Australian Government
Department of Health
Therapeutic Goods Administration

NeeS AU Module 1 and regional information

Specification and guidance for use

Version 2.0, October 2017

TGA Health Safety Regulation

Contents

Introduction

This guidance:

- needs to be used in conjunction with the General dossier requirements
- provides general information on producing an electronic copy of a dossier in the NeeS format
- relates to preparing and structuring the data to be submitted in an electronic format to support applications to:
  - register a medicine under Section 23 of the *Therapeutic Goods Act 1989* (the Act)
  - vary the registration of a medicine Section 9D of the Act.

The NeeS specification is an interim arrangement as applicants plan the move to full eCTD.

Summary of updates in version 2.0

Purpose of the updates

- Support the implementation of applicable parts of the Medicine and Medical Device Review (MMDR) recommendations; namely the notification pathway.
- Allow for the possibility of dossiers supporting requests for multiple changes (see further references in Appendix 1 of this document to 'Work sharing' and/or 'work grouping').
- Provide greater clarity to users.
- Enhance dossier quality (introduce additional validation criteria to assist with dossier quality).
- Allow for automation of some process steps within the TGA.

Summary of NeeS updates

The following documents and specifications have been updated as part of the upgrade to version 2.0:

- AU NeeS specification: Module 1 and regional information (this document)
- Australian regional specification and validation criteria (AU Validation Criteria v3.1.xlsx) and related files

For a comprehensive understanding of the updates introduced in version 2.0 please refer to this document and to the Australian validation criteria where all updates (both new and changes) have been *highlighted in yellow, italicised and include an asterisk**.

Introduction of the NeeS envelope form

An envelope form has been introduced for NeeS submissions to allow greater validation of these submissions and the automation of the uploading processes.

The envelope form stores information within an 'XML envelope like' structure which allows the NeeS sequences to behave in a similar manner to eCTD sequences with XML backbones.

Automation will enable increased efficiencies and improve communication and information on submissions received and processed.

The information contained in the envelope is also linked to many validation criteria. This increases transparency of content and format required to improve the evaluation. It also helps to avoid delays due to missing content for a regulatory activity, or due to qualitative issues with the files provided.

To facilitate the creating of such 'envelope information', the TGA has provided an Excel form which will auto create the required content if filled in correctly. A detailed description of this form and how to complete it forms part of this document.

Please be aware that NeeS continues to be an interim option. The XML form will allow greater usability and control for NeeS submissions; however sponsors are encouraged to transition to eCTD to obtain the benefits of lifecycle management and access to a greater variety of evaluation pathways.

For further information on any of the updates please contact esubmissions@health.gov.au.

Module 1 Section updates

New sections	Rationale
1.3.1.3 Product information – approved	The inclusion of an approved folder clearly distinguishes the approved copy from the working copies
1.3.2.3 Consumer medicine information – approved	

Updated sections	Previous	Rationale
1.3.1.4 Package insert	1.3.1.3 Package insert	Moved section ID to accommodate Product information – approved
1.3.3.1 Label mock-ups and specimens – clean	1.3.3 Label mock-ups and specimens	Section has been divided to clearly distinguish the clean, annotated and newly added approved copies.
1.3.3.2 Label mock-ups and specimens – annotated		
1.3.3.3 Label mock-ups and specimens – approved		

Sequence Type updates

New	Rationale
Notification	To make available, Notifications for both Prescription Medicines and for OTC Medicines
CN	
Duplicate	Requirement inclusion for potential work sharing options.

Where known, additional document requirements have been included within the Document Matrix for each of these new sequence types. As more detail on document requirements becomes available, we will update the Document Matrix that appears on the TGA website.

Separate specifications have **not been developed for NeeS and therefore the sequence types and description updates are the same for NeeS as for eCTD. Please note however that not all registration pathways and therefore sequence types are available to dossiers submitted in NeeS**. For further information please contact streamlinedsubmission@health.gov.au.

Updated Sequence Type	Previous	Rationale
Product Withdrawal	Withdrawal	Name change to better align with the use of this sequence type. Validation criteria have also been amended.

NeeS validation criteria

Updates to the validation criteria for NeeS have been included within version 2.0.

New validation criteria have been included primarily to support the introduction of the NeeS Envelope, as well as new Sections and Sequence Types. Updates have also been made to some current criteria to provide further clarity based on experience gained to date.

Terminology

It is acknowledged that the terminology to describe regulatory activities and electronic submissions differs between regions. To assist users interpret this guidance and specification a brief list of terms used is described below:

Term	Definition
Dossier	a structured set of folders/documents containing the information that supports your request for an evaluation by the TGA
eCTD	electronic Common Technical Document – an electronic standard for the Common Technical Document (CTD) providing the means for transferring information from pharmaceutical companies to agencies
*eCTD application	for the purpose of this document – refers to a collection of electronic documents filed under an e-Identifier and comprises of a number of sequences and regulatory activities
Envelope	Contains the metadata relevant to the eCTD or NeeS sequence. Metadata are referred to as envelope elements
e-Identifier	is a combination of a letter and six digits, for example in NeeS the format, n123456. It is the unique identifier for the NeeS application that tracks the products for the entire lifecycle (previously eSubmission Identifier)
leaf	Structural element of an eCTD submission delivering a document. It provides the link information to the document along with the title associated with the linked content.

Term	Definition
NeeS	Non-eCTD Electronic Submission – an alternative electronic standard to eCTD consisting of PDF Files and PDF Table of Contents linking all content for navigational purposes
regulatory activity	a collection of sequences covering a specific request. Referred to in Australia as a submission e.g. Submission for a new chemical entity (NCE).
sequence	a sequence is a package of information bundled together in an electronic structure providing information to the agency. The contents of a sequence will depend on the regulatory activity type and whether it is the initial sequence of the regulatory activity or a follow-up providing additional data or changes.
Stream	An indication of the clinical team that will deal with a request to register a new product. Each stream corresponds to a therapeutic category. These are available on the TGA website.

*Within Australia the words 'submission' and 'application' have very specific meanings within our regulatory framework and legislation. To avoid confusion 'eCTD application' will be used to describe eCTD related terminology as used by the ICH rather than 'application'.

Implementation/transition plan

To allow for planning and software updates we have incorporated a transition period for the uptake of the new version of the AU NeeS Module 1 specification.

The initial version of this specification was not given a version number. This updated version is given the number 2.0 to avoid confusion with the current NeeS version.

Timelines for implementation of version 2.0

- The AU NeeS Module 1 version 2.0 specification will be effective starting 1 January 2018.
- The AU NeeS Module 1 version 1.0 specification will be accepted until 30 June 2018.

Between 1 January 2018 and 30 June 2018 we will accept both the new version 2.0 and the current version 1.0 of the specification.

Organising NeeS submissions

All dossiers must be structured in accordance with the Common Technical Document (CTD) format, a format Australia initially adopted in 2004.

For electronic dossiers using the NeeS format:

- Use the CTD folder structure as detailed in the Annex to the ICH guideline Organisation of the Common Technical Document for the Registration of Pharmaceuticals for Human Use.
- Make sure the breakdown of the electronic submission conforms with the ICH Granularity Document (the Annex to the Organisation of the Common Technical Document for the Registration of Pharmaceuticals for Human Use).
- Follow the ICH and AU eCTD file naming conventions.

Preparing for your NeeS transaction

Before you submit your regulatory activity in NeeS format, you will need to:

1. Obtain an e-Identifier
2. Complete the NeeS Envelope Form
3. Prepare your cover letter
4. Validate the NeeS submission
5. Structure the folder
6. Select the electronic media
7. Pack and send the dossier

Obtain an e-Identifier

You will need an e-Identifier before you submit your regulatory activity for an application in the NeeS format.

To obtain an e- Identifier:

- send an email to esubmissions@health.gov.au.
- include the following information in your email:
  - the applicant's name as listed in the eBS client database
  - name of active ingredient (the AAN, ABN as applicable; or proposed name) or subject of a NeeS sequence regarding a Master File
  - a description of the Application (application type, dosage form), if referring to a medicine
  - name and address of manufacturing site, if referring to a Master File.

The identifier is:

- made up of a letter and six digits. Example: n123456 ('n' indicates the identifier refers to a NeeS application)
- valid throughout the entire lifecycle of a product unless the product is split from a package as explained elsewhere.

Complete the NeeS Envelope Form

Complete the NeeS Envelope Form as detailed in Appendix 1: The AU NeeS envelope form – guidance.

Place the resulting envelope.xml file in the 1001-cover folder of your NeeS application.

Prepare your cover letter

Include the following information in the cover letter in addition to the CTD requirements for the Cover Letter:

- The e-Identifier, the sequence and related sequence in the subject line.
- A description of the eSubmission:
  - type and number of electronic media
  - approximate submission size
  - any characteristics concerning the media that we might need to know.
- A description of the software used to check the files for viruses and a statement as to whether the submission is virus free.
- The regulatory and information technology points of contact for the submission.
- Information about the validation including:
  - the validation tool and version used
  - any findings e.g. errors, warnings or possible missing documents as designated by the eSubmission Document Matrix that would be expected for your specific sequence type.
- Include a paper copy of the Cover Letter with the physical media containing the NeeS sequence. This is only necessary until we develop an electronic portal.

You do not need to include a copy of the validation report; however an electronic copy of the report needs to be provided if requested.

Validate the NeeS submission

There are two types of NeeS validation findings:

- Pass/Fail – Critical finding:
  - validation findings categorised as 'Pass/Fail' must be addressed
  - non-compliance will lead to rejection of the sequence.
- Best Practice – Best practice recommendations:
  - You should address validation findings categorised as 'Best practice'.
  - We recommend you eliminate best practice recommendations whenever possible.
  - We may request you to fix the sequence and resubmit if there are repeated or excessive issues.

Please minimise sequences with best practice recommendations and address any findings in the Cover Letter.

You must validate your sequence prior to submitting to us. The validation software that you use should be able to validate the AU Module 1 criteria. We also validate each eCTD sequence using the AU Validation Criteria.

Sequences with errors or deficiencies

We will reject sequences with critical validation findings and you will need to re-submit unless you gain our agreement.

If your sequence has content deficiencies, you will need to submit changes in a follow-up sequence.

Related information and guidance

- Australian regional specification and validation criteria 3.1

Structure the folder

Use an application folder named after the e-Identifier. Include in this application folder the sequence folder(s) as sub-folder(s) with their contents.

Example: D:\n123456\0001

Select the electronic media

The size of an eSubmission is only limited by the size of your media format.

Refer to 'Electronic media delivery' in the general dossier requirements for guidance on the types of electronic media you can use for a NeeS sequence to submit as one unit.

Sending your NeeS dossier

If your sequence is less than 100Mb and you have it ready by the time you complete the online pre-submission application form, you can upload it as a zip file directly into the form.

OR

If the file size is small enough to attach to an email, do so and email it to esubmissions@tga.gov.au.

OTHERWISE

Follow the guidance in Part B of general Dossier requirements located at General dossier requirements: Part B: Electronic dossiers.

AU regional content

Regional content refers to the Australian specific information to be included within your NeeS application.

- Regulatory requirements and content for module 1 is described within CTD Module 1.
- The validation criteria to support the content is described within the *NeeS Validation Criteria* spreadsheet in the *AU Validation Criteria 3.1* Excel workbook.
- Use the *NeeS Sequence Matrix* to determine what combination of sequence type and sequence description is relevant to your specific sequence.

Module 1 administrative and prescribing information

The ICH Common Technical Document (CTD) specifies that:

- Module 1 should contain region specific administrative and product information.
- Module 3.2.R should be used for any additional drug substance and/or drug product information specific to Australia.

Regional file formats

Module 1

Table 1 File formats that can be included in Module 1

Section ID	Business Terminology	File Format
1.0	**Correspondence**	
1.0.1	Cover letter	PDF
	XML form	Excel - XML
1.0.2	Lifecycle management tracking table	PDF
1.2	**Administrative Information**	
1.2.1	Application forms	PDF
Other		PDF

Where possible, generate PDFs from an electronic source.

Signatures may be embedded as a graphic file in the PDF.

All PDF files, in any module, should be v1.4, v1.5, v1.6 or v1.7 except where a specific requirement for a later version is defined.

Modules 2 to 5

In addition to the file formats defined for Modules 2 to 5 in the ICH eCTD Specification, we will allow comma separated value (CSV) and plain text (TXT) files in Modules 4 and 5 to allow for specialist analysis, e.g. population pharmacokinetics analysis.

Electronic signatures

Whilst electronic signatures – for example, public key digital signatures – will be crucial, particularly for authentication of electronic submissions and documents, we are currently accepting:

- Digital signatures as an adjunct to written signatures.
- Scanned signatures where the documents make up part of the checksum of a NeeS submission.

Empty or missing sections

In applications for medicines:

- Provide detailed statements justifying the absence of data or specific CTD sections in the relevant Quality Overall Summary and/or Nonclinical/Clinical Overviews e.g. Module 2.3, 2.4, or 2.5.
- Include a statement in the cover letter on the absence of expected Module 1 content (based on information in the Australian regional specification and validation criteria 3.1).

Do Not:

- û Use documents with no substantive content – for example, documents that contain words like “not applicable” - in the NeeS structure. This causes delays for evaluators who must open and assess documents with no substantive content.
- û Provide a justification for content that is typically absent for applications for generic medicines.

Table of contents, bookmarks and hyperlinks

Tables of contents

A NeeS format dossier must contain tables of contents (TOC) in PDF format.

For small dossiers

You may have one TOC referring directly to all dossier documents especially when only one module beside Module 1 is included. Example: certain variations.

For larger dossiers

The main TOC must be linked to module TOCs which are then further linked to the documents in each module.

- Do not include hyperlinks in the module TOCs to the documents in other modules.

The file containing:

- the main, submission-level TOC must be named ctd-toc.pdf and be located in the four digit number named folder for the NeeS submission. This folder comes next to the root or top level folder (named using the e-Identifier).

- the module tables of contents are named m1-toc.pdf, m2-toc.pdf, m3-toc.pdf, m4-toc.pdf and m5-toc.pdf and are located in the corresponding top level module folders.

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

All documents lodged in a NeeS format dossier must be referenced from a hyperlinked table of contents. Hyperlinks for a document should always be provided to the first page of the appropriate file.

Examples for tables of contents

The following examples of the Table of contents are for guidance and illustrative purposes only.

The **bold text** in column 3 indicates where hyperlinks to the individual documents should be added.

Parts of Table 3 are shaded yellow, italicised and include an asterisk; this indicates changes that have been made between the NeeS versions 1.0 and 2.0.*

Table 2 Example: Main CTD table of contents

Module	Title	Hyperlink
Module 1	Administrative and prescribing information for Australia	**Module 1**
Module 2	Common technical document summaries	**Module 2**
Module 4	Nonclinical study reports	**Module 4**
Module 5	Clinical study reports	**Module 5**

Table 3 Example: Module 1 Table of contents Module 1

Module 1	Administrative and prescribing information for Australia	Reference
1.0	Correspondence	1.0
1.0.1	Cover letter *NeeS envelope form**	**1.0.1**
1.0.2	Lifecycle management tracking table	**1.0.2**
1.0.3	Response to request for information	1.0.3
1.2	Administrative information	1.2
1.2.1	Application forms	**1.2.1**
1.2.2	Pre-submission details	**1.2.2**
1.2.3	Patent certification	1.2.3

Module 1	Administrative and prescribing information for Australia	Reference
1.2.4	Change in sponsor	1.2.4
1.3	Medicine information and labelling	1.3
1.3.1	Product information and package insert	1.3.1
1.3.1.1	Product information-clean	**1.3.1.1**
1.3.1.2	Product information-annotated	**1.3.1.2**
*1.3.1.3**	*Product information-approved**	*1.3.1.3**
*1.3.1.4**	Package insert	*1.3.1.4**
1.3.2	Consumer medicines information	1.3.2
1.3.2.1	Consumer medicines information-clean	1.3.2.1
1.3.2.2	Consumer medicines information-annotated	1.3.2.2
*1.3.2.3**	*Consumer medicines information – approved**	*1.3.2.3**
1.3.3	Label mock-ups and specimens	1.3.3
*1.3.3.1**	*Label mock-ups and specimens – clean**	*1.3.3.1**
*1.3.3.2**	*Label mock-ups and specimens – annotated**	*1.3.3.2**
*1.3.3.3**	*Label mock-ups and specimens – approved**	*1.3.3.3**
1.4	Information about the experts	1.4
1.4.1	Quality	1.4.1
1.4.2	Nonclinical	**1.4.2**
1.4.3	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	*Designation applications - supporting documents**	1.5.2
1.5.3	Genetically modified organisms consents	1.5.3

Module 1	Administrative and prescribing information for Australia	Reference
1.5.4	Additional trade name declarations	1.5.4
1.5.5	Co-marketed medicine declarations	1.5.5
1.5.6	Combination medicine consent	1.5.6
1.5.7	OTC product assurances	1.5.7
1.5.8	Umbrella brand assessment	1.5.8
1.6	Master files and Certificates of Suitability	1.6
1.6.1	Relevant external sources	1.6.1
1.6.2	Applicants declaration	1.6.2
1.6.3	Letters of access	1.6.3
1.7	Compliance with meetings and pre-submission processes	1.7
1.7.1	Details of compliance with pre-submission meeting outcomes	**1.7.1**
1.7.2	Details of any additional data to be submitted	1.7.2
1.7.3	Declaration of compliance with pre-submission planning form and planning letter	**1.7.3**
1.8	Information relating to Pharmacovigilance	1.8
1.8.1	Pharmacovigilance systems	1.8.1
1.8.2	Risk management plan	1.8.2
1.9	Summary of biopharmaceutic studies	1.9
1.9.1	Summary of a bioavailability or bioequivalence study	**1.9.1**
1.9.2	Justification for not providing biopharmaceutic studies	1.9.2
1.10	Information relating to paediatrics	1.10
1.11	Foreign regulatory information	1.11
1.11.1	Foreign regulatory status	**1.11.1**
1.11.2	Foreign product information	**1.11.2**

Module 1	Administrative and prescribing information for Australia	Reference
1.11.3	Data similarities and differences	1.11.3
1.11.4	Foreign evaluation reports	1.11.4
1.12	Antibiotic resistance data	1.12

Table 4 Example: Module 2 Table of contents

Module 2	Common technical document summaries	Reference
2.4	Nonclinical overview	**2.4**
2.5	Clinical overview	**2.5**
2.6	Nonclinical written and tabulated summary	**2.6**
2.7	Clinical summary	**2.7**

Table 5 Example: Module 4 Table of contents

Module 4	Nonclinical study reports	Reference
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**
4.3	Literature references	4.3
	Reference 1	**4.3**
	Reference 2	**4.3**
	Reference 3	**4.3**

Table 6 Example: Module 5 table of contents

Module 5	Clinical study reports	References
5.2	Tabular listing of all clinical studies	**5.2**

Module 5	Clinical study reports	References
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**

Bookmarks and hyperlinks

The navigation through a NeeS format dossier is based on:

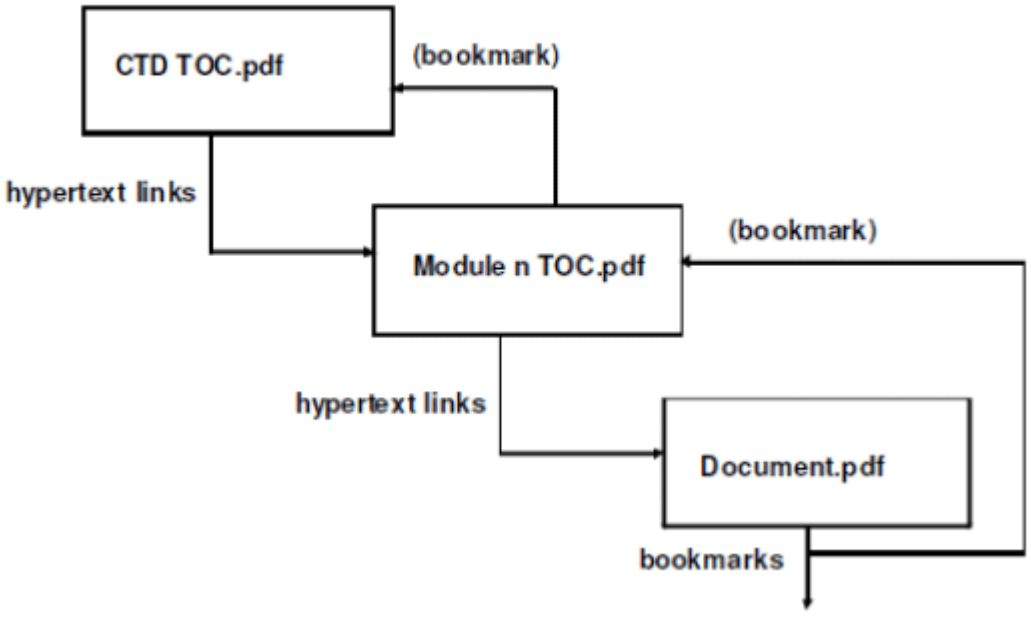
- electronic tables of contents
- bookmarks
- hypertext links.

We can increase the efficiency in evaluating your application if you prepare the documents so we can quickly locate content.

We recommend you:

- Use bookmarks and/or Tables of Content to assist us with navigating through PDF documents to quickly find information.
- Include Table of Contents, and/or if appropriate, a Table of Tables, Table of Figures, etc. on the first page for documents with more than five pages and with multiple sections.

The following image describes the hierarchy for tables of contents and bookmarks.



Related information and guidance

ICH eCTD Specifications - Appendix 7

Baseline submissions

A baseline submission is a resubmission of currently valid documents that you have already provided to us in a paper format. If transitioning from paper we advise that you move directly to eCTD rather than NeeS.

Cover letter for baseline submissions

When making a baseline submission, you need to include a statement about each of the following points in the covering letter:

- the format used for the previous dossier(s)
- when the previous dossier(s) was submitted
- verify that the formatting is the only change to the previous dossier(s) and there are no amendments to content
- all the information in the baseline submission was in the previous version(s) of the dossier
- any omissions in the baseline submission do not cause the content to be misleading.

Changing from paper to NeeS

When changing from paper to NeeS we recommend you:

- use a baseline sequence as a start of a NeeS application
- provide as much content as possible in the NeeS baseline sequence.

You can define the sections provided in a baseline sequence, but make sure that any omissions do not cause the content to be misleading.

We prefer the baseline submission to consist of high quality electronic source documents, but we will accept good quality scanned images with Optical Character Recognition (OCR) as this will help us search the text during the evaluation process.

We do not evaluate the baseline submissions and you do not need hyperlinks between documents.

Baseline sequence

Use the sequence type `Baseline` and sequence description `Reformat` in the lifecycle management table.

Initial baselines of paper submissions

The baseline should:

- normally be submitted as sequence 0000
- always be a separate sequence
- never include new regulatory activities.

The first new regulatory activity – for example, the next variation, in NeeS format should then be submitted as sequence 0001.

Table 7 demonstrates the baseline as an initial NeeS sequence

Sequence	Sequence type	Sequence description	Related sequence
0000	Baseline	Reformat	0000
0001	C-Extension of Indication of COPD	Initial	0001
0002	Supplementary information	Response to Request for Information	0001
0003	H-Minor Variation	Initial	0003
0004	F-Major Variation—New Strength	Initial	0004

Transferring sponsorship

If all products included under an e-Identifier are transferred to a new sponsor, the e-Identifier and the related sequences are transferred to the new sponsor.

Acquiring sponsor

The e-Identifier will transfer with the medicine, unless:

· there were multiple medicines submitted under the same e-Identifier

and

· you only acquired a portion of those in the transfer.

In the case of partial transfers, we will assign new e-Identifiers to the new sponsors.

Begin the first sequence of the new application with the next sequence number that would have been submitted under the old e-Identifier (see Table 1 below). This will indicate to evaluators that the medicine was initially reviewed under a different identifier.

Make sure you include the e-Identifier of the previous eCTD application in the cover letter of the new eCTD application.

Relinquishing sponsor

The future sequences of the medicines that remain under the initial identifier will continue as usual, however you should:

· remove the medicines you transferred from the envelope starting with the next sequence

· mention their removal in the cover letter.

Table 8 eSubmission Identifiers and transfer of Sponsor activities/tasks

Sponsor FFF	Sponsor PPP	Sponsor YYY	Activity/Task
Product A Product B Product C Product D n000111			
0001			Application for Products A, B, C and D from Sponsor FFF
0002			A regulatory activity or notification
Product A Product B n000111	Product C Product D n000222		PPP submits first sequence as 0003 referencing the transfer from n000111 and submitting a regulatory activity.
	0003		
0003	0004		Companies FFF and PPP undertake business as usual, *using their own respective sequences*.
Product A Product B n000111	Product C n000222	Product D n000333	YYY submits first sequence as 0005 referencing n000222.
		0005	Companies FFF, PPP and YYY undertake business as usual.
0004	0005	0006	

Structure and naming requirements

Folder and file structure

The structure of a NeeS format dossier must conform to both:

- the Annex to the ICH guideline *Organisation of the Common Technical Document for the Registration of Pharmaceuticals for Human Use* and
- the requirements set out in CTD Module 1 - Administrative information and prescribing information for Australia.

Name the root folder of the dossier with the e Identifier of the medicine followed by the subfolder name (sequence number) of four digits.

The e-Identifier for a NeeS dossier will be in the format “n” followed by 6 digits.

Example: n123456/0000/

Sequence number

Sequence numbers for eCTD submissions are not applicable for NeeS format dossiers; however, the use of a four digit number in the top level folder name should also be followed for the NeeS format.

The initial submission should normally have a sequence number of 0000.

As additional data is submitted in response to questions etc, the sequence number of the submission will advance, 0001, 0002, etc.

Only in the case of a technically invalid submission should a sequence be replaced with one using the same number, e.g. the initial sequence “0000” will be replaced by another “0000”.

Any time an electronic submission in the NeeS format is submitted, an updated Lifecycle management tracking table named “tracking.pdf” should be placed in Module 1.0.2. This will support transparency and ease tracking of sequences regardless of the format.

Table 9 Example of a Lifecycle management tracking table

Sequence	Sequence type	Sequence description	Related sequence
0000	Baseline	Reformat	0000
0001	C-Extension of Indication of COPD	Initial	0001
0002	Supplementary information	Response to Request for Information	0001
0003	Supplementary information	Pre-Advisory Committee response	0001
0004	Supplementary information	Product Information	0001
0005	F-Major Variation—New Strength	Initial	0005

Folder and file naming conventions

The top level folder will be part of the submitted NeeS.

For Module 1 dossiers

Follow the Australian recommended folder names.

For Modules 2-5, dossiers

Follow the ICH eCTD folder naming conventions as specified in Appendix 3 of the ICH eCTD specification.

File naming

Follow the eCTD file naming conventions described in the *ICH eCTD Specification*.

If you are submitting multiple files in one section and there is only one recommended name, you can use a suffix to the filename: using the file name–var.pdf convention, where the – var component have no dashes or illegal characters (for example*: pharmaceutical–development–container.pdf*).

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

Counting starts from the first digit of the four digit folder name in which the ctd-toc.pdf is placed.

The maximum length of the name of a single folder or file is 64 characters including the extension.

Legend for Table 10 - Recommended folder names for Module 1

Bold text - Fixed folder name

Normal text - Fixed file name component

Italicised text - Variable file name component

Parts of the table below are shaded in yellow and include an asterisk; this indicates changes that have been made between the NeeS versions 1.0 and 2.0.*

Table 10 Recommended folder names for Module 1

Content	Correlating AU Module 1 Section
nXXXXXX (e-Identifier)	
0000	
ctd-toc.pdf	
m1	
m1-toc.pdf	
au	
100-correspondence	1.0 Correspondence
1001-cover	1.0.1 Cover letter

Content	Correlating AU Module 1 Section
cover-*var*.pdf	
*envelope-var.xml**	*Excel>XML form available on TGA website**
1002-tracking	1.0.2 Lifecycle management tracking table
tracking-*var*.pdf	
1003-response	1.0.3 Response to request for information
response-*var*.pdf	
102-admin-info	1.2 Administrative Information
1021-app-form	1.2.1 Application forms
app-form-*var*.pdf	
1022-pre-sub	1.2.2 Pre-submission details
pre-sub-*var*.pdf	
1023-patent	1.2.3 Patent certification
pat-cert-*var*.pdf	
1024-sponsor	1.2.4 Change in sponsor
change-sponsor-*var*.pdf	
103-med-info	1.3 Medicine information and labelling
1031-pi	1.3.1 Product information and package insert
10311-pi-clean	1.3.1.1 Product information – clean
pi-clean-*var*.pdf	
10312-pi-annotated	1.3.1.2 Product information – annotated
pi-annotated-*var*.pdf	
10313-pi-approved*	*1.3.1.3 Product information – approved**
*pi-approved-var.pdf**	
***10314**-pack-ins**	*1.3.1.4** Package insert
pack-ins-*var*.pdf	
1032-cmi	1.3.2 Consumer medicines information
10321-cmi-clean	1.3.2.1 Consumer medicines information – clean

Content	Correlating AU Module 1 Section
cmi-clean-*var*.pdf	
10322-cmi-annotated	1.3.2.2 Consumer medicines information - annotated
cmi-annotated-*var*.pdf	
10323-cmi-approved*	*1.3.2.3 Consumer medicines information – approved**
*cmi-approved-var.pdf**	
1033-mockup	1.3.3 Label mock-ups and specimens
mockup-*var*.pdf	
10331-mockup-clean*	*1.3.3.1 Label mock-ups and specimens – clean**
*mockup-clean-var.pdf**	
10332-mockup-marked-up*	*1.3.3.2 Label mock-ups and specimens – annotated**
*mockup-annotated-var.pdf**	
10333-mockup-approved*	*1.3.3.3 Label mock-ups and specimens – approved**
*mockup-approved-var.pdf**	
104-expert	1.4 Information about the experts
1041-quality	1.4.1 Quality
quality-*var*.pdf	
1042-nonclinical	1.4.2 Nonclinical
nonclinical-*var*.pdf	
1043-clinical	1.4.3 Clinical
clinical-*var*.pdf	
105-specific	1.5 Specific requirements for different types of applications
1051-lit-based	1.5.1 Literature-based submission documents
lit-based-*var*.pdf	
1052-*designation**	*1.5.2 Designation applications - supporting documents**
designation-var.pdf*	
1053-gmo	1.5.3 Genetically modified organisms consents

Content	Correlating AU Module 1 Section
gmo-consents-*var*.pdf	
1054-add-tradename	1.5.4 Additional trade name declarations
add-tradename-*var*.pdf	
1055-co-marketed	1.5.5 Co-marketed medicines declarations
co-marketed-*var*.pdf	
1056-comb-med	1.5.6 Combination medicine consent
comb-med-cons-*var*.pdf	
1057-otc-prod-assurance	1.5.7 OTC product assurances
otc-prod-assurance-*var*.pdf	
1058-umbrella-brand-assess	1.5.8 Umbrella brand assessment
umbrella-brand-assess-*var*.pdf	
106-master-files	1.6 Master files and certificates of suitability
1061-external-sources	1.6.1 Relevant external sources
external-sources-*var*.pdf	
1062-app-decl	1.6.2 Applicant's declaration
app-decl-*var*.pdf	
1063-loa	1.6.3 Letters of access
loa-*var*.pdf	
107-compliance	1.7 Compliance with meetings and pre-submission processes
1071-pre-sub-outcomes	1.7.1 Details of compliance with pre-submission meeting outcomes
pre-sub-outcomes-*var*.pdf	
1072-additional-data	1.7.2 Details of any additional data to be submitted
additional-data-*var*.pdf	
1073-pre-sub-planning	1.7.3 Declaration of compliance with pre-submission planning form and planning letter
pre-sub-planning-*var*.pdf	
108-pharmacovigilance	1.8 Information relating to pharmacovigilance

Content	Correlating AU Module 1 Section
1081-phvig-system	1.8.1 Pharmacovigilance systems
phvigsystem-*var*.pdf	
1082-riskmgt-system	1.8.2 Risk management plan
riskmgtsystem-*var*.pdf	
109-sum-biopharm	1.9 Summary of biopharmaceutic studies
1091-sum-ba-be	1.9.1 Summary of bioavailability or bioequivalence study
sum-ba-be-*var*.pdf	
1092-justif-no-study	1.9.2 Justification for not providing biopharmaceutic studies
justif-no-study-*var*.pdf	
110-paediatrics	1.10 Information relating to paediatrics
paediatrics-*var*.pdf	
111-foreign	1.11 Foreign regulatory information
1111-reg-status	1.11.1 Foreign regulatory status
foreign-reg-status-*var*.pdf	
1112-pi	1.11.2 Foreign product information
foreign-pi-*var*.pdf	
1113-similarities	1.11.3 Data similarities and differences
similarities-*var*.pdf	
1114-eval-reports	1.11.4 Foreign evaluation reports
eval-reports-*var*.pdf	
112-antibiotic	1.12 Antibiotic resistance data
antibiotic-*var*.pdf	

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.

Placement of documents

Go to Australian regional specification and validation criteria 3.1 for guidance on the placement of documents within the CTD structure for particular submission types.

Document Table of contents should be located within the document itself. Provide bookmarks for every entry in the document's Table of Contents to the appropriate location of each document.

If there is no Table of Contents, provide bookmarks to a sufficiently detailed level, typically to Level 3 or 4 headings.

Correspondence

Similar to eCTD, NeeS will support users having a compiled view of the information submitted in the appropriate place in the dossier over time. Therefore, you should also submit formal responses to questions in NeeS format, as well as any correspondence that relates directly to the content of the dossier.

Additional guidance

Module 1.0.3 Responses to requests for information of CTD Module 1 for additional information.

Moving from NeeS to eCTD format applications

You, as the applicant can switch from NeeS to eCTD at the start of any new regulatory activity.

û Do not change from eCTD back to NeeS.

Additional guidance

See the section on 'baseline sequences' in the eCTD AU module 1 and regional information 3.1.

Module specific information

Module 1.0.3 Responses to requests for information

You must provide any additional information or data relating to the submitted dossier (for example, s. 31 responses, and new safety data), in the CTD format and meet the requirements specified in CTD Module 1.

Follow the NeeS folder and file structure and lodge as a new sequence.

Further guidance

Module 1.0.3 Responses to requests for information in CTD Module 1.

If you submit responses to more than one question a single file, use bookmarks within the PDF file to clearly identify each response.

Module 1.2.1: Application form

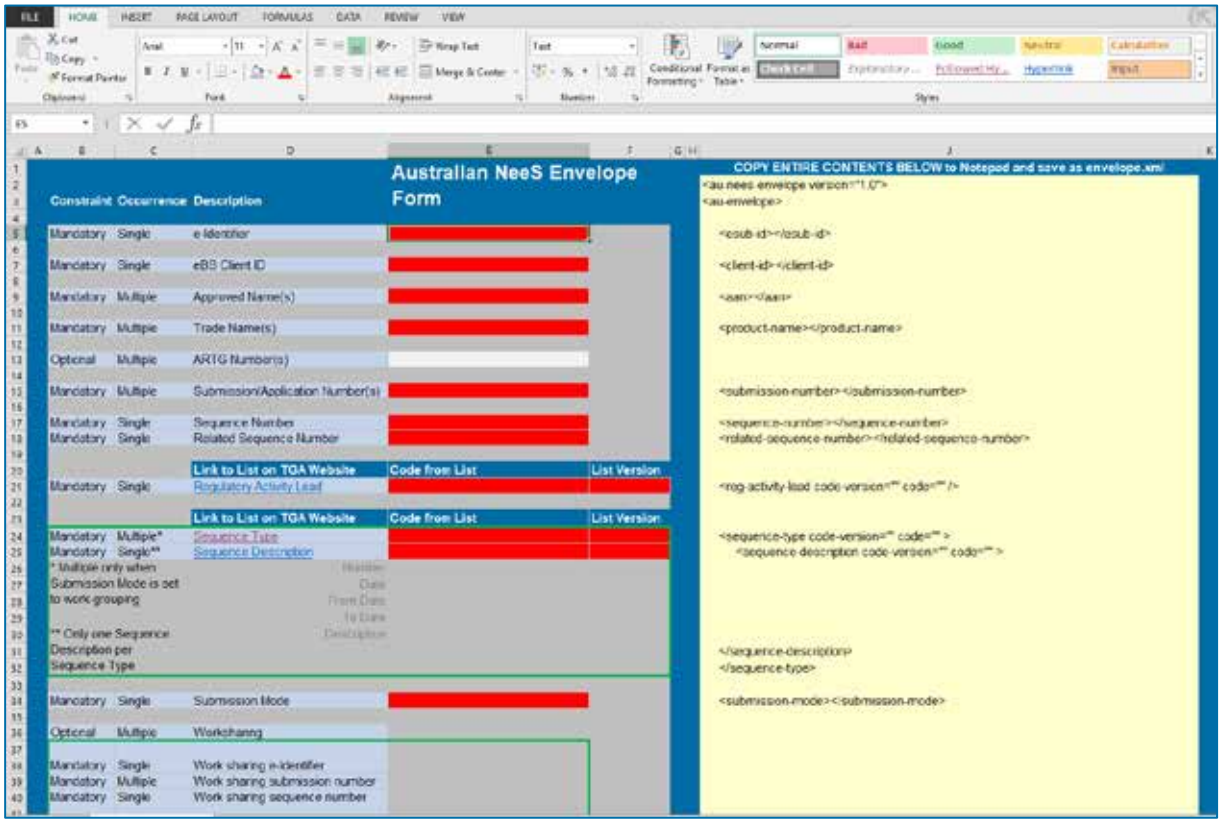
Always provide the application form as a PDF file within the NeeS format structure.

Further guidance

Module 1.2.1 Application forms in CTD Module 1.

Contact streamlinedsubmission@health.gov.au.

Appendix 1: NeeS envelope form – guidance



Structure of the form

The form – an Excel Worksheet - has two main components:

- On the left side, a user friendly form in Excel format with controlled vocabulary and;
- On the right side with yellow background, a preview of the xml content to be copied when the form is complete.

'Constraint' column

Items in this column indicate whether it is mandatory or optional to enter the information in that row.

Note also that the fields that must be filled in for the mandatory content are shaded red in the relevant column.

'Description' column

Items that appear in this column correspond to the elements of the eCTD Envelope. For each of these items a value should be entered in the column immediately to the right.

'Occurrence' column

Items in this column indicate whether it the Envelope element can have only a single value, or whether there may be multiple values of the element. e.g. Approved Name(s), Trade Name(s) and ARTG Number(s).

How to complete the form

Open the AU-ENVELOPE-XML.xlsx file downloaded from the TGA website.

Please refer to Appendix 2: 'NeeS Envelope Items' for further clarification on each of the items listed.

E-Identifier and eBS client ID

Enter the values in each of the fields as they are defined in the appendix. An example of these values correctly entered is shown below.

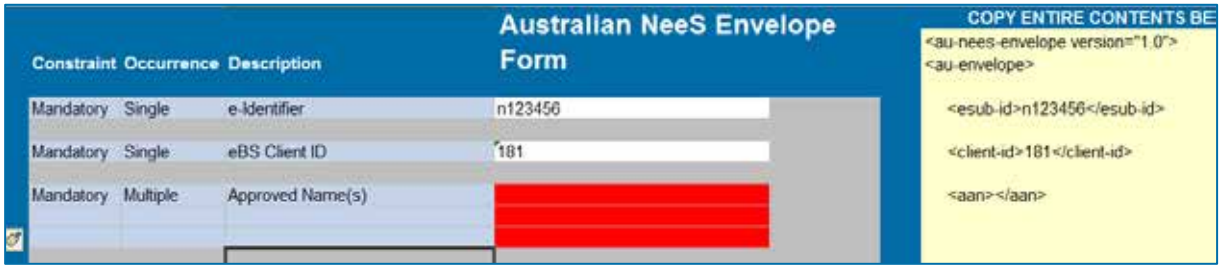
Approved name, Trade name, ARTG Number, and Submission/Application number

Each of these items allows multiple occurrences.

Where there are multiple values to enter, do not place multiple values in a single field. If this occurs, the XML component of the worksheet will not complete correctly and the entire NeeS submission will not validate.

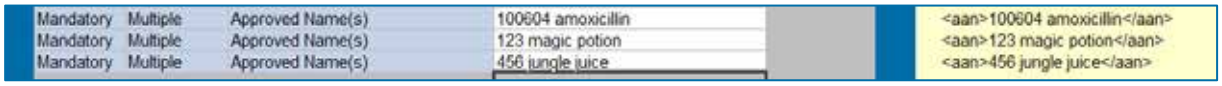
Instead copy the entire row each time an additional value needs to be entered, directly below the row containing the first of the multiple values. Here's a way that always works. There will be other ways depending on which version of MS Excel you have:

1. Insert as many additional rows as needed directly below the first row (*the command is Alt I + R*). In this example there are three Approved names to be added.

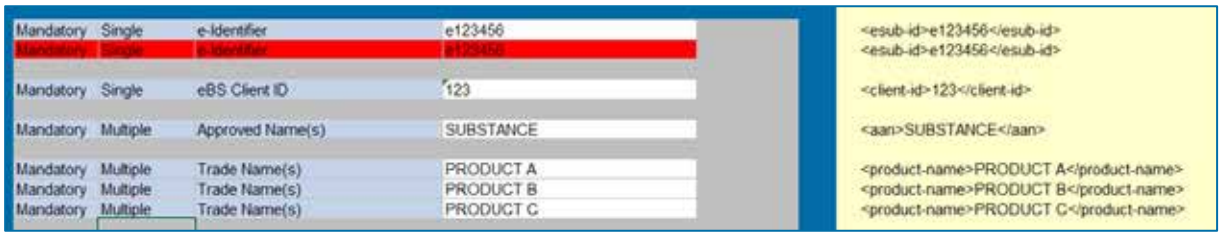


2. Copy the ENTIRE contents of the first row into each of the inserted rows. *(Note that this copies the XML format component of the row as well as the Excel format component, thus ensuring there will be no validation problem from incorrect data entry.)*

3. Enter each approved name, one in each row.



NOTE: If a copy is created of a row that has occurrences defined as single, the row will be marked red. If the row is not removed, your envelope.xml file will not pass validation.



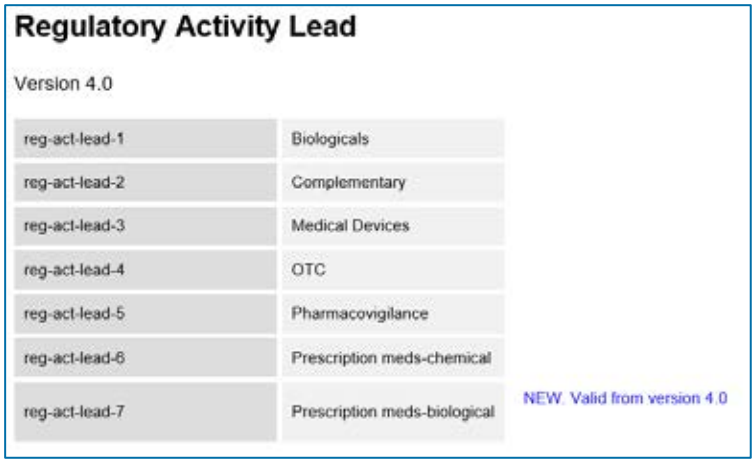
Sequence number and related sequence number

Enter a four (4) digit number for the sequence number and related sequence number. Each NeeS sequence should be submitted sequentially using the next available number for the product application. The related sequence number should indicate the first sequence of a regulatory activity.

Further explanation on correct values for each of these is provided in the Appendix 'NeeS Envelope Items' and the section titled 'related sequence' in the eCTD AU Module 1 and regional information 3.1.

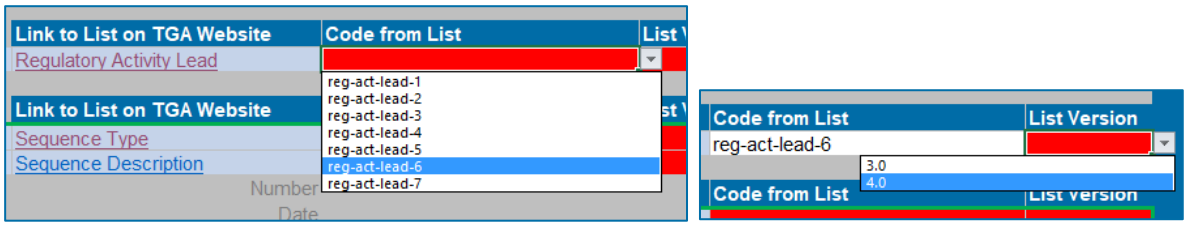
Regulatory activity lead

The Regulatory activity lead, Sequence type and Sequence description items have controlled vocabulary from lists managed on the TGA website. The list on the website will indicate the codes associated with each; the list for Regulatory Activity Lead is shown below.



A dropdown menu has been provided within the form to ensure accurate entry of these values.

Please look up the code and select the code from the dropdown menu.



The lists on the website are updated periodically. Changes are versioned and version numbers are indicated on the online list. Select the version number from the drop down for List Version.

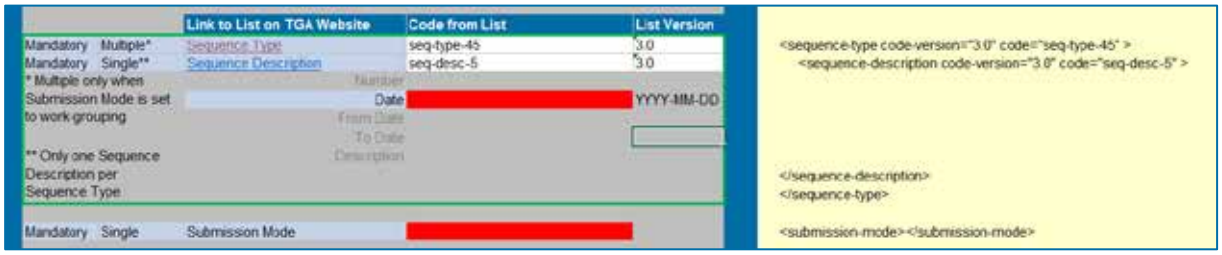
Sequence type and Sequence description

The sequence type for the application must be given. A link to valid sequence types is provided within the form.

Once the sequence type has been selected the corresponding sequence description should be provided. A link to valid sequence descriptions is also provided within the form.

Please refer to the sequence matrix XML document located on the TGA website for information on which sequence descriptions can/should be used with which sequence types. Please note that an invalid combination will lead to validation issues.

Some sequence descriptions require additional information e.g. Date. When the sequence description is selected the required additional fields will be highlighted and any empty corresponding fields will be indicated in red. Dates should be entered YYYY-MM-DD e.g. 2017-09-01.



Submission mode

Please note that the TGA is currently still defining the use of both “work-grouping” and “work-sharing” and until further notice, only “single” should be used and no additional information about work sharing must be entered.

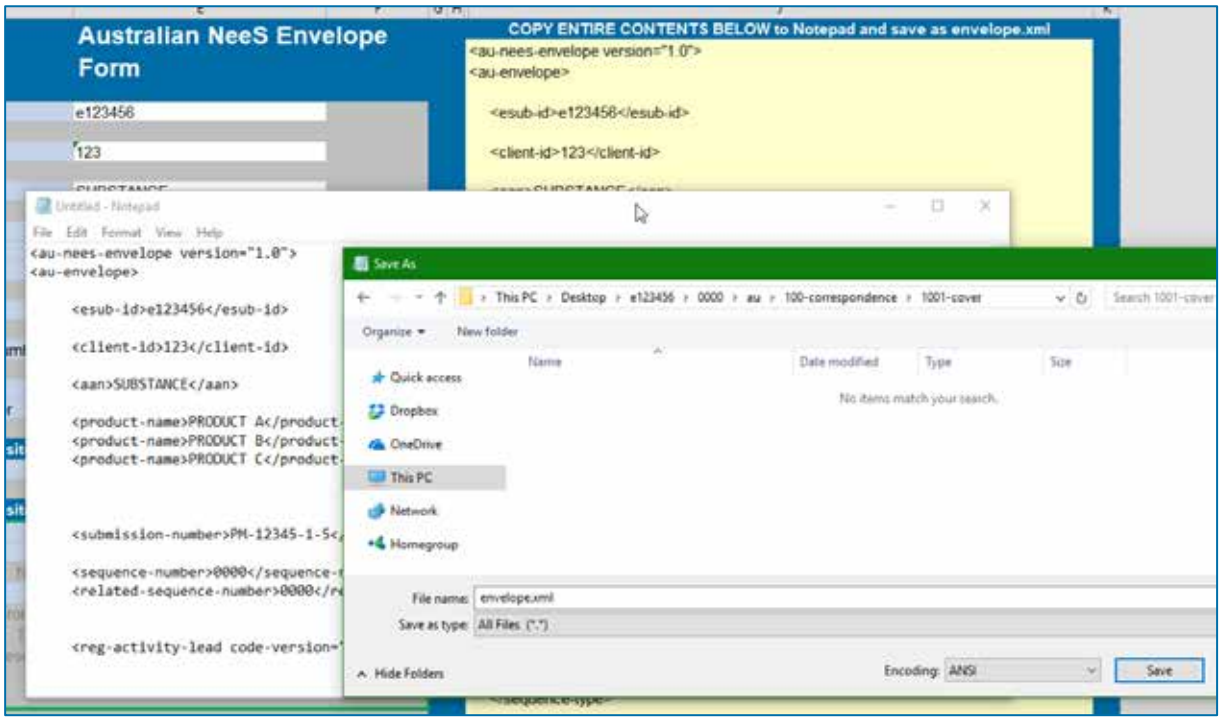
Contact email

Sequences received will ultimately be validated through an automated process. Results of the validation will be sent to the email addresses provided. The email address that you provide here will enable us to contact you regarding any issues with validation of the sequence.

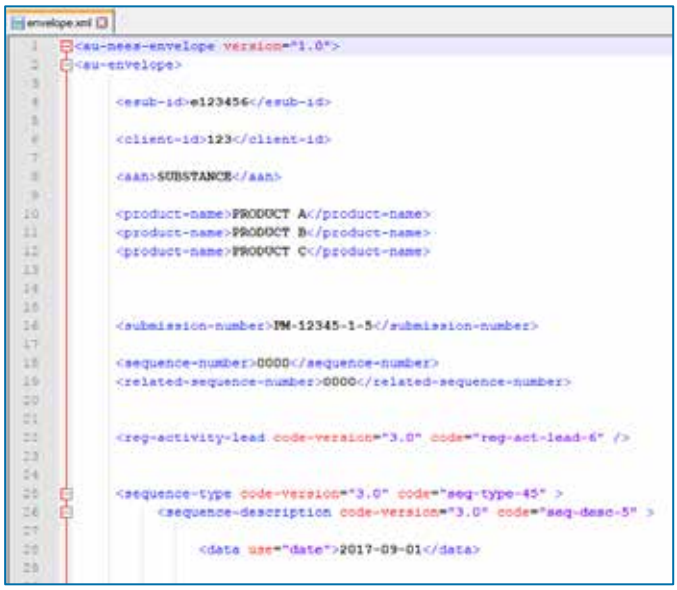
Creating the envelope.xml file

Once all of the sections have been filled in and form is complete, the envelope.xml file can be created from the XML component of the NeeS Envelope Form. The file can be created using Notepad, Notepad++ or any XML Editing software. The examples shown here have been done using Notepad and Notepad++ as these are readily available and either included in most computer setups or available for download from open source for free.

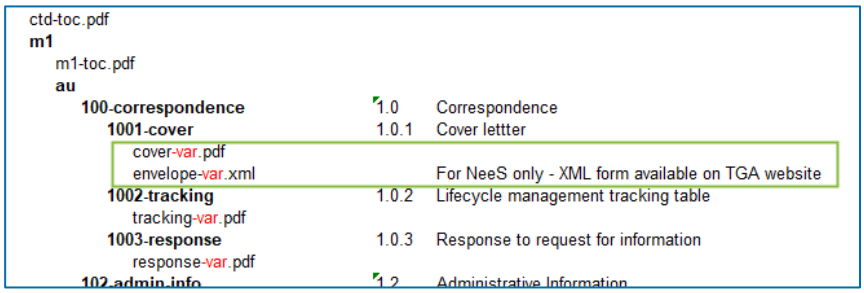
- Select the entire content shaded in yellow in the envelope.xml preview window and copy.
- Open Notepad and paste the content.
- Save the file with the filename as envelope.xml and file type All Files. If desired, it is allowed to add a suffix to the file name e.g. envelope-response170901.xml.



When opened in Notepad++ or an xml editor, the components of the xml are visible through colour coding. The empty lines can be removed but this is not required.



The file should be included in the 1001-cover folder of your NeeS application. It should be referenced by the m1-toc.pdf.



Appendix 2: NeeS envelope items

e-Identifier

This is to be assigned –at your request - by the TGA, and used for the name for the NeeS application folder which contains sequence folders.

Example: n123456

eBS Client ID

Enter the applicant's eBS client ID as used in the eBS client database.

Example: 181

Approved name(s)

The approved name(s) of the ingredient(s) - AAN, ABN, etc. as applicable - as they appear in the Australian Approved Names list.

Example: 100604 amoxicillin.

Trade name(s)

The name or proposed medicine (trade) name to be used on the Certificate of Registration.

Example: incrediPill.

For Master Files, insert name of manufacturing site.

ARTG number

ARTG number(s) must be supplied when known, typically for variations to an already registered good. This can be a four-, five- or six-digit number.

Example: 123456

Submission number(s)

The submission number(s) or application number(s) applicable to the sequence being submitted. These should be provided as follows:

- PM-2017-12345-1-5 Prescription medicines submission numbers: Prefix PM followed by the submission number and stream. If the submission number is not yet known it is appropriate to only include the prefix and the stream i.e., PM-1. NOTE that this will apply whether the activity refers to a biological medicine or other molecular type ('chemical' medicine).
- BA-2017-12345-1 Biologicals submission numbers: Prefix BA followed by the submission number. If the submission number is not yet known it is appropriate to only include the prefix e.g. BA.
- OM-2017-12345-1 OTC medicines submission numbers: Prefix OM followed by the submission number. If the submission number is not yet known it is appropriate to only include the prefix e.g. OM.

- Complementary Medicines: For *registered* complementary medicines the same protocol applies as for OTC medicines as detailed above. For listed complementary medicines no validation is planned at this time.
- PV Pharmacovigilance: No submission number is assigned; PV should be entered for all sequences where pharmacovigilance information is submitted.
- MF Master Files: No submission number is assigned; MF should be entered for all sequences where master file information is submitted.
- MD Medical Devices: Depending on whether the eCTD application is a device *application* or a *conformity assessment*, the prefix should be DA or DC e.g. DA-2017-12345-1.

Allowable *combinations* of the above are:

- PM with PV or MF
- BA with PV or MF
- OM with PV

Sequence number

The four-digit sequence number matching the sequence folder being submitted.

Example: 0000

Related sequence number

The related sequence number is used to group sequences. This enables us to easily evaluate sequences associated with a particular regulatory activity.

It is particularly helpful when separate regulatory activities for the same medicine are in process at the same time – for example, a new chemical entity registration and one of more variations.

All sequences that belong to a specific regulatory activity should contain the same four-digit number in the related sequence number field as demonstrated in the table below.

Table 11 Relating sequence numbers to the associated regulatory activity

Sequence	Related Sequence	Sequence Type	Sequence Description
0001	0001	New Chemical Entity	Initial
0002	0001	Supplementary Information	Response to Request for Information
0003	0001	Supplementary Information	Response to Request for Information
0004	0004	F—Major Variation—New Dosage Form	Initial
0005	0005	Self-Assessment Review (SAR)	Initial

Sequence	Related Sequence	Sequence Type	Sequence Description
0006	0006	G—Minor Variation, New Register Entry—New Container Type	Initial
0007	0004	Supplementary Information	Response to Request for Information
0008	0004	Supplementary Information	Response to Request for Information
0009	0004	Supplementary Information	Product Information
0010	0006	Supplementary Information	Product Information

Each Initial sequence of a regulatory activity will reference itself.

Each Supplementary Information thereafter will reference the initial sequence of the regulatory activity.

The related sequence number should be approached similar to the Submission ID described in the US regional specification 2.3.

Regulatory activity lead

The regulatory activity lead identifies the group within the TGA which is expected to take the lead in the review process.

Sequence type

The sequence type identifies the type of activity that is being submitted, either:

- the regulatory activity type (for the first sequence of the regulatory activity)
- the supplementary information for the follow-up sequences of a regulatory activity that has already commenced.

Sequence description

Content description for the submitted sequence should be one of the values from sequence-description.

Refer to the sequence description for the current list of values.

The examples listed below are a subset of the overall list and show how to handle the different approaches.

1. You can use some values without further information—for example, Initial.
2. You will be required to combine some values with a date—for example, Response to Request for Information—2014 03 30.
3. You enter both the start and end dates for some values—for example, PSUR for Period of 2015-01-01 to 2015-06-30.
4. You add a brief description (fewer than 40 characters) for other values—for example, Uncategorised, DESCRIPTION.

Submission mode

Until the work grouping and work sharing functions are sufficiently developed for specific guidance to be published, the only valid mode is ‘single’ which denotes a single regulatory activity.

Version history

Version	Description of change	Author	Effective date
V1.0	Original publication	Prescription Medicines Authorisation Branch	July 2015
V2.0	Updated	Prescription Medicines Authorisation Branch	January 2018

Therapeutic Goods Administration

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