Australian Government

Department of Health and Ageing

Therapeutic Goods Administration

Guidance for industry on providing regulatory information in electronic format: Non-eCTD electronic submissions (NeeS) for human medicinal products

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	Details of Change	Section	Date
1	First version	All	December 2010

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1 Introduction

This Guidance Document is intended to assist pharmaceutical companies with the submission of regulatory information in electronic format to the Therapeutic Goods Administration (TGA). This document details the requirements for the submission of non-eCTD electronic submissions (NeeS). A separate guidance document covering eCTD submissions is also being published on the TGA website.

It should be stressed that this document reflects the *current* situation and will be regularly updated in the light of changes in legislation together with further experience gained using information submitted in electronic format. NeeS applications should be regarded as an interim format and that applicants should be actively planning their move to full eCTD submissions.

2 General considerations

2.1 – Scope

2.1.1. Type of product

The product types include small molecules, vaccines, and blood products for human medicinal products described in Part 1 of Schedule 10 of the *Therapeutic Goods Regulations 1990*.

2.1.2. Type of submission

This guidance applies to all submissions related to the authorisation and maintenance of medicinal products, including new registrations, variations, PSURs and active substance master files.

2.2 – Structure of submissions

Regulatory information must be structured in accordance with the common technical document (CTD), which for paper submissions became mandatory in the Australia with effect from February 2006.

For NeeS applications the eCTD folder structure is used. The breakdown of the electronic submission should be in conformity with the ICH granularity document and the ICH eCTD file naming conventions and recommended TGA file names (see **Annex 3**).

The difference from an eCTD is that the two relevant XML files, the index.xml and au-regional.xml for the backbone of modules 2 to 5 and module 1 for Australia, respectively and the util folder are not present, so navigation through a NeeS is based on electronic tables of content, bookmarks and hypertext links.

Typically, a NeeS application will cover all dosage forms and strengths of a product with any one invented name. However, if the applicant decides to have one NeeS per strength or dosage form, this would also be acceptable but should be carefully considered in relation to transformation into eCTD at a later stage.

2.2.1. Table of contents and bookmarks

Tables of content should still always be provided by the applicant. The TOCs should always be submitted in PDF format.

All documents in the NeeS dossier should be referenced from a hyperlinked table of contents (TOC). Hyperlinks for each document should always be provided to the first page of the appropriate file.

In the case of small dossiers (e.g. for certain variations), especially when only one module beside module 1 is concerned, it is acceptable to include only a main TOC referring directly to the content documents. However, for larger submissions, the main TOC should always be linked to module TOCs which are then further linked to the documents in each module. The module TOCs should not include hyperlinks to documents in other modules.

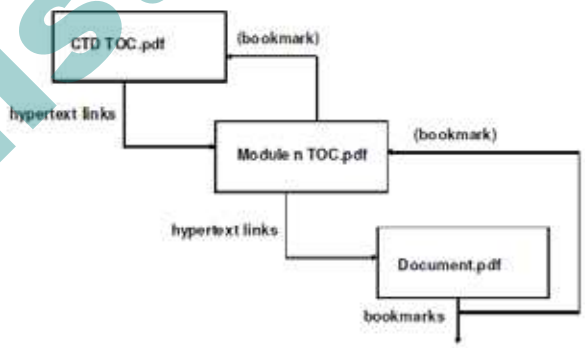
The file containing the main table of contents for the CTD should be named *ctd-toc.pdf* and be located in the top level folder for the NeeS submission. The files containing the module tables of content should be named *m1-toc.pdf*, *m2-toc.pdf*, *m3-toc.pdf*, *m4-toc.pdf* and *m5-toc.pdf* and be located in the corresponding top level module folder.

An example is presented in **Annex 2**. It should be noted that these are just *examples* and are provided for guidance and illustrative purposes only.

Where document TOCs are included they should be located within the same file as the rest of the document. For each document, provide bookmarks for every entry in the document's table of contents to the appropriate location, or where a table of contents does not exist, provide bookmarks to a sufficiently detailed level, typically to Level 3 or 4 headings, as considered appropriate.

An additional function might be provided to allow easy navigation back to the Table of Contents above. This can be achieved through the use of a bookmark linked back to the previous level. This additional function is not mandatory, but when provided it will facilitate the assessment.

The figure below describes diagrammatically this situation.



2.3 – Submission numbering

Sequence numbers, as they are defined for eCTD submissions, are not applicable for NeeS submissions.

The use of a four digit number in the top level folder name is however recommended. The number does not have to be unique.

2.4 – Moving to NeeS format applications

A NeeS format application can normally be started with any application for initial registration or variation of registration. Once the switch to this electronic format is made it is expected that further applications and responses relating to the particular medicinal product are submitted in the same electronic format.

Since there is no life cycle management for NeeS, there is no need to reformat the whole dossier into NeeS format when switching from paper to NeeS.

2.5 – General submission considerations

2.5.1. File and folder structure

Submissions are a collection of documents and each document should be provided as a separate file. The detailed structure of the NeeS should conform to the ICH granularity document and Australian M1 guidance. It is recommended that the root folder of the submission is named with the product (trade) name in lower case followed by the subfolder, name, e.g. mydrug/0000/.

Total folder/file path should not exceed 180 characters.

2.5.2. File naming

The eCTD file naming conventions described in the ICH M2 eCTD specification and Australian M1 guidance (see **Annex 3**) should be followed. If an applicant wishes to submit multiple files in one section, where only one highly recommended name is available, this can be achieved using a suffix to the filename, using the file name-*var*.pdf convention, where the -var component has no dashes or illegal characters.

2.5.3. Placement of documents

Guidance on the placement of documents within the CTD structure for particular submission types can be found on the TGA website.
(www.tga.gov.au/docs/html/eugctd.htm)

2.6 – Correspondence

In addition to the NeeS application, information may need to be exchanged to assist the processing or handling of the application. Not all such correspondence need to be included in the NeeS dossier.

Accordingly, the correspondence sent via the usual electronic means (email etc) only needs to be in full NeeS format if it relates directly to the content of the dossier.

2.7 – Paper requirements

The practical guidance for the paper submission of regulatory information in support of a registration or variation application when using the electronic common technical document ("eCTD") as the source submission applies to NeeS submissions as well.

2.8 – Hardware

The TGA will not accept any hardware (laptops, desktops, zip drives, etc.) from sponsors in connection with the submission of information in electronic format. The electronic information should be directly readable and usable on the TGA's hardware and software.

2.9 – File formats

Detailed guidance on the specific file formats can be found in the ICH eCTD specification document.

2.9.1. PDF

In general terms the majority of documents included in electronic submissions should be in PDF format.

Portable document format (PDF) is an open, de facto, electronic publishing standard, created by Adobe Systems Incorporated. There are several alternative suppliers of PDF software. Applicants need to check that the PDF documents meet the following key requirements:

- files should be legible with Acrobat Reader, version 5.0 or higher
- PDF file version 1.4 only should be used
- documents should be generated from electronic source documents and not from scanned material, except where access to the source electronic file is unavailable or where a signature is required. See Annex 1 for further guidance on text searchable documents.

2.9.2. Extensible mark-up language (XML)

Extensible mark-up language (XML) is the format for the backbone files for the eCTD but not in a NeeS dossier. Details on XML can be found in the ICH eCTD specification document, Appendix 7.

2.9.3. Other file formats

Other file formats such as rich text (RTF) or MS Word formats may be required in addition to the PDF requirement of the NeeS, especially for the provision of product information documents.

These files should not be added within the NeeS structure. They should be provided in a separate folder called, for example, 'workingdocuments' on the same CD/DVD containing the NeeS.

2.10 – Bookmarks and hypertext links

Navigation through an electronic submission is greatly enhanced by the intelligent use of bookmarks and hypertext links. ICH guidance states: 'It is expected that any document that has a table of contents (TOC) will have bookmarks' (see the eCTD specification for details). Documents without TOCs should have bookmarks included where it aids in the navigation around the document content. For example, a four page document summarising findings could require bookmarks to aid navigation. However, a 300 page file containing a single data listing might not require bookmarks as there is no further internal structure.

In general terms, bookmarks and hyperlinks should be used to aid navigation.

Additional details on creating bookmarks and hypertext links in PDF documents can be found in the ICH eCTD specification, Appendix 7.

Each document should be referred to from a table of content (the overall TOC or any module TOC as applicable).

2.11 – Other technical information

2.11.1. Security issues

The physical security of the submission during transportation is the responsibility of the applicant. Once received by the TGA, security and submission integrity is the sole responsibility of the TGA.

2.11.2. Password protection

Submission or file level security is not permitted. If one-time security settings or password protection of an electronic submission is used this could constitute grounds for the rejection of the submission.

2.11.3. Virus protection

The applicant is responsible for checking the submission for viruses. Checking should be performed with an up-to-date virus checker and be confirmed in the cover letter. After receipt at the TGA, a similar internal virus check will be performed. If a virus is detected it will constitute grounds for rejection of the submission.

2.11.4. Electronic signatures

The TGA requires that certain specific electronic documents (cover page for submission) are authenticated by separate signed paper copies.

2.11.5. Transmission media

Currently CD-ROM, CD-R, DVD-R are considered acceptable media standards (USB keys, hard drives etc are not acceptable). Sponsors should provide the electronic information on the smallest number of discs possible, taking into consideration the size of the submission.

If an individual NeeS submission is of such a size as to span several CDs, the provision of a DVD is recommended. However, if the sponsor is unable to provide a DVD, and the application spans multiple CDs, then, where possible, individual CTD modules should be

kept together and not be split over multiple CDs (i.e. a single CD should contain all of module 1, another all of module 2, etc.).

A separate CD/DVD should be provided for each NeeS submission. When submitting several applications for the same medicinal product (trade name) concurrently, it would be acceptable to provide them on a single CD/DVD.

This should always be clearly described in the cover letter and indicated on the disc (see 2.11.6).

2.11.6. Labelling of media

Each CD or DVD submitted with a NeeS should include the following label information, clearly presented and printed on the media:

- format: NeeS
- applicant's name
- product (trade) name(s)
- AAN of the active substance(s)
- full submission number(s)
- number of media units per full set and an indication of the place of the individual CD/DVD within this set (e.g. 1(5), 2(5), etc.)
- submission type(s) of each NeeS submission(s) contained on the CD/DVD (e.g. new chemical entity, extension of indications).

2.11.7. Procedure for sending electronic information

Electronic media sets should be submitted at the same time as any required paper documentation. The electronic media should be packed adequately to prevent damage and the package should include a cover letter.

2.12.8. Archiving and working copies

Six copies of the full electronic dossier must be provided for category 1 and category 2 submissions.

3 Module specific information

3.1 – Module 1.2: Administrative information (application forms)

The application form should always be provided as a PDF file within the NeeS structure and provided as a signed paper copy. For this specific PDF file a newer version than PDF version 1.4 may be appropriate and acceptable.

3.2 – Module 1.3.1: Product information

For NeeS applications, product information should be supplied as PDF files within the NeeS structure. For products already registered and changes to the product information are proposed, submission dossier must include both the 'annotated' Australian PI and a 'clean' Australian PI. A 'clean' Australian PI incorporates all the changes proposed but removes the revision marks and comments.

An MS Word file version should also be submitted to facilitate assessment. These files should not be added within the NeeS structure. They should be provided in a separate folder called, for example, 'workingdocuments' on the same CD/DVD containing the NeeS (see also section 2.9.3).

3.3 – Module 1 – responses

The organisation of the submission of electronic information in response to a list of questions from the TGA should follow the same basic principles as the first submission. The written response should be submitted following the recommended response folder and file structure. In this case the written response document should be placed in a folder named for example mydrug/0000/m1-0-2-responses-quest. Appropriate navigation in the submission should follow the same concepts as described in section 2.2.1.

Annex 1 Guidance on text searchable documents

1 – General

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 evaluation report.

This short document provides some guidance about what must be text searchable and the ways to ensure that files are created appropriately.

1.1. Creating text searchable files

Portable document files (PDFs) 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 is the only way to create searchable text. PDF files created in this way tend to be much larger in size, for the same number of pages (from 10 to 100 times as large), and the quality of the text that is created will almost certainly not be a 100% match to the original text. It is noted that tools for checking and correcting this text tend to be somewhat cumbersome. For these reasons, applicants are recommended to use scanning/OCR only as a last resort.

Applicants 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 applicant 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.

2 – Documents that must always be text searchable

Text searchable means the PDF should be produced wherever possible from a text source, such as MS Word, but if soured from a scanned original then it **must be** OCR format.

The following must always be text searchable:

- key administrative documents in module 1 including, the cover letter, application form, product information documents
- any document in module 2 of the submission (QOS, non-clinical overview and summaries, clinical overview and summaries)
- the main body of text and main tables in any non-clinical or clinical report required to support the main claim of the submission

- 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).

3 – Documents that do not need to be text searchable

The PDF of documents from this category 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 format.

Documents in this category are:

- 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 to support the main claims of the application)
- the blank case report form in a clinical study report
- patient data listings (when supplied)
- case report forms (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.

4 – Further information

If applicants are uncertain whether or not a particular document should be text searchable, they should contact the TGA for guidance.

Annex 2 Example tables of contents

These tables of contents are *examples* and are provided for illustrative and guidance purposes only. The blue underlined text illustrates where hyperlinks to the individual documents may be added.

In these examples there are some "Not applicable" documents shown. "Not applicable" documents should not appear in the dossier and nor should they be included in the TOCs.

The following is an example of a CTD TOC (main TOC)

Module 1	Administrative information and prescribing information for Australia	Module 1
Module 2	Common technical document summaries	Module 2
Module 3	Quality	Module 3
Module 4	Non-clinical study reports	Module 4
Module 5	Clinical study reports	Module 5

The following are examples of module TOCs.

Module 1	**Administrative information and prescribing information for Australia**	
1.0	Letter of application	1.0
1.0.0	Electronic lodgement cover sheet	1.0.0
1.0.1	Letter of application	1.0.1
1.0.2	Responses to questions	1.0.2
1.1	Comprehensive table of contents	1.1
1.2	Application forms	1.2
1.2.1	Application form	1.2.1
1.2.2	Pre-submission details	1.2.2
1.2.3	Patent certification	1.2.3
1.3	Medicine information documents, packaging, and labelling	1.3
1.3.1	Proposed Australian product information and package insert	1.3.1
1.3.2	Proposed Australian consumer medicine information	1.3.2
1.3.3	Therapeutic goods and use of human embryos or human embryonic stem cells or material derived from them	1.3.3
1.3.4	Label mock-ups and specimens	1.3.4
1.4	Information about the experts	1.4
1.4.1	Information about the expert – Quality	1.4.1
1.4.2	Information about the expert – Non-clinical	1.4.2
1.4.3	Information about the expert – Clinical	1.4.3
1.5	Specific requirements for different types of applications	1.5
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1.5.3	Genetically modified organisms: Consent from the Office of the Gene Technology Regulator	1.5.3
1.5.4	Additional trade name declarations	1.5.4
1.5.5	Co-marketed medicine declarations	1.5.5
1.6	Drug and plasma master files and Certificates of Suitability of Monographs of the European Pharmacopoeia	1.6
1.6.1	Relevant external sources	1.6.1

Module 1	Administrative information and prescribing information for Australia	
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1.6.3	Letters of access	1.6.3
1.6.4	Certificates of suitability (including Annexes)	1.6.4
1.7	Good manufacturing practice	1.7
1.7.1	List of Australian manufacturer names and licence numbers	1.7.1
1.7.2	GMP clearance letters for all overseas manufacturing sites	1.7.2
1.7.3	Copies of applications for TGA GMP clearances	1.7.3
1.8	Compliance with meetings and pre-submission processes	1.8
1.8.1	Details of compliance with pre-submission meeting outcomes	1.8.1
1.8.2	Details of any additional data to be submitted	1.8.2
1.8.3	Declaration of compliance with pre-submission planning form and planning letter	1.8.3
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1.10.3	Data set similarities and differences	1.10.3
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1.11.1	Summary of a bioavailability or bioequivalence study	1.11.1
1.11.2	Justification for not providing appropriate biopharmaceutic studies	1.11.2
1.12	Paediatric development program	1.12
1.12.1	References to paediatric development program	1.12.1
1.13	Information relating to pharmacovigilance	1.13
1.13.1	Risk management plan for Australia	1.13.1
Annex I	Antibiotic resistance data	Annex I
Annex II	Overseas evaluation reports	Annex II

Module 2	Common technical document summaries	
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2.3.S.2	Manufacture	2.3.S.2
2.3.S.3	Characterisation	2.3.S.3
2.3.S.4	Control of drug substance	2.3.S.4
2.3.S.5	Reference standards or materials	2.3.S.5
2.3.S.6	Container closure system	2.3.S.6
2.3.S.7	Stability	2.3.S.7
2.3.S	Drug substance - Substance-S – Manufacturer	2.3.S
2.3.S.1	General information	2.3.S.1
2.3.S.2	Manufacture	2.3.S.2
2.3.S.3	Characterisation	2.3.S.3
2.3.S.4	Control of drug substance	2.3.S.4
2.3.S.5	Reference standards or materials	2.3.S.5
2.3.S.6	Container closure system	2.3.S.6
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2.3.P.4	Control of excipients	2.3.P.4
2.3.P.5	Control of drug product	2.3.P.5

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2.7	Clinical summary	2.7
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2.7.2	Summary of clinical pharmacology studies	2.7.2
2.7.3	Summary of clinical efficacy	2.7.3
2.7.4	Summary of clinical safety	2.7.4
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3.2.S.1.2	Structure (substance-manufacturer)	3.2.S.1.2
3.2.S.1.3	General properties (substance-manufacturer)	3.2.S.1.3
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3.2.S.4.5	Justification of specification (substance-manufacturer1)	3.2.S.4.5
3.2.S.5	Reference standards or materials (substance-manufacturer1)	3.2.S.5
3.2.S.6	Container closure system (substance-manufacturer1)	3.2.S.6
3.2.S.7	Stability (substance-manufacturer1)	3.2.S.7
3.2.S.7.1	Stability summary and conclusions (substance-manufacturer1)	3.2.S.7.1
3.2.S.7.2	Post-approval stability protocol and stability commitment (substance-manufacturer1)	3.2.S.7.2
3.2.S.7.3	Stability data (substance-manufacturer1)	3.2.S.7.3
3.2.P	Drug product	3.2.P
3.2.P.1	Description and composition of the drug product	3.2.P.1
3.2.P.2	Pharmaceutical development	3.2.P.2
3.2.P.2.1	Components of the drug product	3.2.P.2.1
3.2.P.2.2	Drug product	3.2.P.2.2
3.2.P.2.3	Manufacturing process development	3.2.P.2.3
3.2.P.2.4	Container closure system	3.2.P.2.4
3.2.P.2.5	Microbiological attributes	3.2.P.2.5
3.2.P.2.6	Compatibility	3.2.P.2.6
3.2.P.3	Manufacture	3.2.P.3
3.2.P.3.1	Manufacturer(s)	3.2.P.3.1
3.2.P.3.2	Batch formula	3.2.P.3.2
3.2.P.3.3	Description of manufacturing process and process controls	3.2.P.3.3
3.2.P.3.4	Controls of critical steps and intermediates	3.2.P.3.4
3.2.P.3.5	Process validation and/or evaluation	3.2.P.3.5

Module 3	Quality	
3.2.P.4	Control of excipient – compendial	3.2.P.4
3.2.P.4.1	Specifications	3.2.P.4.1
3.2.P.4.2	Analytical procedures	Not Applicable
3.2.P.4.3	Validation of analytical procedures	Not Applicable
3.2.P.4.4	Justification of specifications	Not Applicable
3.2.P.4.5	Excipients of human or animal origin	3.2.P.4.5
3.2.P.4.6	Novel excipients	3.2.P.4.6
3.2.P.4	Control of excipient - non-compendial excipient	1 3.2.P.4
3.2.P.4.1	Specifications	3.2.P.4.1
3.2.P.4.2	Analytical procedures	3.2.P.4.2
3.2.P.4.3	Validation of analytical procedures	3.2.P.4.3
3.2.P.4.4	Justification of specifications	3.2.P.4.4
3.2.P.4.5	Excipients of human or animal origin	3.2.P.4.5
3.2.P.4.6	Novel excipients	3.2.P.4.6
3.2.P.5	Control of drug product	3.2.P.5
3.2.P.5.1	Specifications	3.2.P.5.1
3.2.P.5.2	Analytical procedures	3.2.P.5.2
3.2.P.5.3	Validation of analytical procedures	3.2.P.5.3
3.2.P.5.4	Batch analyses	3.2.P.5.4
3.2.P.5.5	Characterisation of impurities	3.2.P.5.5
3.2.P.5.6	Justification of specification(s)	3.2.P.5.6
3.2.P.6	Reference standards or materials	3.2.P.6
3.2.P.7	Container closure system	3.2.P.7
3.2.P.8	Stability	3.2.P.8
3.2.P.8.1	Stability summary and conclusions	3.2.P.8.1
3.2.P.8.2	Post-approval stability protocol and stability commitment	3.2.P.8.2
3.2.P.8.3	Stability data	3.2.P.8.3
3.2.R	Regional information	3.2.R
3.2.A	Appendices	3.2.A
3.2.A.1	Facilities and equipment – manufacturer	3.2.A.1
3.2.A.1	Facilities and equipment – manufacturer1	3.2.A.1
3.2.A.1	Facilities and equipment – manufacturer2	3.2.A.1
3.2.A.2	Adventitious agents safety evaluation – manufacturer	3.2.A.2
3.2.A.2	Adventitious agents safety evaluation – manufacturer1	3.2.A.2
3.2.A.3	Novel excipients	3.2.A.3
3.3	Literature references	3.3
3.3	Reference 1	3.3
3.3	Reference 2	3.3
3.3	Reference 3	3.3

Module 4	Nonclinical study reports	
4.2	Study reports	4.2
4.2.1	Pharmacology	4.2.1
4.2.1.1	Primary pharmacodynamics	4.2.1.1
	study report 1	4.2.1.1
	study report 2	4.2.1.1
	study report 3	4.2.1.1
4.2.1.2	Secondary pharmacodynamics	4.2.1.2
	study report 1	4.2.1.2
	study report 2	4.2.1.2
	study report 3	4.2.1.2
4.2.1.3	Safety pharmacology	4.2.1.3
	study report 1	4.2.1.3
	study report 2	4.2.1.3
	study report 3	4.2.1.3

Module 4	Nonclinical study reports	
4.2.1.4	Pharmacodynamic drug interaction	4.2.1.4
	study report 1	4.2.1.4
	study report 2	4.2.1.4
	study report 3	4.2.1.4
4.2.2	Pharmacokinetics	4.2.2
4.2.2.1	Analytical methods and validation reports	4.2.2.1
	study report 1	4.2.2.1
	study report 2	4.2.2.1
	study report 3	4.2.2.1
4.2.2.2	Absorption	4.2.2.2
	study report 1	4.2.2.2
	study report 2	4.2.2.2
	study report 3	4.2.2.2
4.2.2.3	Distribution	4.2.2.3
	study report 1	4.2.2.3
	study report 2	4.2.2.3
	study report 3	4.2.2.3
4.2.2.4	Metabolism	4.2.2.4
	study report 1	4.2.2.4
	study report 2	4.2.2.4
	study report 3	4.2.2.4
4.2.2.5	Excretion	4.2.2.5
	study report 1	4.2.2.5
	study report 2	4.2.2.5
	study report 3	4.2.2.5
4.2.2.6	Pharmacokinetic other pharmacokinetic studies drug linteractions (nonclinical)	4.2.2.6
	study report 1	4.2.2.6
	study report 2	4.2.2.6
	study report 3	4.2.2.6
4.2.2.7	Other pharmacokinetic studies	4.2.2.7
	study report 1	4.2.2.7
	study report 2	4.2.2.7
	study report 3	4.2.2.7
4.2.3	Toxicology	4.2.3
4.2.3.1	Single-dose toxicity	4.2.3.1
	study report 1	4.2.3.1
	study report 2	4.2.3.1
	study report 3	4.2.3.1
4.2.3.2	Repeat-dose toxicity	4.2.3.2
	study report 1	4.2.3.2
	study report 2	4.2.3.2
	study report 3	4.2.3.2
4.2.3.3	Genotoxicity	4.2.3.3
4.2.3.3.1	In vitro	4.2.3.3.1
	study report 1	4.2.3.3.1
4.2.3.3.2	In vivo	4.2.3.3.2
	study report 1	4.2.3.3.2
	study report 2	4.2.3.3.2
4.2.3.4	Carcinogenicity	4.2.3.4
4.2.3.4.1	Long-term studies	4.2.3.4.1
	study report 1	4.2.3.4.1
4.2.3.4.2	Short- or medium term studies	4.2.3.4.2
	study report 1	4.2.3.4.2

Module 4	Nonclinical study reports	
	study report 2	4.2.3.4.2
4.2.3.4.3	Other studies	4.2.3.4.3
	study report 1	4.2.3.4.3
	study report 2	4.2.3.4.3
	study report 3	4.2.3.4.3
4.2.3.5	Reproductive and developmental toxicity	4.2.3.5
4.2.3.5.1	Fertility and early embryonic development	4.2.3.5.1
	study report 1	4.2.3.5.1
4.2.3.5.2	Embryo-foetal development	4.2.3.5.2
	study report 1	4.2.3.5.2
	study report 2	4.2.3.5.2
4.2.3.5.3	Prenatal and postnatal development, including maternal function	4.2.3.5.3
	study report 1	4.2.3.5.3
	study report 2	4.2.3.5.3
	study report 3	4.2.3.5.3
4.2.3.5.4	Studies in which the offspring (juvenile animals) are dosed and/or further evaluated	4.2.3.5.4
	study report 1	4.2.3.5.4
4.2.3.6	Local tolerance	4.2.3.6
	study report 1	4.2.3.6
4.2.3.7	Other toxicity studies	4.2.3.7
4.2.3.7.1	Antigenicity	4.2.3.7.1
	study report 1	4.2.3.7.1
	study report 2	4.2.3.7.1
4.2.3.7.2	Immunotoxicity	4.2.3.7.2
	study report 1	4.2.3.7.2
4.2.3.7.3	Mechanistic studies	4.2.3.7.3
	study report 1	4.2.3.7.3
4.2.3.7.4	Dependence	4.2.3.7.4
	study report 1	4.2.3.7.4
	study report 2	4.2.3.7.4
4.2.3.7.5	Metabolites	4.2.3.7.5
	study report 1	4.2.3.7.5
	study report 2	4.2.3.7.5
	study report 3	4.2.3.7.5
4.2.3.7.6	Impurities	4.2.3.7.6
	study report 1	4.2.3.7.6
4.2.3.7.7	Other	4.2.3.7.7
	study report 1	4.2.3.7.7
4.3	Literature references	4.3
	Reference 1	4.3
	Reference 2	4.3
	Reference 3	4.3

Module 5	Clinical study reports	
5.1	Table of Contents	5.1
5.2	Tabular listing of all clinical studies	5.2
5.3	Clinical study reports	5.3
5.3.1	Reports of biopharmaceutic studies	5.3.1
5.3.1.1	Bioavailability (BA) study reports	5.3.1.1
	study report 1	5.3.1.1
	study report 2	5.3.1.1

Module 5	Clinical study reports	
	study report 3	5.3.1.1
5.3.1.2	Comparative BA and bioequivalence (BE) study reports	5.3.1.2
	study report 1	5.3.1.2
	study report 2	5.3.1.2
5.3.1.3	In vitro-in vivo correlation study reports	5.3.1.3
	study 51002 – title page	5.3.1.3
	study 51002 – synopsis	5.3.1.3
	study 51002 – body	5.3.1.3
	study 51002 – appendix-16-1-1	5.3.1.3
	study 51002 – appendix-16-1-2	5.3.1.3
	study 51002 – appendix-16-1-3	5.3.1.3
	study 51002 – appendix-16-1-4	5.3.1.3
	study 51002 – appendix-16-1-5	5.3.1.3
	study 51002 – appendix-16-1-6	5.3.1.3
	study 51002 – appendix-16-1-7	5.3.1.3
	study 51002 – appendix-16-1-8	5.3.1.3
	study 51002 – appendix-16-1-9	5.3.1.3
	study 51002 – appendix-16-1-10	5.3.1.3
	study 51002 – appendix-16-1-11	5.3.1.3
	study 51002 – appendix-16-1-12	5.3.1.3
	study 51002 – appendix-16-2-2	5.3.1.3
	study 51002 – appendix-16-2-7	5.3.1.3
	study 51002 – appendix-16-3-1	5.3.1.3
	study 51002 – appendix-16-3-2	5.3.1.3
5.3.1.4	Reports of bioanalytical and analytical methods for human studies	5.3.1.4
	study 51003 – title-page.pdf	5.3.1.4
	study 51003 – synopsis.pdf	5.3.1.4
	study 51003 – body	5.3.1.4
	study 51003 – appendix-16-1-1.pdf	5.3.1.4
	study 51003 – appendix-16-1-2.pdf	5.3.1.4
	study 51003 – appendix-16-1-3.pdf	5.3.1.4
	study 51003 – appendix-16-1-4.pdf	5.3.1.4
	study 51003 – appendix-16-1-5.pdf	5.3.1.4
	study 51003 – appendix-16-1-7.pdf	5.3.1.4
	study 51003 – appendix-16-1-8.pdf	5.3.1.4
	study 51003 – appendix-16-1-9.pdf	5.3.1.4
	study 51003 – appendix-16-1-10.pdf	5.3.1.4
	study 51003 – appendix-16-1-11.pdf	5.3.1.4
	study 51003 – appendix-16-1-12.pdf	5.3.1.4
	study 51003 – appendix-16-2-2.pdf	5.3.1.4
	study 51003 – appendix-16-2-7.pdf	5.3.1.4
	study 51003 – appendix-16-3-1.pdf	5.3.1.4
	study 51003 – appendix-16-3-2.pdf	5.3.1.4
5.3.2	Reports of studies pertinent to PK using human biomaterials	5.3.2
5.3.2.1	Plasma protein binding study reports	5.3.2.1
	study report 1	5.3.2.1
5.3.2.2	Reports of hepatic metabolism and drug interaction studies	5.3.2.2
	study report 1	5.3.2.2
5.3.2.3	Reports of studies using other human biomaterials	5.3.2.3
	study report 51006	5.3.2.3
5.3.3	Reports of human PK studies	5.3.3
5.3.3.1	Healthy subject PK and initial tolerability study reports	5.3.3.1

Module 5	Clinical study reports	
	study report 1	5.3.3.1
	study report 2	5.3.3.1
5.3.3.2	Patient PK and initial tolerability study reports	5.3.3.2
	study report 1	5.3.3.2
5.3.3.3	Intrinsic factor PK study reports	5.3.3.3
	study report 1	5.3.3.3
5.3.3.4	Extrinsic factor PK study reports	5.3.3.4
	study report 1	5.3.3.4
5.3.3.5	Population PK study reports	5.3.3.5
	study report 1	5.3.3.5
5.3.4	Reports of human PD studies	5.3.4
5.3.4.1	Healthy subject PD and PK/PD study reports	5.3.4.1
	study report 1	5.3.4.1
5.3.4.2	Patient PD and PK/PD study reports	5.3.4.
	study report 1	5.3.4.2
	study report 2	5.3.4.2
5.3.5	Reports of efficacy and safety studies (confusion)	5.3.5
5.3.5.1	Study reports of controlled clinical studies pertinent to the claimed indication	5.3.5.1
	study ab12345 – synopsis	5.3.5.1
	study ab12345 – report body	5.3.5.1
	study ab12345 – protocol	5.3.5.1
	study ab12345 – protocol amendment a	5.3.5.1
	study ab12345 – randomisation code	5.3.5.1
	study ab12345 – adverse events listings	5.3.5.1
	study ab12345 – blank CRF	5.3.5.1
	study ab12345 – demographic table	5.3.5.1
	study ab12345 – ethics committee approval	5.3.5.1
	study cd98765 – synopsis	5.3.5.1
	study cd98765 – report body	5.3.5.1
	study cd98765 – protocol	5.3.5.1
	study cd98765 – randomisation code	5.3.5.1
	study cd98765 – adverse events listings	5.3.5.1
	study cd98765 – blank CRF	5.3.5.1
	study cd98765 – demographic table	5.3.5.1
	study cd98765 – ethics committee approval	5.3.5.1
5.3.5.2	Study reports of uncontrolled clinical studies	5.3.5.2
	study report 51015	5.3.5.2
5.3.5.3	Reports of analyses of data from more than one study	5.3.5.3
	study report 51016	5.3.5.3
5.3.5.4	Other clinical study reports	5.3.5.4
	study report 51017	5.3.5.4
5.3.6	Post-marketing experience	Not Applicable
5.3.7	Case report forms and individual patient listings when submitted	5.3.7
	study ab12345 – appendix 16-3-1	5.3.7
	study ab12345 – appendix 16-3-2	5.3.7
	study ab12345 – appendix 16-4	5.3.7
	study cde98765 – appendix 16-3-1	5.3.7
	study cde98765 – appendix 16-3-2	5.3.7
	study cde98765 – appendix 16-4	5.3.7
	study 51002 – appendix 16-3-1	5.3.7
	study 51002 – appendix 16-3-2	5.3.7
	study 51002 – appendix 16-4	5.3.7

Module 5	Clinical study reports	
	study 51003 – appendix 16-3-1	5.3.7
	study 51003 – appendix 16-3-2	5.3.7
	study 510023 – appendix 16-4	5.3.7
5.4	Literature references	5.4
	Reference 1	5.4
	Reference 2	5.4
	Reference 3	5.4

Annex 3 Naming of files

	Module 1 Administrative information and prescribing information for Australia The name of the folder for module 1 should be m1.	
Section in CTD	**Description**	**Folder name**
1.0	Letter of application	m1-0-letter-applic
1.0.0	Electronic lodgement cover sheet	m1-0-0-elect-lodge
1.0.1	Letter of application	m1-0-1-letter-applic
1.0.2	Responses to questions	m1-0-2-responses-quest
1.1	Comprehensive table of contents	m1-1-toc
1.2	Application forms	m1-2-applic-form
1.2.1	Application form	m1-2-1-applic-form
1.2.2	Pre-submission details	m1-2-2-pre-submission
1.2.3	Patent certification	m1-2-3-patent-certification
1.3	Medicine information documents, packaging, and labelling	m1-3-aust-labelling-packaging
1.3.1	Proposed Australian product information and package insert	m1-3-1-proposed–pi
1.3.1.1	Proposed Australian product information and package insert	m1-3-1-1-proposed–pi
1.3.1.2	Proposed Australian product information and package insert - annotated	m1-3-1-2-annotated-proposed–pi
1.3.2	Proposed Australian consumer medicine information	m1-3-1-proposed–cmi
1.3.3	Therapeutic goods and use of human embryos or human embryonic stem cells or material derived from them	m1-3-3-embryo-declaration
1.3.4	Label mock-ups and specimens	m1-3-4-label-mock-up
1.4	Information about the experts	m1-4-expert
1.4.1	Information about the expert - Quality	m1-4-1-quality
1.4.2	Information about the expert – Non-clinical	m1-4-2-non-clinical
1.4.3	Information about the expert - Clinical	m1-4-3-clinical
1.5	Specific requirements for different types of applications	m1-5-specific-requirements
1.5.1	Literature based submission documents	m1-5-1-literature-based
1.5.2	Orphan drug designation	m1-5-2-orphan

1.5.3	Genetically modified organisms: Consent from the Office of the Gene Technology Regulator	m1-5-3-gmo-consents
1.5.4	Additional trade name declarations	m1-5-4-attitional-trad-name
1.5.5	Co-marketed medicine declarations	m1-5-5-co-marketed-medicine
1.6	Drug and plasma master files and Certificates of Suitability of Monographs of the European Pharmacopoeia	m1-6-drug-master-files-cert-of-suitability
1.6.1	Relevant external sources	m1-6-1-dmf-pms-cos-
1.6.2	Sponsor's declaration	m1-6-2-sponsors declaration
1.6.3	Letters of access	m1-6-3-letters of access
1.6.4	Certificates of suitability (including Annexes)	m1-6-4-cert-of-suitability
1.7	Good manufacturing practice	m1-7-good-manufacturing-pactice
1.7.1	List of Australian manufacturer names and licence numbers	m1-7-1-aust-mfrs
1.7.2	GMP clearance letters for all overseas manufacturing sites	m1-7-2-os-mfrs
1.7.3	Copies of applications for TGA GMP clearances	m1-7-3-os-mfrs-without-clearance
1.8	Compliance with meetings and pre-submission processes	m1-8-meetings
1.8.1	Details of compliance with pre-submission meeting outcomes	m1-8-1-compliance-pre-sub-meeting
1.8.2	Details of any additional data to be submitted	m1-8-2-additional data-details
1.8.3	Declaration of compliance with pre-submission planning form and planning letter	m1-8-3-compliance-pre-sub-form
1.9	Individual patient data	m1-9-indiv-patient-data
1.9.1	Individual patient data	m1-9-1-indiv-patient-data
1.10	Overseas regulatory status	m1-10-overseas-reg-status
1.10.1	Overseas regulatory status	m1-10-1-overseas-reg-status
1.10.2	Product information from Canada, the Netherlands, New Zealand, Sweden, UK and USA	m1-10-2-other-countries-pi
1.10.2.1	US prescribing information	m1-10-2-1-us
1.10.2.2	EU summary of product characteristics	m1-10-2-2-eu
1.10.2.3	Canadian product monograph	m1-10-2-3-canada
1.10.2.4	NZ data sheet	m1-10-2-4-new-zealand
1.10.3	Data set similarities and differences	m1-10-3-dataset-similarities
1.11	Summary of biopharmaceutic studies	m1-11-summary-biopharm-studies
1.11.1	Summary of a bioavailability or bioequivalence study	m1-11-1-summary-biopharm-studies
1.11.2	Justification for not providing appropriate biopharmaceutic studies	m1-11-2-justification- no-biopharm-studies
1.12	Paediatric development program	m1-12-paediatrics
1.12.1	References to paediatric development program	
1.13	Information relating to pharmacovigilance	m1-13-pharmacovigilance

1.13.1	Risk management plan for Australia	m1-13-1-riskmgt-system
Annex I	Antibiotic resistance data	m1-annex1-antibiotic-resist
Annex II	Overseas evaluation reports	m1-annex2-other-countries-evaluation-report

	Module 2 Summaries The name of the folder for module 2 should be m2.	
Section in CTD	**Description**	**Folder name**
2.1	Table of contents	21-toc
2.2	Introduction	22-intro
2.3	Quality overall summary	23-qos
2.4	Nonclinical overview	24-nonclin-over
2.5	Clinical overview	25-clin-over
2.6	Nonclinical written and tabulated summaries	26-nonclin-sum
2.7	Clinical summary	27-clin-sum

	Module 3 Quality The name of the folder for module 3 should be m3.	
Section in CTD	**Description**	**Folder name**
3.1	Table of contents	31-toc
3.2	Body of data	32-body-data
3.2.S	Drug substance	32s-drug-sub
3.2.S	Drug substance [name] [manufacturer]	substance-1-manufacturer-1
3.2.S.1	General information (name, manufacturer1)	32s1-gen-info
3.2.S.2	Manufacture (name, manufacturer1)	32s2-manuf

3.2.S.3	Characterisation (name, manufacturer1)	32s3-charac
3.2.S.4	Control of drug substance (name, manufacturer1)	32s4-contr-drug-sub
3.2.S.4.1	Specification (name, manufacturer1)	32s41-spec
3.2.S.4.2	Analytical procedures (name, manufacturer1)	32s42- analyt-proc
3.2.S.4.3	Validation of analytical procedures (name, manufacturer1)	32s43-val-analyt-proc
3.2.S.4.4	Batch analyses (name, manufacturer1)	32s44-batch-analys
3.2.S.4.5	Justification of specification (name, manufacturer1)	32s45-justif-spec
3.2.S.5	Reference standards or materials (name, manufacturer1)	32s5-ref-stand
3.2.S.6	Container closure system (name, manufacturer1)	32s6-cont-closure-sys
3.2.S.7	Stability (name, manufacturer1)	32s7-stab
3.2.P	Drug product (name, dosage form)3	32p-drug-prod
3.2.P	Drug product (name, dosage form) – name	product-1
3.2.P.1	Description and composition of the drug product (name, dosage form)	32p1-desc-comp
3.2.P.2	Pharmaceutical development (name, dosage form)	32p2-pharm-dev
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