Draft
Guidance for Industry on Providing Regulatory Submissions for Prescription Medicines in Electronic Format (eCTD) in Australia

Version 1.5 – January 2009
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1. INTRODUCTION

The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) is a unique project that brings together regulatory authorities and experts in the pharmaceutical industry from around the world to discuss scientific and technical aspects of product registration. This group has coordinated the international harmonisation of regulatory guidelines for prescription medicines leading to the creation of a set of specifications for their submission, the Common Technical Document (CTD). The specifications on the CTD were finalised in November 2000 and have been in use at the TGA since November 2004.

Subsequent to the development of the CTD, an expert subcommittee of the ICH, the ICH M2 Expert Working Group, developed specifications for an electronic form of the CTD, the eCTD. Version 3.2.2 of this specification was finalised in 2008 and, while remaining harmonised with the content of CTD, the specifications enumerate technology in implementing the CTD specification electronically, adding functionality such as ease of use, life cycle management, and information accessibility.

The eCTD maintains the structure of the CTD in its organisation of modules, sections, and documents and applies a technological philosophy that encompasses the use of open standards. These open standards include proprietary standards that through their widespread use have been considered de facto standards. The principal technologies applied include Extensible Markup Language (XML), Extensible Stylesheet Language (XSL), Document Type Definition (DTD), Portable Document Format (PDF) and content assurance through a checksum mechanism (MD5). These technologies combined form the modules, sections, and documents of an eCTD submission and an assurance that the content sent is the same as the content received.

While open standards allow for the eCTD being compiled, viewed/reviewed using readily accessible software such as common Internet browsers, scanners and XML parsers, such technology is unable to take full advantage of the benefits associated with an eCTD submission. In recognition of this, numerous vendors have developed software to facilitate these processes and, through the inclusion of additional functionality, have improved the useability of eCTD and the productivity of the viewer/reviewer or those involved in the compilation of an eCTD submission while preserving the open standard of the content. It is expected that sponsors wishing to submit an eCTD will put software into place to allow them to easily create eCTDs.

This guidance document for industry is intended to assist sponsors of prescription medicines in the submission of regulatory information in eCTD format to the Therapeutic Goods Administration (TGA) in Australia. It is based on the ICH eCTD Specifications and Australian Module 1 CTD. Experience gained with electronic submission of new chemical entities (NCEs) containing full dossiers, Product Information (PI) and applicable Periodic Safety Update Reports (PSURs), national legislation, current ICH and European Union standards in the area of electronic submissions and the experience of other overseas regulatory agencies has been taken into consideration.
This guidance document for industry is intended to supplement the *Australian Regulatory Guidelines for Prescription Medicines* (ARGPM) where you can find guidance (and definitions) on the requirements for a submission to register a new prescription medicine or vary an existing medicine registration and is available at [http://www.tga.gov.au/pmeds/argpm.htm](http://www.tga.gov.au/pmeds/argpm.htm). It also supplements the regulatory information on how a CTD is to be structured. Further details on the CTD are available at [http://www.tga.gov.au/docs/html/eugctd.htm](http://www.tga.gov.au/docs/html/eugctd.htm).

It must be stressed that this guidance document reflects the current situation and will be regularly updated in light of changes to: Australian legislation such as the *Therapeutic Goods Act 1989* and Regulations; the ICH eCTD Specification; and/or the Australian Module 1 CTD; and with further experience gained within the TGA using information submitted in an electronic format.

### 2. SCOPE

#### 2.1 General

The initial objectives of the TGA in accepting an eCTD can be summarised as follows:

- consistency with international practice for data dossiers
- improved data flow for regulatory activities between TGA and industry
- reduction of (internal) paper-flow (logistics and administrative burden)
- reduction of physical archiving space
- facilitation of the review process

#### 2.2 Lodgement of submissions

The TGA is moving towards prescription medicine submissions by electronic lodgement (PEL) onto PREMIER (our information management system for prescription medicine information and evaluation for registration). PEL does not support the uploading of the eCTD dossier into TGA repositories but does allow the details of the submission, and individual applications, to be recorded electronically directly into TGA systems.

The process for lodging applications and other documentation of the regulatory lifecycle will become fully electronic. Submissions will be lodged through TGA electronic Business Services (eBS)/Premier and the supporting data in the form of eCTDs. The eBS submission/application process and eCTD data submissions will complement each other but the one will not replace the other. More information about electronic lodgement will be provided on the TGA eBS website [http://www.ebs.tga.gov.au/](http://www.ebs.tga.gov.au/) when available.
2.3 Type and format of submissions

All submissions, regardless of type, should be submitted as eCTDs i.e. any submission of
updated documents/information made in the context of any application. Types of submissions
and types of dated that may be submitted are as follows:

<table>
<thead>
<tr>
<th>Types of submission include</th>
<th>Types of data that may be submitted</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Category 1</td>
<td>• Supporting data</td>
</tr>
<tr>
<td>• Category 2</td>
<td>• Answers to questions, including Section 31 responses</td>
</tr>
<tr>
<td>• Category 3</td>
<td>• Additional Data</td>
</tr>
<tr>
<td>• Safety-Related Notification</td>
<td>• Supplementary Data</td>
</tr>
<tr>
<td>• Self-Assessable Notification</td>
<td>• Pre-ADEC Response</td>
</tr>
<tr>
<td>• Minor Editorial Change to Product Information</td>
<td>• Report</td>
</tr>
<tr>
<td>• Correction of an Error</td>
<td>• Withdrawal letter</td>
</tr>
<tr>
<td>• Section 14 Exemption</td>
<td>• Product Information/Consumer Medicine Information</td>
</tr>
<tr>
<td>• Request for Orphan Drug Designation</td>
<td>• Master file</td>
</tr>
<tr>
<td>• Periodic Safety Update Report</td>
<td></td>
</tr>
<tr>
<td>• Master file</td>
<td></td>
</tr>
</tbody>
</table>

Initially, it is likely that the first submission that you make in respect to a particular product
will not be a submission for a new product such as a new chemical entity (NCE) or a New
Generic (also known as ‘essentially similar’) but maybe further advanced along the lifecycle
of the product such as a variation to the conditions of approval of registration (for example,
Safety Related Notifications (SRNs), Self-Assessable Notifications (SANs) or Category 3
variations). Data relating to a particular application or approval should continue to be
provided in paper until the finalisation of that activity, e.g. a Section 31 response to an existing
submission should continue to be provided as hardcopy if the initial data dossier for the
submission was provided in hardcopy.

Once the switch to eCTD is made, it will be mandatory to submit as eCTDs all further
submissions/reports for that product.

It is expected that all of the products for which a sponsor is responsible will be covered by a
data dossier (whether CTD or eCTD). Even if some of the information is confidential from
the sponsor (e.g. manufacturing processes), it is expected that, for example, the application
form and prescribing information (i.e. Module 1) will be held in a dossier.

For new applications, detailed statements justifying absence of data or specific CTD sections
should be provided in the relevant quality overall summary and/or non-clinical/clinical
overviews. Note that placeholder documents highlighting 'no relevant content' should not be
placed in the eCTD structure, as these would create a document lifecycle for non-existent
documents and unnecessary complication and maintenance of the eCTD.

2.3.1 Responses to questions using the eCTD structure

The eCTD structure can be used to accommodate the responses to questions in the following
way:

• A document which lists all the questions with the corresponding narrative text
  response for each question should be placed in the ‘Responses to Questions’ section of
  Module 1.
Where responses also contain new or updated data/documents relating to Modules 3, 4 and/or 5, such data/documents should be placed in the relevant sections of those Modules. This may also apply to Module 1 (e.g. revised product information), as well as to Module 2 in cases where extensive data/documents would require inclusion of the relevant summaries and/or overview sections.

Where new or updated documents are required, hyperlink(s) from an appropriate location(s) in the list of questions document to the new or updated document(s) elsewhere in the eCTD dossier should be included.

2.3.2 Periodic Safety Update Reports

Periodic Safety Update Reports (PSURs) should be included in Module 5 (m5) and named as m5-3-6-reports-of-postmarketing-experience. The file name should also indicate the relevant dates of the PSUR.

<table>
<thead>
<tr>
<th>CTD Specification Sections</th>
<th>PDF Document Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 5.3.6 Reports of Post-Marketing Experience</td>
<td>m5-3-6-reports-of-postmarketing-experience</td>
</tr>
<tr>
<td>• For PSUR reports, add date to name, e.g.</td>
<td>m5-3-6-rep-postmarket-exp-psur-01-jul-31-dec-07</td>
</tr>
<tr>
<td></td>
<td>m5-3-6-rep-postmarket-exp-psur-01-jan-30-jun-06</td>
</tr>
</tbody>
</table>

2.3.3 Sponsor’s Pre-ADEC Response

Prior to referral of an application to the Australian Drug Evaluation committee (ADEC), the sponsor has an opportunity to respond to the Delegate’s Request for ADEC Advice and proposed recommendation. The sponsor’s pre-ADEC response comprises the following documents:

• A3 – Pre-ADEC covering letter
• A3a – Sponsor’s Comment on Evaluations
• A3b – International Regulatory History
• A3c – Adverse Reactions Update
• A3d – Comments on PI (if necessary)
• A3e – Comments on Foreign PI (if necessary)
• A3f – PSUR
• C1 – Australian Product Information (PI) (an annotated and a non annotated version)
• C1a – Australian Consumer Medicine Information (CMI) (an annotated and a non annotated version)
• C2 – Approved European SmPC
• C2a – Approved US Package Insert
• C2b – Approved Canadian Monograph
These components of the pre-ADEC response should be included in the eCTD as detailed in the following table.

<table>
<thead>
<tr>
<th>Pre-ADEC Response component</th>
<th>PDF Document Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>A3 – Pre-ADEC covering letter</td>
<td>m1-0-cover-letter</td>
</tr>
<tr>
<td>A3a – Sponsor’s Comment on Evaluations</td>
<td>m1-au/ Responses-to-questions*</td>
</tr>
<tr>
<td>A3b – International Regulatory History</td>
<td>m1-10-1-countries-with-similar-app</td>
</tr>
<tr>
<td>A3c – Adverse Reactions Update</td>
<td>m1-au/ Responses-to-questions*</td>
</tr>
<tr>
<td>A3d – Comments on PI</td>
<td>m1-au/ Responses-to-questions*</td>
</tr>
<tr>
<td>A3e – Comments on Foreign PI</td>
<td>m1-au/ Responses-to-questions*</td>
</tr>
<tr>
<td>A3f – PSUR</td>
<td>m5-3-6-reports-of-postmarketing-experience (see Section 2.3.2)</td>
</tr>
<tr>
<td>C1 – Product Information</td>
<td>m1-3-1-proposed-pi (see Section 4.1)</td>
</tr>
<tr>
<td>C1a – Consumer Medicine Information</td>
<td>m1-3-2-proposed-cmi (see Section 4.1)</td>
</tr>
<tr>
<td>C2 – Approved European SmPC</td>
<td>m1-10-2-other-countries-pi</td>
</tr>
<tr>
<td>C2a – Approved US Package Insert</td>
<td>m1-10-2-other-countries-pi</td>
</tr>
<tr>
<td>C2b – Approved Canadian Monograph</td>
<td>m1-10-2-other-countries-pi</td>
</tr>
</tbody>
</table>

*These file should be collated into one pdf file.

2.3.4 Drug (Active substance) master file (DMF)

Documentation should be broken down into the individual CTD sections and named according to the CTD format. In choosing the level of granularity for reports the applicant should consider that, when relevant information is changed at any point in the product's life cycle, replacements of complete files should be provided. All documents should be submitted in PDF format.

For new applications the following documents should be included:

- Covering letter - with a clear indication of the DMF’s current edition and the TGA DMF file number (if known), and whether the active substance is currently approved for manufacture of a medicine registered in Australia. Please also clearly state the name and address of the Master File Holder, and of the Manufacturing Site, as there are often several address involved, and this will clarify matters and aid processing.
- Sponsor’s part (comprising relevant individual CTD documents).
- Restricted part (comprising relevant individual CTD documents).
- Quality overall summary (comprising relevant individual CTD documents)
- Letter of access.

The DMF holder should submit the restricted part by CD, as part of a submission of the complete new DMF or update. To tie the Registration Submission and the restricted part of the DMF together once it reached the TGA, it should be made clear in the covering letters that the submissions are related.

2.4 Paper versus electronic

During the transition period in implementing eCTD submissions there may be:

- a requirement to lodge a paper copy of the data dossier
- the possibility that not all application types will have electronic applications available through PEL.

This Guidance will be updated in these eventualities.
2.5 eCTD versus non-eCTD format electronic dossiers

It will remain possible to submit documentation on CD or DVD which is not in the eCTD format during the transition period. This will be accepted with a single paper copy, but again, once the switch to eCTD for a product is made, then all further data relating to the product must be in the eCTD format.

3. MEDIA

3.1 Media Requirements

The eCTD may only be submitted in CD or DVD (single or dual layer). The disc must not be bootable or have autostart programs. Only one copy is required to be submitted. Sponsors must provide the electronic information on the smallest number of media units possible, taking into consideration the size of the submission. Currently both CD-ROM and DVD ISO 9660 are considered an acceptable media standard.

If more than one CD-ROM or DVD is needed, avoid spanning the content of a Part or a Module of the dossier over two CD-ROMs or DVDs.

Hard media (e.g. CD, DVD) must be used for the submission of all eCTDs. eMail can be used for eCTD in addition to hard media, but not as the sole medium for submission. It is appreciated that it may be necessary, at certain times in the evaluation process, to submit an eCTD submission or documents via email in the first instance in order to ensure that the documents are received in a timely manner by TGA and work can commence. It is expected, however, that this interim ‘working’ eCTD or documents will be followed as soon as reasonably possible by an exact copy of the same submission on hard media, (or an eCTD submission if only the documents were submitted previously) and it is this eCTD which will become the formal TGA record. eCTDs will be appropriately processed once received on hard media. The TGA strongly advises that eCTD sequences should ONLY be submitted via CD or DVD as far as possible to ensure that only one communication channel is used.

3.2 Other Media

The TGA will not accept any hardware (laptops, desktops, thumb drives, hard drive, etc.) from sponsors in connection with the eCTD submission. The TGA will not accept floppy discs.

3.3 System Compatibility

The eCTD (as provided) must be directly readable and usable on TGA hardware and software. Although it is the policy of the TGA to maintain desktop configurations and IT infrastructure in line with common office standards, the electronic information provided in the eCTD must not only be readable on the latest operating system, but support a reasonable number of backward versions of windows operating systems.
4. FILE FORMATS

4.1 General

Currently, the following file formats are compliant with the National Archives Regulations and are accepted by both the TGA eCTD specifications and the ICH and EU eCTD specifications:

- **Module 2 Overviews and Summaries** – Overviews and summaries in the CTD Module 2 must always be provided electronically as both PDF and file formats Microsoft (MS) Word 2003 or Rich Text Format (RTF).
- **General Narratives** – Portable Document Format (PDF). File formats MS Word 2003 and RTF are accepted but always in addition to the PDF files made of the same documents. Both document types must be stored together in the eCTD.
- **Graphics** – PDF or when appropriate or when PDF is not possible, use Joint Photographic Experts Group (JPEG), Portable Network Graphics (PNG), Scalable Vector Graphics (SVG) or Graphics Interchange Format (GIF). Special formats for very high resolutions may be appropriate and acceptable on a case-by-case basis, on consultation with TGA.
- **Structure** – Extensible Markup Language (XML)

TGA requires RTF/Word documents (Word being the preferred format) for Product Information Consumer Medicines Information and labelling documents and M2.2 – 2.5 in addition to the PDF for the purposes of review and document manipulation. The Module 2 summaries (2.6, 2.7) are **not** required in RTF/Word format. Whilst RTF is an accepted eCTD format, Word documents are considered, as an aid to review and are not a formal part of the eCTD submission. The following principles apply to the submission of Word documents with the eCTD:

- PDFs (and other accepted file formats) only are to be referenced in the eCTD XML backbone. Word documents should **not** be included in the eCTD backbone, as they are provided as an aid to review and inclusion within the eCTD would require unnecessary management of the lifecycle of these documents in addition to the formal PDF documents.
- Word documents required for review in Modules 1 and 2 should be located in a separate folder to the eCTD and not referenced in the XML backbone, but made available on the same hard media. For submissions made in support of the product lifecycle, both ‘clean’ and ‘track changes’ copies of Product Information documents should be provided where applicable.
- The filenames for Word/RTF documents should be succinct and meaningful, and should match as far as possible the corresponding leaf titles for the PDF documents submitted in the eCTD.
- An indication should be given in the filename as to whether the document is ‘highlighted’ or ‘clean’, if applicable. (This indication should also be given for PDF files in the eCTD leaf title).

Although RTF documents can be included in the eCTD XML backbone, they are considered, if submitted in addition to PDF, as electronic ‘working’ documents and so it is recommended that, if submitted, they are included in a separate folder.
4.2 Portable Document Format (PDF)

PDF is an open, de facto, published format created by Adobe Systems Incorporated (http://www.adobe.com). There are several suppliers of the software required to produce PDF documents. The following points can be made in relation to PDF files:

- Files must be legible with Acrobat Reader, version 7 or lower.
- PDF files produced from an electronic source document are highly preferred over PDF files produced from scanned paper, since those 'electronic' PDF files provide the maximum functionality to the reviewers in terms of search and print capabilities, and copy and paste functionality. The overviews/summaries in the CTD Module 2 should always be generated from an electronic source document.
- If scanning is unavoidable, readability and file size must be balanced; the following is recommended: resolution 300 dpi (photographs up to 600 dpi), avoid greyscale or colour where possible, use only lossless compression techniques.
- All fonts used in a document must belong to the standard provided fonts with Adobe or MS Word 2003 and must be consistent with the Australian Regulatory Guidelines for Prescription Medicines (ARGPM) and the TGA Module 1 CTD.
- If colours other than black are used, the coloured pages must be tested on a black and white printer for acceptable reproduction and legibility prior to submission.
- Print area for pages must fit on an A4 sheet of paper; margins must allow binding in multi-ring binders without affecting readability.
- Landscape-oriented tables must automatically appear in landscape on screen.

4.3 Extensible Markup Language (XML)

XML is developed by a working group of the World Wide Web Consortium (W3C). It is an open-source language developed to improve on previous mark-up languages including Standard Generalised Markup Language (SGML) and Hypertext Markup Language (HTML). Additional details on XML can be found in the ICH eCTD Specification Document, Appendix 7.

4.4 Text Searchable Files

Sponsors are requested to ensure that all submissions contain the maximum amount of text searchable content. Documents with searchable text will aid the evaluator, or any other user, in searching for specific terms and also in copying and pasting information into another document, such as an assessment report.

The TGA recognize that not all documents need to be text searchable. This appendix provides some guidance about what must be text searchable and the ways to ensure that files are created appropriately.

4.4.1 Creating Text Searchable Files

PDF files with searchable text can be created by all PDF tools from a source file in a text format (e.g. MS Word, SAS, MS PowerPoint, Rich Text Files, etc.). When created in this way, the file will usually be the smallest in size (measured in kilobytes or megabytes) that they can be.
If the only version of a document available is in paper, then scanning to PDF and using an Optical Character Recognition (OCR) routine will create searchable text. It is recommended that sponsors use OCR only as a last resort as:

- PDF files created in this way tend to be much larger in size, for the same number of pages;
- the quality of the text that is created will almost certainly not be a 100% match to the original text; and
- the tools for checking and correcting this text tend to be somewhat cumbersome.

Sponsors are reminded that the text produced by the OCR routine should be “hidden” behind the image of the original page so that the user can refer to the picture of the page and the text on it as final verification of the data. As a result, the sponsor should ensure that, as a minimum, the text on the scanned image is legible to the user. Poor quality images should not be provided and you should note that these can only inevitably lead to poor quality OCR text.

### 4.4.2 Documents that must always be text searchable

The PDF should be produced wherever possible from a text source, such as MS Word, but if sourced from a scanned original then they must be OCR’d.

- Key administrative documents in Module 1 including, the cover letter, application form, labelling documents
- Any document in Module 2 of the submission (QOS, Preclinical Overview and Summaries, Clinical Overview and Summaries).
- The main body of text and main tables in any preclinical or clinical report required to support the main claim of the application.
- The main body of text in any reports, methods, analytical procedures, etc. supplied in Module 3 of the submission
- The main body of text of Periodic Safety Update Reports (PSURs)
- The main body of text of Risk Management Plans
- Any English translation of a document originally written in a foreign language (see also below)

### 4.4.3 Documents that do not need to be text searchable

The PDF should be produced wherever possible from a text source, such as MS Word, but if sourced from a scanned original then there is no need for OCR.

- Any original GMP certificate
- Any original certificate of analysis
- Any manufacturer’s licences
- Any certificates of suitability
- Any Manufacturing Authorisation
- Any document written in a foreign language where a translation is provided in English (however, the translation should be text searchable, see above)
- Any literature references sourced from journals, periodicals and books (except when these are used in a bibliographic application so support the main claims of the application).
The blank case report form (CRF) in a Clinical Study Report
- Patient data listings (when supplied)
- CRFs (when supplied)
- Any page with a signature that does not contain other information key to the understanding of the submission
- Applicants should consider providing signatures on separate pages from key text in reports, overviews, etc.

5. SECURITY

5.1 General

There are various aspects related to security. The physical security of the submission during transportation/transmission is the responsibility of the Sponsor. Once received within the TGA, security and submission integrity is the sole responsibility of the TGA. In this respect, it should be noted that the TGA abides by the Australian Government Information and Communications Technology Security Manual as embodied in the Defence Signals Directorate Publication ACSI 33. This manual includes appropriate measures to prevent loss, unauthorised duplication and/or access or theft of regulatory information presented both on paper and electronic media that are distributed throughout the TGA.

5.2 Password protection

One-time security settings or password protection of electronic submissions for security purposes is not acceptable during transportation/transmission from the applicant to the Agency.

Applicants should also not include any file level security settings or password protection for individual files in the eCTD. Applicants should allow printing, annotations to the documents, and selection of text and graphics. Internal security and access control processes in the regulatory authority should maintain the integrity of the submitted files.

5.3 Virus protection

The applicant is responsible for checking the submission for viruses. Checking must be performed with an up-to-date and well-recognised virus-checker. Certification from the sponsor is required within the covering letter (see 5.2) that virus checking was performed. After receipt of the submission at the TGA, a similar internal virus check will be performed. If a virus is detected it can constitute grounds for refusal of the electronic submission.

5.4 Electronic signatures

For the moment, electronic signatures are currently not accepted at the TGA as being legally equivalent to handwritten signatures. The authenticity of certain documents (covering letters, Application Forms, Embryo Declarations) must be guaranteed within the covering letter (see 5.2) with a handwritten signature. Until a clear internal procedure is developed for the use, tracking and maintenance of electronic signatures, only handwritten signatures will be accepted at the TGA for official purposes.
6. PROCEDURE FOR SENDING ELECTRONIC INFORMATION

6.1 Obtaining an eCTD number

eCTD dossiers may only be submitted in conjunction with PEL (electronic lodgement of prescription medicine submissions, see section 1.2).

Within eBS there will be a facility to acquire a new eCTD ID for each sponsor for each product/active ingredient (there may be a number of separate and distinct goods within the sponsor’s product suite for the active ingredient), and that facility will ensure that the uniqueness of the eCTD ID for the sponsor/ product suite’s data dossier. It will be possible to have more than one dossier for an active ingredient if there are different datasets required, such as for greatly different dosage forms. The distinction between such datasets will need to be identified to the eBS ID facility. During the electronic lodgement process, you will be asked to provide the eCTD IDs.

The eCTD ID is a unique identifier and is retained for the life of the data dossier (although the sequence numbers or related sequence will change) and must be quoted in all future submissions that reference that data dossier. An example of how related sequence should be used is at Appendix 1.

The eCTD ID must be recorded against the data dossier in the eCTD generating software prior to checksum and CD/DVD generation. Each eCTD data submission will also include the Premier submission ID.

6.2 Cover letter

The cover letter must identify the type of submission and that it is an eCTD submission and include, as a minimum, the following information.

6.2.1 General information

- Identify the type of submission and that it is an eCTD submission
- Company name, address, contact details and signature (see Section 4.4)
- eCTD ID reference eg E2009-1234-0000
- Submission date (DD-MM-YYYY)
- Premier Submission number
- Type of new submission (see section 1.3).
- Submission sequence number, see attachment 1
- AUST R numbers of affected products (where relevant)
- Product invented name(s)
- Name of the active substance(s)
- Certification that virus checking has been undertaken by <NAME OF VIRUS CHECK>.

6.2.2 Required information

- Statement that the electronic submission type is structured in compliance with this industry guidance, the ARGPM, the TGA Module 1 and eCTD Specification Documents
- Index and number of media units per full set
6.3 Packaging and labelling

The eCTD dossier and its cover letter must be forwarded as soon as possible after the PEL submission is lodged. The electronic media must be adequately packed to prevent damage to the media and their content. The package containing the electronic information must include the cover letter (see Section 5.2). All the media units must be appropriately labelled as described in the covering letter including a labelled jewel case/cover. The media label must state the:

- eCTD ID
- PEL submission ID
- sequence number
- sponsor name and Client ID
- product name and the submission type, eg submission data, S31 response, etc

6.4 Address

The electronic submission must be submitted to the following addresses:

<table>
<thead>
<tr>
<th>Postal Address:</th>
<th>Courier Address:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Records Management Section</td>
<td>Records Management Section</td>
</tr>
<tr>
<td>Therapeutic Goods Administration</td>
<td>Therapeutic Goods Administration</td>
</tr>
<tr>
<td>PO Box 100</td>
<td>136 Narrabundah Lane</td>
</tr>
<tr>
<td>Woden ACT 2606</td>
<td>Symonston ACT 2609</td>
</tr>
<tr>
<td>Australia</td>
<td>Australia</td>
</tr>
</tbody>
</table>

7. WHAT HAPPENS TO YOUR ELECTRONIC SUBMISSION

7.1 Validation

On receipt in the TGA, your submission will be logged and identified and the following items will be checked during validation:

- required paper copies
- adequate covering letter (see section 5.2 above)
- virus check at the TGA
- checksum validation
- compliance with general requirements of this guidance document
- compliance with the TGA Module 1 and eCTD Specification Documents
- security settings or password protection
- no physical corruption on disk, or any other serious defect, incident, etc associated with the initial processing of the electronic submission
- validation rules

If errors are found during the validation process the sponsor will be notified and requested to submit a new disk. Legislative timeframe clocks will not start until a valid eCTD is received.
7.2 Defective disks

If, during the further administrative handling of the electronic submission or during the actual review process, serious defects are found and those defects are reproducible on the original copy of the electronic submission as received from the sponsor, the sponsor will be required to resubmit a new disk. Examples of such defects could be a substantial number of non-functioning hyperlinks, hyperlinks to non-existing documents, PDF documents with encryption securities to allow viewing but not printing, etc. As a consequence, this might lead to a serious delay in the review process. In the event that the electronic submission does not meet the TGA requirements, the TGA will contact the sponsor. Legislative timeframe clocks will stop from the date the sponsor is notified until the date a valid new disk is received.

7.3 Archiving and working copies

Once media units are received, the information will be uploaded to the eCTD review tool as a working copy over the TGA internal network. The original set of media units received (including any defective disks) will be maintained as a Commonwealth Record under the National Archives Regulations and cannot be returned to the sponsor.

8. QUESTIONS

Any questions arising before or after the submission of electronic information can be directed by email aet.application.entry.team@tga.gov.au with reference to 'electronic submission'.

9. REGIONAL REQUIREMENTS

The eCTD is an international standard and is implemented in the EU (EMEA), US (FDA) and Japan (MHLW). However, whilst once of the primary objectives of introducing the eCTD is to facilitate the preparation of applications intended for multiple regions, care must be taken over the adaptation of the submission to meet regional requirements, as these can, and do, differ.

Particular areas of divergence between eCTD requirements for the US and the EU include:

- The requirement for the Study Tagging File (STF) in the US, which is not used in the EU (although a submission containing the STF will not be rejected in the EU).
- Information relating to datasets e.g. data definitions, analysis datasets etc., ISS and ISEs (not submitted in the EU).
- The use of SAS transport files for data in the US, which is a format not accepted by EMEA.
- The use of node extensions, which are not accepted in the US but accepted in the EU (it should be noted however that node extensions are handled in differing ways by review tools, and so their use should be limited where possible).
- Module 1 content and DTD.

Applicants should pay attention to the particular requirements of each region and ensure that the eCTD submission, if previously prepared for another region,. has been adapted accordingly for submission to the TGA.
## APPENDIX 1: EXAMPLE RELATED SEQUENCE NUMBERING

<table>
<thead>
<tr>
<th>Sequence</th>
<th>Submission Description</th>
<th>Related Sequence</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0000</td>
<td>Category 1 application for a NCE or New Generic application</td>
<td>&lt;none&gt;</td>
<td>This is a new regulatory submission and so no related sequence is included</td>
</tr>
<tr>
<td>0001</td>
<td>Responses to PCE Section 31 for the NCE or New Generic application</td>
<td>0000</td>
<td>This is continued activity for the regulatory submission initiated in 0000 and so the related sequence points to the beginning of that submission</td>
</tr>
<tr>
<td>0002</td>
<td>Responses to TOX Section 31 for the NCE or New Generic application</td>
<td>0000</td>
<td>This is continued activity for the regulatory submission initiated in 0000 and so the related sequence points to the beginning of that submission</td>
</tr>
<tr>
<td>0003</td>
<td>Updated, agreed product information for the NCE or New Generic application</td>
<td>0000</td>
<td>This is the completion of the regulatory activity for this submission initiated in 0000 and so the related sequence points to the beginning of that submission</td>
</tr>
<tr>
<td>0004</td>
<td>Category 3 application for a change in manufacturing site for the approved product</td>
<td>&lt;none&gt;</td>
<td>This is a new regulatory submission and so no related sequence is included</td>
</tr>
<tr>
<td>0005</td>
<td>Category 1 application for EXTENSION OF INDICATION (EOI) for the approved product</td>
<td>&lt;none&gt;</td>
<td>This is the beginning of a new regulatory submission and so no related sequence is included</td>
</tr>
<tr>
<td>0006</td>
<td>Responses to PCE Section 31 for the change in manufacturing site for the approved product</td>
<td>0004</td>
<td>This is continued activity for the regulatory submission initiated in 0004 and so the related sequence points to the beginning of that submission</td>
</tr>
<tr>
<td>0007</td>
<td>Responses to CLIN Section 31 EOI for the approved product</td>
<td>0005</td>
<td>This is continued activity for the regulatory submission initiated in 0005 and so the related sequence points to the beginning of that submission</td>
</tr>
<tr>
<td>0008</td>
<td>Periodic Safety Update Report for the approved product</td>
<td>&lt;none&gt;</td>
<td>This is new regulatory activity and so no related sequence is included</td>
</tr>
<tr>
<td>0009</td>
<td>Supplementary data for EOI for the approved product</td>
<td>0005</td>
<td>This is continued activity for the regulatory submission initiated in 0005 and so the related sequence points to the beginning of that submission</td>
</tr>
<tr>
<td>0010</td>
<td>Safety related notification for the approved product</td>
<td>&lt;none&gt;</td>
<td>This is a new regulatory submission and so no related sequence is included</td>
</tr>
<tr>
<td>0011</td>
<td>Updated, agreed product information for the EOI for the approved product</td>
<td>0005</td>
<td>This is the completion of the regulatory activity for this submission initiated in 0005 and the related sequence points to the beginning of that submission</td>
</tr>
</tbody>
</table>