for the use of the product in the trial (called the Proposed Usage Guidelines), a pharmaceutical data sheet, and a summary of the preclinical data and a clinical summary.

It is important to note that the TGA does not receive, evaluate or comment directly on the trial protocol. The primary responsibility of the TGA is to review the safety of the product. The TGA decides whether or not to object to the proposed usage guidelines for the product. If an objection is raised with the sponsor, the trial cannot proceed until the objection has been



overcome. If the TGA has no objection, the researcher submits the data package to the relevant HREC.

Even if no objection is raised, the TGA usually provides comments on the accuracy or interpretation of the summary information supplied by the sponsor.

The HREC in each host institution/organisation is responsible for approving the proposed trial protocol after reviewing the summary information received from the sponsor and the investigator and any additional comments from the TGA. The HREC is also able to request any additional information they believe is necessary to undertake review of the proposed research.

There are therefore two CTX forms (Parts) that must be submitted by the sponsor to the TGA:

- Part 1 constitutes the formal CTX application. This form is completed by the sponsor of the trial and submitted directly to TGA with data for evaluation.
- Part 2 is used to notify the commencement of each new trial conducted under the CTX as well as new sites in ongoing CTX trials.

This form is submitted by the investigator on behalf of the sponsor to the HREC and to the Approving Authority. Once the HREC and the Approving Authority approvals have been received by the principal investigator, the trial can commence on the condition that the sponsor of the trial submits the Part 2 form to the TGA within 28 days of commencing to supply the goods.

The sponsor may conduct additional clinical trials without further assessment by the TGA, provided such use falls within the original approved Proposed Usage Guidelines. However, HREC approval of each protocol and approval from the institution/organisation for the conduct of each trial are still required. A notification (using the Part 2 form) for each subsequent trial must be made to TGA.

The Therapeutic Goods Regulations require that the notification be in a form approved by the Secretary of the Department of Health and Aged Care. Sponsors must use the current CTX Part 2 form (located at **Appendix 3**); otherwise the notification will be invalid.

### **HREC Responsibilities in relation to the Regulation of Clinical Trials**

This section should be read in conjunction with the *National Statement on Ethical Conduct in Research Involving Humans, 1999* (the National Statement).

The difference between CTN and CTX is the level of involvement of the TGA in reviewing data about the therapeutic good involved in the trial before the trial begins.

In CTN trials the TGA does not review any data before the trial begins. The responsibility for this review lies with the HREC and the principal investigator. The HREC and the institution are responsible for establishing what information should be provided in support of an application and how that application will be handled by the committee.

In CTX trials the TGA reviews summary data about the therapeutic good (medicine or medical device). TGA then provides comment to the HREC about the product. The TGA

also stipulates the minimum data which must be provided to the HREC. This data includes summary information about the product, the overseas regulatory status of the product and the Proposed Usage Guidelines for the product. The HREC and the institution may require additional information to be provided in support of an application.

HRECs are responsible for reviewing clinical trial protocols for both CTX and CTN. The responsibility for the conduct of the trial rests with the principal investigator and the sponsor. The HREC provides advice to the sponsor and the institution on the trial before it begins and during the course of the trial.

Approval for the trial to be conducted at the site rests with the institution or body where the trial is to be conducted (called the Approving Authority).

Clinical trials, both CTN and CTX must be conducted according to the protocol which the HREC has approved, Good Clinical Practice (GCP) and the National Statement. Should the HREC become aware that the trial is not being conducted according to these standards, the HREC should inform the principal investigator that the use is inconsistent with the approved protocol or any other condition to which approval for use was given (National Statement paragraph 2.44).

The HREC should also advise the Sponsor, the Approving Authority and the TGA of their concerns. This may lead to investigation and withdrawal of the approval of the trial by the sponsor, the Approving Authority or the TGA.

Having approved a trial protocol, under both CTN and CTX, the HREC is assuming responsible for monitoring the conduct of the trial. In signing the CTN and the CTX form they are agreeing to this responsibility.

HRECs also need to be aware of relevant State and Territory laws pertaining to the supply of therapeutic goods or to issues relating to medical practice which may be relevant to a clinical trial proposal.

The National Statement outlines requirements and obligations of HRECs when they consider and reach decisions regarding clinical trials. While the whole document is relevant the following sections are particularly important for clinical trials with therapeutic goods:

- general guidance in Section 2;
- guidance specifically in relation to clinical trials and trial protocols in Section 12;
- obligations relevant to monitoring of clinical trials for both HRECs and their institutions in guidelines 2.33 - 2.38 and 12.9;
- obligations of the HREC in relation to suspension or discontinuation of research in guidelines 2.44.

## **TGA recommendations to HRECs reviewing a trial proposal**

Each proposed protocol and related informed consent form should be reviewed in conjunction with data provided by the sponsor to support the proposal. If the HREC does not understand any part of the proposal or wishes to see more information it should, consistent with guideline 2.8 of the National Statement, ask for the necessary information and defer the proposal until it is satisfied that the interests of trial participants have been safeguarded.

When assessing the appropriateness of the protocol for clinical trials involving the use of unregistered medicines, the HREC should consider the mechanisms proposed, if any, for continued access to treatment with the unregistered medicinal products by patients for whom treatment has been found to be effective and where long term therapy would be appropriate following completion of the trial. The HREC should consider the advisability of having a post study supply component in the research protocol.

The process of the CTX scheme is intended to provide sufficient guidance for HRECs to proceed without needing to seek further information. However, at no time should an HREC be constrained from asking for further information or seeking advice, especially in order to secure participant safety and welfare.

In relation to proposals to conduct a trial under the CTN Scheme, the HREC will need to determine whether the clinical trial would be best considered under the CTN or CTX scheme, or does not meet the requirements of either scheme. In some institutions, a proposal for a clinical trial may be reviewed by a research or drug subcommittee before the HREC. An HREC may wish to consult additional expertise from sources outside its institution. The HREC may determine that it does not wish to review the proposed trial under the CTN scheme and recommend its review under the CTX scheme.

It is not possible for the TGA to give directions on when a CTN or CTX should be used. The decision will be influenced by many factors including the size of the institution, the experience of the investigator, the experience and expertise of the HREC and related committees and the nature of the therapeutic good involved. Should the HREC be unsure of the decision advice from another more experienced HREC or the TGA could be sought.

If the HREC is of the opinion that it is appropriate for the trial to proceed and approves the protocol, the proposal is usually considered by the institution/organisation that makes the final decision on whether the trial may proceed. If approval to conduct the trial is given, the sponsor submits the relevant clinical trial notification form to the TGA. The chairperson of the HREC should sign the form.

No HREC should give ethical endorsement to any trial about which it has reservations. Any reservations the HREC may have should be resolved with the investigator or sponsor before the form is signed or conditions should be specified to ensure ongoing compliance should this be required.

In signing a notification form and approving a clinical trial protocol, the HREC accepts responsibility for monitoring the progress and conduct of the trial. This is a significant ongoing role for the HREC and one that the Therapeutic Goods Regulations impose solely on the HREC. The TGA is not required to undertake routine monitoring of clinical trials.

## TGA recommendations for monitoring clinical trials

The National Statement sets out obligations relevant to monitoring for both HRECs and their institutions (guidelines 2.33 - 2.38 and 12.9). The HREC and its institution may adopt such review mechanisms as are appropriate, including the appointment of a monitor, independent of both the researcher and the sponsor. The TGA recommends that HRECs have clearly defined mechanisms that require researchers to advise them of:

- any serious unexpected adverse events that occur during the trial, including those that have occurred at other sites involved in the study [see below].
- new information from other published or unpublished studies which may have an impact on the continued ethical acceptability of the trial, or which may indicate the need for amendments to the trial protocol; and
- deviations from, or changes to, the protocol that either eliminate immediate hazards to trial participants, significantly affect the conduct of the trial, or increase risks to participants.

It is also recommended by TGA that any such information be accompanied by comment from the researchers on what implications, if any, they believe the new information has for the trial.

Serious adverse events are those noxious and unintended responses to the drug that:

- result in death;
- require in-patient hospitalisation or prolongation of existing hospitalisation;
- result in persistent or significant disability/incapacity;
- result in birth defects;
- are life threatening.

An event should be considered **unexpected** if the nature, severity or frequency of that event is not documented in the current Australian Product Information if the product is approved for marketing, or in the most current Investigator's Brochure if the product is unapproved.

It should be noted that the TGA does not receive overseas reports of individual adverse reactions. The TGA requires sponsors to report all individual reports of adverse reactions, which occur in Australia. Good Clinical Practice requires sponsors of trials to inform investigators at all participating sites of individual reports at all sites world wide. HRECs should develop procedures to ensure they are able to handle such reports appropriately.

The TGA does require that sponsors report any significant safety concerns or actions taken as a result of the analysis of adverse reaction reports within Australia and overseas, including action by overseas regulatory agencies. The TGA will ensure that any such advice has been reported to the Australian investigators and the HREC.

The HREC, as well as the researcher, must consider a serious adverse or unexpected event in the context of information on the drug as well as the underlying disease. For example, a fatal or serious outcome may be identical to, or resemble, the primary efficacy endpoint of the study. Such an event would be considered disease-related. Some assessment of whether the event is drug-related should be undertaken and appropriate measures taken to protect patient safety. Reports of serious and/or unexpected events occurring at other institutions

participating in the study are also of value to the HREC. Such reports may signal events not yet seen at their institution, for example, by virtue of the fact that enrolment numbers are lower than elsewhere. Review of the details of these events along with an assessment of causality and the actions taken in other institutions will help guide the HREC in taking appropriate steps to protect patient well being.

Guidelines 2.44, 2.45 and 12.10 of the National Statement outline the circumstances when research should be discontinued. TGA recommends that if an HREC has concerns about the conduct of a clinical trial they should seek advice firstly from the investigator and sponsor. If the researcher has not allayed their concerns despite adequate time to do so, then they should consider withdrawing ethical approval. The HREC should advise the researcher, the relevant institution/s and the TGA of any decision to withdraw approval.

An HREC may discuss any concerns they have with any aspect of a clinical trial with the TGA. TGA has the authority to conduct an audit of a clinical trial where necessary on safety grounds and to investigate non-compliance with the trial protocol or accepted standards for the conduct of a trial.

### **TGA Administrative Requirements - implications for HRECs**

In relation to clinical trials conducted under the CTN and CTX Schemes, sponsors are required to notify the trials to TGA by sending a completed clinical trial notification form (CTN form (**Appendix 2**) or CTX Part 2 form (**Appendix 3**)) to the TGA. The forms include separate sections for details of the HREC. They require the chairperson of the HREC to certify that the HREC has approved the clinical trial protocol and has assumed responsibility for monitoring the conduct of the trial, having regard to the advice provided by the National Statement. Also, the HREC is required to certify it has notified its existence to AHEC. An ethics committee which has not notified its existence to AHEC is not recognised as an ethics committee under the Act. In such a case, the conditions under which an exemption from Part 3 of the Act is created to allow lawful supply of the unapproved good will not have been met, the therapeutic goods cannot be supplied and, therefore, the trial cannot commence.

The TGA also recommends that the HREC inform the TGA if it withdraws its approval of a clinical trial, including reasons for the withdrawal.

### 3. THE SPECIAL ACCESS SCHEME

#### Legislation

The Special Access Scheme (SAS) refers to arrangements which provide for the import and/or supply of an unapproved therapeutic good on a single patient, case by case basis under Sections 18 and 19(1)(a) of the Act. These arrangements are:

- supply to a patient and notification to the TGA (as delegate of the Secretary) by a medical practitioner that the patient is in category A, under section 18 of the Act.

Category A patients are defined in regulation 12A(5) as persons who are 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.

A medical practitioner who forms the view that his/her patient meets that definition can, having obtained the informed consent of the patient or the patient's legal representative and completed the relevant notification form, import and/or supply the unapproved therapeutic good to that patient without approval from the TGA.

- approval from the TGA to supply an unapproved therapeutic good to a single patient is given under section 19(1)(a) of the Act.
- approval from an 'external delegate' (external to TGA) to supply an unapproved therapeutic good to a single patient is given under section 19(1)(a) of the Act.

A person, who is not employed by the TGA or the Commonwealth Department of Health and Aged Care, may be given a delegation under Section 57(3) of the Act to approve the supply of unapproved therapeutic goods by another practitioner. These external delegates are provided with a set of treatment protocols for those therapeutic goods that can be approved. Medical practitioners within an institution may make an application to the external delegate at that institution for approval to supply unapproved therapeutic goods.

When issuing an authority to supply an unapproved therapeutic good, the TGA will specify to whom authority is given and for which particular drugs and their indication.

#### **HREC Responsibilities in relation to Supply of Unapproved Therapeutic Goods under Section 19(1)(a) of the Act (Special Access Scheme/External Delegates)**

HREC responsibilities in relation to the Special Access Scheme are primarily concerned with the granting of approvals under section 19(1)(a) of the Act by 'external delegates'. In accordance with Regulation 47A(6)(b), all applications approved by an external delegate must be approved by an HREC. In practice, external delegations are rare and thus, HRECs will not be asked to deliberate on such issues as a matter of routine.

## **TGA recommendations to the HREC**

Before agreeing to an approval by an external delegate, the HREC should be provided with the following information:

- the product for which approval is sought;
- whether that unapproved product is included on the list of products which can be approved by the external delegate;
- details about the product to be prescribed, including an assessment of the efficacy and safety of the product;
- the medical condition (also known as the 'indication') for which approval is being sought;
- an assessment of the seriousness of the condition being treated;
- the intended mode of use/treatment regimen and whether this conforms to the treatment protocol; and
- the clinical justification for use of the unapproved product, including the nature and availability of alternative treatments.

The HREC could also consider their knowledge of the practitioner requesting the supply from previous research activities of the practitioner that have been considered or monitored by the HREC.

In deciding whether to agree to approval by the external delegate, the HREC should be aware that the external delegate should be guided by the same considerations as would apply within TGA for granting of approvals under Section 19(1)(a) of the Act. These considerations are outlined in detail in **Section 5** (pages 19 20) of this document.

Although not specifically required under the Act, an HREC may also be asked to comment on the appropriateness of an informed consent form used in conjunction with the use of an unapproved good. One of the conditions TGA imposes on approvals to supply an unapproved therapeutic good is that the patient gives their informed consent. The issue of informed consent in relation to the supply of unapproved products is discussed in **Section 6** (page 23) of this document as well as in the National Statement.

## 4. AUTHORISED PRESCRIBERS

### Legislation

Under subsections 19(5-9) of the Act and Regulation 12B, the TGA is able to grant a medical practitioner authority to prescribe a specified unapproved therapeutic good or class of unapproved therapeutic goods to specified recipients or classes of recipients (identified by their medical condition). An Authorised Prescriber can then prescribe that product for that condition (also known as the 'indication') and no approval from the TGA is required for each individual patient. The legislation requires:

- An Authorised Prescriber to be a medical practitioner;
- A medical practitioner to obtain endorsement from an appropriate HREC; or
- Where a medical practitioner does not have access to an HREC and this can be demonstrated to TGA, the medical practitioner may obtain endorsement from a specialist college having an established expertise relevant to the use of the medicines concerned.

Under regulation 12B(4) medical devices may only be approved for medical practitioners practising in hospitals. Approval must be obtained from the HREC at the institution at which the practitioner practices. Approval will not be given to medical practitioners to use medical devices outside the hospital setting.

Thus, endorsement of the prescriber by the HREC is critical to the Section 19(5) approval process by TGA.

### **TGA recommendations to HRECs endorsing medical practitioners for the purposes of authorisation under Section 19(5) of the Act**

The following information is presented as a guide for an HREC when considering a request from a medical practitioner for endorsement as an Authorised Prescriber. The HREC needs to assess not only the safety of the product in relation to its proposed use, but also the suitability of the medical practitioner. The HREC should consider:

- the indication for which the product will be prescribed;
- whether the practitioner is seeking to treat a condition in his/her area of specialty or training and expertise. In general, endorsement should be given only when the practitioner has training and expertise appropriate for the proposed use of the product. The consideration could include knowledge that the HREC may have from the practitioner's research activities that have been considered by the HREC and such other information as the HREC requests the practitioner to provide;
- details about the product to be prescribed, including an assessment of the efficacy and safety of the product. This should take into account the regulatory status of the product in overseas countries with regulatory standards comparable to those in Australia (ie, USA, UK, The Netherlands, Canada and Sweden), or if not approved in any of these countries, whether the product has been the subject of clinical trials either in Australia or these overseas countries. In addition, it is important to consider whether the product has been officially withdrawn from the Australian market or refused registration because of safety concerns;
- for medicines, the route of administration and dosage form;



- the clinical justification for the use of the product. This should include an appraisal of the nature of alternative treatments (ie marketed products) available for the indication and the circumstances under which the unregistered product could be used in preference to marketed products; and
- information to be given to the patient about the product; and
- the informed consent form.

Guidance on how HRECs should use this information, particularly in relation to how to balance the seriousness of the condition being treated against the level of evidence provided in support of the efficacy and safety of the product, is provided in **Section 5** (pages 19-20). The HREC may also wish to seek advice from a Scientific or Research Subcommittee or a Drug and Therapeutics Subcommittee, if available, when considering the above issues.

The HREC should also ascertain that the unregistered product is not intended for use in a clinical trial. Approval as an Authorised Prescriber is not appropriate in this circumstance. Clinical trials being conducted in Australia require notification under the CTN scheme or approval under the CTX scheme.

The HREC may consider it appropriate to impose conditions on the endorsement. The nature of any conditions imposed will be a matter for the HREC to decide. Examples of possible conditions are:

- a requirement for the Authorised Prescriber to provide regular reports to the HREC outlining the number of patients for whom the unregistered product has been prescribed; and
- requirements for reporting any suspected adverse reactions.

### **What happens when a section 19(5) authorisation is revoked by the TGA?**

The HREC may also receive requests for endorsement from medical practitioners who have had their Authorisation revoked by the TGA as a result of a registered product having become available for the specified indication. When a product either containing the same active ingredient or in the same therapeutic class as the unregistered product is evaluated and registered for treatment of the specified indication, the TGA will revoke existing 19(5) authorisations for unregistered products.

If the Authorised Prescriber wishes to continue to use the unapproved product, he/she is required to submit a new application to TGA for Authorisation under section 19(5). The applicant is required by TGA to provide, as part of the application:

- sufficient clinical justification as to why the registered product is not suitable for use in the patient group; and
- a new letter of endorsement from an HREC for continued use of the unapproved product. The HREC's letter of endorsement should state that endorsement has been given with the full knowledge that an evaluated and approved treatment has become available.

This course of action is imposed in part because it is the TGA's responsibility to encourage at all times the availability of approved (fully evaluated) products. To do otherwise would remove the incentive for a sponsor to seek registration of the unapproved product or for other sponsors to seek registration of alternative products for treatment of the indication.

## **Review of an endorsement**

The TGA recommends that an HREC review its endorsement of the Authorised Prescriber if it becomes aware of:

- inappropriate use of the product by the Authorised Prescriber;
- a concern about the safety of the product;
- failure of the Authorised Prescriber to comply with conditions imposed by the HREC; or
- failure of the Authorised Prescriber to comply with State/Territory legislation.

An HREC may become aware of such circumstances as a result of complaints from patients, or from medical or nursing staff at the institution concerned. If, as a result of its reconsideration, the HREC is satisfied that the welfare and /or rights of patients are not or will not be protected, the TGA recommends the HREC advise its institution and the TGA of its concerns.

The TGA has the authority to inquire about the use of unregistered therapeutic goods and, where necessary, release information about inappropriate use of therapeutic goods to relevant State and Territory authorities.

The HREC should advise the TGA whenever it withdraws an endorsement. Withdrawal of endorsement by the HREC will result in the TGA revoking the Authorisation. The TGA recommends that when an HREC withdraws its endorsement, the HREC should be satisfied that there are appropriate arrangements in place for alternative treatment of patients.

## **TGA Administrative requirements - implications for HRECs**

The TGA requires, as part of a medical practitioner's application to become an Authorised Prescriber, a letter of endorsement from the HREC. It is recommended that the letter include:

- a clear statement that endorsement is being given for the purpose of the medical practitioner becoming an authorised prescriber under Section 19(5) of the Act;
- the name of the medical practitioner being endorsed;
- the drug and indication for which endorsement has been given;
- the site(s) at which use is covered by the endorsement;
- any conditions the HREC has imposed on the endorsement; and
- the signature of the chairman of the HREC over his/her official title.

An example of a letter of endorsement is given at **Appendix 4**.

## 5. THE CRITERIA USED BY DELEGATES IN DECIDING WHETHER TO APPROVE SUPPLY OF UNAPPROVED THERAPEUTIC GOODS

(The following is provided for the information of HRECs.)

Applications for approval to supply unapproved products need to address criteria relating to the patient, the product and the prescriber. Applicants can also provide any other information they consider important. In considering whether to grant approval, the delegate will generally consider the quality and extent of the information provided and balance the position in relation to each of the criteria. Applications should address each criterion set out below and supply the information requested. In reaching a decision, the delegate will have regard to each of the criteria and approval is unlikely to be granted if each of the criteria have not been met.

Approval is given on a patient by patient basis to reflect the needs of different patients. The major criteria for determining whether approval should be given relate to the patient, the product and the prescriber.

### *Criterion 1 - The patient*

The application should contain adequate clinical justification for the use of the product, including an appraisal of the seriousness of the patient's condition being treated. When making an application, the practitioner will need to supply the following information:

<i>Patient details</i>	Initials Date of birth (or age) Sex Patient ID or unit record number Diagnosis If applying for an extension of use under SAS - previous approval number, if available
------------------------	--

<i>Clinical justification</i>	This should include an appraisal of the seriousness of the patient's condition and details of past treatment. If other registered treatments are available, the applicant will need to justify the use of the unregistered product in preference to those treatments. This should include an appraisal of the expected benefits from the use of the unapproved product.
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### *Criterion 2 - The product*

The application should indicate how the product is to be used and include an appraisal of the efficacy and safety of the proposed use of the product. The application should include:

<i>Product details</i>	For <b>unapproved medicines</b>  Active ingredient Trade name Company/supplier (sponsor) Dose form
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## For **unapproved medical devices**

Name of device  
Company/sponsor

### *Administration and monitoring regime*

Dosage  
Route of administration  
Duration of treatment  
Details of the techniques to determine both the efficacy of the treatment and the occurrence and severity of any adverse reaction. This could be provided in terms of clinical, biochemical, haematological and/or immunological monitoring. Monitoring should occur throughout treatment and in some cases it may be appropriate for monitoring to continue for a period thereafter. In the event that a practitioner requests an extension of use under SAS, outcomes of monitoring, including measures of patient response and safety parameters, are required.

### *Efficacy/safety data*

Efficacy and safety data sufficient to support the proposed use of the product. A copy of any reference articles from which the data have been obtained should be included. Such references can range from evidence from published randomised controlled trials through evidence from published non-randomised trials and case reports, to consensus opinion. The level of evidence required will depend on the seriousness of the condition (see how to balance the criteria).

### ***Criterion 3 - The prescriber***

The application should be received from a doctor with qualifications and/or expertise appropriate to the condition being treated and the proposed use of the product. The application should contain:

#### *Prescriber details*

Name  
Postal address  
Qualifications  
Hospital and hospital department, if applicable  
Phone number  
Fax number, if available

### **How to balance the criteria**

The following is a guide only. It does not cover all possibilities but may give the delegate and others a general guide as to how the complex issues impacting a decision may be balanced.

There is a hierarchy of evidence of efficacy and safety of the product, a hierarchy of evidence that affects the patient's condition and a hierarchy of qualifications relating to the requesting doctor. There is thus a complex interaction of these hierarchies which will affect the decision to be made.

The product hierarchy effectively differentiates between:

- products which are not approved in Australia but approved in countries with a regulatory standard comparable to that in Australia (ie, USA, UK, Sweden, Canada, The Netherlands);
- products which are not approved in Australia but approved in countries other than those with regulatory standards comparable to that in Australia;
- products which are currently under evaluation within TGA;
- products that are not approved anywhere and are still undergoing clinical trials.

These products can be further classified according to the types of evidence available. This can range from

- ◆ evidence from published randomised controlled trials [highest level of evidence]
- ◆ evidence from published non-randomised trials
- ◆ individual case reports,
- ◆ consensus opinion of specialist colleges and societies [lowest level of evidence].

The efficacy and safety data submitted in support of the application should be weighed against the seriousness of the condition. As a general rule, the less serious the clinical need, the higher the degree of evidence needed to support the use of the product. For example, a product that has been approved in a country with a regulatory system comparable to our own (USA, UK, Sweden, The Netherlands and Canada) is likely to be approved for supply under the SAS for any condition for which it has been approved in those countries. On the other hand, if the only evidence available is that from published case reports, it is unlikely that use of the product would be approved for anything but the most serious (almost life-threatening) of conditions. In this case, the prescriber will also have to demonstrate that other conventional therapies are unsuitable or unlikely to control the condition (clinical justification).

With respect to the clinical justification for the use of the unapproved product, the extent to which the application should address the use of available approved therapies will depend on the seriousness of the patient's condition and the amount of information that is known about the product. As a general rule, the less serious the clinical need, the greater the requirement to demonstrate those available therapies are clinically unacceptable.

In circumstances where the product has been previously withdrawn from, or refused entry to, the Australian market because of safety concerns, it will be expected that all conventional therapy has been tried and failed, or has been accompanied by unacceptable adverse reactions. The clinical justification should address the risk/benefit balance of using the proposed therapy.

The delegate may be aware of information of which the applicant is not based on general knowledge or previous applications eg overseas status of a product. The delegate is responsible for undertaking a limited search for information but the process time of an application will be improved if the applicant supplies all relevant information about the patient and the product to be used in the initial application.

In the event that another product is evaluated by TGA and approved for treatment of an indication, the level of evidence required in support of an application to use an unapproved product instead of the new product for that indication is high. This is particularly so for

products with the same active ingredient or with active ingredients in the same therapeutic class.

Medical devices that are only a variation of a previous model or duplicate of the intended performance of an already approved medical device would require a very high level of evidence for approval of an application.

The clinical justification should include discussion as to why the newly approved product is not acceptable for the treatment of the individual patient and this should be based on medical reasons and not on grounds of cost or convenience. This requirement is imposed in part because it is the TGA's responsibility to encourage at all times the availability of approved (fully evaluated) products. To do otherwise would remove the incentive for a sponsor to seek registration of the unapproved product or for other sponsors to seek registration of alternative products for treatment of the indication. If a medical practitioner has an interest in the continued, long-term supply of a particular product, he/she should strongly encourage the sponsor to seek registration of that product in Australia.

## **6. INFORMED CONSENT IN RELATION TO THE USE OF UNAPPROVED PRODUCTS**

Unapproved therapeutic goods have undergone little or no evaluation of quality, safety or efficacy by the Therapeutic Goods Administration. Accordingly, use of all such goods carries with it some risks that have not been defined in the Australian context. As such, use of these products is considered to be experimental and should be guided by the principles and practices outlined in the National Statement. The National Statement contains detailed guidance in relation to informed consent.

Specifically in relation to the supply of unapproved therapeutic goods, TGA recommends that HRECs consider whether the consent forms and/or patient information conveys the following information adequately:

- the product is not approved (ie registered or listed) in Australia;
- any risks and side effects that are known;
- the possibility of unknown risks and late side effects; and
- any alternative treatments using approved products which are available.

If the HREC is considering an application to supply unapproved products derived from any biological tissue including human blood or plasma, it needs to be aware that the TGA can give no guarantee as to the quality, safety or efficacy of these products, particularly as regards any prion or viral inactivation.

In this instance it is suggested that the HREC require the practitioner to use a consent form with wording identical, or as close as possible, to that used in the form titled 'Consent to Treatment and Indemnity for Use of Products Derived from Human Blood or Plasma' which is located at **Appendix 5**.

**APPENDIX 1. EXCERPTS FROM THE LEGISLATION**



## *The Therapeutic Goods Act*

### **18 Exempt Goods**

- (1) The regulations may, subject to such conditions (if any) as are specified in the regulations, exempt:
  - (a) all therapeutic goods, except those included in a class of goods prescribed for the purposes of this paragraph; or
  - (b) specified therapeutic goods; or
  - (c) a specified class of therapeutic goods;from the operation of this Part (except section 31A and sections 31C to 31F).
- (2) An exemption in terms of paragraph (1)(a) has effect only in relation to such classes of persons as are prescribed for the purposes of this subsection.
- (3) Where the regulations revoke an exemption, the revocation takes effect on the day, not being earlier than 28 days after the day on which the regulations are made, specified in the regulations.

### **19 Exemptions for Special and Experimental Uses**

- (1) The Secretary may, by notice in writing, grant an approval to a person for the importation into, or the exportation from Australia or the supply in Australia of specified therapeutic goods that are not registered goods, listed goods or exempt goods:
  - (a) for use in the treatment of another person: or
  - (b) for use solely for experimental purposes in humans;and such an approval may be given subject to conditions as are specified in the notice of approval.
- (1A) An approval for the purpose mentioned in paragraph (1)(b) is subject to conditions (if any) specified in the regulations. Those conditions (if any) are in addition to any conditions imposed on the approval under subsection (1).
- (2) An application for an approval must be made to the Secretary and must:
  - (a) in the case of an application for use of the kind referred to in paragraph (1)(a) - be accompanied by such information relating to the goods the subject of the application as is required by the Secretary; and
  - (b) in the case of an application for use of the kind referred to in paragraph (1)(b):
    - (i) be made in writing; and
    - (ii) be accompanied by such information relating to the goods the subject of the application as is required by the Secretary; and
    - (iii) be accompanied by the prescribed evaluation fee.
- (3) Without limiting the conditions to which an approval under subsection (1) may be made subject, those conditions may include a condition relating to the charges that may be made for the therapeutic goods to which the approval relates.

- (4) Where an application for an approval is made, the Secretary must, after having considered the application and, in the case of an application for the use of therapeutic goods for experimental purposes in humans, after having evaluated the information submitted with the application, notify the applicant of the decision on the application within 28 days of making the decision and, in the case of a decision not to grant the approval, of the reasons for the decision.
- (4A) The use by a person for experimental purposes in humans of specified therapeutic goods that are the subject of an approval granted to someone else under paragraph (1)(b) is subject to the conditions (if any) specified in the regulations relating to one or more of the following:
- (a) the preconditions on the use of the good for those purposes;
  - (b) the principles to be followed in the use of the goods for those purposes;
  - (c) the monitoring of the use, and the results of the use, of the goods for those purposes;
  - (d) the monitoring of the use, and the results of the use, of the goods for those purposes;
  - (e) the circumstances in which the person must cease the use of the goods for those purposes.
- (5) The Secretary may, in writing, authorise a specified medical practitioner to supply:
- (a) specified therapeutic goods for use in the treatment of humans; or
  - (b) a specified class of such goods to the class or classes of recipients specified in the authority.
- (5A) An authority may be given subject to conditions (if any) specified in the authority.
- (5B) The Secretary may impose conditions (or further conditions) on an authority given to a person under subsection (5) by giving the person written notice of the conditions (or further conditions).
- (6) An authority under subsection (5) may only be given:
- (a) to a medical practitioner included in a class of medical practitioners prescribed by the regulations for the purposes of this paragraph; and
  - (aa) to a medical practitioner who has the approval of an ethics committee to supply the specified therapeutic goods or the specified class of such goods; and
  - (b) in relation to a class or classes of recipient prescribed by the regulations for the purposes of this paragraph.

Paragraph (AA) does not apply in the exceptional circumstances (if any) prescribed by the regulations for the purposes of this subsection.

- (7) The regulations may prescribe the circumstances in which therapeutic goods may be supplied under an authority under subsection (5).
- (8) The giving of an authority under subsection (5) does not render the Commonwealth or Secretary or a delegate of the Secretary liable to a person in

respect of loss, damage or injury of any kind suffered by a person as a result of, or arising out of, the use of therapeutic goods by that person or another person

- (9) In this section, "medical practitioner" means a person who is registered, in a State or internal Territory, as a medical practitioner.

## **20 Offences relating to importation, exportation, manufacture and supply of therapeutic goods**

- (1) A person is guilty of an offence if:
- (a) The person intentionally:
    - (i) imports into Australia therapeutic goods for use in humans; or
    - (ii) exports from Australia therapeutic goods for use in humans; or
    - (iii) manufactures in Australia therapeutic goods for use in humans; or
    - (iv) supplies in Australia therapeutic goods for use in humans; and
  - (b) none of the following subparagraphs applies in relation to the goods:
    - (i) the goods are registered goods or listed goods in relation to the person;
    - (ii) the goods are exempt goods;
    - (iii) the goods are subject to an approval or authority under section 19;
    - (iv) the goods are subject of an approval under section 19A.

(1AA) An offence against subsection (1) is punishable on conviction by a fine not more than 240 penalty units.

(1A) It is a defence to a prosecution under subsection (1) if the defendant proves that the defendant was not the sponsor of the goods at the time of the importation, export, manufacture or supply, as the case may be.

(2) – (3) [Relates to registered or listed goods]

## **22 General Offences relating to this Part**

(1) - (5) - [Relates to registered or listed goods]

(6) A person must not intentionally or recklessly make a claim, by any means, that the person or another person can arrange the supply of therapeutic goods (not being exempt goods) that are not registered goods or listed goods.

- (7) A person is guilty of an offence if:
- (a) the person intentionally does not act or omits to do an act; and
  - (b) the person was reckless as to whether the act or omission would breach:
    - (i) a condition of an exemption applicable under regulations made for the purposes of subsection 18(1); or
    - (ii) a condition of an approval under section 19; or
    - (iii) a condition applicable under regulations made for the purposes of subsection 19(4A); or
    - (iv) a condition of an approval under section 19A.

- (7AA) An offence against subsection (7) is punishable on conviction by a fine of not more than 60 penalty units.
- (7A) A person who whom an authority under subsection 19(5) has been granted must not supply the therapeutic goods to which the authority relates except in accordance with:
- (a) the authority; and
  - (aa) the conditions (if any) to which the authority is subject; and
  - (b) the regulations made for the purpose of subsection 19(7).

Maximum penalty: 60 penalty units

- (8) - [Relates to goods approved under 19A]

### **31A Secretary may require information etc. about exempt goods**

#### *Exempt goods for use for experimental purposes in humans*

- (1) If therapeutic goods are exempt under section 18(1) from the operation of this Part (except this section and sections 31C to 31F) to allow for their use for experimental purposes in humans, the Secretary may give the sponsor a written notice requiring the sponsor to give to the Secretary specified information or documents relating to one or more of the following:
- (a) the supply of the goods;
  - (b) the handling of the goods;
  - (c) the monitoring of the supply of the goods;
  - (d) the results of the supply of the goods;
  - (e) any other matter prescribed by the regulations for the purpose of this paragraph in relation to medicines of that kind.

#### *Statement by medical practitioner about medicine*

- (2) If a medicine is exempt under section 18(1) from the operation of this Part (except this section and sections 31C to 31F) because a medical practitioner has signed a statement in accordance with regulation 12A of the *Therapeutic Goods Regulations 1990*, the Secretary may give the medical practitioner a written notice requiring the medical practitioner to give to the Secretary specified information or documents relating to one or more of the following:
- (a) the condition of the person to whom the medicine is to be given or is given;
  - (b) the supply of the medicine;
  - (c) the handling of the medicine;
  - (d) the monitoring of the supply of the medicine;
  - (e) the results of the supply of the medicine;
  - (f) any other matter prescribed by the regulations for the purpose of this paragraph in relation to medicines of that kind

*Compliance period*

- (3) A notice under subsection (1) or (2) must specify a reasonable period within which the person to whom the notice is given must comply with it. The period must be at least 14 days starting on the day on which the notice is given.

**31B Secretary may require information relating to approvals and authorities under section 19**

*Approval under subsection 19(1)*

- (1) The Secretary may give to a person who is granted an approval under subsection 19(1) in relation to specified therapeutic goods a written notice requiring the person to give to the Secretary specified information or documents relating to one or more of the following:
  - (a) the supply of the goods;
  - (b) the handling of the goods;
  - (c) the monitoring of the supply of the goods;
  - (d) the results of the supply of the goods;
  - (e) any other matter prescribed by the regulations for the purpose of this paragraph in relation to medicines of that kind.
- (2) The Secretary may give notice to a person using specified therapeutic goods that are the subject of an approval granted to someone else under paragraph 19(1)(b) a written notice requiring the person to give the Secretary specified information or documents relating to either or both of the following:
  - (a) the use of the goods;
  - (b) any other matter prescribed by the regulations for the purposes of this paragraph in relation to goods of that kind.

*Authority under subsection 19(5)*

- (3) The Secretary may give to a person who is granted an authority under subsection 19(5) in relation to specified therapeutic goods, or a specified class of therapeutic goods, a written notice requiring the person to give to the Secretary specified information or documents relating to one or more of the following:
  - (a) the supply of the goods;
  - (b) the handling of the goods;
  - (c) the monitoring of the supply of the goods;
  - (d) the results of the supply of the goods;
  - (e) any other matter prescribed by the regulations for the purpose of this paragraph in relation to medicines of that kind.

*Compliance period*

- (4) A notice under subsection (1), (2) or (3) must specify a reasonable period within which the person to whom the notice is given must comply with it.

The period must be at least 14 days starting on the day on which the notice is given.

### **31C Requirements in relation to information or documents sought under section 31A or 31B**

*When information or documents must be given etc.*

- (1) A person to whom a notice is given under section 31A or 31B must give the Secretary:
  - (a) the information or documents specified in the notice within the period specified in the notice; and
  - (b) the information specified in the notice in the form (if any) specified in the notice.

*Way in which information given*

- (2) A notice mentioned in subsection (1) may require information to be given in accordance with specified software requirements:
  - (a) on a specified kind of data processing device; or
  - (b) by way of a specified kind of electronic transmission.

*Offence*

- (3) A person mentioned in subsection (1) is guilty of an offence if the person fails to comply with that subsection.

Note: The privilege against self-incrimination is not a reasonable excuse for the purposes of subsection (3). However, the information given and the fact that a document was given under this section (and other information, documents or things obtained because of giving the information or document) generally cannot be used in a prosecution (see section 31 F).

*Penalty*

- (4) An offence against subsection (3) is punishable on conviction by a fine of not more than 60 penalty units.

### **7 31 D False and misleading information**

- (1) A person to whom a notice is given under section 31A or 31B is guilty of an offence if:
  - (a) the person gives information to the Secretary in compliance or purported compliance with subsection 31C(1); and
  - (b) the person does so knowing that the information:
    - (i) is false or misleading; and
    - (ii) omits any matter or thing without which the information is misleading.

Maximum penalty: Imprisonment for 12 months

- (2) Subsection (1) does not apply as a result of subparagraph (1)(b)(i) if the information is not false or misleading in a material particular.

Note: A defendant bears an evidential burden in relation to the matter in subsection (2)

- (3) Subsection (1) does not apply as a result of subparagraph (1)(b)(ii) if the information did not omit any matter or thing without which the information is misleading in a material particular.

Note: A defendant bears an evidential burden in relation to the matter in subsection (3)

### **31 E False or misleading documents**

- (1) A person is guilty of an offence if:
- (a) the person produces a document to the Secretary; and
  - (b) the person does so knowing that the document is false or misleading; and
  - (c) the document is produced in compliance or purported compliance with subsection 31C(1).

Maximum penalty:                      Imprisonment for 12 months

- (2) Subsection (1) does not apply if the document is not false or misleading in a material particular.

Note: A defendant bears an evidential burden to the matter in subsection (2).

- (3) Subsection (1) does not apply to a person who produces a document if the document is accompanied by a written statement signed by the person or in the case of a body corporate by a competent officer of the body corporate:
- (a) stating that the document is, to the knowledge of the first-mentioned person false or misleading in a material particular; and
  - (b) setting out, or referring to, the material particular in which the document is, to the knowledge of the first-mentioned person, false or misleading.

Note: A defendant bears an evidential burden to the matter in subsection (3).

### **31 F Self-incrimination**

- (1) A person is not excused from giving information or a document under section 31C on the ground that the giving of the information or document would tend to incriminate the person or expose the person to a penalty.

- (2) However, in the case of an individual:
- (a) the information given; or
  - (b) the giving of the information; or
  - (c) any information, document or thing obtained as a direct or indirect consequence of giving the information or document; is not admissible in evidence in criminal proceedings against the individual (except proceedings under, or arising out of, section 31D or 31E).

**Delegation**

- (1) Subject to subsections (2), (6) and (8), the Minister or the Secretary may, by signed instrument, declare to:
  - (a) an officer of the Department; or
  - (b) an officer of an authority of the Commonwealth that has functions in relation to therapeutic goods; or
  - (ba) an APS employee in an Agency (within the meaning of the Public Service Act 1999) that has functions in relation to therapeutic goods; or
  - (c) a person occupying or acting in an office, or holding an appointment, declared by the regulations to be an office or appointment the occupant or holder of which may be a delegate under this section;all or any of his or her powers and functions under this Act.
- (2) The powers of the Secretary under paragraph 19(1)(a) may be delegated under subsection (1) only to a person referred to in paragraph (1)(a) or (c) who is registered, or eligible for registration, in a State or internal Territory, as a medical or dental practitioner or as a pharmacist.
- (3) Subject to the regulations, the Secretary may, in such circumstances as are prescribed, by signed instrument, delegate all or any of his or her powers under paragraph 19(1)(a) to a person who is registered, in a State or internal Territory, as medical or dental practitioner.
- (4) A delegate under subsection (3) is, in the exercise of a delegated power, subject to the direction of:
  - (a) the Secretary; or
  - (b) an officer of the Department authorised in writing by the Secretary; or
  - (c) a person referred to in paragraph (1)(c).
- (5) Without limiting the generality of matters that may be dealt with by regulations made for the purposes of subsection (3), the regulations may make provision in relation to the following:
  - (a) the persons who may be delegates;
  - (b) the circumstances in which delegates may grant approvals for the purposes of paragraph 19(1)(a);
  - (c) the conditions to which any approvals granted by delegates are to be subject;
  - (d) requiring information to be given by delegates to the Secretary.
- (6) The powers of the Secretary under subsection 19(5) may be delegated only to a person referred to in paragraph (1)(a) or (c) who is registered or eligible for registration, in a State or internal Territory as a medical or dental practitioner.
- (7) The regulations may prescribe the circumstances in which, and the requirements subject to which, delegates may grant authorities under subsection 19(5).



(8) [relates to 19A]

(9) [relates to 6AA and 23AA]

### ***The Therapeutic Goods Regulations***

## **12 Exempt goods**

(1) [Relates to schedule 5]

(1AA)[Relates to medical devices]

(1A) For the purposes of subsection 18(1) of the Act, the therapeutic goods or classes of therapeutic goods specified in an item in column 2 or Schedule 5A are exempt from the operation of Part 3 of the Act (except section 31A and 31C to 31F) subject to compliance with the relevant conditions specified in column 3 of that Schedule.

(1B) [Relates to anti-D immunoglobulin]

(3) If:

- (a) therapeutic goods that, in relation to a provision of Part 3 of the Act, are exempt goods cease to be exempt goods; and
- (b) the sponsor of the goods has applied for registration or listing of the goods before the goods until the application for registration or listing is determined.

the goods are taken to be exempt goods until the application for registration or listing is determined.

## **12A UNAPPROVED MEDICINES – EXEMPTION IN LIFE THREATENING CASES**

(1) For the purposes of subsection 18(1) of the Act, all medicines, other than medicines of a class or kind listed in the 9th Schedule to the Poisons Standard, as in force from time to time, are exempted, subject to subregulation (2), from the operation of Part 3 of the Act (except section 31A and sections 31C to 31F).

(2) The exemption of a medicine is subject to the following conditions:

- (a) the medicine is to be given to a person who satisfies the following criteria:
  - (i) the person is a Category A patient (as defined in subregulation (5)); and
  - (ii) the person, or the guardian of the person, has given informed consent (as defined in subregulation (5)) to the goods being given to the person; and
  - (iii) the medical practitioner by whom, or at whose direction, the therapeutic good is to be given to the person has signed a statement in relation to the person in the form approved by the Secretary for the purposes of this paragraph; and

- (b) the good is dispensed on the prescription of a medical practitioner who has prescribed the medicine in accordance with good medical practice.
- (3) A person who signs a statement referred to in subparagraph (2)(a)(iii) must send a copy of the statement to the Secretary within 4 weeks of signing it.  
Maximum Penalty: \$1,000.
- (4) This regulation does not affect the operation of regulation 12.
- (5) In this regulation:

***Category A patient*** means a person 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;

***informed consent***, in relation to treatment or proposed treatment, means consent freely given by a person on the basis of information concerning the potential risks and benefits of the treatment that was sufficient information to allow the person to make an informed decision whether to consent to treatment.

#### **12AA Applications for special and experimental uses.**

Without limiting the information that may be required by the Secretary under subsection 19(2) of the Act, that information may include, in relation to therapeutic goods that subject of an application under subsection 19(1) of the Act for the use described in paragraph 19(1)(b) of the Act:

- (a) the names of the members of the ethics committee that has given approval for each proposed clinical trial of the goods and that will have responsibility for monitoring that conduct of each trial; and
- (b) the name of, and the contact details for, the principal investigator for each trial; and
- (c) the name of the person who will be in charge of the trial (or each trial site, if the trial is to be conducted at more than 1 site), unless that person is the principal investigator; and
- (d) information about whether or not any conditions specified by the committee have been met.

#### **12 AB Goods imported, etc, for experimental uses**

- (1) For subsection 19(1A) of the Act, this regulation specifies conditions attaching to an approval for the importation, exportation or supply of therapeutic goods for use solely for experimental purposes in humans.
- (2) Before any clinical trials proposed to be undertaken in relation to the goods are started, the National Manager, Therapeutic Goods Administration, must receive from the person to whom the approval is granted, and the principal investigator for each trial site:

- (a) a written assurance that clinical trials will be conducted in accordance with the Guidelines for Good Clinical Practice (the *Practice Guidelines*), as in force from time to time, published jointly by the International Conference on Harmonisation on Technical Requirements for Registration of Pharmaceuticals for Human Use and the Committee for Medicinal Products; and
- (b) a written undertaking;
  - (i) to comply with requests by an authorised person, whether made before or after the start of a trial, to give information about the conduct of the trial; and
  - (ii) allow an authorised person to do the things mentioned in regulation 12AC.

**12 AC Powers of authorised persons in relation to goods imported, etc, for experimental uses**

- (1) An authorised person may, in relation to a clinical trial mentioned in regulation 12AB:
  - (a) enter the site of the trial; and
  - (b) search the site and any thing on the site; and
  - (c) inspect, examine, take measurements of, or conduct tests on (including by the taking of samples), any thing on the site that relates to the trial; and
  - (d) take photographs, make video recordings or make sketches of the site or any thing on the site; and
  - (e) inspect any book, record or document on the site that relates to the trial; and
  - (f) request the principal investigator to:
    - (i) answer any questions put by the authorised person; and
    - (ii) produce any book, record or document requested by the authorised person.
- (2) An authorised person is not entitled to do a thing mentioned in subregulation (1) if:
  - (a) the principal investigator or any other person present at the site concerned and in apparent control, requests the authorised person to produce his or hers identity card for inspection; and
  - (b) the authorised person fails to comply with the request.

*Note* For identity card; see section 52 of the Act.

- (3) The principal investigator, or any other person present at the site and in apparent control, is entitled to observe a search conducted under paragraph (1)(b), but must not impede the search.
- (4) Subregulation (3) does not prevent 2 or more areas of the site being searched at the same time.

**12AD Use of goods for experimental purposes – specified conditions**

For subsection 19(4A) of the Act, the following conditions are specified:

- (a) the use of therapeutic goods in a clinical trial must be in accordance with the Practice Guidelines;
- (b) the use must be comply with a procedural protocol determined by the ethics committee that gave approval for the clinical trial of the goods and that has the function of monitoring the conduct of the trail at each trial site;
- (c) the use must be in accordance with the ethical standards set out in the National Statement on Ethical Conduct in Research Involving Humans, as in force from time to time, published by the National Health and Medical Research Council;
- (d) the use must cease if the ethics committee mentioned in paragraph (b) informs the principal investigator that the use is inconsistent with:
  - (i) the protocol mentioned in paragraph (b);or
  - (ii) any condition subject to which approval for the use was given.

## **12B Exemptions for special and experimental use**

- (1) For paragraph 19(6)(a) of the Act, in relation to therapeutic goods that are medicines, a medical practitioner is in the prescribed class of medical practitioners if he or she is engaged in clinical practice outside a hospital and:
  - (a) has demonstrated that, in relation to the proposed supply, he or she does not have access to an ethics committee that could approve the supply; and
  - (b) has, from a specialist college having an established expertise relevant to use of the medicines concerned, endorsement to supply the medicines.
- (2) The class of recipients prescribed for the purposes of paragraph 19(6)(b) of the Act is the class of recipients consisting of persons each of whom is suffering from a life-threatening, or otherwise serious, illness or condition.
- (3) For the purposes of paragraph 19(7) of the Act, the prescribed circumstances in which a medicine, or a class of medicines, may be supplied in accordance with an authority under section 19(5) of the Act are that the supplier of the medicine or class of medicines complies with the treatment directions (if any) mentioned in the authority for the medicine or class of medicine.
- (4) For the purposes of paragraph 19(7) of the Act, the prescribed circumstances in which a therapeutic device, or a class of therapeutic devices, may be supplied in accordance with an authority under section 19(5) of the Act are:
  - (a) that the medical practitioner whom the Secretary authorises under subsection 19(5):
    - (i) is a specialist in clinical practice at a hospital: and
    - (ii) is endorsed by the ethics committee of that hospital; and
  - (b) that the authority states the particular therapeutic intervention, or class of therapeutic intervention, for which the authorised person may supply the therapeutic device or class of therapeutic devices.

#### **47A Delegations – powers under paragraph 19(1)(a) of the Act.**

- (1) In this regulation, *delegation* means a delegation, under subsection 57(3), of the Act, of powers of the Secretary under paragraph 19(1)(a) of the Act, that relates to specified therapeutic goods.
- (2) A delegation may only be to a person who:
  - (a) is a medical practitioner registered in a State or Territory and employed by an institution that has an ethics committee; and
  - (b) subject to subregulation (3), is proposed by the medical superintendent or, if there is no medical superintendent, the person occupying a position comparable to that of medical superintendent, of the institution, as a person to be a delegate under subsection 57(3) of the Act.
- (3) If:
  - (a) a person proposes another person under paragraph (2)(b) as a person to be a delegate; and
  - (b) that other person becomes a delegate;  
the first-mentioned person must supervise each approval that the delegate grants under the delegation.
- (4) A delegation must describe the person or class of persons to be treated with the therapeutic goods to which the delegation relates.
- (5) A delegation may be made for the purpose of allowing the delegate to grant an approval in relation to:
  - (a) a particular item of therapeutic goods; or
  - (b) a particular class of therapeutic goods;  
for treating a specific illness or condition.
- (6) A delegate may grant an approval under a delegation only if:
  - (a) A medical practitioner other than the delegate has stated in writing that the person to be treated with the item of therapeutic goods to which the approval relates has an illness or condition that requires treatment with the item; and
  - (b) An ethics committee has agreed to the granting of approval under paragraph 19(1)(a) of the Act for the use, in the circumstances in which the delegate grants the approval, of the item of therapeutic goods to which the delegation relates.
  - (c)

### Schedule 5A excerpt

<u>Column 1</u>	<u>Column 2</u>	<u>Column 3</u>
Item	Therapeutic goods	Conditions
3	Therapeutic goods used solely for experimental purposes in humans	<p>(a) before starting to use the goods, the sponsor must notify the Secretary:</p> <ul style="list-style-type: none"><li>(i) in a form approved by the Secretary; and</li><li>(ii) in accordance with the requirements (if any) determined by the Secretary for the form of notification;</li></ul> <p>that the sponsor intends to sponsor a clinical trial using specified goods; and</p> <p>(b) the notification must be accompanied by the relevant notification fee referred to in item 14 or 14A of Schedule 9; and</p> <p>(c) the approval of the goods for this purpose must be given by the sponsor (if the sponsor is conducting the trial), or by the body or organisation conducting the trial for the sponsor, having regard to the advice of the ethics committee that has, or will assume, responsibility for monitoring the conduct of the trial; and</p> <p>(d) the terms of the approval by the sponsor, body or organisation referred to in paragraph (c) must be no less restrictive than the terms advised by the ethics committee;</p> <p>(e) and the Secretary must not, at any time:</p> <ul style="list-style-type: none"><li>(i) have become aware that to conduct or continue the trial would be contrary to the public interest; and</li><li>(ii) have directed that the trial not be conducted, or be stopped; and</li></ul> <p>(f) the sponsor (if the sponsor is conducting the trial), or the body or organisation conducting the trial for the sponsor, must not receive, or have received, advice from the ethics committee that is inconsistent with the continuation of the trial; and</p> <p>(g) the conditions set out in regulation 12AD must be complied with, as if that regulation applied to a person using therapeutic goods under this item.</p>

**APPENDIX 2. NOTIFICATION OF INTENT TO SUPPLY UNAPPROVED  
THERAPEUTIC GOODS UNDER THE CLINICAL TRIAL NOTIFICATION  
(CTN) SCHEME  
(CTN FORM)**







# Notification of Intent to Supply Unapproved Therapeutic Goods under the Clinical Trial Notification (CTN) Scheme

## Therapeutic Goods Act 1989

To be used for:

- initial notifications of clinical trials involving medicines and/or medical devices under the Clinical Trial Notification (CTN) Scheme; or
- notification of one or more additional sites for a Clinical Trial previously reported under the Clinical Trial Notification (CTN) Scheme

**THIS IS THE FORM APPROVED BY THE SECRETARY OF THE DEPARTMENT OF HEALTH  
AND AGED CARE**

On completion please send this form to the Therapeutic Goods Administration:

*Courier address*

**The Business Manager  
Business Management Unit  
Therapeutic Goods Administration  
136 Narrabundah Lane  
Symonston ACT 2609  
Australia**

*or*

*Postal address*

**The Business Manager  
Business Management Unit  
Therapeutic Goods Administration  
PO Box 100  
Woden ACT 2606  
Australia**

Cheques should be made payable to "Therapeutic Goods Administration"



## PLEASE READ THE FOLLOWING INSTRUCTIONS BEFORE COMPLETING THIS FORM

- Notification under the CTN scheme (or application under the Clinical Trial Exemption (CTX) scheme) is required for clinical investigational use of:
  - any medicine or device not entered in the Australian Register of Therapeutic Goods, including any new formulation of an existing product or any new route of administration; or
  - a marketed medicine or device beyond the conditions of its marketing approval, including new indications extending the use of the product to a new patient group and the extension of doses or duration of treatments outside the approved range.
- **Before completing this form, all parties providing certification should read about their respective responsibilities in the clinical trial.** These roles are outlined in the following documents:
  - Access to Unapproved Therapeutic Goods - Clinical Trials in Australia, TGA, 2000
  - The National Statement on Ethical Conduct in Research Involving Humans, NHMRC, 1999
  - Guidelines for the Ethical Review of Research Proposals for Human Somatic Cell Gene Therapy and Related Therapies, NHMRC, 1999
- Under the *Therapeutic Goods Act 1989*, the **Therapeutic Goods Administration (TGA)** has the authority to enquire into and/or audit clinical trials, where necessary, on safety grounds and to investigate non compliance with either **Good Clinical Practice guidelines or legislative requirements. In addition, information concerning the supply and use of unregistered therapeutic goods may be released to State and Territory regulatory authorities under section 61 of the *Therapeutic Goods Act 1989*.** Completion of this notification form requires the sponsor of the trial, principal investigator, Human Research Ethics Committee and the approving authority to agree, in writing, to make all records available to TGA on request and to cooperate with TGA investigations. The sponsor of the trial is also required to acknowledge the potential for release of information about the use of unregistered therapeutic goods to State and Territory regulatory authorities.
- For the purpose of notifying a Clinical Trial of Medicines or Medical Devices, the "**sponsor of the trial**" is the company, organisation, institution, body or individual (enterprise) that initiates, organises and supports a clinical study of an investigational product on human subjects. As a result, the sponsor of the trial takes responsibility for the overall conduct of the trial. The "**approving authority**" is the body, organisation or institution that approves the conduct of the trial at the site. Thus, the Human Research Ethics Committee (HREC) can also be the Approving Authority for a particular trial site. The same person can sign on behalf of the HREC and the Approving Authority but they should indicate their position or capacity in relation to each. Also, the same person may sign on behalf of the sponsor of the trial and the Approving Authority. However, because of the potential for conflict of interest, the same person cannot sign on behalf of the sponsor of the trial and the HREC.
- **Key points for sponsors of the trial** to check before completing and submitting the CTN form to the Therapeutic Goods Administration (TGA) are:
  - You will need to have a TGA Enterprise ID in order for your notification fee to be accepted and receipted by the TGA Business Management Unit. If you have not conducted business with the TGA before, you will need to obtain an Enterprise ID. Enterprise Details Forms (1531(9602)) are available from the Experimental Drugs Section or the TGA Business Management Unit and can be submitted simultaneously with this notification.
  - You will need to obtain signatures from the relevant Human Research Ethics Committee, Approving Authority and Principal Investigator for **each** site at which the trial will be conducted.
  - Sites may be notified in any sequence. That is, all sites can be notified in the first instance; notified in groups; or notified singly. The fee for notification of a multi site trial is the same as that for a single site trial providing the sites involved in the multi site trial are declared simultaneously. However, if sites are notified individually or added for an existing trial, an additional fee equivalent to the fee for a single site applies to each notification. Full details of the fee structure for the CTN scheme can be obtained from the Business Management Unit of TGA.
  - Each new and/or additional trial site must be notified to the TGA prior to the trial commencing at that site.
  - You must assign a protocol number to each new trial. Take care not to assign to a new trial a protocol number used previously. Also, check that the protocol number notified to the TGA matches the version of the protocol approved by the Human Research Ethics Committee. When notifying additional sites, quote the protocol number exactly.
  - The TGA assigns a unique clinical trial number. The clinical trial number will appear on an acknowledgement letter from the TGA. Subsequent notifications to TGA of additional trial sites and other correspondence relating to the clinical trial post acknowledgement, such as reporting of adverse reactions, should include the protocol number and the clinical trial number as points of reference.
  - A CTN notification is not effective until the correct fee has been paid.

For office use only

Total Fee Paid \$  Receipt Number   
Enterprise ID Code  TGAIN Number

## SECTION 1. TO BE COMPLETED BY THE SPONSOR OF THE TRIAL

### 1.1 Notification Type

Complete this section for all notifications. Select one box only. If multiple sites are being notified, complete a 'Trial Site Details' page for each site.

Initial notification of a single CTN site (new trial)  Subsequent notification of a single additional CTN site   
Initial notification of multiple CTN sites (new trial)  Subsequent notification of multiple additional CTN sites

### 1.2 Use of Restricted Goods

 Complete this section for all notifications of medicines only.

Does this trial involve the use of any medicine as an abortifacient or for "post-coital" or "emergency" contraception in women, or the use of a progesterone antagonist or a vaccine against human chorionic gonadotrophin for any purpose? Yes  No

### 1.3 Sponsor of the trial

 Complete this section for all notifications. In cases where a trial is sponsored by an individual, that person's name may also be the enterprise business name. Business details can be provided to TGA via the Enterprise Details Form. If in doubt, contact the Experimental Drugs Section.

Sponsor name (Enterprise Business Name)   
Enterprise ID Code (If known)

### 1.4 Trial details

Protocol Number  (Complete for all notifications; maximum of 20 characters)  
If adding a site, Clinical Trial Number  (assigned by TGA; see acknowledgment letter for previously notified sites. Leave blank if unsure)

**Title of study** Complete for all notifications. Maximum of 255 characters. Title should indicate the aim of the trial and give a broad description of the trial. Include, for example: phase, indication(s) being treated, main medicines and comparators, use of placebo-control, focus of the study, patient population and any other significant or novel aspects. "A Trial of X" is not adequate. Similar detail is required for device trials.


**Trial Type** Complete for initial notification only of trials involving the use of medicines; tick relevant box(es) or otherwise describe.

Phase 1  Phase 2  Phase 3  Phase 4  Bioavailability/bioequivalence

Describe if necessary

**This trial**

Complete for initial notification only; tick only those boxes which are applicable. Note: For the purpose of this document, gene therapy includes related therapies that overlap with the traditional concept of gene therapy by virtue of the fact that they introduce DNA into somatic cells. For example, modifications to immunisation strategies in which DNA, rather than protein, is used to generate an immune response for the purposes of prevention or treatment of chronic viral infection or as part of cancer treatment, would be considered a related therapy.

involves the use of a medicine	<input type="checkbox"/>	involves the use of a device	<input type="checkbox"/>
is placebo controlled	<input type="checkbox"/>	Is comparator controlled	<input type="checkbox"/>
is also being conducted in other countries	<input type="checkbox"/>	involves gene therapy	<input type="checkbox"/>
<b>Expected trial start date</b> (Complete for initial notification)	<input type="text" value="/ /"/>	<b>Expected trial completion date</b> (Complete for all notifications)	<input type="text" value="/ /"/>

**Medicine details**

Complete for all notifications of clinical trials involving medicines. Do not use for clinical trials involving the use of devices only. List the therapeutically active components in formulations being used in the trial. All medicines being trialed should be listed, including comparators. The form has space for three medicines. For more than four, attach details of additional medicines in the same format. For the Active Name, enter the active ingredient name using where possible, the Australian Approved Name (AAN). If no AAN, BAN or USAN has been assigned, a code name (see below) or chemical name must be given. For the Code Name, enter code name/s used currently or previously to identify the drug. For the Dosage Form, enter a primary descriptor for dosage form (eg. tablet, injection) and include a secondary descriptor (eg. sustained release, microsphere emulsion) where necessary, particularly if a new dosage form is the focus of the trial.

1	Active name	<input type="text"/>		
	Trade name	<input type="text"/>	Code name	<input type="text"/>
	Dosage form	<input type="text"/>	Strength	<input type="text"/>
			Biological origin	<input type="checkbox"/>
2	Active name	<input type="text"/>		
	Trade name	<input type="text"/>	Code name	<input type="text"/>
	Dosage form	<input type="text"/>	Strength	<input type="text"/>
			Biological origin	<input type="checkbox"/>
3	Active name	<input type="text"/>		
	Trade name	<input type="text"/>	Code name	<input type="text"/>
	Dosage form	<input type="text"/>	Strength	<input type="text"/>
			Biological origin	<input type="checkbox"/>
4	Active name	<input type="text"/>		
	Trade name	<input type="text"/>	Code name	<input type="text"/>
	Dosage form	<input type="text"/>	Strength	<input type="text"/>
			Biological origin	<input type="checkbox"/>



**1.6 Sponsor certification**

Complete this section last for all notifications. In the Name field, print the name of the person signing the form on behalf of the company, organisation, institution, body or individual sponsoring the trial. (Do not enter a company or organisation name here - the entity name appears in Section 1.3) In the Position field, state the person's position within, or relationship to, the entity sponsoring the trial.

I, the undersigned, certify:

- all details contained in this form are true and accurate, and all required information and signatures have been included;
- the sponsor of the trial named in section 1.3 of this form is taking overall responsibility for the conduct of the trial;
- the sponsor of the trial has met or agrees to meet all Human Research Ethics Committee conditions of approval;
- the investigator(s) has/have training and experience relevant to the conduct of this trial;
- the participating institution has resources adequate for the proper conduct of the trial;
- the sponsor of the trial has received an undertaking from the investigator(s) to conduct the trial in accordance with the Guidelines for Good Clinical Practice as described in regulation 12AB(2)(a) of the Therapeutic Goods Regulations and the National Statement of Ethical Conduct in Research Involving Humans as described in regulation 12AD(c) of the Therapeutic Goods Regulations;
- the sponsor of the trial agrees to report all serious and unexpected adverse reactions to the Therapeutic Goods Administration;
- the sponsor of the trial agrees to conduct the trial in accordance with the Guidelines for Good Clinical Practice as described in regulation 12AB(2)(a) of the Therapeutic Goods Regulations and the National Statement of Ethical Conduct in Research Involving Humans as described in regulation 12AD(c) of the Therapeutic Goods Regulations;
- the sponsor of the trial agrees to comply with requests by an authorised person, whether made before or after the start of a clinical trial, to give information about the conduct of the clinical trial and allow an authorised officer (regulation 47AA of the Therapeutic Goods Regulations) to do the things mentioned in regulation 12AC and regulation 12AB of the Therapeutic Goods Regulations; and
- the sponsor of the trial accepts that information concerning the use of unregistered therapeutic goods may be released to State and Territory regulatory authorities.

Name (Print)

Position

Signature   
/ /

Phone

Fax

## SECTION 2. TO BE COMPLETED BY THE PRINCIPAL INVESTIGATOR

*The principal investigator is the person responsible for the conduct of the clinical trial at a trial site. In the case of a trial being conducted by a team of individuals at the site, the principal investigator is the responsible leader of the team.*

### Principal investigator certification

I, the undersigned:

- am the principal investigator at the site shown in section 1.5 of this form;
- agree to personally supervise the clinical trial at this site in accordance with the relevant current protocol(s) and will only make changes in a protocol after approval by the sponsor;
- have received and read the trial protocol and other relevant information;
- have met or agree to meet all Human Research Ethics Committee conditions of approval for this trial:
- acknowledge my obligations with respect to monitoring patient safety, record management and reporting requirements for adverse events;
- agree to ensure that all associates, colleagues and employees assisting in the conduct of the trial are informed of their obligations in meeting the above requirements;
- agree to promptly report to the Human Research Ethics Committee all unanticipated problems and will not make any changes to the trial without Human Research Ethics Committee and sponsor approval, except where necessary to eliminate apparent immediate hazards to subject safety;
- agree to conduct the clinical trial(s) in accordance with the Guidelines for Good Clinical Practice as described in regulation 12AB(2)(a) of the Therapeutic Goods Regulations and the National Statement of Ethical Conduct in Research Involving Humans as described in regulation 12AD(c) of the Therapeutic Goods Regulations;
- agree to comply with requests by an authorised person, whether made before or after the start of a clinical trial, to give information about the conduct of the clinical trial and allow an authorised officer (regulation 47AA of the Therapeutic Goods Regulations) to do the things mentioned in regulation 12AC and regulation 12AB of the Therapeutic Goods Regulations; and
- accept that information concerning the use of unregistered therapeutic goods may be released to State and Territory regulatory authorities.

Name (Print)

Phone

Signature

  
/ /

Fax



### SECTION 3. TO BE COMPLETED BY THE HUMAN RESEARCH ETHICS COMMITTEE RESPONSIBLE FOR MONITORING THE TRIAL

This section must be completed by a Human Research Ethics Committee (HREC) that satisfies the following definition of an ethics committee, as set out in the Therapeutic Goods Act 1989, otherwise the notification is invalid :

A committee constituted and operating in accordance with guidelines issued by the National Health and Medical Research Council as in force from time to time and which has notified its existence to the Australian Health Ethics Committee.

HREC certification should not be given until all conditions of approval of the protocol by that HREC have been met. Wherever possible, the certification should be completed by the Chair or Deputy Chair of the Human Research Ethics Committee. Guidelines for the approval of clinical trials by HRECs are located at Chapter 12, The National Statement on Ethical Conduct in Research Involving Humans, 1999 and in the TGA publication 'HRECs and the Therapeutic Goods Legislation'.

For trials of gene therapy and related therapies, the proposal must be approved by all relevant bodies as per the NHMRC Guidelines for Ethical Review of Research Proposals for Human Somatic Cell Gene Therapy and Related Therapies.

HREC name

HREC address   
 Postcode

Protocol Number approved by HREC

Does the trial for which approval is being given involve the use of gene therapy or a related therapy? (See NHMRC Guidelines for Ethical Review of Research Proposals for Human Somatic Cell Gene Therapy and Related Therapies)

Yes  No

If the trial involves gene therapy or a related therapy, has the Gene and Related Therapies Research Advisory Panel (GTRAP) agreed that the trial can be conducted under the CTN Scheme?

Yes  No

#### Human Research Ethics Committee Certification

I, the undersigned, certify:

- I am a member of the above named Human Research Ethics Committee;
- the above named Human Research Ethics Committee is a properly constituted ethics committee and operates in accordance with the guidelines issued by the National Health and Medical Research Council and has notified its existence to the Australian Health Ethics Committee;
- the above named Human Research Ethics Committee, having regard to the guidance provided by the *National Statement on Ethical Conduct in Research Involving Humans* and, where applicable, the *Guidelines for Ethical Review of Research Proposals for Human Somatic Cell Gene Therapy and Related Therapies*, has approved the clinical trial protocol identified above and has assumed responsibility for monitoring the conduct of the trial; and
- the above named Human Research Ethics Committee agrees to comply with requests by an authorised person, whether made before or after the start of a clinical trial, to give information about the conduct of the clinical trial and allow an authorised officer (regulation 47AA of the Therapeutic Goods Regulations) to do the things mentioned in regulation 12AC and regulation 12AB of the Therapeutic Goods Regulations.

Name (Print)

Position

Signature   
/ /

Phone

Fax

## SECTION 4. TO BE COMPLETED BY THE AUTHORITY APPROVING THE CONDUCT OF THE TRIAL

Complete for all notifications. In cases where the Human Research Ethics Committee or Approving Authority for more than one site is the same, it is still necessary to submit a Trial Site Details Page for **each** site. The bodies approving the conduct of the trial at each site need to be declared individually. This requirement also still applies in cases where, for example, an Area Health Service or Hospitals Group may encompass several different institutions.

The Approving Authority must appoint a person to be responsible for giving approval on its behalf. The terms of approval for the conduct of the trial must be consistent with the Human Research Ethics Committee's (HREC) recommendations and these terms must be no less restrictive than the HREC advice.

Approving Authority name	<input type="text"/>
Address	<input type="text"/>
	<input type="text" value="Postcode"/>

### Approving Authority Certification

I, the undersigned

- am authorised to represent the body, organisation or institution at which the above mentioned clinical trial will be conducted and, having regard to the advice and approval of the trial protocol by the Human Research Ethics Committee responsible for monitoring the trial at this site, give approval for this trial to proceed;
- undertake that the use of the drug will comply with all relevant Commonwealth and State or Territory legislation; and
- undertake to comply with requests by an authorised person, whether made before or after the start of a clinical trial, to give information about the conduct of the clinical trial and allow an authorised officer (regulation 47AA of the Therapeutic Goods Regulations) to do the things mentioned in regulation 12AC and regulation 12AB of the Therapeutic Goods Regulations.

Name (Print)	<input type="text"/>	Position	<input type="text"/>
Signature	<input type="text" value="/ /"/>	Phone	<input type="text"/>
		Fax	<input type="text"/>

**APPENDIX 3. SUPPLY OF UNAPPROVED THERAPEUTIC GOODS UNDER  
THE CLINICAL TRIAL EXEMPTION (CTX) SCHEME**

**PART 2 NOTIFICATION OF THE CONDUCT OF A TRIAL UNDER A CTX  
APPROVAL**





# Supply of Unapproved Therapeutic Goods under the Clinical Trial Exemption (CTX) Scheme

## Therapeutic Goods Act 1989

### PART 2 NOTIFICATION OF THE CONDUCT OF A TRIAL UNDER THE CTX SCHEME

To be used for CTX Scheme trials of medicines and medical devices

This form must be sent to the Therapeutic Goods Administration within 28 days of commencing supply of the goods:

*For medicines*

The Medical Advisor  
Experimental Drugs Section  
Drug Safety and Evaluation Branch  
Therapeutic Goods Administration  
PO Box 100  
Woden ACT 2606  
Australia

or

*For medical devices*

Chief Clinical Advisor  
Conformity Assessment Branch  
Therapeutic Goods Administration  
PO Box 100  
Woden ACT 2606  
Australia

For Office Use Only – EDS/CAB

Date Notification received

CTX Number



## PLEASE READ THE FOLLOWING INSTRUCTIONS BEFORE COMPLETING PART 2

- A sponsor cannot commence a CTX trial until:
  - written approval has been received from the TGA regarding the CTX application (Part 1);and
  - approval for the conduct of the trial has been obtained from an ethics committee and the institution at which the trial will be conducted.

There are two forms, each reflecting these separate processes (Parts), that must be submitted by the sponsor. Part 1 constitutes the formal CTX application. It must be completed by the sponsor and submitted to TGA with data for evaluation. Part 2 (this form) is used to notify the commencement of each new trial conducted under the CTX scheme as well as new sites in ongoing CTX trials. The notification, containing certifications of the sponsor, principal investigator, HREC and Approving Authority, is required to inform the TGA of the conduct of each specific trial and to demonstrate that all of the parties involved in the conduct of individual trials have complied with legislative and regulatory requirements and agree to release information to the TGA about the conduct of the trial in the event of an inquiry or audit of the trial by the TGA. There is no fee for notification of trials under the CTX scheme. Part 2 must be completed and submitted to TGA within 28 days of either the commencement of each new trial or the addition of a new site in an ongoing CTX trial.

- Under the *Therapeutic Goods Act 1989*, the Therapeutic Goods Administration (TGA) has the authority to inquire into and/or audit clinical trials, where necessary, on safety grounds and to investigate non compliance with either Good Clinical Practice guidelines or legislative requirements. In addition, information concerning the supply and use of unregistered therapeutic goods may be released to State and Territory regulatory authorities under section 61 of the Therapeutic Goods Act 1989. Completion of this notification form requires the sponsor of the trial, principal investigator, Human Research Ethics Committee and the approving authority to agree, in writing, to make all records available to TGA on request and to cooperate with TGA investigations. The sponsor and principal investigator at each site are also required to acknowledge the potential for release of information about the supply and handling of unregistered therapeutic goods to State and Territory regulatory authorities.
- For the purpose of notifying a Clinical Trial of Medicines or Medical Devices, the "**sponsor of the trial**" is the company, organisation, institution, body or individual (enterprise) that initiates, organises and supports a clinical study of an investigational product on human subjects. As a result, the sponsor of the trial takes responsibility for the overall conduct of the trial. The "**approving authority**" is the body, organisation or institution that approves the conduct of the trial at the site. Thus, the Human Research Ethics Committee (HREC) can also be the Approving Authority for a particular trial site. The same person can sign on behalf of the HREC and the Approving Authority but they should indicate their position or capacity in relation to each. Also, the same person may sign on behalf of the sponsor of the trial and the Approving Authority. However, because of the potential for conflict of interest, the same person cannot sign on behalf of the sponsor of the trial and the HREC.
- **Key points for sponsors of the trial** to check before completing and submitting this notification to the Therapeutic Goods Administration (TGA) are:
  - You will need to obtain signatures from the relevant Human Research Ethics Committee, Approving Authority and Principal Investigator for **each** site at which the trial will be conducted.
  - Sites may be notified in any sequence. That is, all sites can be notified in the first instance; notified in groups; or notified singly. There is no fee associated with the notification of trials conducted under the CTX scheme.
  - You must assign a protocol number to each new trial. Take care not to assign to a new trial a protocol number used previously. Also, check that the protocol number notified to the TGA matches the version of the protocol approved by the Human Research Ethics Committee. When notifying additional sites, quote the protocol number exactly.
  - The TGA assigns a unique clinical trial number. The clinical trial number will appear on an acknowledgement letter from the TGA. Subsequent notifications to TGA of additional trial sites and other correspondence relating to the clinical trial post acknowledgement, such as reporting of adverse reactions, should include the protocol number and the clinical trial number as points of reference.

## SECTION 1. TO BE COMPLETED BY THE SPONSOR OF THE TRIAL

### 1.1 Sponsor of the trial

Complete this section for all notifications. Use name stated in CTX application

Sponsor name  
(Enterprise Business Name)

Enterprise ID Code

### 1.2 Investigational drug/ medical device

Use active name(medicines) or device name. Details must be consistent with those contained in CTX application (Part 1 form).

1.

2.

3.

CTX Number

Complete for all notifications. Use the number assigned by TGA to the CTX application

Relevant TGA file  
number(s) from  
previous  
correspondence

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### 1.3 Notification Type

Complete this section for all notifications. Select one box only. If multiple sites are being notified, complete a 'Trial Site Details' page for each site.

Initial notification of a new CTX trial (single site)

Subsequent notification of a single additional site

Initial notification of a new CTX trial (multiple sites)

Subsequent notification of multiple additional sites

### 1.4 Trial details

Protocol Number  
(Complete for all notifications;  
maximum of 20 characters)

Trial start date

Expected completion date



Title of study

Maximum of 255 characters. Title should indicate the aim of the trial and give a broad description of the trial. Include, for example: phase, indication(s) being treated, main medicines and comparators, use of placebo-control, focus of the study, patient population and any other significant or novel aspects. "A Trial of X" is not adequate. Similar detail is required for device trials.


**Trial Type**

Complete for trials involving the use of medicines only; tick relevant box(es) or otherwise describe.

Phase 1  Phase 2  Phase 3  Phase 4  Bioavailability/bioequivalence

Describe if necessary

**This trial**

Complete for initial notification of new trial only; tick only those boxes which are applicable.

is placebo controlled  is a multicentre trial   
is also being conducted in other countries  Is comparator controlled

**Comparators**

1	Active name	<input type="text"/>		
	Trade name	<input type="text"/>	Dosage form	<input type="text"/>
	Route of administration	<input type="text"/>	Strength	<input type="text"/>
2	Active name	<input type="text"/>		
	Trade name	<input type="text"/>	Dosage form	<input type="text"/>
	Route of administration	<input type="text"/>	Strength	<input type="text"/>
3	Active name	<input type="text"/>		
	Trade name	<input type="text"/>	Dosage form	<input type="text"/>
	Route of administration	<input type="text"/>	Strength	<input type="text"/>

## 1.5 Trial site details

Complete for all notifications. Submit a Trial Site Details page for each site at which the trial will be conducted. Enter the name and location of the site (eg. name and address of hospital, institution, clinic or practice). For large institutions, the address need not include specific department details unless essential to identify the location or unless the unit /body/practice operates as a separate entity within the campus. In some rare circumstances, it will be appropriate to notify a trial as a composite site trial. For example, a GP-based trial conducted by a general practice network may need to be notified as a composite site trial. The site details should indicate clearly that there are multiple sites involved and include the name, address and contact numbers for the principal investigator. A list of all practices (sites) involved should be submitted as an attachment. The ethics committee and approving authority for such a trial must have appropriate authority for all sites operating. A sponsor intending to notify a composite site for the first time should contact the Experimental Drugs Section if they have any questions regarding the use of composite sites.

Site

Site address

<input type="text"/>
<input type="text"/>

Post code

**1.6 Sponsor certification**

Complete this section last for all notifications. In the Name field, print the name of the person signing the form on behalf of the company, organisation, institution, body or individual sponsoring the trial. In the Position field, state the person's position within, or relationship to, the entity sponsoring the trial.

I, the undersigned, certify:

- the TGA has approved the supply of the investigational product(s) listed in section 1.2 of this form;
- all details contained in this form are true and accurate and all required information and signatures have been included;
- the sponsor of the trial has met or agrees to meet all Human Research Ethics Committee conditions of approval;
- the sponsor of the trial named in section 1.1 of this form is taking overall responsibility for the conduct of the trial;
- the investigator(s) has/have training and experience relevant to the conduct of this trial;
- the participating institution has resources adequate for the proper conduct of the trial;
- the sponsor of the trial has received an undertaking from the investigator(s) to conduct the trial in accordance with the Guidelines for Good Clinical Practice as described in regulation 12AB(2)(a) of the Therapeutic Goods Regulations and the National Statement of Ethical Conduct in Research Involving Humans as described in regulation 12AD(c) of the Therapeutic Goods Regulations;
- the sponsor of the trial agrees to report all serious and/or unexpected adverse reactions to the Therapeutic Goods Administration;
- the sponsor of the trial agrees to conduct the trial in accordance with the Guidelines for Good Clinical Practice as described in regulation 12AB(2)(a) of the Therapeutic Goods Regulations and the National Statement of Ethical Conduct in Research Involving Humans as described in regulation 12AD(c) of the Therapeutic Goods Regulations;
- the sponsor of the trial agrees to comply with requests by an authorised person, whether made before or after the start of a clinical trial, to give information about the conduct of the clinical trial and allow an authorised officer (regulation 47AA of the Therapeutic Goods Regulations) to do the things mentioned in regulation 12AC and regulation 12AB of the Therapeutic Goods Regulations; and
- the sponsor accepts that information concerning the use of unregistered therapeutic goods may be released to State and Territory regulatory authorities.

Name (Print)

Position

Signature   
/ /

Phone

Fax

## SECTION 2. TO BE COMPLETED BY THE PRINCIPAL INVESTIGATOR

*The principal investigator is the person responsible for the conduct of the clinical trial at a trial site. In the case of a trial being conducted by a team of individuals at the site, the principal investigator is the responsible leader of the team.*

### Principal investigator certification

I, the undersigned:

- am the principal investigator at the site shown in section 1.5 of this form;
- agree to personally supervise the clinical trial at this site in accordance with the relevant current protocol(s) and will only make changes in a protocol after approval by the sponsor;
- have received and read the trial protocol and other relevant information;
- have met or agree to meet all Human Research Ethics Committee conditions of approval for this trial:
- acknowledge my obligations with respect to monitoring patient safety, record management and reporting requirements for adverse events;
- agree to ensure that all associates, colleagues and employees assisting in the conduct of the trial are informed of their obligations in meeting the above requirements;
- agree to promptly report to the Human Research Ethics Committee all unanticipated problems and will not make any changes to the trial without Human Research Ethics Committee and sponsor approval, except where necessary to eliminate apparent immediate hazards to subject safety;
- agree to conduct the trial in accordance with the Guidelines for Good Clinical Practice as described in regulation 12AB(2)(a) of the Therapeutic Goods Regulations and the National Statement of Ethical Conduct in Research Involving Humans as described in regulation 12AD(c) of the Therapeutic Goods Regulations;
- agree to comply with requests by an authorised person, whether made before or after the start of a clinical trial, to give information about the conduct of the clinical trial and allow an authorised officer (regulation 47AA of the Therapeutic Goods Regulations) to do the things mentioned in regulation 12AC and regulation 12AB of the Therapeutic Goods Regulations; and
- accept that information concerning the use of unregistered therapeutic goods may be released to State and Territory regulatory authorities.

Name (Print)

Phone

Signature

Fax

### SECTION 3. TO BE COMPLETED BY THE HUMAN RESEARCH ETHICS COMMITTEE RESPONSIBLE FOR MONITORING THE TRIAL

This section must be completed by a Human Research Ethics Committee (HREC) that satisfies the following definition of an ethics committee, as set out in the Therapeutic Goods Act 1989, otherwise the notification is invalid:

A committee constituted and operating in accordance with guidelines issued by the National Health and Medical Research Council as in force from time to time and which has notified its existence to the Australian Health Ethics Committee.

HREC certification should not be given until all conditions of approval of the protocol by that HREC have been met. Wherever possible, the certification should be completed by the Chair or Deputy Chair of the Human Research Ethics Committee. Guidelines for the approval of clinical trials by HRECs are located at Chapter 12, The National Statement on Ethical Conduct in Research Involving Humans, 1999 and in the TGA publication 'HRECs and the Therapeutic Goods Legislation'.

For trials of gene therapy and related therapies, the proposal must be approved by all relevant bodies as per the NHMRC Guidelines for Ethical Review of Research Proposals for Human Somatic Cell Gene Therapy and Related Therapies.

HREC name

HREC address

<input type="text"/>	
<input type="text"/>	Postcode

Protocol Number approved by HREC

#### Human Research Ethics Committee Certification

I, the undersigned, certify:

- I am a member of the above named Human Research Ethics Committee;
- the above named Human Research Ethics Committee is a properly constituted ethics committee and operates in accordance with the guidelines issued by the National Health and Medical Research Council and has notified its existence to the Australian Health Ethics Committee;
- the above named Human Research Ethics Committee, having regard to the guidance provided by the *National Statement on Ethical Conduct in Research Involving Humans* and, where applicable, the *Guidelines for Ethical Review of Research Proposals for Human Somatic Cell Gene Therapy and Related Therapies*, has approved the clinical trial protocol identified above and has assumed responsibility for monitoring the conduct of the trial; and
- the above named Human Research Ethics Committee agrees to comply with requests by an authorised person, whether made before or after the start of a clinical trial, to give information about the conduct of the clinical trial and allow an authorised officer (regulation 47AA of the Therapeutic Goods Regulations) to do the things mentioned in regulation 12AC and regulation 12AB of the Therapeutic Goods Regulations.

Name (Print)

Position

Signature

  
  
/ /

Phone

Fax

## SECTION 4. TO BE COMPLETED BY THE AUTHORITY APPROVING THE CONDUCT OF THE TRIAL

Complete for all notifications. In cases where the Human Research Ethics Committee or Approving Authority for more than one site is the same, it is still necessary to submit a Trial Site Details Page for **each** site. The bodies approving the conduct of the trial at each site need to be declared individually. This requirement also still applies in cases where, for example, an Area Health Service or Hospitals Group may encompass several different institutions.

The Approving Authority must appoint a person to be responsible for giving approval on its behalf. The terms of approval for the conduct of the trial must be consistent with the Human Research Ethics Committee's (HREC) recommendations and these terms must be no less restrictive than the HREC advice.

Approving Authority name

Address   
 Postcode

### Approving Authority Certification

I, the undersigned

- am authorised to represent the body, organisation or institution at which the above mentioned clinical trial will be conducted and, having regard to the advice and approval of the trial protocol by the Human Research Ethics Committee responsible for monitoring the trial at this site, give approval for this trial to proceed;
- undertake that the use of the drug will comply with all relevant Commonwealth and State or Territory legislation; and
- undertake to comply with requests by an authorised person, whether made before or after the start of a clinical trial, to give information about the conduct of the clinical trial and allow an authorised officer (regulation 47AA of the Therapeutic Goods Regulations) to do the things mentioned in regulation 12AC and regulation 12AB of the Therapeutic Goods Regulations.

Name (Print)

Position

Signature   
/ /

Phone

Fax

**APPENDIX 4. HREC LETTER OF ENDORSEMENT FOR AUTHORISED  
PRESCRIBERS**

## ETHICS COMMITTEE LETTERHEAD

[Dr's name]  
[Title (if applicable)]  
[Dr's address]

Dear Dr [     ],

### **Ethics committee endorsement for the purpose of becoming an Authorised Prescriber of an unapproved product under section 19(5) of the Therapeutic Goods Act**

The [name] Human Research Ethics Committee hereby endorses you for the purpose of becoming an Authorised Prescriber under section 19(5) of the Therapeutic Goods Act.

This endorsement is restricted to the following circumstances:

Unapproved product:	[drug/ device: trade and generic names if available]
Indication for use:	[illness/condition/class of patient]
Site(s) covered by the endorsement:	[hospital/rooms etc]
Conditions imposed by the HREC:	[provision of usage reports to HREC] [reporting of adverse events to HREC]

Please present a copy of this endorsement letter to the TGA as part of your application to become an Authorised Prescriber.

Yours sincerely

[     ]  
Chair  
[     ] Human Research Ethics Committee  
Date     /     /



**APPENDIX 5. CONSENT TO TREATMENT AND INDEMNITY FOR USE OF  
PRODUCTS DERIVED FROM HUMAN BLOOD OR PLASMA**

**SPECIAL ACCESS SCHEME**  
**Consent to Treatment and Indemnity for Use of**  
**Products Derived from Biological Tissues including Human Blood or Plasma**

I, .....  
(name of patient or parent/guardian)

understand that the Commonwealth can give no guarantee as to the quality, safety or efficacy of  
.....(name of product),

particularly as regards any prion or viral inactivation procedures used in its manufacture.  
Accordingly, the Commonwealth can accept no liability for its safety, quality or efficacy.

I understand that this product is not registered for use in Australia but that use of the product may  
be approved under the provisions of the Special Access Scheme.

I confirm that the above statements have been explained to me and with this knowledge agree to  
administration of the product to me/my ward.

**Patient's name:** .....

**Signature of patient:** ..... **Date:** .....  
(or parent/guardian)

**Signature of witness:** ..... **Date:** .....

I have explained the above statements to the patient or the patient's parent/guardian.

**Treating physician:** .....

**Signature:** ..... **Date:** .....

*Fax completed form together with request for SAS approval to:  
The SAS Officer, TGA on 02 6232 8112*