Introduction to changes to the TGA’s Clinical Trial Notification (CTN) process

Adelina Tan
Director, Experimental Products
Scientific Evaluation and Special Product Access Branch
Market Authorisation Division, TGA
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Introduction overview

• Background
• Benefits
• What preparation is required by clinical trial sponsors?
Background

• The current CTN process is paper based and quite burdensome administratively

• Responding to sponsors request for an electronic lodgement system – improved efficiency

• Errors in data reporting

Inaccuracies in clinical trial statistics for the reporting period 2009-2012
Benefits

• Improved external and internal tracking of documents (no lost signed originals)
• Reduction in need to follow up information that may not be legible (typed over hand written)
• Sponsor instantly knows that the CTN has been received by the TGA (no need to contact the TGA to confirm receipt)
Benefits

• The status of the CTN is known to the sponsor e.g. under review
• Variations to the original application are streamlined by using the original data set
• Reports will be more detailed and with a higher degree of accuracy
Benefits

• All clinical trial documentation relevant to the CTN will be accessible on TGA Business Services (TBS)
• There will be no need for Sponsor, Principal Investigator (PI), Human Research Ethics Committee (HREC) or Approving Authority (AA) certification on the form
• A guide on how to complete the CTN form will be available on TBS and the form will contain tool tips
Benefits

• More accurate, timely and detailed reports, if organisations request information from the TGA

• Clinical trial activities and trends can be identified - could improve Australia as a better choice for the conduct of clinical trials

• TGA time currently spent on administrative activities can be value added to review of CTN submissions space

• Closing the loop - much easier for sponsors to inform the TGA when a clinical trial is complete
What preparation is required by clinical trial sponsors?

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TGA Business Services

28 April 2015

TGA Business Services establishes a base for electronic commerce, electronic lodgement of data packages in support of applications for entry of products onto the Australian Register of Therapeutic Goods and enables online client access to legally appropriate information. The Terms and Conditions for using TGA Business Services are available.

Open TGA Business Services
Go to the TGA Business Services website.

TGA Business services: getting started with the TGA
Introduction to TGA online services for sponsors, agents and manufacturers.

TGA Business Services: how to use the site
The TGA Business Services site allows industry to manage some therapeutic good registration applications, and view and cancel their current entries on the Australian Register of Therapeutic Goods (ARTG).

TGA Business Services forms
What preparation is required by clinical trial sponsors?

- Apply for your client identification number – about 3 working days
- Apply for access to TBS – about 3 working days
- Once the TBS Helpdesk receives your completed Organisation details form, a Administrator Account is created for the nominated person – this enables that person to control who has access to the information
What preparation is required by clinical trial sponsors?

• Administrator for the organisation will be able to set up different user accounts e.g. Drafter, Submitter, Finance

• The users of your account can then access your secure TBS portal to:
  – submit CTN forms
  – pay invoices online
What preparation is required by clinical trial sponsors?

- TGA webpage – TGA Business Services – how to use the site
  - Video
  - Frequently asked questions
- TBS Helpdesk available to answer further enquiries
  - Email: ebs@tga.gov.au
  - Phone: 1800 010 624
CTN/ Clinical Trial Exemption (CTX) online submission - overview

- Unapproved therapeutic goods
- Clinical trials
- Online submission form for CTN/CTX
What is an unapproved therapeutic good?

- Generally, therapeutic goods must be entered in the Australian Register of Therapeutic Goods (ARTG) to be lawfully supplied in or exported from Australia.
- Goods that do not appear on the ARTG, or ARTG goods being used outside of marketing approval are considered unapproved goods.
- Unapproved goods have not been evaluated by the TGA for quality, safety or efficacy.
Avenues to supply unapproved therapeutic goods

Use in clinical trials
- CTN
  - Section 18(1), Section 31A(1), Reg 12 & Schedule 5A, Item 3

Personal Importation
- CTX
  - Section 19, esp 19(1)(b)
  - Section 31B(1) & (2) & Regs 12AA-AD

Special Access Scheme
- Category A
  - Section 18, Section 31A(2) & Reg 12A

Authorised Prescriber
- Category B
  - Section 19, esp 19(1)(a)* Section 31B(1)

Exemptions for 'supply in the interests of public health'

Temporary supply problem
- Section 19A(1)

Therapeutic breakthrough
- Section 19A(2)

TGA officers

Authorised by external delegate
- Reg 47A

Introduction to changes to the TGA’s Clinical Trial Notification (CTN) process
TGA’s role in clinical trials differs from some other regulators

• Main focus is on **access to unapproved medicines and devices** for trials rather than end-to-end regulation of trials

• **CTX/CTN schemes required** for any product not entered on the ARTG or use of a product in a clinical trial beyond the conditions of its marketing approval
# CTN vs CTX Schemes - overview

<table>
<thead>
<tr>
<th>CTN</th>
<th>CTX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Notification process</td>
<td>Approval process</td>
</tr>
<tr>
<td>One step process</td>
<td>Two step process – part 1 (approval) part 2 (notification)</td>
</tr>
<tr>
<td>Medicines, devices or biologicals</td>
<td>Medicines, devices or biologicals but <strong>required</strong> for certain class 4 biologicals</td>
</tr>
<tr>
<td>No TGA review of data prior to trial</td>
<td>TGA evaluates the proposed Usage Guidelines</td>
</tr>
<tr>
<td>Trial cannot commence without valid notification and fee paid</td>
<td>Trial cannot commence without Part 1 being approved</td>
</tr>
<tr>
<td>Assurances pertaining to the trial conduct and protocol are provided by the sponsor, HREC, PI and AA</td>
<td>Assurances pertaining to the trial conduct and protocol are provided by the sponsor, HREC, PI and AA</td>
</tr>
<tr>
<td>Each additional trial site notified before commencing trial at that site</td>
<td>May conduct <strong>any number of clinical trials</strong>, provided use of the product falls within the original approved Usage Guidelines</td>
</tr>
</tbody>
</table>

- Each additional trial site notified before commencing trial at that site

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Legal responsibilities

• All trials must have an Australian sponsor who initiates, organises and supports a clinical study and carries the medico-legal responsibility.
Guidelines for Clinical Trials

• Conduct of the proposed trial should be in accordance with:
  – National Health Medical Research Council (NHMRC)
    National Statement on Ethical Conduct in Research Involving Humans (2007)
  – Declaration of Helsinki
  – Note for Guidance on GCP or the ISO 14155 Clinical Investigation of Medical Devices
  – relevant Commonwealth and/or State/Territory laws
Guidelines for manufacturing

• Generally, a facility manufacturing therapeutic goods, including Investigational Medicinal Products (IMP) and placebo, for supply in Australia must comply with appropriate GMP standards and must be licensed accordingly.

• The TGA has adopted the *PIC/S Guide for Good Manufacturing Practice for Medicinal Products 2009*, with Annex 13 of this guide referring to the manufacture of IMP.
Clinical trial statistics

2014 total new trials – 967
Total notifications (number of sites) – 3762

New trial notifications that include a therapeutic good received by phase

<table>
<thead>
<tr>
<th></th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Jul-Dec</td>
<td>Jan-Jun</td>
<td>Jul-Dec</td>
</tr>
<tr>
<td>Phase 1</td>
<td>85</td>
<td>65</td>
<td>132</td>
</tr>
<tr>
<td>Phase 2</td>
<td>128</td>
<td>86</td>
<td>102</td>
</tr>
<tr>
<td>Phase 3</td>
<td>155</td>
<td>131</td>
<td>70</td>
</tr>
<tr>
<td>Phase 4</td>
<td>34</td>
<td>28</td>
<td>32</td>
</tr>
<tr>
<td>Bioavailability/equivalence</td>
<td>5</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>None specified</td>
<td>9</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td>Total</td>
<td>416</td>
<td>326</td>
<td>355</td>
</tr>
</tbody>
</table>

*this number now combines those CTNs which involve device(s)
Online submission of CTN / CTX

• Currently paper driven, manually entered into a database
• New form completed and submitted online
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Introducing changes to the TGA's Clinical Trial Notification (CTN) process

![Clinical Trial Notification (CTN) process screenshot]

The screenshot illustrates the Clinical Trial Notification (CTN) process for eBusiness Services, focusing on the section for Trial Details.

Key features highlighted in the screenshot include:

- **Contact Information**: Fields for the contact name (Adelina Tan), contact phone number (0262328046), and email address (adelina@domain.com.au).
- **Protocol Number**: Blank field.
- **Expected Trial Start Date**: 22/06/20131.
- **Expected Completion Date**: 19/12/1990.
- **Potential use of restricted goods**: Yes.
- **Title of Study**: Blank field.
- **Trial Type**: Phases 1, 2, and 3.
- **This Trial**: Involves animal experiments.
- **Total Number of Patients to be Enrolled in Trial Therapeutic Area**: Blank field.

The screenshot also highlights an error message: "The string entered is not a valid email address."
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The Medicine Details form includes fields for:

- Trade/Product/Code Name
- Is this a combination product?
- Dosage Form
- Presentation
- Route of Administration
- Formulation
- Indication
- Dosage and Frequency
- Intended Use
- For a medicine not in Phase 1, is the medicine manufactured in Australia?
- Manufacturer details

The form also includes buttons for adding ingredients and removing selected ingredients.
Why placebos should be entered on the CTN
Under the *Therapeutic Goods Act 1989*, therapeutic goods means goods:
(a) that are **represented in any way** to be...
(i) **for therapeutic use**; or...
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### Introduction to changes to the TGA’s Clinical Trial Notification (CTN) process

#### Submissions

<table>
<thead>
<tr>
<th>Approval Area</th>
<th>Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsor</td>
<td>All Sponsors</td>
</tr>
<tr>
<td>Filter on</td>
<td>Received</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Received</th>
<th>Identifier</th>
<th>Workflow Status</th>
<th>Description</th>
<th>Product Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015-06-11</td>
<td>CT-2015-CRN-0016</td>
<td>Under Review</td>
<td>A single phase 1 study with 200 mice and one shot of buprop.</td>
<td>Alphapharm Pty Ltd</td>
</tr>
<tr>
<td>2015-06-11</td>
<td>CT-2015-CRN-0019</td>
<td>Under Review</td>
<td>An open-label lesion controlled study of Electroportation Therapy (EPT) for the treatment of Cullen's.</td>
<td>Alphapharm Pty Ltd</td>
</tr>
</tbody>
</table>

- **Biologicals**
- **Clinical Trials**
  - Clinical Trial Notification Application
  - Submission
- **Export Only Medicine**
- **Listed Medicine**
- **Manufacturers**
- **Medical Device**
- **Medicine Shortages**
- **Over The Counter Medicine**
- **Substance**
- **Prescription Medicine**
- **Lodge Supporting Documentation**
- **Maintain User Account**
- **Your TGA Information**
- **Sponsor Cancellation**
- **Online Invoice Payment**
- **Public TGA Information**
- **News**
- **Help**
- **Training**
- **Secure Email**
- **Logout**
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Before submitting your application(s) please read the declaration below and click the Accept button to proceed with this submission; or click on the Decline button to return to the Submission form.

In this declaration, unless the contrary intention appears:
- It means the individual assigned to the eTGA login ID associated with the submission of this form to the TGA.
- Secretary means the Secretary of the Department of Health and includes a delegate of the Secretary.
- Sponsor means the company, organization, institution, body or individual that is notifying the TGA as named in the ‘Sponsor Name’ field located on the application tab of this notification.

Declaration

By clicking the Accept button:

I declare that I am authorised by the sponsor to notify the TGA on its behalf in relation to this clinical trial.

I acknowledge that:

- The sponsor is taking overall responsibility for the trial.
- The relevant goods only remain exempt by reason of their use in the clinical trial only for so long as:
  - the approval of the goods for the trial has been given by the sponsor having regard to the advice of the ethics committee responsible for monitoring the conduct of the trial, or terms no less restrictive than terms advised by that committee.
  - the sponsor has not received advice from the committee that is not inconsistent with the continuation of the trial.
  - the requirements in regulation 12AD of the Therapeutic Goods Regulations 1990 (in the case of therapeutic goods other than medical devices) and regulation 7.5 of the Therapeutic Goods (Medical Devices) Regulations 2002 (in the case of medical devices) are complied with, indicating that the use of therapeutic goods in the trial must be in accordance with the Guidelines for Good Clinical Practice as defined in the Therapeutic Goods Regulations.
  - the Secretary has not under Item 3 of Schedule 2A of the Therapeutic Goods Regulations (in the case of therapeutic goods other than medical devices) or Item 2.3 in Part 2 of Schedule 4 of the Therapeutic Goods (Medical Devices) Regulations 2002 directed that the trial not be conducted on the basis that the Secretary has become aware that to conduct the trial would be contrary to the public interest.
  - the Secretary can under the Therapeutic Goods Act 1989 (the Act), require the sponsor to provide specified information or documents relating to exempt goods.
  - the Secretary can provide information obtained in response to an authority of the Commonwealth, or a State or Territory that has functions in relation to therapeutic goods or the registration of medical practitioners or pharmacists in the relevant State or Territory.
  - it is an offence under the Act to fail to provide that information or documents required by the Secretary, or to provide information or documents that are false or misleading in a material particular to the Secretary.
  - it is a requirement of the Guidelines on Good Clinical Practice that the sponsor report all serious and unexpected adverse reactions arising from the use of the relevant goods in the trial to the TGA.
  - it is a serious offence under Commonwealth law to provide information for the purposes of this notification that is false or misleading in a material particular.

I declare that all information provided for the purposes of the notification is true and accurate and that all required information has been included.
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Questions?

Enquiries: clinical.trials@tga.gov.au