Check the TGA website for up-to-date guidance

The most up-to-date information about prescription medicine registration in Australia is on the TGA website <http://www.tga.gov.au>. Now that guidance is presented in a series of web pages, updates are likely to be more common than in the past. If you subscribe to the TGA guidelines email alert service, you will be emailed every time the TGA web guidance is updated.

TGA web pages are dated, and can be printed.

A PDF format is being provided during the transition between the former version of the ARGPM (Australian Regulatory Guidelines for Prescription Medicines) and the new web format. Please note that information in the PDF should not be relied upon to be up-to-date.

About the Therapeutic Goods Administration (TGA)

- The Therapeutic Goods Administration (TGA) is part of the Australian Government Department of Health and Ageing, and is responsible for regulating medicines and medical devices.
- The TGA administers the Therapeutic Goods Act 1989 (the Act), applying a risk management approach designed to ensure therapeutic goods supplied in Australia meet acceptable standards of quality, safety and efficacy (performance), when necessary.
- The work of the TGA is based on applying scientific and clinical expertise to decision-making, to ensure that the benefits to consumers outweigh any risks associated with the use of medicines and medical devices.
- The TGA relies on the public, healthcare professionals and industry to report problems with medicines or medical devices. TGA investigates reports received by it to determine any necessary regulatory action.
- To report a problem with a medicine or medical device, please see the information on the TGA website <http://www.tga.gov.au>.
# Version history

<table>
<thead>
<tr>
<th>Version</th>
<th>Description of change</th>
<th>Author</th>
<th>Effective date</th>
</tr>
</thead>
<tbody>
<tr>
<td>V1.0</td>
<td>Updated for web publication</td>
<td>Therapeutic Goods Administration</td>
<td>25/06/2013</td>
</tr>
<tr>
<td>V1.1</td>
<td>Updated document links</td>
<td>Therapeutic Goods Administration</td>
<td>12/07/2013</td>
</tr>
<tr>
<td>V1.2</td>
<td>Updated document links</td>
<td>Therapeutic Goods Administration</td>
<td>05/08/2013</td>
</tr>
<tr>
<td></td>
<td>Inclusion of Section 7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>V1.3</td>
<td>Removed storage box size requirement from Section 5.6</td>
<td>Office of Medicines Authorisation</td>
<td>25/09/2013</td>
</tr>
</tbody>
</table>
Contents

Introduction 7

1 When to provide hard and electronic submission dossiers for prescription medicines 7

2 General submission dossier requirements 8
   2.1 CTD Format 8
      2.1.1 If CTD Modules or documents are not required 8
      2.1.2 If documents are required, but not provided 8
      2.1.3 Related information and guidance on justifications 8
   2.2 Formatting for documents 9
      2.2.1 Language 9
      2.2.2 Fonts 9
      2.2.3 Legibility 9
      2.2.4 Page numbering of submission dossiers 9
   2.3 Physical condition of the submission dossier and security during transport 10

3 Electronic submission dossiers for prescription medicines 10
   3.1 File format for electronic copies of the submission dossier 10
      3.1.1 Related information and guidance 10
   3.2 Security on electronic files 11
   3.3 Transmission media 11
      3.3.1 Number of discs used 11
      3.3.2 Labelling of each disc submitted with a NeeS submission dossier 12
   3.4 Number of copies of the electronic submission dossier 12
   3.5 Packing and dispatch of electronic submission dossiers 12
4 Using electronic formats to print the hard copy dossier

4.1 Structure of paper dossier produced from NeeS or eCTD format 13

4.2 Use of tab identifiers 13

4.3 Printed table of contents 13

4.3.1 NeeS format 13

4.3.2 eCTD format 13

4.4 Headers and footers 14

4.5 Reference to previous submissions and lifecycle attributes 14

5 Hard copy submission dossiers for prescription medicines 14

5.1 Paper size and printing 14

5.2 Binding 15

5.3 Dividing the submission dossier into volumes (binders) 15

5.3.1 Volume contents 15

5.3.2 Tab identifiers and other requirements 17

5.3.3 Multiple versions of a document 17

5.3.4 Related information and guidance 17

5.4 Volume identification in a submission dossier 18

5.4.1 Module and volume numbering 18

5.4.2 Numbering of copies 18

5.4.3 Contents that span more than one volume 19

5.5 How many hard copies are required? 19

5.6 Packing a submission dossier for dispatch 20

5.6.1 Labelling requirements 20

5.6.2 Address for dispatching the submission dossier 21
6 Subsequent or additional data

6.1 When responding to s. 31 request for information

6.1.1 For hard copy data

Did you know?

7 Submission dossier checklist for prescription medicines
Introduction

This guidance is to assist sponsors to prepare submission dossiers for:

- category 1 and 2 applications
- category 3 applications
- other variations to registered prescription medicines.

1 When to provide hard and electronic submission dossiers for prescription medicines

Provide both hard and electronic copies of the submission dossier for Category 1 and 2 applications, with the exception of applications for additional trade names.

For all other application types provide the submission dossier in hard copy. In addition to the hard copy an electronic copy will be accepted.

Ensure that your letter of application or cover letter contains a declaration that the hard and electronic copies of the submission dossier are either:

- identical (including signatures)
- if not identical, ensure the declaration specifies any differences.

Note: You may include the individual patient data (located in Module 5) in the electronic copy of the submission dossier only.
2 General submission dossier requirements

2.1 CTD Format

Use the CTD format for hard copy dossiers regardless of whether any previous application was/was not in CTD format.

Use non-eCTD electronic submission (NeeS) format for the electronic copy of dossier. Ensure Module 1 complies with the Australian CTD Module 1 requirements, and that Modules 2, 3, 4, and 5 comply with the EU CTD documents adopted in Australia.

Do not modify the overall organisation of the CTD format.

Note: Applications may not be effective if the submission dossier does not comply with the CTD format AND/OR the submission dossier is not complete.

2.1.1 If CTD Modules or documents are not required

Do not include modules and documents that are not required for a specific application, or application type. It is not necessary to include ‘not applicable’ pages or tab identifiers for CTD documents that are not required.

2.1.2 If documents are required, but not provided

If you do not include a required document, or do not comply with a guideline, provide, where applicable, a robust scientific justification.

2.1.3 Related information and guidance on justifications

- Electronic format submission dossiers for prescription medicines
- Hard copy submission dossiers for prescription medicines
- Mandatory requirements for an effective application
- Section 2.3 of Information for sponsors completing a pre-submission planning form
2.2 Formatting for documents

2.2.1 Language

Ensure:

- all information in the submission dossier is in English and legible
- any acronyms and abbreviations are defined the first time they are used in each module.

For information that is not in English, include both:

- a copy of the information in the original language
- a full translation of the information into English.

Note: You are responsible for the translation.

2.2.2 Fonts

Ensure font sizes for:

- text is no smaller than 12 points
- text in tables is no smaller than 10 points
- footnote text is no smaller than 10 points.

2.2.3 Legibility

Ensure that:

- all text and tables are of a style and size that are large enough to be easily legible, even after photocopying or when printed
- shading in tables does not impair clarity or legibility.

2.2.4 Page numbering of submission dossiers

Ensure:

- each document is numbered sequentially, and divided from other documents by a tab
- page numbering is at the document level and not at the volume or level
- all documents have page numbers.
Do not:

- number the entire submission dossier consecutively by page
- number documents with more than one set of page numbers.

When cross referencing to documents:

- refer to the module, volume, tab identifier, and page number. Example: see Module 3, Volume 6, 3.2.P.4.3 Method validation, p 23.

2.3 Physical condition of the submission dossier and security during transport

You are responsible for:

- The physical security of the submission dossier during transportation.
- The submission dossiers arriving at the TGA undamaged (e.g. not crushed, broken, wet, contaminated, etc).

3 Electronic submission dossiers for prescription medicines

3.1 File format for electronic copies of the submission dossier

Ensure the:

- product information documents are in both MS Word and PDF format
- remaining documents are PDF documents
- PDF documents are text searchable (produced from an electronic source document).

3.1.1 Related information and guidance

- Electronic submission dossier requirements
3.2 Security on electronic files

Ensure there are no:

- submission or file-level security; one-time security settings; or password protection applied to any files
- security settings to open any individual file, including:
  - passwords
  - certificate security
  - adobe policy server settings.

Do not apply any further security settings to an individual file, except literature references in Modules 3.3, 4.3, and 5.4 that have pre-existing security.

For example, in Adobe Acrobat all restrictions should be 'allowed' when viewing the Document Properties > Security settings > Permissions >.

3.3 Transmission media

Provide the electronic copy of the submission dossier on either CD-R or DVD-R.

Ensure discs are:

- single-sided
- single or dual layer
- archival quality.

Ensure that you do not use:

- double-sided discs
- rewritable discs (protection, authenticity, and stability of information cannot be guaranteed)
- other storage media, including:
  - USB keys
  - solid state storage devices
  - hard drives
- zipped files when sending CDs or DVDs.

3.3.1 Number of discs used

Provide the electronic information on the smallest number of discs possible.

Use a single DVD if an individual NeeS format submission dossier will span several CDs.
Do not split individual CTD modules over multiple discs when the application spans multiple discs. For example, a single disc should contain all of Module 1, another all of Module 2, and so on.

3.3.2 Labelling of each disc submitted with a NeeS submission dossier

Ensure each disc includes the following label information, clearly presented and printed on both the disc and its case:

- name of sponsor
- name of medicine
- AAN of the active substance(s)
- submission ID
- format: NeeS
- the four digit number(s) used for the NeeS contained on the CD/DVD (0000 or a sequential number).

3.4 Number of copies of the electronic submission dossier

Provide three (3) copies of the complete electronic submission dossier for applications for New Chemical Entities, Fixed Combinations and Extension of Indications.

For all other applications provide one (1) copy of the complete electronic submission dossier.

3.5 Packing and dispatch of electronic submission dossiers

Lodge the electronic copy of the submission dossier with the hard copies of the submission dossier.

Ensure the electronic copy is safely packed to arrive at the TGA undamaged.
4 Using electronic formats to print the hard copy dossier

4.1 Structure of paper dossier produced from NeeS or eCTD format

Ensure that the structure of a paper submission dossier produced from a NeeS or eCTD electronic format dossier is in accordance with the sequence of documents as referenced in either:

- the XML backbone of the eCTD
- the overall table of contents of the NeeS.

Ensure the sequence of documents meets CTD regulatory requirements.

Where a document appears in several locations of the eCTD backbone or NeeS table of contents, ensure it only appears once in the hard copy submission dossier.

4.2 Use of tab identifiers

Ensure tab identifiers are used in the table of contents as references to documents.

4.3 Printed table of contents

4.3.1 NeeS format

Ensure the comprehensive table of contents includes a complete list of all documents provided in the application (by Module).

The NeeS Table of contents are printed directly (either a single ctd-toc.pdf for the entire submission the individual module ToCs—mx-toc.pdf).

4.3.2 eCTD format

Ensure the index.xml and au-regional backbones, as viewed using style sheets and converted to PDF, are printed and serve as the Table of contents in the paper submission dossier.

For Module 1, print the au-regional.xml via the style sheet to create the Table of contents.
Place the comprehensive Table of contents for all based on index.xml before Modules 2, 3, 4, and 5 of the paper submission dossier. There is no need to create module specific Table of contents.

### 4.4 Headers and footers

Ensure the header and footer information in the paper submission dossier is identical to the information contained in the documents in the NeeS or eCTD format dossier.

### 4.5 Reference to previous submissions and lifecycle attributes

In the eCTD, references to previous submissions or operation attributes in XML leaves can be used for automated lifecycle management of submissions.

They are interpreted and processed by eCTD viewing tools to present a history of the information on a medicinal product.

The paper submission dossier should be identical in content to the eCTD sequence or NeeS format submission, and need not contain content that may be referred to from the submission but provided electronically in a previous submission.

### 5 Hard copy submission dossiers for prescription medicines

#### 5.1 Paper size and printing

Use standard A4 paper for all applications. Ensure there is a wide left-hand margin so that information is not obscured by binding. Prepare text and tables using margins that allow the document to be printed on A4 paper.

When printing documents double sided, ensure:

- legibility is not impaired
- margin space is sufficient on all sides so that information is not obscured when the page is placed in a binder
- page numbers are applied to both sides of each page
- binders are of a type that will open flat.
5.2 Binding

Lodge all data (including responses to TGA requests for information) that exceeds 20 pages in a binder (volume). Ensure binders have durable covers, and allow the content to be dismantled and reassembled.

Ensure the external dimensions of binders do not exceed:

- 270 mm in width
- 320 mm in height
- 80 mm in thickness.

Note: Do not overfill binders as this can lead to loss of contents.

5.3 Dividing the submission dossier into volumes (binders)

Provide the hard copy of the submission dossier in binders. Each binder is called a ‘volume’. The amount of information in a volume is restricted by the size of the binder.

5.3.1 Volume contents

A volume can contain several documents from within one module, providing they are in consecutive order, as specified by the relevant CTD module.

An illustration of how this is achieved can be seen in Figure 1 below:
Therapeutic Goods Administration

Figure 1: CTD format submission dossier

**Note:** The only exception to this is a requirement that a particular document be the only document within a volume. For example, provide Module 1 Annex 1, Annex 2, and the risk management plan in individual volumes, without any other CTD documents.
5.3.1.1 Related information and guidance

- CTD Module 1 (Annex 1 and 2, and Module 1.13)

5.3.2 Tab identifiers and other requirements

Ensure all documents are separated by appropriately named tab identifiers.

The name for the tab identifier is the name of the document (e.g. 'application form') or the section heading according to the CTD format (e.g. 3.2.P.4.2). If the full name of the document is too long for the tab identifier, an alternative name that adequately identifies the document can be substituted.

For Category 1 and 2 applications (other than applications for additional trade names), ensure documents from different CTD modules are in separate volumes.

For all other application types, documents from different CTD modules may be included within the same volumes.

Where additional data is provided to the TGA (e.g. s.31 request responses, or the submission of new safety data), and the information is spread across more than one module, ensure each module is submitted in a separate volume(s). See 'Subsequent data' below for further information.

5.3.3 Multiple versions of a document

Where there are multiple versions of a specific document (e.g. for a fixed combination product the dossier might contain one Module 3.2.S for one drug substance, and another Module 3.2.S for the other drug substance), the documents are to be:

- included in the relevant module sequentially
- titled to include the name of the active ingredient (or component) and manufacturer, or other identifying details, for example:
  - Module 3.2.S Amoxycillin trihydrate, Manufacturer XYZ
  - Module 3.2.S Clavuianic Acid, Manufacturer XYZ.

5.3.4 Related information and guidance

- General Questions and Answers. Common technical document for the registration of pharmaceuticals for human use - Step 5 (CPMP/ICH/5552/02 Rev 2)
5.4 Volume identification in a submission dossier

Label each volume on both the side and the front of the binder.

Include the following information on the front and side labelling for each volume:

- name of sponsor
- name of medicine
- submission number
- module and volume number
- copy number
- content of volume (expressed as CTD document(s)).

5.4.1 Module and volume numbering

Number the volumes for each module separately and sequentially using the format:

- \( x \) of \( y \) volumes (\( x \) is the number for the specific volume and \( y \) is the total number of volumes submitted for the respective module).

For example:

Module 3
Volume 1 of 6

5.4.2 Numbering of copies

Multiple copies of some modules are required to allow for the concurrent evaluation of a Category 1 or Category 2 application by relevant evaluation areas.

Ensure the copies are numbered sequentially, for example:

Module 2
Volume 1 of 6
Copy 1 of 2

5.4.2.1 Related information and guidance

- How many copies are required?
5.4.3 Contents that span more than one volume

Label each volume to show the section(s) it contains, for example, a label of 'Section 3.2.P.4' would indicate:

3. – Module 3—Quality
2. – Body of data
P. – Product
4. – Control of excipients

Whilst modules can be split across volumes do not split documents within the modules unless the document will not fit into a single binder.

5.4.3.1 Related information and guidance

- Binder requirements

5.5 How many hard copies are required?

Multiple hard copies of some modules are required to allow for the concurrent evaluation of a Category 1 or Category 2 application by the relevant evaluation areas.

Provide hard copy submission dossiers in the quantities indicated in the table below:

<table>
<thead>
<tr>
<th>Module</th>
<th>Category 1/category 2 applications (excluding additional trade names)</th>
<th>Category 1 additional trade name application</th>
<th>Category 3 application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Module 1</td>
<td>1-3 a</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Module 2</td>
<td>1-3 a</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Module 3</td>
<td>1</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Module 4</td>
<td>1</td>
<td>-</td>
<td>- b</td>
</tr>
<tr>
<td>Module 5</td>
<td>1</td>
<td>-</td>
<td>- b</td>
</tr>
</tbody>
</table>

a. Provide one (1) copy of Module 1 and Module 2 for each Module 3, 4 and 5 submitted i.e., if the application requires the submission of Module 3 and 5 data, two (2) copies of Modules 1 and 2 must be submitted.

b. By legislative definition, a Category 3 application does not require evaluation of nonclinical, clinical, or bioequivalence data. Therefore, Module 4 and 5 data are not required in a Category 3 application.
5.6 Packing a submission dossier for dispatch

Ensure:

- that applications consisting of more than two binders are boxed
- the binders fit into boxes
- the boxes are of a quality sufficient to protect the contents from damage in transit.

Pack boxes with the binder spines to the sides or bottom of the box to prevent binder failure and loss of contents. Use bubble, plastic or shrink wrap around the sides of the box to protect the folders.

Ensure that:

- Individual folders are not bubble-wrapped.
- Polystyrene beads, peanut shells, or other loose materials are not used for packaging.
- The weight of any one box does not exceed 16 kg.
- All boxes are shrink wrapped on the pallet.

5.6.1 Labelling requirements

Number each box sequentially, with box 1 containing volume 1 of Module 1. Clearly identify the contents (including type of submission) for each box on the box label, by copy and module.

Ensure submission dossiers consisting of 10 boxes or more are:

- Shipped using a pallet
- stacked on a pallet in reverse numerical order, with the last box at the base and the first box (box 1) clearly identified and at the top of the pallet.

Include the following information on the shipping manifest:

- details of the sponsor
- submission ID number
- total numbers of pallets
- numbers of boxes per pallet encompassing which box numbers and numbers of copies, i.e., sponsor xxx, submission ID yyy, total number of pallets z, pallet 1 [contains] boxes 1 to 10, pallet 2 [contains] boxes 11 to 20, total [number] of application copies.

Attach to, or insert, the shipping manifest information to the top flap of box 1.

If you are including a completed Submission Dossier Checklist, place this inside the top of box 1.
5.6.2 **Address for dispatching the submission dossier**

Address the submission dossier to:

Postal address:

Office of Medicines Authorisation  
Therapeutic Goods Administration  
PO Box 100  
Woden ACT 2606  
Australia  

Street address (for deliveries):

Therapeutic Goods Administration  
136 Narrabundah Lane  
Symonston ACT 2609  
Australia

6 **Subsequent or additional data**

When providing subsequent or additional application-related information after the submission dossier has been lodged with the TGA (e.g. a s. 31 response, new safety data), ensure:

- the additional information is in CTD format  
- modules are not combined into single volumes (binders) for Category 1 and 2 applications.

If you are providing additional information in Modules 3, 4, or 5, (e.g. a new study), you may also need to provide an updated Module 2, continuing the relevant additional expert comment that discusses the new study.

6.1 **When responding to s. 31 request for information**

Unless stated otherwise in the request from the TGA, provide the response as:

- one hard copy in CTD format  
- one electronic copy of the response on CD/DVD in NeeS format.

6.1.1 **For hard copy data**

Ensure the volumes:

- meet all the requirements, including tab identifiers for each new/revised document  
- are labelled as a s. 31 response  
- show the s. 31 request number (and/or the submission number where applicable) in addition to the module and volume number.
Did you know?

The TGA is required to keep submission dossiers for a period of 70 years.

TGA keeps all submissions in acid-free archival-standard boxes to ensure they remain intact and legible throughout their lifetime. However, these boxes will not prevent the degradation of the information if the paper, binders, plastic inserts etc. provided by the sponsor are not acid-free.

While the TGA is preparing to transition to a fully electronic submission dossier:

- Ensure submission dossiers are acid-free.
- Use acid-free inserts (as a minimum) to protect the contents of the volume from an acidic binder.

6.1.1.1 Related information and guidance

- National Archives of Australia preserving paper files.

7 Submission dossier checklist for prescription medicines

The submission dossier checklist is not mandatory for the submission of applications, however it can be used to assist you to standardise the format, packaging and dispatch of both hard copy and electronic copy submission dossiers.

If you are including a completed version of this checklist with your submission, include in Module 1, box 1 of your submission.

- Form: Submission dossier checklist for prescription medicines