

SG-HSA eCTD Question and Answers Document

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1. General

1.1 When will HSA make eCTD submissions mandatory?

eCTD will be implemented in phases and the adoption by industry will be on a voluntary basis during the initial roll-out. HSA will provide advance notice to the industry on subsequent phases.

1.2 Does HSA recommend any eCTD solution provider to help me publish my dossier in eCTD format?

HSA does not provide any recommendation on solution providers for the industry. It is the responsibility of the companies to ensure that they acquire the right solution for their needs. eCTD is an international standard and any software that is compliant with ICH and SG-HSA eCTD Specifications and Validation Criteria will be compatible with the review system used by HSA to evaluate eCTD applications.

1.3 Are there additional fees for companies to submit eCTD?

No. There are no additional fees imposed on eCTD submissions.

1.4 Are there any advantages for companies to submit eCTDs instead of via PRISM/CD?

Submitting eCTD through the portal is an entirely paperless submission with the advantage of system validation to ensure successful receipt of the package by HSA. Unlike how documents are attached in PRISM, eCTD allows companies to submit common dossiers for multiple strengths in a single application and by uploading a single zip file. eCTD also enables content reuse without the need to re-submit documents. It also facilitates lifecycle management for both industry and HSA.

1.5 What version of eCTD is being implemented and is the current version compatible with eCTD 4.0 submissions?

Internationally, the eCTD is currently implemented using the ICH eCTD Specifications version 3.2.2. The eCTD Specifications for version 4.0 have been released and some agencies are in the process of implementing plans to migrate. It is the intention of Singapore to also migrate at a later time point.

1.6 If I submit in eCTD, can I later submit variations or amendments in another format?

After eCTD submissions have commenced for a product, any subsequent variations should continue in eCTD. eCTD has a defined lifecycle management that allows the content to be filtered and viewed so that the evaluator can see the current view of the application, as well as content which was previously approved.

Other formats lack the XML infrastructure to be able to build the above views and therefore switching between eCTD and non-eCTD formats should be avoided.

1.7 Can I convert my current registered product from PRISM/CD submissions to eCTD?

HSA is applying a phased approach to implementing eCTD submissions, beginning with new therapeutic product registrations. Please contact HSA if you are interested in switching to eCTD submissions for your registered therapeutic products.

1.8 Will I be able to submit test submissions during the initial phase?

After HSA has launched eCTD in Singapore, you will be able to submit test submissions during the first 3 months. The contents of test submissions will not be reviewed by HSA and will be deleted from the system once testing is complete.

2. Portal

2.1 How do I register my company to submit eCTD packages through the eCTD portal?

You need to register your company to use the eCTD portal eService via CorpPass. The CorpPass Administrator for your company should provide access to the required personnel within your company who needs to submit eCTD packages. Note that the personnel should have SingPass to login to eCTD e-services.

2.2 As a CorpPass Admin, how can I provide access to eCTD portal to my colleagues?

eCTD will be a registered e-service, just like other Singapore government e-services. You can select the eCTD e-service and provide access to your colleagues via your CorpPass Admin account.

2.3 I am a DMF holder located outside Singapore. Can I submit my DMF in eCTD format via the portal to HSA?

Yes, you may submit the eCTD to HSA as long as you have a CorpPass account. Please visit www.corppass.gov.sg (Services > Register for Corppass > Foreign Entity) for more information.

2.3 Can I submit eCTD through PRISM or storage media?

No. The eCTD Portal will be the only method to submit eCTD Sequences to HSA. Refer to the SG-HSA eCTD Specifications for more details.

2.4 What is the file format and size limit of the packages?

All packages must be compressed into a Zip file, without any encryption or password protection. The current limit is 50GB.

2.5 How will I know if my package has been successfully transmitted?

A receipt will be shown on the screen once the package is successfully transmitted. The receipt will contain the Transmission ID, Individual's Name, Company Name, Application Type, Product Type, Application Number, Submission Type, Submission Number, Sequence Number, Filename, File Size and Datetime Submitted (at confirmation step, not initial upload). You can save the receipt as a PDF or XML file.

3. Content

3.1 Can eCTD submissions be in ACTD format?

eCTD submissions should always be prepared in accordance with ICH specifications.

3.2 Is it always necessary to provide a Note to Evaluator?

It is good practice to submit a Note to Evaluator, especially in every "Initial" Sequence of a Submission. Assuming that the evaluator who will be evaluating the Sequence is not the same as the evaluator who evaluated previous Sequences, the Note to Evaluator is your direct communication to the Evaluator and is a good opportunity to address questions that you may be able to predict to reduce the number of iterations required for the evaluation.

3.3 Can I still submit documents in Word format?

Source files are submitted in MS Word format. Refer to *SG-HSA eCTD Specifications* for more information.

4. Document navigation

4.1 Are bookmarks mandatory?

Bookmarks should be created for all documents with 5 or more pages and that contain multiple sections, tables, or figures. They serve as an electronic table of content and increase the efficiency of evaluation. Bookmarks are not required for Literature References or Educational/RMP Materials.

4.2 Are there any requirements for Hyperlinking?

The review system used by the HSA will provide an analysis of all hyperlinks provided in the application which may be consulted during the screening activities. You should provide hyperlinks where they are encouraged e.g., 2.4-2.7 & 5.2.

Module 1: Hyperlinks should be created in the Response documents in 1.0.4 Response to Input Request to the section that is addressed and/or has been updated.

Modules 2/3: The frequent changes to Module 3, coupled with the detailed granularity of the Quality sections which make content locations more predictable, means that hyperlinks to Module 3 from 2.3 are discouraged.

Module 4: The lack of major changes to Modules 4, coupled with a less granular structure of the Study sections, means that hyperlinks to Module 4 are encouraged. Specifically, any reference to a specific study in the 2.4 Overview or the 2.6 Written and Tabulated Summaries should be linked to that study in 4.2

Module 5: The lack of major changes to Modules 5, coupled with a less granular structure of the Study sections, means that hyperlinks to Module 5 are encouraged. Specifically, any reference to a specific study in the 2.5 Overview, the 2.7 Summaries and Synopsis of Individual Studies or 5.2 Tabular Listing of All Clinical Studies should be linked to that study in 5.3

4.3 Can I hyperlink to content submitted in earlier Sequences?

Yes, since the eCTD is contained in a predictable structure, it is possible to create hyperlinks to documents provided in earlier Sequences. Hyperlinks must be made using a relative path.

5. Technical presentation

5.1 How do I obtain my Application Number and Submission Number?

The Application Number is derived from the Submission Number associated with the first Sequence provided.

Please refer to the section 2.3 of the *SG-HSA eCTD Specifications* for information regarding the Submission Number.

For the first Sequence, the Application Number and Submission Number should be identical with the exception that the Application Number will have a prefix "e". For example:

Submission Number: 2212345A

Application Number: e2212345A

5.2 How do I create Application Folders?

The Application Folder name is derived from the Application Number(s) used in the first Sequence without the ending letter if the last digit of the Application Number is a letter. The "e" and any other letters from the Application Number should be written in lower case. If multiple Application Numbers exist, the folder should represent the range from the first number to the last number.

The Application Folder name can never be changed over time. Please see the eCTD Specifications for more details.

5.3 What is the Document Matrix?

The Document Matrix is provided to help Applicants make sure that the content expected for a particular Submission Type is provided or content not allowed for a Submission Type is not provided. It is also used during validation to check that the documents expected for your specific Submission Type have been submitted.

5.4 What is the Submission Type Matrix?

The Submission Type Matrix is provided to help Applicants make sure that they do not group Submission Types that need to be submitted in separate Sequences. It is also used during validation to check that the combinations of Submission Types are acceptable.

5.5 Can I reference files already submitted in other Applications or Sequences?

Yes, this is encouraged. Reusing content already submitted earlier helps facilitate the review process. Content reuse is allowed within the same Sequence, between Sequences of the same Application and between Sequences of different Applications. See the *SG-HSA eCTD Specifications* for more information on how content reuse should be implemented.

5.6 If a file is required in multiple sections of the CTD structure, should it be published in each of the sections?

No, the file should only be published once and then referenced in each of the locations of the eCTD backbone. Cases of content reuse should be addressed in the Note to Evaluator and you should indicate at which referenced location the document was physically published.

5.7 What is the difference between a Leaf Title and a File Name?

A leaf title is what is seen by an evaluator when viewing an eCTD Application via the XML file, whereas the file name is not visible to the evaluator in the review system. There are also fewer restrictions on leaf titles than on file names - Capital Letters are allowed, Special Characters are allowed, there are fewer limitations on length, although it is recommended to keep titles short and well below the ICH 512 characters suggested. A file name is what is seen when viewing a folder structure without the XML and Style Sheet. For eCTDs, the file names are unimportant.

5.8 Can I change the information in the Envelope over time?

Yes, the information provided in the Envelope should represent the Application at the time the Sequence is submitted. The Envelope provides Application and Submission Information and should reflect the Sequence. For example, if additional products are added over time, i.e., additional strengths, those Application Numbers should be added to the Envelope. If products are removed e.g., via a Transfer of Application or Withdrawal, the Application Numbers should be removed from the Envelope.

6. Validation

6.1 If my submission passes validation, does it mean the application has been accepted for evaluation?

No. The acceptability of the eCTD dossier for evaluation is determined during the screening process. Refer to the *Guidance on Therapeutic Product Registration* for more information.

6.2 Can I submit an application if there are validation Warnings?

Yes, but you must address the Warnings in the Cover Letter. Warnings generally lead to a less efficient evaluation so should be fixed whenever possible. The HSA officer will determine whether the issues should be resolved. Any adjustments should generally be addressed in the next Sequence.

6.3 Can I submit an application if there are validation Errors?

No, if any validation errors are found, the Sequence will be rejected before it can be passed on to the evaluation teams.

7. Post-marketing information

7.1 Where should pharmacovigilance reports related to post-marketing information (e.g. PBRERs, RMP reports, Clinical study reports) be submitted?

Please submit pharmacovigilance reports related to post-marketing information in section 5.3.6 (Reports of Postmarketing Experience) using Node Extensions. It is recommended to use Leaf Titles that identify the category of the content (e.g. Leaf Title beginning with PBRER, RMP report, or Clinical study report).

The submission of PBRERs is only required when requested by HSA on an ad-hoc basis or as part of the product's post-approval registration condition.

If the documents are submitted to fulfil post-marketing registration conditions, please select Submission Type PV-PBRER/RMP Reports.

If the documents submitted are requested as part of a pre-authorisation application dossier, please select the associated application (e.g. Submission Type NDA, MAV-1).

7.2 Where do I submit new educational/RMP materials or post-authorisation revisions to educational/RMP materials requiring HSA's approval?

Draft copies of new educational/RMP materials should be submitted in section 1.8.3 (Educational/RMP Materials) under the associated application (e.g. Submission Type NDA).

Post-authorisation revisions to educational/RMP materials requiring HSA's approval (i.e. affecting clinical/safety content) should be submitted with a concurrent variation to update the product information. The proposed revised materials should be submitted in section 1.8.3 (Educational/RMP Materials) under the associated application for the variation (e.g. Submission Type MAV-1).

7.3 Following approval of contents by HSA, how do I submit the finalised artwork of educational/RMP materials?

Please submit the finalised artwork of educational/RMP materials as a "Closing information" Sequence Type in section 1.8.3.3 (Finalised Artwork - Educational/RMP Materials) under the relevant application type (e.g. Submission Type NDA). The finalised artwork should not be provided in the "Initial" Sequence Type. It should also not contain new or unapproved content.

7.4 Where do I submit RMP materials requested by HSA for documentation purposes (e.g. Letter of Undertaking, Patient Informed Consent Form)?

If the RMP materials are part of a proposed RMP submitted with the pre-market application (e.g. pregnancy prevention programme, controlled access programme), please submit in section 1.8.1 (Singapore-Specific Annex) under the associated application (e.g. Submission Type NDA).

If the RMP materials are submitted post-authorisation (e.g. new materials, revisions to existing materials), please submit in section 1.8.3.3 (Finalised Artwork - Educational/RMP Materials) under Submission Type PV-EDU/RMP Materials-N. The reasons for the submission should be highlighted in a cover letter and submitted in section 1.0.1 (Cover Letter) under Submission Type PV-EDU/RMP Materials-N.

7.5 Where do I submit post-authorisation administrative revisions to educational materials that do not require HSA's review (e.g. change in company address, correction of typographical errors)?

Please submit the finalised copy of post-authorisation administrative revisions in section 1.8.3.3 (Finalised Artwork - Educational/RMP Materials) under Submission Type PV-EDU/RMP Materials-N.

The administrative revisions should be highlighted in a cover letter and submitted in section 1.0.1 (Cover Letter) under Submission Type PV-EDU/RMP Materials-N.

As the administrative revisions do not require HSA's approval, please retain the existing approval date on the materials.

Version	Description of Change	Author	Effective Date
0.9	Initial version for industry consultation	Singapore eCTD Project Team	2023-05-02