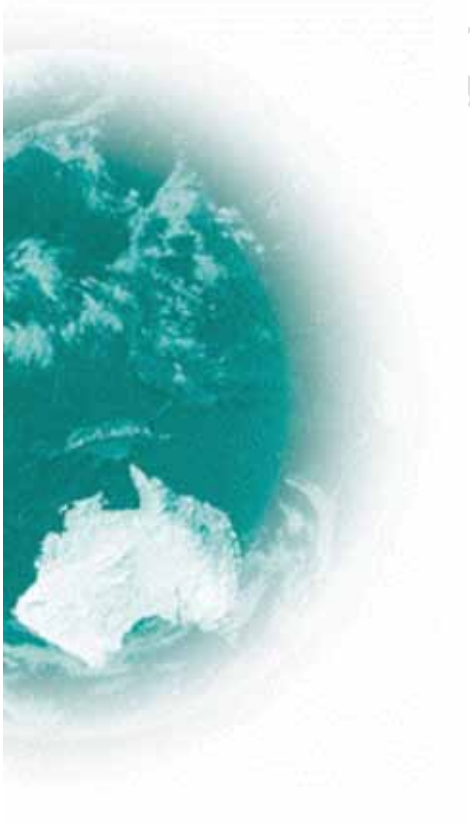
Australian Government

Department of Health and Ageing

Therapeutic Goods Administration

Electronic format requirements for industry for providing regulatory information

Non-eCTD electronic submissions (NeeS) for human medicinal products



Version: 2.0

March 2011

Document change record

	Details of Change	Section	Date
1	First version	All	January 2011
2	Corrections to Annex II—highlighting of hyperlinks and corrections to module numbers; updated to reflect TGA style guide; harmonisation of terminology with the streamlined submission process; consolidation of separate sections on TOCs, bookmarks, and submission media; linking provided to external documents; ambiguity in folder naming conventions resolved; introduction updated to explain process towards fully electronic submission process	All	March 2011

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1. Introduction

Lodgement of an electronic copy of a submission dossier is mandatory under the prescription medicines streamlined submission process as detailed in transitional draft *CTD—Module 1: Administrative information and prescribing information for Australia* (CTD—Module 1).

The electronic copy of the submission dossier should be lodged in non-eCTD electronic submissions (NeeS) format. This document provides general information on producing an electronic copy of a submission dossier in NeeS format, with references to further, more detailed information. The NeeS format for electronic submission dossiers is an interim format and sponsors should plan to adopt the eCTD format for the lodgement of electronic submission dossiers.[1]

The TGA is engaged in a process which will result, in the longer term, in the phasing out of paper submission dossiers. This transition to a fully electronic environment is complex and requires several intervening phases. The first phase was the TGA requirement under the streamlined submission process that submission dossiers be lodged in both paper and electronic format. The second phase was mandating the regulatory requirements for an electronic submission dossier. The ability of the TGA to meet the timeframes in the streamlined submission process and thereby provide certainty to sponsors is contingent upon sponsor lodgement of a quality electronic submission dosser that meets TGA regulatory requirements.

The third and subsequent phases will progress towards the goal of fully electronic eCTD submission.

This document will be updated periodically to reflect changes in legislation, and to provide further clarification where required.

2. General requirements

2.1 Scope

This document applies to the electronic copy of all submissions related to the registration, and variations to the registration, of human medicinal products described in Part 1 of Schedule 10 of the Therapeutic Goods Regulations 1990. This includes periodic safety update reports (PSURs) and active substance master files. For further information, see Part A of transitional draft *CTD—Module 1*.

2.2 Using the NeeS format

Sponsors can choose the NeeS format when lodging an application for initial registration or variation of registration. Once the NeeS format is chosen, it is expected that further applications and responses relating to the particular medicinal product are submitted in this same electronic format.

2.3 Organisation of NeeS submissions

All electronic submission dossiers must be structured in accordance with the common technical document (CTD) format, which for paper submissions became mandatory in Australia in February 2006. Information on the CTD format is provided on the TGA website.

[1] As the TGA does not have the necessary software to fully manipulate eCTD format submission dossiers, the acceptance of an eCTD dossier is subject to the following conditions at this time:

- eCTD dossiers will only be accepted for new chemical entity or new combination submissions
- eCTD dossiers must contain active links.

For NeeS format submission dossiers, the eCTD folder structure is used, as detailed in the *ICH granularity document* (International Conference on Harmonisation). Submission dossiers must follow the ICH eCTD folder naming conventions for modules 2 to 5 as specified in Appendix 3 of the *ICH Electronic common technical document specification*. Submission dossiers must follow the recommended TGA folder names (see Annex III) for module 1.

Navigation through a NeeS format submission dossier is based on electronic tables of contents, bookmarks, and hypertext links. This differs from the eCTD format in that two relevant XML files, the index.xml and au-regional.xml that provide the backbone of modules 2 to 5, and module 1 for Australia, respectively, and the *util* folder are not present.

Typically, a NeeS format submission dossier will include all dosage forms and strengths of a product with any one active ingredient. However, if the sponsor decides to have one NeeS format submission dossier 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.

2.4 Submission numbering

Sequence numbers, as defined for eCTD submissions, are not applicable for NeeS format submission dossiers. The use of a four digit number in the top level folder name is, however, recommended.

2.5 Structure and naming requirements

2.5.1. File and folder structure

Submission dossiers are a collection of documents and each document should be provided as a separate file. The structure of a NeeS format submission dossier must conform to the *ICH granularity document* and requirements set out in the transitional draft *CTD—Module 1*. It is recommended that the root folder of the submission dossier is named with the product (trade) name in lower case followed by the subfolder name: for example mydrug/0000/.

The number of characters in a folder/file path should not exceed 180 characters.

2.5.2. File naming

The eCTD file naming conventions described in the *ICH eCTD Specification* must be followed. If a sponsor 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 (for example: *pharmaceutical-development-container.pdf*)

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.

2.5.4. Empty folders

Where there is no content for a specific folder, the folder can be omitted. However, when the content is normally expected, a justification must be provided, in accordance with relevant guidelines, as to why the data/study has not been provided.

2.6 Tables of contents, bookmarks and hypertext links

2.6.1. Tables of contents

A NeeS format submission dossier must contain tables of contents (TOC) provided in PDF format. Tables of contents can be provided at the submission (main), module, and document levels. All documents lodged in a NeeS format submission dossier must be referenced from a hyperlinked table of contents. Hyperlinks for a document must always be provided to the first page of the appropriate file.

In the case of small submission dossiers (for example, for certain variations), especially when only one module beside module 1 is included, it is acceptable to have only one TOC referring directly to all submission dossier 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 must not include hyperlinks to documents in other modules. If the same document is used in more than one module, it must be provided in each module.

The file containing the main, submission-level table of contents must be named ctd-toc.pdf and located in the top level folder of the submission dossier. The files containing the module tables of contents 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.

Example tables of contents are provided in Annex II. It should be noted that these are examples and are provided for guidance and illustrative purposes only.

Where TOCs are included at the document level, they must be located within the same file as the rest of the document.

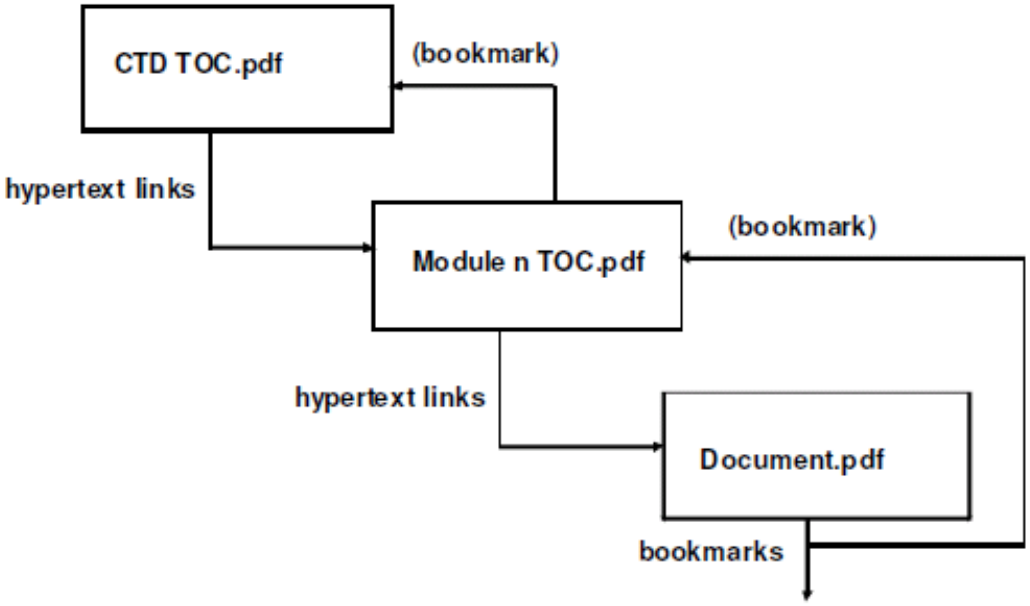
2.6.2. Bookmarks and hypertext links

Bookmarks and hypertext links allow for navigation through the documents in an electronic submission. It is expected any document that has a table of contents will have bookmarks (see the *ICH eCTD Specification* for details). Bookmarks are typically required for each document. If a table of contents is provided for the document, there should be a bookmark for each entry in the table of contents. Where there is no table of contents for a document, bookmarks should be provided to a sufficiently detailed level, typically to level 3 or 4 headings. A four-page document summarising findings could require bookmarks to aid navigation. However, a 300 page document containing a single data listing might not require bookmarks if there is no further internal structure.

An additional function might be provided to allow easy navigation back to the table of contents of the level 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 facilitates assessment of the submission dossier.

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

The figure below describes this hierarchy for tables of contents and bookmarks.



2.7 Lodging correspondence

During the submission process, information may be exchanged between the sponsor and the TGA to assist the processing or handling of the application. Not all such correspondence needs to be included in the NeeS format submission dossier. Correspondence sent via electronic means (for example, by email) only needs to be lodged in full in NeeS format if it relates directly to the content of the submission dossier. See section 1.0.2 Responses to requests for information, of transitional draft *CTD – Module 1* for additional information.

2.8 Paper requirements

Where a paper submission dossier is to be derived from a NeeS format electronic submission dossier, the guidance provided for this process for dossiers in eCTD format is applicable. See *Paper format: Requirements for industry for providing regulatory information* for further information.

2.9 File formats

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

2.9.1. PDF

In general terms, the majority of documents included in an electronic submission dossier should be in portable document format (PDF). This format is an open, de facto, electronic publishing standard.

There are several suppliers of PDF software. Sponsors must check PDF documents meet the following key requirements:

- files must be legible with Adobe Acrobat Reader, version 5.0 or higher
- PDF file version 1.4 must be used
- documents must 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 I for further guidance on text searchable documents.

2.9.2. Other file formats

Other file formats such as rich text format (RTF) or MSWord formats may be required in addition to PDF for a NeeS format submission dossier, for example, 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, 'working documents' on the same CD/DVD containing the NeeS format submission dossier.

2.10 Other technical information

2.10.1. Security issues

The physical security of the submission dossier during transportation is the responsibility of the sponsor.

2.10.2. Password protection

Submission or file level security is not permitted. If one-time security settings or password protection are used, this could constitute grounds for considering a submission not effective and therefore not accepted for evaluation.

2.10.3. Virus protection

The sponsor is responsible for ensuring the submission dossier does not contain any viruses. Virus checking should be performed with an up-to-date virus checker and be confirmed in the cover letter. After receipt by the TGA, a further virus check will be performed. If a virus is detected, it may constitute grounds for considering the submission not effective.

2.10.4. Electronic signatures

The TGA requires that certain specific electronic documents (for example, the cover page for the submission dossier) are authenticated by separate signed paper copies. See Part A of the transitional draft *CTD Module 1* for more information.

2.10.5. Transmission media

CD-ROM, CD-R, DVD-R are considered acceptable media standards. USB keys, hard drives, or other similar media are not acceptable. Discs should be archival quality. Protection, authenticity, and stability of information cannot be guaranteed on rewritable discs and these must not be used.

Sponsors must provide the electronic information on the smallest number of discs possible, taking into consideration the size of the submission dossier. If an individual NeeS format submission dossier is of such a size as to span several CDs, the provision of the submission dossier on a single DVD is recommended. However, if the sponsor is unable to provide a DVD, and the application spans multiple CDs, where possible individual CTD modules should not be split over multiple CDs (for example, a single CD should contain all of module 1, another all of module 2, and so on).

A separate CD/DVD must be provided for each copy of a NeeS format submission dossier. See section 2.10.8 for more information.

2.10.6. Labelling of media

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

- format: NeeS
- sponsor'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 the set (for example, 1(5), 2(5))
- application type(s) in the submission (for example, new chemical entity, extension of indications).

2.10.7. Procedure for sending electronic information

Electronic media sets must be submitted at the same time as any required paper documentation. The electronic media must be packed adequately to prevent damage.

2.10.8. Number of electronic copies required

Six copies of the complete electronic submission dossier must be provided for category 1 and category 2 submissions. See Part A of transitional *CTD Module 1* for more information.

3. Module specific information

3.1 Module 1.2: Administrative information (application forms)

The application form must always be provided as a PDF file within the NeeS format structure and also submitted as a signed paper copy (see section 1.2 Application forms, of transitional draft *CTD Module 1* for more information). 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 format submissions, product information (PI) must be supplied in PDF files within the NeeS structure. For products already registered where changes to the PI are proposed, the 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 MSWord file version must also be submitted to facilitate assessment. These files must not be added within the NeeS structure but provided in a separate folder called, for example, 'working documents' on the same CD/DVD containing the NeeS format submission (see also section 2.9.2).

3.3 Module 1: responses

The organisation of the submission of electronic information in response to a consolidated s. 31 request for information from the TGA must follow the same basic principles as the initial submission. The written response must be lodged following the recommended Australian response folder and file structure (see also section 1.0.2 Responses to requests for information, in transitional draft *CTD Module 1*). 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 2.6.

Annex I—Guidance on text searchable documents

I.1 General

Sponsors must ensure all submissions contain the maximum amount of text searchable content. Documents with text searchable content 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 annex provides some guidance about what must be text searchable and ways to ensure files are created appropriately.

I.1.1 Creating text searchable files

Portable document format (PDF) files with text searchable content can be created by all PDF tools from a source file in a text format (for example, MSWord, SAS, MSPowerPoint, rich text files). Creating a file in this way minimises the file size (measured in kilobytes or megabytes).

If the document is not available electronically (it only exists in paper form), then scanning to PDF and using an optical character recognition (OCR) routine is the only way to create text searchable content. 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 rarely matches the original text entirely. Tools for checking and correcting this text tend to be somewhat cumbersome. For these reasons, scanning/OCR is recommended only as a last resort.

Text produced by the OCR routine should be 'hidden' behind the image/picture of the scanned document so the user can refer to the 'picture' of the page and the text in it as final verification of the data. The sponsor must ensure that, as a minimum, the text in the scanned image is legible to the user. Poor quality images must not be provided, and poor quality images produce poor quality OCR text.

I.2 Documents that must be text searchable

Text searchable means the PDF must be produced wherever possible from a text source such as MSWord. If sourced from a scanned original, it must be in OCR format.

The following must always be text searchable:

- key administrative documents in module 1 including the cover letter, application form, and product information documents
- any document in module 2 of the submission, including 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 (for example, in any reports, methods, analytical procedures) 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 section 1.3 below for more information).

I.3 Documents that do not need to be text searchable

The PDF of documents from this category must be produced wherever possible from a text source, such as MSWord, but if sourced from a scanned original, there is no need for OCR format.

Documents in this category are:

- any original GMP certificate
- any original certificate of analysis
- any manufacturer's licence
- any certificates of suitability
- any manufacturing authorisation
- any document written in a foreign language where a translation is provided in English (however, the translation must be text searchable, see section 1.2)
- 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
    - sponsors should consider providing signatures on separate pages from key text in such documents as reports or overviews.

I.4 Further information

If sponsors are uncertain whether or not a particular document must be text searchable, they should contact the TGA for guidance at bpr.project@tga.gov.au.

Annex II—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.

II.1 Example 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

II.2 Example module TOCs

Module 1	**Administrative information and prescribing information for Australia**	**Reference**
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
1.2	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
1.5.1	Literature based submission documents	1.5.1
1.5.2	Orphan drug designation	1.5.2
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
1.6.2	Sponsor's declaration	1.6.2
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
1.9	Individual patient data	1.9
1.9.1	Individual patient data	1.9.1
1.10	Overseas regulatory status	1.10
1.10.1	Overseas regulatory status	1.10.1
1.10.2	Product information from Canada, the Netherlands, New Zealand, Sweden, UK and USA	1.10.2
1.10.3	Data set similarities and differences	1.10.3
1.11	Summary of biopharmaceutic studies	1.11
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
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Annex II	Overseas evaluation reports	Annex II

Module 2	**Common technical document summaries**	**Reference**
2.2	Introduction	2.2
2.3.S	Drug substance–Substance–R Maleate–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
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
2.3.S.7	Stability	2.3.S.7
2.3.P	Drug product–substance–dosage form–Manufacturer3	2.3.P
2.3.P.1	Description and composition of the drug product	2.3.P.1
2.3.P.2	Pharmaceutical development	2.3.P.2
2.3.P.3	Manufacture	2.3.P.3
2.3.P.4	Control of excipients	2.3.P.4
2.3.P.5	Control of drug product	2.3.P.5

2.3.P.6	Reference standards or materials	2.3.P.6
2.3.P.7	Container closure system	2.3.P.7
2.3.P.8	Stability	2.3.P.8
2.3.A	Appendices	2.3.A
2.3.A.1	Facilities and equipment	2.3.A.1
2.3.A.2	Adventitious agents safety evaluation–Substance–S–Manufacturer	2.3.A.2
2.3.A.2	Adventitious Agents Safety Evaluation–Substance–R–Manufacturer	2.3.A.2
2.3.A.3	Novel excipients	2.3.A.3
2.3.R	Regional information	2.3.R
2.4	Nonclinical overview	2.4
2.5	Clinical overview	2.5
2.6	Nonclinical written and tabulated summary	2.6
2.6.1	Introduction	2.6.1
2.6.2	Pharmacology written summary	2.6.2
2.6.3	Pharmacology tabulated summary	2.6.3
2.6.4	Pharmacokinetics written summary	2.6.4
2.6.5	Pharmacokinetics tabulated summary	2.6.5
2.6.6	Toxicology written summary	2.6.6
2.6.7	Toxicology tabulated summary	2.6.7
2.7	Clinical summary	2.7
2.7.1	Summary of biopharmaceutic studies and associated analytical methods	2.7.1
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
2.7.5	Literature references	2.7.5
2.7.6	Synopses of individual studies	2.7.6

Module 3	**Quality**	**Reference**
3.2	Body of data	3.2
3.2.S	Drug substance (substance–manufacturer)	3.2.S
3.2.S.1	General information (substance–manufacturer)	3.2.S.1
3.2.S.1.1	Nomenclature (substance–manufacturer)	3.2.S.1.1
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
3.2.S.2	Manufacture (substance–manufacturer)	3.2.S.2
3.2.S.2.1	Manufacturer(s) (substance–manufacturer)	3.2.S.2.1
3.2.S.2.2	Description of manufacturing process and process controls (substance–manufacturer)	3.2.S.2.2
3.2.S.2.3	Control of materials (substance–manufacturer)	3.2.S.2.3
3.2.S.2.4	Control of critical steps and intermediates (substance–manufacturer)	3.2.S.2.4
3.2.S.2.5	Process validation and/or evaluation (substance–manufacturer)	3.2.S.2.5
3.2.S.2.6	Manufacturing process development (substance–manufacturer)	3.2.S.2.6
3.2.S.3	Characterisation (substance–manufacturer)	3.2.S.3
3.2.S.3.1	Elucidation of structure and other characteristics (substance–manufacturer)	3.2.S.3.1
3.2.S.3.2	Impurities (substance–manufacturer)	3.2.S.3.2

3.2.S.4	Control of drug substance (substance–manufacturer)	3.2.S.4
3.2.S.4.1	Specification (substance–manufacturer)	3.2.S.4.1
3.2.S.4.2	Analytical procedures (substance–manufacturer)	3.2.S.4.2
3.2.S.4.3	Validation of analytical procedures (substance–manufacturer)	3.2.S.4.3
3.2.S.4.4	Batch analyses (substance–manufacturer)	3.2.S.4.4
3.2.S.4.5	Justification of specification (substance–manufacturer)	3.2.S.4.5
3.2.S.5	Reference standards or materials (substance–manufacturer)	3.2.S.5
3.2.S.6	Container closure system (substance–manufacturer)	3.2.S.6
3.2.S.7	Stability (substance–manufacturer)	3.2.S.7
3.2.S.7.1	Stability summary and conclusions (substance–manufacturer)	3.2.S.7.1
3.2.S.7.2	Post–approval stability protocol and stability commitment (substance–manufacturer)	3.2.S.7.2
3.2.S.7.3	Stability data (substance–manufacturer)	3.2.S.7.3
3.2.S	Drug substance (substance–manufacturer1)	3.2.S
3.2.S.1	General information (substance–manufacturer1)	3.2.S.1
3.2.S.1.1	Nomenclature (substance–manufacturer1)	3.2.S.1.1
3.2.S.1.2	Structure (substance–manufacturer1)	3.2.S.1.2
3.2.S.1.3	General properties (substance–manufacturer1)	3.2.S.1.3
3.2.S.2	Manufacture (substance–manufacturer1)	3.2.S.2
3.2.S.2.1	Manufacturer(s) (substance–manufacturer1)	3.2.S.2.1
3.2.S.2.2	Description of manufacturing process and process controls (substance–manufacturer1)	3.2.S.2.2
3.2.S.2.3	Control of materials (substance–manufacturer1)	3.2.S.2.3
3.2.S.2.4	Control of critical steps and intermediates (substance–manufacturer1)	3.2.S.2.4
3.2.S.2.5	Process validation and/or evaluation (substance–manufacturer1)	3.2.S.2.5
3.2.S.2.6	Manufacturing process development (substance–manufacturer1)	3.2.S.2.6
3.2.S.3	Characterisation (substance–manufacturer1)	3.2.S.3
3.2.S.3.1	Elucidation of structure and other characteristics (substance–manufacturer1)	3.2.S.3.1
3.2.S.3.2	Impurities (substance–manufacturer1)	3.2.S.3.2
3.2.S.4	Control of drug substance (substance–manufacturer1)	3.2.S.4
3.2.S.4.1	Specification (substance–manufacturer1)	3.2.S.4.1
3.2.S.4.2	Analytical procedures (substance–manufacturer1)	3.2.S.4.2
3.2.S.4.3	Validation of analytical procedures (substance–manufacturer1)	3.2.S.4.3
3.2.S.4.4	Batch analyses (substance–manufacturer1)	3.2.S.4.4
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
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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
3.2.P.4	Control of excipient—compendial	3.2.P.4
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3.2.P.4.6	Novel excipients	3.2.P.4.6
3.2.P.4	Control of excipient—non-compendial excipient	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
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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
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3.2.P.8	Stability	3.2.P.8
3.2.P.8.1	Stability summary and conclusions	3.2.P.8.1
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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
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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
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
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4.2.2.4	Metabolism	4.2.2.4
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	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 Iinteractions (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

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4.2.3.2	Repeat-dose toxicity	4.2.3.2
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	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
	study report 2	4.2.3.4.2
4.2.3.4.3	Other studies	4.2.3.4.3
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	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
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	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**	**Reference**
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
	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
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	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
	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	5.3.4.2
	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	5.3.6
5.3.7	Case report forms and individual patient listings when submitted	5.3.7
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	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
	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 III—Naming of folders

Module 1: Administrative information and prescribing information for Australia The name of the folder for module 1 should be m1		
CTD Section	**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	M1–12–1–paediatrics
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

The naming of folders in modules 2 to 5 must follow the format described in Appendix 3: General Considerations for the CTD Modules of the *ICH eCTD specification*.