ประกาศสำนักงานคณะกรรมการอาหารและยา
เรื่อง รายละเอียดการยื่นคำขอขึ้นทะเบียนตำรับยาโดยวิธีทางอิเล็กทรอนิกส์

อาศัยอำนาจตามความในข้อ ๒ ข้อ ๓ ข้อ ๔ และ ข้อ ๕ ของประกาศกระทรวงสาธารณสุข เรื่อง การยื่นคำขอขึ้นทะเบียนตำรับยาโดยวิธีทางอิเล็กทรอนิกส์ ลงวันที่ ๒๖ ตุลาคม ๒๕๕๘ เลขาธิการคณะกรรมการอาหารและยาประกาศกำหนดรายละเอียดการยื่นคำขอขึ้นทะเบียนตำรับยาโดยวิธีทางอิเล็กทรอนิกส์ไว้ ดังต่อไปนี้

ข้อ ๑ ประกาศฉบับนี้ให้ใช้บังคับนับแต่วันถัดจากวันประกาศในราชกิจจานุเบกษาเป็นต้นไป

ข้อ ๒ โครงสร้างข้อมูลและข้อกำหนดเฉพาะของประเทศไทยในการยื่นคำขอขึ้นทะเบียนตำรับยาโดยวิธีทางอิเล็กทรอนิกส์ หลักเกณฑ์และวิธีการขอรับหมายเลขประจำคำขอที่ยื่นโดยวิธีการทางอิเล็กทรอนิกส์ (e-Identifier number) และการนำส่งข้อมูลเข้าระบบของสำนักงานคณะกรรมการอาหารและยา เป็นไปตามภาคผนวก ๑ ที่แนบท้ายประกาศฉบับนี้

ข้อ ๓ ในกรณีที่ผู้รับอนุญาตจะยื่นคำขอขึ้นทะเบียนตำรับยาโดยวิธีการทางอิเล็กทรอนิกส์และจะจัดเตรียมเอกสารตามรูปแบบอาเซียน (ACTD) ให้จัดเตรียมเอกสารตามโครงสร้างตามภาคผนวก ๒ ที่แนบท้ายประกาศฉบับนี้

ข้อ ๔ รายละเอียดและวิธีการในการตรวจสอบความถูกต้องของไฟล์ข้อมูลที่ยื่นคำขอขึ้นทะเบียนตำรับยาโดยวิธีทางอิเล็กทรอนิกส์ ให้เป็นไปตามภาคผนวก ๓ ที่แนบท้ายประกาศฉบับนี้

ข้อ ๕ มาตรฐานและโครงสร้างข้อมูลของการจัดเตรียมเอกสารคำขอขึ้นทะเบียนตำรับยาโดยวิธีทางอิเล็กทรอนิกส์ ให้ใช้มาตรฐานตามไอซีเอช อีซีทีดี (ICH eCTD) ตามภาคผนวก ๔ ที่แนบท้ายประกาศฉบับนี้

ประกาศ ณ วันที่ ๑๗ ธันวาคม พ.ศ. ๒๕๕๘

ลงชื่อ บุญชัย สมบูรณ์สุข
(นายบุญชัย สมบูรณ์สุข)
เลขาธิการคณะกรรมการอาหารและยา

ภาคผนวก ๑

ประกอบด้วย

๑. โครงสร้างข้อมูลและข้อกำหนดเฉพาะของประเทศไทย (TH eCTD Specification Module 1 and Regional Information)

๒. หลักเกณฑ์และวิธีการขอรับหมายเลขประจำคำขอที่ยื่นโดยวิธีการทางอิเล็กทรอนิกส์ (e-Identifier number)

๓. การนำส่งข้อมูลเข้าระบบของสำนักงานคณะกรรมการอาหารและยา

TH eCTD Specification

Module 1 and Regional Information

Version 1.0

Version History

Version	Description of change	Effective date
V0.90	Original draft publication for pilot implementation and industry review	01/07/2014
V0.91	Inconsistencies with Schema updated. Updated Heading 1.3.1.3.3.1	07/08/2014
V0.92	Update format of eSubmission Identifier Require document in Business Protocol	07/10/2014

V1.0	Approved Version
	
	- Update Module 1 Specification
	- Clarification
	  o Introduction
	  o Business Protocol
	  o File Reuse
	  o Lifecycle Operation
		01/12/2015

Change Control

Factors that could affect the content of the specification include, but are not limited to:

- Change in the content of the Module 1 for the CTD, either through the amendment of information at the same level of detail, or by provision of more detailed definition of content and structure
- Change to the regional requirements for applications that are outside the scope of the CTD
- Update of standards that are already in use within the eCTD
- Identification of new standards that provide additional value for the creation and/or usage of the eCTD
- Identification of new functional requirements
- Experience of use of the eCTD by all parties, in particular Module 1

We will:

- provide a practical timeframe for future changes to minimize impact on industry.
- introduce changes at scheduled intervals to allow stability.

Feedback is welcome and encouraged. Please send any comments or questions to drug_esubmission@fda.moph.go.th . Common questions will be compiled into a Question and Answer document and updated as necessary http://drug.fda.moph.go.th/eng

Table of Contents

1. Glossary of Terms

Term	Definition
Application	The term Application is used for THAI FDA's medicine registration process and is the top group of a series of sequences for the same product (e.g. active ingredient). One Application is usually defined for the complete life cycle of the specific product.
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.
Dossier	A collection of files and documents that contains data (administrative, quality, nonclinical and clinical) relating to a therapeutic good.
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
ICH E3	ICH Harmonised Tripartate Guidance Structure and Content of Clinical Study Reports
Leaf	Structural element delivering a document. It provides the link information to the document along with the title associated with the linked content.
Node Extensions	Additional heading structures beyond those defined by the specifications – generally equated to an additional subfolder in a defined section.
Regulatory Activity	The term Regulatory Activity is a subgroup of an Application which can be a group or series of related sequences for one approval process (e.g. one variation) One Regulatory Activity is usually defined for the lifecycle of the specific approval process.
RPS	Regulated Product Submission Release 1 (RPS) is a Health Level Seven (HL7) standard to facilitate the processing and review of regulated product information. It is the standard for the next eCTD version titled ICH eCTD v4.0.
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.
Submission	Generic term that can refer to an application, a regulatory activity type and/or a sequence. Often used when not referring specifically to a particular hierarchical level of the application. The THAI FDA recognises that this definition differs from the legal definitions used under Thai law. This definition will be applied to this and related documents.
W3C	World Wide Web Consortium – international standards organization for the world wide web.

2. Introduction

This document specifies Module 1 and the regional information of 2.3.R and 3.2.R of the electronic Common Technical Document (eCTD) for Thailand (TH).

This document should be read together with the ICH eCTD Specification to prepare a valid eCTD submission for Thailand. The latest version of the ICH eCTD Specification can be found at: http://www.ich.org/products/electronic-standards.html.

In line with desires to create a structure friendly to harmonization with other regions, much of this guidance has been modelled from the Australia, Canadian and European guidance on creating an eCTD. Large portions of the text are based on explanations given in those documents which can be found in the Reference section of this document.

The EU structure is being used as a proven structure and to increase reusability from applications already submitted in the EU region. Additional documents required by Thailand but not covered by the EU structure and not specifically addressed by this document will be added to section 1.A Additional Data.

Policy Objective

The objective is to ensure sponsors have access to all the information needed to provide a dossier to the THAI FDA in the eCTD format.

Policy Statement

This document outlines the creation of a regional backbone file according to the Thai Module 1 schema. This backbone file is to be used in the preparation and filing of medicine regulatory transactions in eCTD format established by the International Conference on Harmonisation (ICH).

Scope and Application

This document applies to all regulatory activities relating to medicines and being provided to the THAI FDA in eCTD format. Additional guidance documents that can or are meant to be read in conjunction with this guidance are listed in the Reference section.

Background

Given the desire to adopt the eCTD v4.0 / Regulated Product Submissions (RPS) in the foreseeable future, the decision has been made to move to a World Wide Web Consortium (W3C) Schema approach to define the new Module 1.

This specification will change over time. Future changes will be accompanied by a well thought out introduction to minimize the impact on industry and introduced at scheduled intervals to allow stability.

Commencing in July 2014, the THAI FDA has engaged with the industry to pilot the electronic Common Technical Document format submission using Version 0.90 of the Thailand eCTD Module 1 and Regional Specification. The version of this document is to be

considered as an approved version to accompany the official acceptance of eCTD intended to replace paper applications.

Applicants can submit their applications with version 1.0 of the Thailand eCTD Module 1 and Regional Specification from 1 January 2016. The transition period will be define in separate announcement.

3. Business Protocol

Obtaining the eSubmission Identifier

Prior to filing the first regulatory transaction for an application in an electronic format, the applicant should submit a request to the THAI FDA online service to obtain an eSubmission identifier.

If the applicant wishes to provide single dossiers for the same active ingredient, dosage form and therapeutic group but has more than one strength, only one eSubmission identifier will be issued to cover all strengths.

A request for an eSubmission identifier should made via email until Dec-16 or THAI FDA website . The request will require the following information:

- Licensee Number
- Description of Application.
- Dosage Form
- INN or Generic Name
- Strength
- WHO ATC Code
- Sequence Type
- Application form
- CPP (In case of Importer)

The eSubmission Identifier will be issued within 10 days of application. The Applicant must check on the THAI FDA online service for a response informing them of their eSubmission Identifier. After receiving the identifier, the Applicant must then make an appointment for submission within 30 days.

The Cover Letter as Transmission Letter

A paper copy of the cover letter should be included with the submission to serve as a transmission letter which can be found in the Reference.

The cover letter should include:

- The eSubmission identifier in the subject line;
- A description of the electronic submission including type and number of electronic media, approximate submission size, and if appropriate, characteristics concerning the media;
- A statement that the submission is virus free with a description of the software used to check the files for viruses;
- The regulatory and information technology points of contact for the submission; and
- A reference to the validation report, an indication of which validation tool and version was used as well as a statement addressing any issues found in the accompanying validation report.

The letter should not contain any scientific information. Responses to questions raised by THAI FDA should not be included in the cover letter, since they have been assigned a specific location in Module 1.R.

The paper copy of the cover letter will not be needed once the THAI FDA has a portal for the secure electronic transmission of data in place.

Validation Report

An electronic copy of the validation report created should be submitted. A folder should be created in the application folder named after the eSubmission identifier with the naming convention of the sequence number followed by validation-report e.g. "0000-validation-report". The validation report should be limited to only items listed in the validation criteria, additional checks should not be included.

Expected Structure of Submitted Media

Content should be submitted in an application folder named after the eSubmission identifier. The sequence folder and its contents should be placed in this application folder. If an application is too large and must be split and submitted on multiple items e.g. DVDs, the overall folder structure should be included on each media so that content can be easily merged.

Media Formats

The media formats acceptable when submitting an eCTD regulatory activity are:

- Compact Disc-Recordable (CD-R) conforming to the Joliet specification;
- Digital Versatile Disc-Random Access Memory (DVD-RAM) Universal Disc Format (UDF) standard;
- Digital Versatile Disc-Recordable (DVD+R/-R) recorded in the Universal Disc Format (UDF) standard;

Ensure that you do not use:

- double-sided discs,
- rewritable discs (protection, authenticity, and stability of information cannot be guaranteed),
- compressed or zipped files (except for validation reports).

Delivery of the eCTD Application

The Applicant will need to make an appointment and deliver the application personally at the Division of Policy System Development. The eCTD will be validated and imported into the THAI FDA Review System together with the applicant. Once accepted and submitted, the applicant will be given back their media to keep.

Feedback on Validation of Application

THAI FDA will inform applicants if there are problems experienced during the upload of an eCTD sequence during the appointment.

4. TH Regional Information

4.1. Regional Content

4.1.1. Module 1 Administrative and Prescribing Information

The ICH Common Technical Document (CTD) specifies that Module 1 should contain region-specific administrative and product information. The content and numbering of Module 1 for Thailand is modelled after the EU Module 1 content as described in the 2008 version of the Notice to Applicants. Additional documents specifically required by Thailand not covered by the EU structure will be added to 1.A Additional Data.

The following items listed in the Notice to Applicants may be included for an initial submission:

- a cover letter
- an application form(Form MA-1)
- product information documents
- information on the experts
- specific requirements for different types of applications
- an environmental risk assessment
- product interchangeability equivalence evidence
- information relating to pharmacovigilance
- information relating to clinical trials
- information relating to paediatrics

In addition, other items such as answers to regulatory questions can be included under 1.R and rationale for variations documentation could also be included in or as an appendix to the Cover Letter.

It should be noted, that for subsequent submissions in the lifecycle of a medicinal product, e.g. for a variation, not all of the above mentioned types of document need to be included in Module 1. Consult the various legal documents for guidance on the exact documents to be submitted in such a case.

4.1.2. Module 2.3.R & 3.2.R Regional Information

2.3.R Regional Information

A brief description of the information specific to the region, as provided under 3.2.R should be included, where appropriate.

3.2.R Regional Information

Any additional drug substance and/or drug product information specific to the region should be provided in section 3.2.R of the application.

Where similar or relevant information has been provided in another section of Module 3 or where there is supporting or related information from other modules of the application, the applicant is encouraged to clearly cross-reference to the location of that information. Cross-referencing should be sufficiently detailed, so as to allow the appropriate information to be easily located within the dossier.

Applicants should include the following information in Module 3.2.R, where appropriate:

- Process validation scheme for the drug product
- Certificates of suitability
- Medical Device
- Supplier's declarations regarding compliance with packaging standards and colouring standards.

4.1.3. Node Extensions

Node extensions are a way of providing extra organisational information to the eCTD. The node extension should be visualised as an extra heading in the CTD structure and should be displayed as such when the XML backbone is viewed.

Consideration should be given regarding the impact of changing node extension structures during the lifecycle as this can lead to a higher level of complexity in the cumulative view of a submission.

The following rules govern the use of node extensions for TH:

- Node extensions must not be used where ICH-specified sub-headings already exist e.g. indication, manufacturer, drug substance, and drug product are all-ICH specified node extensions.
- Node extensions must only be used at the lowest level of the eCTD structure e.g. a node extension can be used at the level 5.3.5.1 but is not allowed at the level 5.3.
- Node extensions are mainly to be used to group together documents made up of multiple leaf elements e.g. a clinical study made up of separate files for the synopsis, main body and individual appendices could be grouped together under a node extension with the Study Identifier as its Title attribute.
- Node extensions may be nested as this is allowed by the eCTD DTD. However, as noted in Bullet 2, the first node extension must be at the lowest level in the eCTD structure e.g. in Module 5.3.7 a node extension may be added to group together files with the Study Identifier as Title attribute. Further node extensions may be added as children of the Study Identifier node, separating Case Report Forms (CRFs), if submitted, from individual patient listings.
- The content associated with a node extension can be placed in a separate sub folder in the submission; this is recommended for studies in Module 5 where study reports are provided as multiple files. However, there is no specific requirement for an additional subfolder.

4.1.4. Study Tagging Files

The THAI FDA does not currently have any plans to mandate study tagging files (STFs) for evaluation purposes however applicants wishing to re-use content submitted in other regions where STFs have been used can do so. If provided, STFs will be validated and must be conform to standards and specifications. Also, data pertaining to the number and size of ICH E3 16.3 CRFs and non ICH E3 documents will be collected for informational purposes.

4.2. Regional File Formats

4.2.1. Module 1

In addition to the common format PDF, as defined by the ICH eCTD Specification Document, XML will also be accepted whenever a structured exchange standard exists for the content. Currently there are no structured exchange standards for content, however it is expected that these may be introduced in the future for content such as the tracking table, application forms, etc.

Note that all PDF files included in an eCTD irrespective of the module should be v1.4, v1.5, v1.6 or v1.7 except where a specific requirement for a later version is defined (see ICH Q&A for further details regarding PDF version acceptability).

It is preferred that PDFs be generated from an electronic source. Signatures may be embedded as a graphic file in the PDF text if desired.

4.2.2. Modules 2 to 5

No additional file formats are defined for Modules 2 to 5 other than those mentioned in the ICH eCTD Specification Document.

4.3. Use of Electronic Signatures

The use of advanced electronic signatures e.g. digital signatures, will be crucial in achieving pure electronic communication between the pharmaceutical industry and regulatory agencies, particularly for authentication of electronic submissions and documents contained therein. Currently the use of digital signatures for electronic submissions is not fully supported within the THAI FDA. Digital signatures can be used but only as an adjunct to any required written signatures. Scanned signatures would ordinarily be used where the documents make up part of the checksum of an eCTD submission.

4.4. Handling of Empty or Missing eCTD Sections

For new applications, including generic applications, detailed statements justifying the absence of data or specific CTD sections should be provided in the relevant Quality Overall Summary and/or Nonclinical/Clinical Overviews e.g. Module 2.3, 2.4, or 2.5. Note that placeholder documents highlighting no relevant content should not be placed in the eCTD structure. Such documents would create a document lifecycle for non-existent documents causing unnecessary complications and maintenance of the eCTD submissions.

For a generic application, there is no need to provide a justification for content that is typically absent.

4.5. Updating Backbone Attributes/Metadata

4.5.1. Updating ICH Attributes

Updating XML backbone attributes such as `manufacturer` during the eCTD lifecycle is possible, however, consideration should be given regarding the impact of changing backbone attributes during the lifecycle as this can lead to a higher level of complexity in the cumulative view of a submission.

4.5.2. Updating TH Envelope Information

The TH envelope information can be updated during the lifecycle as is necessary to reflect changes in the application metadata e.g. adding and removing duplicate product names.

4.6. Bookmarks, TOCs and Hyperlinks

The evaluation process is made more efficient if content documents are prepared in such a manner that will aid the assessor to quickly and effectively locate content. The navigation through PDF documents is made easier, especially in larger documents, if bookmarks and/or TOCs are made available to quickly access information within the document. Based on experience in other regions, the THAI FDA recommends that documents with more than five pages and with multiple sections should provide a Table of Contents, and/or if appropriate, a Table of Table, Table of Figures, etc. on the first page of the document to ease further navigation through the document.

Hyperlinks are recommended when they would aid the evaluation in ways not already possible through the use of the eCTD index.xml and document navigation aids (bookmarks and TOCs). Applicants should consider when creating cross document hyperlinks that they can cause confusion later in lifecycle and therefore be distracting for an efficient review.

For more information on creating bookmarks and hyperlinks in PDF documents, please refer to Appendix 7 in the ICH eCTD Specifications.

4.7. File Reuse

As prescribed in the Appendix 6 of the ICH eCTD Specifications, the THAI FDA accepts and encourages applicants to make active use of file reuse. Applicants should not submit the same document multiple times. File reuse should be used when a file is submitted multiple times within one sequence, a file already submitted in an earlier sequence is being referenced again or if a file submitted in another application is being referenced in a new application.

Please note that the THAI FDA is implementing a flat repository structure to make cross application referencing possible. Links to content provided in other applications simply need to be directed out of the current application structure and into the structure of the corresponding application. Both the source and target applications should be in the same folder on the same level when references are created. All application will be stored using the eSubmission Identifier to make cross referencing easily predictable and possible.

We accept and encourage you to reuse files when you:

- Need to submit a file several times within one sequence.
- Are referring to a file that has already been submitted in a previous sequence.
- Are referencing a file submitted in another application.

If referencing content in another application, the link in the xml file should be created as shown below.

```
<m1-4-3-clinical>
  <leaf ID="N32c04822abdb4f79b269f81751ae924f" operation="new" xlink:href=
  "104-expert/1041-quality/quality.pdf" checksum="84bb1d0f34241377b395b41be4c96842"
  checksum-type="MD5">
    <title>Expert Dr. A. Jones</title>
  </leaf>
  <leaf ID="Nba9e2cd05ca04ca39fb33e41277be3aa" operation="new" xlink:href=
  "../../../0000/m1/th/104-expert/1042-nonclinical/nonclinical.pdf" checksum=
  "7ef64a29ff976baf1dfd9f8652e228f5" checksum-type="MD5">
    <title>Expert Dr. B. Schmidt</title>
  </leaf>
  <leaf ID="N88345a5375e449f080c68fc58f015a9c" operation="new" xlink:href=
  "../../../../e5700001/0000/m1/th/104-expert/1043-clinical/clinical.pdf" checksum=
  "922833d161180729ad59c23ba2e0444e" checksum-type="MD5">
    <title>Expert Dr. C. Smith</title>
  </leaf>
</m1-4-3-clinical>
```

This directs the hyperlink out of the application and into the referenced application using the eSubmission ID of that application (referencing itself if directing into another sequence of the same application).

5. TH Module 1 General Architecture

5.1. The Thai Module 1 Backbone File

The Thai Module 1 eCTD backbone file comprises three main components:

- A fixed eXtensible Markup Language (XML) root element;
- The envelope elements; and
- The eCTD heading elements describing the actual files provided.

Creating the Module 1 eCTD Backbone File

To create the Thai Module 1 backbone file for a given sequence:

1. Create an XML file with the appropriate XML declaration using an authenticated eCTD preparation software. See The XML Root Element below.
2. Create an envelope with elements containing the appropriate metadata values describing this sequence. See the The Envelope Elements below.
3. Create heading elements as needed for this sequence, as described in the

4. The Heading Elements below. These elements will be of two broad types:
   - Heading elements, organizing the content in the Module 1 to meet the THAI FDA's review requirements.
   - Leaf elements, providing a file system reference to each file being submitted in the regulatory transaction as part of Module 1, along with other information such as eCTD check-sum and life-cycle information.
5. Name the Thai Module 1 eCTD backbone file th-regional.xml and place it in the th subfolder within the Module 1 i.e. m1 subfolder of the regulatory transaction.
6. Validate the resulting backbone using a suitable eCTD validation tool.

Style-Sheets

The TH Module 1 is provided with a standard style-sheet that is used to view content. Note that the style-sheet has been designed to display the complete Module 1 table of contents i.e. all sections, irrespective of whether files are actually present in those sections or not. The style-sheet is provided so that content in Module 1 can be opened using a browser by the applicant, the THAI FDA will not be using it to review content.

5.2. The XML Root Element

All Thai Module 1 backbone files prepared for the THAI FDA will contain the standard XML root element. Note that the required text includes an XML declaration and the root element `th_ectd` with its attributes linking this XML file to the XML definition prepared by the THAI FDA. The line breaks inside of the `th_ectd` element as shown in the excerpts below are not mandatory.

```
<?xml version="1.0" encoding="UTF-8"?>
<?xml-stylesheet href="../../util/style/th-regional.xsl" type="text/xsl"?>
<th_ectd xmlns="th_ectd"
         xmlns:xlink="http://www.w3.org/1999/xlink"
         xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
         schema-version="1.0"
         xsi:schemaLocation="th_ectd ../../util/dtd/th-regional.xsd">
```

5.3. The Envelope Elements

XML Element	Description	Constraint	Occurrence	Defined Values
esub-id	eSubmission Identifier	Mandatory	Single	
sequence-type	Sequence Type	Mandatory	Single	X
reg-activity-lead	Regulatory Activity Lead	Mandatory	Single	X
licensee	Licensee	Mandatory	Single	
licensee-type	Licensee Type	Mandatory	Single	X
licensee-name	Licensee Name	Mandatory	Single	
Inn	INN or Generic Name	Mandatory	Multiple	
product-name	Product Name	Mandatory	Multiple	
sequence	Sequence Number	Mandatory	Single	
related-sequence	Related Sequence Number	Mandatory	Single	
seq-description	Sequence Description	Mandatory	Single	X
email	Contact email	Mandatory	Single	

eSubmission Identifier

Prior to submitting the first sequence of an eCTD, an eSubmission Identifier must be assigned. This is done by following the steps described in the Business protocol section of this document. The identifier must be entered as assigned in the envelope and should also to be used as the name for the application folder in which the sequence folders are submitted. The identifier is made up of a letter and seven digits.

Example: e1234567

Sequence Type

Identifies the type of activity that is being submitted with the sequence, either the regulatory activity type if it is the first sequence of the regulatory activity or supplementary information if it is a follow-up to information already submitted for the regulatory activity.

Example: A : Pharmaceutics - New Chemical Entity

Sequence Type	
List Value	**Description**
a-ph-newce	A: Pharmaceutics - New Chemical Entity
a-ph-newse	A: Pharmaceutics - New Salt or Ester of Existing Active Ingredient
a-ph-newdosage	A: Pharmaceutics - New Dosage Form
a-ph-newroute	A: Pharmaceutics - New Route of Administration
a-ph-newcomb	A: Pharmaceutics - New Combination
a-ph-abridge	A: Pharmaceutics – Abridge application
a-ph-newothers	A: Pharmaceutics - New Medicinal Product (Others)
a-ph-newgen	A: Pharmaceutics - New Generic
a-ph-generic	A: Pharmaceutics - Generic
a-ph-house	A: House Hold Remedies
b-bio-vaccine	B: Biologics - Vaccine
b-bio-blood	B: Biologics - Blood and Plasma Derived Product
b-bio-cell	B: Biologics - Cell- and Tissue- Based Therapy Product
b-bio-biotech	B: Biologics - Biotechnology Product
b-bio-biosimilar	B: Biologics - Biosimilar Product
b-bio-abridge	B: Biologics – Abridge application
b-bio-others	B: Biologics - Others
c-vet-newprod	C: Veterinary - New Medicinal Product
c-vet-newgeneric	C: Veterinary - New Generic Medicinal Product
c-vet-generic	C: Veterinary - Generic Medicinal Product
c-vet-premixed	C: Veterinary - Medicated Premixed
c-vet-bio	C: Veterinary - Biologics
d-traditional	D: Traditional Medicinal Product
f-var-major	F: Variation - Major Variation (MaV)
f-var-minor-pa	F: Variation - Minor Variation (MiV-PA)
f-var-minor-n	F: Variation - Minor Variation (MiV-N)
f-var-others	F: Variation - Others
g-clin-authapp	G: Clinical Trial Authorization Application
g-clin-authamend	G: Clinical Trial Authorization Amendments
h-review-smph	H: Review of SMP Application
h-riskmgtplan	H: Risk Management Plan
h-pv	H: Pharmacovigilance
h-psur	H: Periodic Safety Update Report
i-dmf	I: Drug Master Files
i-pmf	I: Plasma Master Files

i-vamf	I: Vaccine Antigen Master File
i-tmf	I: Tissue Master File
j-suppl	J: Supplementary Information
k-orphan	K: Orphan Drug Application
k-emergency	K: Emergency Used Application
l-consult	L: Consultative Application
z-undefined-regact	Z: Undefined Regulatory Activity

Regulatory Activity Lead

Identifies the group within the THAI FDA which is expected to take the lead in the review process.

Example: pharma

Defined Values	Description
Biologicals	Biological Product Review
Pharmaceuticals	Pharmaceutical Product Review
Pharmacovigilance	Pharmacovigilance Review
Cosmetic	Cosmetic Review
Medical-Devices	Medical Device Review

Licensee Number

The licensee number that is legally responsible for the application in Thailand. The licensee number of the company should be provided.

Example: 12345/2557

Licensee Type

The licensee type of Licensee Number for the application in Thailand. The licensee type of the company should be provided.

Example: Manufacturer

Defined Values	Description
Importer	Importer
Manufacturer	Manufacturer

Licensee Name

The licensee name that is legally responsible for the application in Thailand. The licensee name of the company should be provided in all capital letter.

Example: INCRIDIBLE PHARMA

INN or Generic Name

The INN or Generic Name of the active ingredients used in the product.

Example: amoxicillin

Product Name

The name or proposed product (trade) name(s) to be used on the Certificate of Registration. If duplicate products are being submitted within one application, all products should be listed.

Example: SuperPill

Sequence Number

Four digit sequence number matching the sequence folder being submitted.

Example: 0000

Related Sequence Number

The related sequence number is used to group sequences within an eSubmission. This will allow easy reviewing of sequences associated with a particular regulatory activity among the multiple activities submitted during the lifecycle of the eSubmission. The four (4)-digit related sequence no. for each regulatory activity is the sequence-number of the initial sequence of that regulatory activity. Therefore, all sequences that belong to a specific regulatory activity should contain the same four (4)-digit number in the related sequence no field.

Sequence	Related Sequence	Sequence Type	Sequence Description
0000	0000	A: Pharmaceutics - New Chemical Entity	Initial Application
0001	0000	J: Supplementary Information	Response to Request for Information Date: 01-December-2015
0002	0000	J: Supplementary Information	Response to Request for Information Date: 15-December-2015
0003	0000	J: Supplementary Information	Response to Request for Information Date: 30-December-2015

0004	0004	F: Variation - Major Variation (MaV)	Initial Variation
0005	0005	H: Periodic Safety Update Report	Initial Report
0006	0006	F: Variation - Minor Variation (MiV-PA)	Initial Variation
0007	0004	J: Supplementary Information	Response to Request for Information Date: 10-Febuary-2016
0008	0004	J: Supplementary Information	Response to Request for Information Date: 11-March-2016
0009	0004	J: Supplementary Information	Product Information
0010	0006	J: Supplementary Information	Product Information

Each Initial sequence of a regulatory activity will reference itself. Each Supplementary Information provided 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 specifications 2.3.

Example: 0001

Sequence Description

The sequence description is used to provide a free text description of the submission. The description provided here should also be used in the node title for 1.0 Cover Letter and 1.R Response to Questions. It is encouraged that applicants provide a short, precise but informative description. It should not repeat information provided in the Sequence Type attribute but rather provide additional clarification to information being submitted. The list below provides a few examples for such a field:

- Initial Application: Initial Application
- Response: Response to LOQ dated 2014-06-13
- Response: Response to Validation Questions
- Response: Providing Quality Supplementary Information

Email

The email is used to notify the applicant in case of change in application status.

Example: regulatory@incridiblepharma.com

5.4. The Heading Elements

The Thai Module 1 headings are based on the headings from the EU specifications (version 2.0). Additional structure has been added to some sections to better meet Thai requirements. In particular, an element has been specified for the tracking table, specific elements for the labelling, SPC and Package Leaflet as well as two additional elements for the Specific Requirements for Different Types of Applications. Some sections have been deemed not applicable while others have been designated as optional.

Content should be provided as `leaf-nodes`. The `leaf-node` element can be comprised of one or multiple `leaf` elements and/or `node-extensions`. Titles for the `leaf-nodes` should be descriptive and helpful for identifying the content and does not need to repeat information in the parent structure. In the following description of the heading elements, the `leaf-node` has been added where specific `leaf title` recommendations exist. Where the `leaf-node` is not specified, it is up to the applicant to provide an appropriate description of the content in the `leaf title`.

1.0 Cover Letter and Tracking Table

Section ID	Business Terminology	XML-Element
1.0	**Cover**	m1-0-cover
1.0.1	Tracking Table	m1-0-1-tracking
1.0.2	Cover Letter	m1-0-2-cover-letter

During lifecycle, the cover letter should always be submitted with the lifecycle operator `new` and the tracking table should be submitted with the lifecycle operator `replace`.

The suggested naming convention for the cover letter `leaf title` is the sequence number followed by the sequence description as provided in the envelope e.g. "0000 Initial Application".

1.2 Application Form

Section ID	Business Terminology	XML-Element
1.2	**Application Forms**	m1-2-forms
1.2.1	Application Form	m1-2-1-form
1.2.1.1	<Sequence Number> <Description>	leaf-node
1.2.2	Annexes	m1-2-2-annexes
1.2.2.1	<Sequence Number> <Description of Annex>	leaf-node

During lifecycle, the application form should normally be submitted with the lifecycle operator `new` unless under rare occasions a correction to an application form already submitted is being provided in which case, `replace` can be used.

The application form should be placed under 1.2.1 and the suggested naming convention for the `leaf title` is the sequence number followed by a description of the file being submitted e.g. "0000 Application Form New Generic".

Any annexes to be provided e.g. declaration documents from the applicant including Proxy Letter, Letter of Authorization, and Certificates such as CPP CFS and GMP should be provided under 1.2.2 and the suggested naming convention for the leaf title is the sequence number followed by a brief, precise and recognizable identification of the Annex content.

1.3 Product Information

Section ID	Business Terminology	XML-Element
1.3	**Product Information**	m1-3-pi
1.3.1	SPC, Labelling and Package Leaflet	m1-3-1-spc-label-pl
1.3.1.1	Labelling	m1-3-1-1-label
1.3.1.1.1	<Description of Labelling>	leaf-node
1.3.1.2	SPC	m1-3-1-2-spc
1.3.1.3	Package Leaflet	m1-3-1-3-pl
1.3.1.3.1	Package Leaflet - Thai	m1-3-1-3-pl-th
1.3.1.3.2	Package Leaflet - English	m1-3-1-3-pl-en
1.3.1.3.3	Package Leaflet - Other Language	m1-3-1-3-pl-ot
1.3.1.3.3.1	<Language> <Description>	leaf-node
1.3.2	Mock-up	m1-3-2-mockup
1.3.3	Specimen	m1-3-3-specimen
1.3.4	Consultation with Target Patient Groups	m1-3-4-consultation
1.3.5	Product Information already approved in Other States	m1-3-5-approved
1.3.5.1	Foreign Regulatory Status	m1-3-5-1-status
1.3.5.2	Foreign Product Information	m1-3-5-2-pi
1.3.5.2.1	<Country> <Product Information Type>	leaf-node
1.3.5.3	Data Similarities and Differences	m1-3-5-3-similarities
1.3.6	Braille	m1-3-6-braille

The Product Information should be provided in PDF format within the eCTD. Working documents are not needed and do not need to be provided within the eCTD framework for Thailand.

The Product Information section for Thailand reflects a more granular and defined approach than that of the EU specifications. Both the sections for Product Information and the Product Information already approved in other Countries have been expanded to define the product information type and languages expected as well as a breakdown of the type of information wanted where the product information has already been approved in other countries.

1.3.1 Product Information has been broken down into three specific sections for Labelling, SPC and the Package leaflet. No other product types are expected. If one file is submitted for this section, it should be submitted under 1.3.1.1 Labelling.

The `leaf title` provided for 1.3.1.1 Labelling should describe the labelling that is being provided. Multiple documents can be provided or all information can be combined in one document.

1.3.1.3 Package Leaflet has been broken down into language sections for English, Thai and Other languages and it is recommended that separate files be submitted for each language.

1.3.4 Consultation with Target Patient Groups is not required for Thai applications but can be provided.

1.3.5 Product Information already approved in other Countries has been broken down into three sections. One file should be provided for the Foreign Regulatory Status as a tabular summary. During the lifecycle, the status should always use the operator `replace`. Details of Foreign Product Information should be provided, especially if already approved in ASEAN, EU, US, Canada, Australia or PIC/S regulated countries. The `leaf title` provided for 1.3.5.2 should indicate the originating country and product information type being provided. Data Similarities and Differences should be provided using the THAI FDA form. During the lifecycle, the Data Similarities and Differences file should always us the operator `replace`.

1.3.6 Braille should is option but should be provided if braille is to be used in the production information and packaging.

1.4 Information about the Experts

Section ID	Business Terminology	XML-Element
1.4	**Information about the Experts**	m1-4-expert
1.4.1	Quality	m1-4-1-quality
1.4.2	Non-Clinical	m1-4-2-non-clinical
1.4.3	Clinical	m1-4-3-clinical

Currently there is no mandate for information to be provided for this section, however, the THAI FDA would appreciate Information about the Experts.

1.5 Specific Requirements for Different Types of Applications

Section ID	Business Terminology	XML-Element
1.5	**Specific Requirements for Different Types of Applications**	m1-5-specific
1.5.1	Information for Bibliographical Applications	m1-5-1-bibliographic
1.5.2	Information for Generic, 'Hybrid' or Bio-similar Applications	m1-5-2-generic-hybrid-bio-similar
1.5.2.1	Information for Generic Application	m1-5-2-1-generic
1.5.2.2	Information for 'Hybrid' Applications	m1-5-2-2-hybrid
1.5.2.3	Information for Bio-similar Applications	m1-5-2-3-bio-similar
1.5.3	(Extended) Data/Market Exclusivity	m1-5-3-data-market-exclusivity
1.5.4	Exceptional Circumstances	m1-5-4-exceptional-circumstances
1.5.5	Conditional Marketing Authorisation	m1-5-5-conditional-ma
1.5.6	Additional Trade Name Declarations	m1-5-6-trade-name
1.5.7	Co-marketed Medicines Declarations	m1-5-7-co-marketed

This section has been taken from the EU structure and additional types of applications have been added. Section 1.5.2 has been broken down into three sections and given a section number to make expectations and cross referencing clearer.

Section 1.5.6 should be included when the application seeks the registration of an additional trade name for an existing registered prescription medicine. This may be either:

- a stand-alone additional trade name application
- in combination with other application types

For example, an extension of indications in addition to the additional trade name.

Please note that trade names are to:

- identify the products within a range of dose forms and strengths
- include distinguishing letters so they are not confused with those already in the Thai Register of Medicinal Product
- identify the strengths of the active ingredients in the trade name for fixed combinations.

The trade names proposed must not:

- be registered already (unless a further identifier is proposed)
- be inappropriate (for example, must not be advertorial)
- look or sound like other trade names (potential to cause prescribing and dispensing errors).

Section 1.5.7 should be included when:

- a cross-licensing agreement exists between the applicant of the application and a third party applicant
- the third party sponsor authorises the THAI FDA to use information on its product (that is either on the Thai Register of Medicinal Product or under evaluation) for the benefit of the first party's application
- the applicant's product will be identical or very similar to the third-party's product

Please note that you must ensure the third party has lodged their data before lodging the application. Failure to provide the third part's data may result in an application being considered not effective.

To avoid delays in evaluating the application, requests to make corrections or variations to the Thai Register of Medicinal Product entry for the third party's already registered product must be submitted to the THAI FDA well in advance of lodging the co-marketed medicine application.

1.6 Environmental Risk Assessment

Section ID	Business Terminology	XML-Element
1.6	**Environmental Risk Assessment**	m1-6-environrisk
1.6.1	Non-GMO	m1-6-1-non-gmo
1.6.2	GMO	m1-6-2-gmo

Only one file should be provided for 1.6 Environmental Risk Assessment. It is not allowed to provide content in both 1.6.1 and 1.6.2.

1.7 Product Interchangeability Equivalence Evidence

Section ID	Business Terminology	XML-Element
1.7	**Product Interchangeability Equivalence Evidence**	m1-7-productinter
1.7.1	BE Protocol	m1-7-1-beprotocol
1.7.2	BE study report	m1-7-2-bestudy
1.7.3	Comparative in vitro dissolution/release studies	m1-7-3-beinvitro
1.7.4	Comparative clinical studies	m1-7-4-beclinic
1.7.5	Comparative pharmacodynamics studies	m1-7-5-bepharmaco
1.7.6	Other	m1-7-6-beother

1.8 Information relating to Pharmacovigilance

Section ID	Business Terminology	XML-Element
1.8	**Information relating to Pharmacovigilance**	m1-8-pharmacovigilance
1.8.1	Pharmacovigilance System	m1-8-1-pharmacovigilance-system
1.8.2	Risk-management System	m1-8-2-risk-management-system

1.8.3	SMP Protocol	m1-8-3-smp

During lifecycle, 1.8.2 Risk management plan should always use the lifecycle operator `replace`.

1.9 Information relating to Clinical Trials

Section ID	Business Terminology	XML-Element
1.9	**Information relating to Clinical Trials**	m1-9-clinical-trials

Currently there is no mandate for information to be provided for this section, however, the THAI FDA would appreciate a statement to the effect that clinical trials performed outside Thailand meet ethical requirements.

1.10 Information relating to Paediatrics

Section ID	Business Terminology	XML-Element
1.10	**Information relating to Paediatrics**	m1-10-paediatrics

Currently there is no mandate for information to be provided for this section, however, the THAI FDA would appreciate any appropriate information on this topic to be provided if available.

1.R Responses to Questions

Section ID	Business Terminology	XML-Element
1.R	**Responses to Questions**	m1-responses
1.R.1	<Sequence Number> <Sequence Description>	leaf-node

When responding to questions posed by the THAI FDA, a document addressing these questions should be provided. Where possible, hyperlinks should be created linking the topic addressed with the sections where changes have been made. The `leaf title` should provide the sequence number and the sequence description as provided in the envelope e.g. "0000 Response to LOQ – Quality from 2014-06-04".

1.A Additional Data

Section ID	Business Terminology	XML-Element
1.A	**Additional Data**	m1-additional-data
1.A.1	Assessment report from other regulatory agency	m1-a-1-assessment-report
1.A.2	Checklist Form /Self Assessment Report	m1-a-2-self-assessment
1.A.3	Information on Development Studies	m1-a-3-development-studies
1.A.4	COA from Institute of Biological Product	m1-a-4-coa-biologic
1.A.5	Comparison Table	m1-a-5-comparison-table

1.A.6	Information of Exportation	m1-a-6-exportation
1.A.7	Declaration from applicant	m1-a-7-declaration
1.A.8	Template of Database entering	m1-a-8-database-entering
1.A.99	Other	m1-a-99-other

Any data provided that would not logically belong in one of the specified sections can be provide in the 1.A.99 Other. The `leaf title` should be descriptive of the content being provided.

5.5. The Node Extension Element

Structures beyond the heading elements can be defined through node extension elements. In addition, wherever a `leaf` element is allowed in the schema, a `node-extension` element is also allowed. The `node-extension` structure allows the sponsor to effectively make arbitrary heading structures as desired. This advanced concept can be helpful in organizing multiple large collections of files which are all needing to be placed under a single normal eCTD heading.

The fact that the schema allows the node-extension structure is in compliance with general ICH eCTD specifications, but should not be interpreted as a blanket permission to use the structures anywhere or without consideration. Sponsors may use these structures where needed to assist reviewers but may want to contact the THAI FDA for advice if the usage is novel.

The optional `node-extension` element contains a single mandatory `title` element, followed by at least one `leaf` element, and followed by another optional `node-extension` element. The element can be repeated.

The node extension `title` element should be short, precise and informative. Information already categorized by heading elements need not be repeated. The most important identifying information should be placed at the beginning to prevent reviewers from having to scroll to the end of the title.

5.6. The Leaf Elements

Content for each heading element is provided through `leaf` elements. This optional element contains one other element, the `title` element along with a number of attributes, all based upon the ICH eCTD definition provided in the Electronic Common Technical Document Specification (Version 3.2.2). This element can be repeated. The schema will additionally ensure the checksum-type attribute contains either “MD5” or “md5”.

The leaf `title` element should be short, precise and informative. Information already categorized by heading elements need not be repeated. The most important identifying information should be placed at the beginning to prevent reviewers from having to scroll to the end of the title.

5.7. Files and Folders

5.7.1. File and Folder Naming Conventions

Naming conventions for the content files are irrelevant for eCTD review as the leaf titles provided in the XML files will be used to identify content. The naming conventions used by other regions can be reused for Thai eCTDs. Naming conventions will not be validated as part of the TH eCTD Validation Criteria. It is, however, required that all file and folder names be submitted in English and not in Thai.

All content must be referenced by the appropriate XML files for efficient navigation. Applicants should concentrate on providing precise but informative leaf titles to aid reviewers.

While naming conventions for content will not be validated, it is expected that the basic construction of the eCTD be maintained and adherence to the following naming conventions will be required.

Folder	File	Description
e1234567		Application folder with eSubmission identifier e.g. e1234567
0000		Sequence folder with four digit sequence number e.g. 0000
	index.xml	Index file in accordance with ICH
	index-md5.txt	MD5 checksum in accordance with ICH
m1		Content folder for Module 1 documents in accordance with ICH
th		Thai country specific folder
	th-regional.xml	Thai regional index file for Module 1
m2		Content folder for Module 2 documents in accordance with ICH
m3		Content folder for Module 3 documents in accordance with ICH
m4		Content folder for Module 4 documents in accordance with ICH
m5		Content folder for Module 5 documents in accordance with ICH
util		Util folder in accordance with ICH
dtd		DTD and schema folder in accordance with ICH
	th-regional.xsd	Thai regional backbone schema for Module 1
	xlink.xsd	W3C schema for XLink 1.1 (referenced from th-regional.xsd)
	xml.xsd	W3C schema for XML namespace (referenced from th-regional.xsd)
	ich-ectd-3-2.dtd	ICH DTD for Modules 2 to 5
style		Style sheet folder in accordance with ICH
	ectd-2-0.xsl	ICH style sheet for Modules 2 to 5
	th-regional.xsl	Style sheet for Thai regional backbone
0000-validation-report		Folder for validation report to be provided with the submitted sequence.

5.7.2. Folder and File Name Path Length

The overall folder and file name path length starting from the sequence number should not exceed 180 characters, for any file in any module. This is a TH regional requirement based on existing requirements in the EU. It is acknowledged that this is less than the ICH agreed overall path length.

5.7.3. Lifecycle operations

The following four lifecycle operations defined under the ICH eCTD specification:

- New
- Replace
- Delete
- Append

We encourage you to: Use New, Replace, and Delete.

Only use Append as part of the study tagging files (STF) as defined by the ICH eCTD Backbone File Specification for Study Tagging Files. If you use Append for any other purpose, you will receive a validation warning which need to include an explanation in the cover letter.

6. eCTD Preparation Tools

The THAI FDA does not mandate or recommend any particular software product for eCTD preparation. However, based upon other agency observations and experience the THAI FDA recommends that applicants:

- Prepare the eCTD using an authenticated commercial eCTD preparation software. There are a wide variety of options available to sponsors for commercial eCTD preparation software, both in terms of multiple vendors and in terms of approaches e.g. installed software, software as a service, service providers. Sponsors are encouraged to find a solution which supports current and ongoing TH eCTD requirements and meets their overall business needs.
- Validate the prepared regulatory activity using an authenticated commercial eCTD validation tool.

Sponsors are encouraged to use a validation tool which supports checking current and ongoing TH eCTD requirements. These validation tools are not just XML checkers or parsers, but actually evaluate the technical content of the regulatory activity. There are numerous options available to sponsors, several of which are free. This minimizes the possibility of technical validation errors with eCTD regulatory transactions sent to the THAI FDA which introduce delays into the overall regulatory process.

A list of validation tools that the THAI FDA feels support the Thai validation requirements will be maintained on the THAI FDA website at http://drug.fda.moph.go.th/eng . Vendors of validation tools are encouraged to demonstrate their tool's compliance and will be listed if they are in-line with validation criteria.

7. References

The following documents should be read in connection with this specification to ensure conformity with overall eCTD requirements. Where applicable, these specifications should be followed unless otherwise stated in this specification document.

ICH Electronic Common Technical Document Specification (Version 3.2.2)

ICH The eCTD Backbone File Specification for Study Tagging Files (Version 2.6.1)

eCTD Specification and Related files – ICH links to specifications and related files including change control process, change request forms and their Q&A document.

Notice to Applicants Volume 2 B(June 2006), Medicinal products for human use. Presentation and format of the CTD dossier. Provides information on expected content for the CTD. The THAI FDA will adopt these expectations unless expectations are otherwise stated in the Section 5.4

TH Regional Specification and Validation Criteria – source document for Module 1 elements, envelope attributes, eCTD Validation criteria and naming conventions for the TH Module 1 sections added by this specification and not covered by the EU naming conventions. The numbering of the validation criteria has been maintained to correlate with EU criteria. Where requirements were removed, no renumbering of remaining requirements was done. Requirements that were added were appended to the EU criteria.

Example of Cover Letter

Example of Tracking Table

The following documents were referenced during the creation of this specification and many sections were modelled on their content.

AU eCTD Specification

EU Module 1 eCTD Specification (Version 2.0)

Guidance Document: Creation of the Canadian Module 1 Backbone

ภาคผนวก ๒

การจัดเตรียมเอกสาร
กรณีจัดเอกสารตามรูปแบบอาเซียน

การจัดเตรียมเอกสารคำขอขึ้นทะเบียนตำรับยา ตามแบบ ACTD *เข้าสู่รูปแบบการยื่น แบบ* eCTD

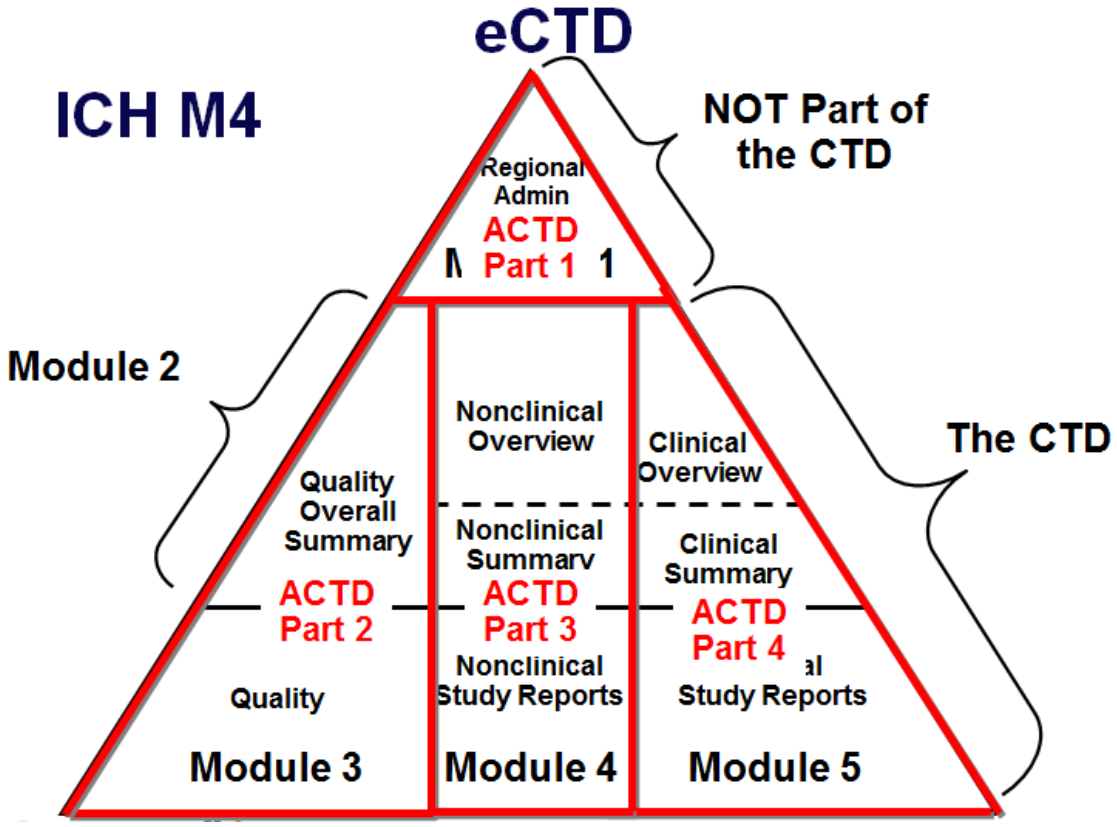
Version 1.0

ประวัติการแก้ไข

Version	รายละเอียดโดยสรุป	วันที่
0.90	ประกาศใช้ในช่วงการทดลองระบบ และมีวิธีการ Mapping ACTD part P9 2 ทางเลือก ทางเลือกที่ 1 : เฉพาะกรณียาสามัญ / ยาสามัญใหม่ ที่แยกข้อมูล ทางเลือกที่ 2 : เฉพาะกรณียาสามัญ / ยาสามัญใหม่ ที่ไม่แยกข้อมูล	01/07/2014
0.92	1. เพิ่มเติมการ Mapping BA/BE - BE protocol 2. เพิ่มตารางประวัติการแก้ไข 3. ปรับวิธีการ Mapping ACTD part P9 เหลือทางเลือก เดียว คือแยก P9 ไว้ใน 1.A	03/08/2015
0.921	แก้ไขการ Mapping BE protocol ให้รวมอยู่ใน P9	15/08/2015
1.0	ปรับปรุงให้สอดคล้องกับ TH eCTD SpecificationModule 1 and Regional Information, Version 1.0	17/12/2015

Table of Contents

eCTD and ACTD Structure



1. Module 1 TH eCTD

Module 1 Th eCTD Structure	ACTD Structure
1 Administrative Information and Prescribing Information	
1.0 Cover Letter	
1.0.1 Tracking Table	History of Sequence - Required by Validation Criteria
1.0.2 Cover Letter	Overview of application and sequence - Required by Validation Criteria
1.2 Application Form	
1.2.1 Application Form	1.2 แบบคำขอขึ้นทะเบียนตำรับยาแบบ ASEAN HARMONIZATION (แบบ ย.1)
1.2.2 Annexes	
1.2.2.1 Letter of Authorization	6.5.5 หนังสือมอบอำนาจ (authorization form)
1.2.2.2 Manufacturing License	2.1.1 สำเนาใบอนุญาตผลิตยาแผนปัจจุบัน
1.2.2.3 Production Permit	5.1 คำขออนุญาตผลิตยาตัวอย่างเพื่อขอขึ้นทะเบียนตำรับยา .แบบ ผย)8) (Production permit for drug sample)
1.2.2.4 GMP Certificate	2.1.2 สำเนาหนังสือรับรอง GMP ของผู้ผลิต 2.2.3 สำเนาหนังสือรับรอง GMP ของผู้ผลิตต่างประเทศ
1.2.2.5 Importing License	2.2.1 สำเนาใบอนุญาตนำหรือสั่งยาแผนปัจจุบันเข้ามาในราชอาณาจักร
1.2.2.6 Import Permit	5.2 คำขออนุญาตนำหรือสั่งยาตัวอย่างเข้ามาในราชอาณาจักร เพื่อขอขึ้นทะเบียนตำรับยา (แบบ น .ย.8) (Import permit for drug sample)
1.2.2.7 CPP-CFS Certificate	2.2.2 หนังสือรับรองผลิตภัณฑ์ยา
1.3 Product Information	
1.3.1 SPC, Labelling and Package Leaflet	
1.3.1.1 Labelling	
1.3.1.1.1 Product Description	3. ฉลาก (Labeling)
1.3.1.2 SPC	4.1 ข้อมูลโดยสรุปของผลิตภัณฑ์ตามแบบ Summary of Product Characteristics (SPC) หรือ Product Data Sheet
1.3.1.3 Package Leaflet	
1.3.1.3.1 Package Leaflet - Thai	4.1 ข้อมูลโดยสรุปของผลิตภัณฑ์ตามแบบ Summary of Product Characteristics (SPC) 4.2 เอกสารกำกับยา (Package Insert, PI) 4.3 เอกสารข้อมูลสำหรับผู้ป่วย

Module 1 Th eCTD Structure	ACTD Structure
1.3.1.3.1 Package Leaflet - English	4.1 ข้อมูลโดยสรุปของผลิตภัณฑ์ตามแบบ Summary of Product Characteristics (SPC) 4.2 เอกสารกำกับยา (Package Insert, PI) 4.3 เอกสารข้อมูลสำหรับผู้ป่วย
1.3.1.3.1 Package Leaflet - Other Language	4.1 ข้อมูลโดยสรุปของผลิตภัณฑ์ตามแบบ Summary of Product Characteristics (SPC) 4.2 เอกสารกำกับยา (Package Insert, PI) 4.3 เอกสารข้อมูลสำหรับผู้ป่วย
1.3.2 Mock-up	Optional
1.3.3 Specimen	7. รูปถ่ายยาที่ขอขึ้นทะเบียน (เฉพาะยาเม็ด แคปซูล และยาเหน็บ)
1.3.4 Consultation with Target Patient Groups	Optional
1.3.5 Product Information already approved in the Other States	
1.3.5.1 Foreign Regulatory Status	6.3 คำรับรองการแจ้งข้อมูลการขึ้นทะเบียนยาในประเทศต่าง ๆ
1.3.5.2 Foreign Product Information	Optional
1.3.5.2.1 Data Similarities and Differences	Optional
1.3.5.3 Data Similarities and Differences	Optional
1.3.6 Braille	Optional
1.4 Information about the Experts	
1.4.1 Quality	Optional
1.4.2 Non-clinical	Optional
1.4.3 Clinical	Optional
1.5 Specific Requirements for Different Types of Applications	
1.5.1 Information for Bibliographical Applications	Optional
1.5.2 Information for Generic, Hybrid or Bio-similar Application	Optional
1.5.2.1 Information for Generic Application	- เอกสารอ้างอิงการเป็นยาสามัญ (ขทย AR)
1.5.2.2 Information for Hybrid Application	- เอกสารอ้างอิงการเป็นยาสามัญใหม่ (ขทย NGR)
1.5.2.3 Information for Bio-similar Application	- เอกสารอ้างอิงการเป็นยาชีววัตถุคล้ายคลึง
1.5.3 (Extended) Data/Market Exclusivity	Optional
1.5.4 Exceptional Circumstances	Optional

Module 1 Th eCTD Structure	ACTD Structure
1.5.5 Conditional Marketing Authorization	6.2 คำรับรองเงื่อนไขการขึ้นทะเบียนตำรับยา 6.5.2 คำรับรองเงื่อนไขการขึ้นทะเบียนตำรับยาเฉพาะกลุ่ม
1.5.6 Additional Trade Name Declarations	**Optional**
1.5.7 Co-marketed Medicines Declarations	**Optional**
1.6 Environmental Risk Assessment	
1.6.1 Non-GMO	**Mandatory Selection - Required by Validation Criteria**
1.6.2 GMO	**Mandatory Selection - Required by Validation Criteria**
1.7 Product Interchangeability Equivalence Evidence	
1.7.1 BE Protocol	**P9 หลักฐานแสดงความเท่าเทียมกันในการออกฤทธิ์ของผลิตภัณฑ์ (Product Interchangeability Equivalence evidence) (รวมถึงโครงการศึกษาวิจัย BE, including BE protocol)**
1.7.2 BE study report	
1.7.3 Comparative in vitro dissolution/release studies	
1.7.4 Comparative clinical studies	
1.7.5 Comparative pharmacodynamics studies	
1.7.6 Other	
1.8 Information relating to Pharmacovigilance	
1.8.1 Pharmacovigilance System	**Optional**
1.8.2 Risk-management System	**Optional**
1.8.3 SMP Protocol	**Optional**
1.9 Information relating to Clinical Trials	**Optional**
1.10 Information relating to Pediatrics	**Optional**
1.R Responses to Questions	**Optional**
1.R.1 RESPONSE DESCRIPTION	**Optional**
1.A Additional Data	
1.A.1 Assessment report from other regulatory agency	**Optional**
1.A.2 Checklist Form /Self Assessment Report	Checklist From (eg. แบบ ขทย .ND1 เป็นต้น)
1.A.3 Information on Development Studies	P.2.1 ข้อมูลของการศึกษาพัฒนา)Information on Development Studies) –Optional

Module 1 Th eCTD Structure	ACTD Structure
1.A.4 COA from Institute of Biological Product	ผลวิเคราะห์ยาชีววัตถุซึ่งอยู่ภายใต้การดูแลของสถาบันชีววัตถุ กรมวิทยาศาสตร์การแพทย์ ยกเว้นฮอร์โมนและเอ็นไซม์ (BIOLOGICS)
1.A.5 Comparison Table	8.0 ข้อมูลเปรียบเทียบข้อดี ข้อเสีย - ระหว่างยาใหม่ที่ขอขึ้นทะเบียนกับยาในกลุ่มการบำบัดรักษาโรคเดียวกันที่ได้ขึ้นทะเบียนในประเทศไทยแล้วทั้งในแง่ประสิทธิผลและความปลอดภัย (comparison table with exiting products)
1.A.6 Information of Exportation	- หนังสือติดต่อระหว่างประเทศผู้ค้า หรือ Invoice หรือ Proforma Invoice หรือ Letter of Credit (กรณีส่งออก) 6.5.4 หนังสือแจ้งชื่อยาสำหรับส่งออก
1.A.7 Declaration from applicant	คำรับรองต่าง ๆ เช่น - 6.1 คำรับรองผู้ยื่นคำขอขึ้นทะเบียนตำรับ ยาสามัญ / ยาสามัญใหม่ / ยาใหม่ / ยาชีววัตถุใหม่ / ยาวัคซีน - 6.2 คำรับรองเงื่อนไขการขึ้นทะเบียนตำรับยา 6.4 คำรับรองการแจ้งข้อมูลสิทธิบัตรยา 6.5.2 คำรับรองเงื่อนไขการขึ้นทะเบียนตำรับยาเฉพาะกลุ่ม 6.5.3 คำรับรองเงื่อนไขการขึ้นทะเบียนตำรับยาเพื่อการส่งออกต่างประเทศ 6.5.6 คำรับรองการเรียกเก็บยา เป็นต้น
1.A.8 Template of Database entering	9.0 แบบบันทึกข้อมูลทะเบียนตำรับยา (Optional)
1.A.99 Other	

2. Module 2 eCTD

Module 2 eCTD Structure (Based on EU CTD region)	ACTD Structure		
	Part / Section		Content
2.1 Common Technical Document Summaries (Modules 2-5)			
2.2 Introduction	Admin	A	-A (Section A) : คำนำ (Introduction)
2.3 Quality Overall Summary			
2.3.1 Introduction	Quality	B	**Optional**
2.3.S Drug Substance - NAME - MANUFACTURER	Quality	B	S วัตถุดิบตัวยาสำคัญ (Drug Substance)
2.3.S.1 General Information	Quality	B	S1 ข้อมูลทั่วไป (General Information) S.1.1 ชื่อ (Nomenclature) S.1.2 โครงสร้าง (Structure) S.1.3 คุณสมบัติทั่วไป (General Properties)
2.3.S.2 Manufacture	Quality	B	S2 การผลิต (Manufacture) S.2.1 ผู้ผลิต (อาจมีมากกว่าหนึ่ง) Manufacturer(s)) S.2.2 คำอธิบายกระบวนการผลิตและวิธีควบคุมกระบวนการผลิต (Description of Manufacturing Process and Process Controls) S.2.3 การควบคุมวัตถุดิบ (Control of Materials) S.2.4 การควบคุมขั้นตอนการผลิตที่สำคัญ และ สารมัธยันตร์ (Controls of Critical Steps and Intermediates) S.2.5 การตรวจสอบความถูกต้องของกระบวนการผลิตและ หรือ การประเมินผล/ (Process Validation and/or Evaluation) S.2.6 การพัฒนากระบวนการผลิต (Manufacturing Process Development)
2.3.S.3 characterization	Quality	B	S3 การตรวจลักษณะเฉพาะ (characterization) S.3.1 การแสดงโครงสร้างและลักษณะเฉพาะอื่นๆ (Elucidation of Structure and Other Characteristics) S.3.2 สารเจือปน (Impurities)
2.3.S.4 Control of Drug Substance	Quality	B	S4 การควบคุมวัตถุดิบตัวยาสำคัญ (Control of Drug Substance) S.4.1 ข้อกำหนดมาตรฐาน (Specification) และหนังสือรับรองการวิเคราะห์ (Certificate of Analysis) S.4.2 วิธีการวิเคราะห์ (Analytical Procedure) S.4.3 การตรวจสอบความถูกต้องของวิธีการวิเคราะห์ (Validation of Analytical Procedures) S.4.4 การวิเคราะห์การผลิตแต่ละรุ่น (Batch Analysis)

Module 2 eCTD Structure (Based on EU CTD region)	ACTD Structure		
	Part / Section		Content
			S.4.5 การชี้แจงเหตุผลของข้อกำหนดมาตรฐาน (Justification of Specification)
2.3.S.5 Reference Standards or Materials	Quality	B	S5 สารมาตรฐานหรือวัสดุมาตรฐาน (Reference Standards or Materials)
2.3.S.6 Container Closure System	Quality	B	S6 ระบบปิดของภาชนะบรรจุ (Container Closure System)
2.3.S.7 Stability	Quality	B	S7 ความคงสภาพ (Stability)
2.3.P Drug Product - NAME	Quality	B	P ผลิตภัณฑ์ยา (DRUG PRODUCT)
2.3.P.1 Description and Composition of the Drug Product	Quality	B	P1 ลักษณะยาและส่วนประกอบ (Description and Composition)
2.3.P.2 Pharmaceutical Development	Quality	B	P2 การพัฒนาทางเภสัชกรรม (Pharmaceutical Development) P.2.1 ข้อมูลของการศึกษาพัฒนา (Information on Development Studies) P.2.2 ส่วนประกอบของผลิตภัณฑ์ยา (Components of the Drug Product) P.2.3 ผลิตภัณฑ์สำเร็จรูป (Finished Product) P.2.4 การพัฒนากระบวนการผลิต (Manufacturing Process Development) P.2.5 ระบบปิดของภาชนะบรรจุ (Container Closure System) P.2.6 คุณสมบัติทางจุลชีววิทยา (Microbiological Attributes) P.2.7ความเข้ากันได้ของผลิตภัณฑ์ (Compatibility)
2.3.P.3 Manufacture	Quality	B	P3 การผลิต (Manufacture) P.3.1 สูตรยาต่อรุ่นการผลิต (Batch Formula) P.3.2 กระบวนการผลิตและวิธีการควบคุมกระบวนการผลิต (Manufacturing Process and Process Controls) P.3.3 การควบคุมขั้นตอนการผลิตที่สำคัญ และ สารมัธยันตร์ (Controls of Critical Steps and Intermediates) P.3.4 การตรวจสอบความถูกต้องของกระบวนการ และ/หรือ การประเมินผล (Process Validation and/or Evaluation)
2.3.P.4 Control of Excipients	Quality	B	P4 การควบคุมสารปรุงแต่ง (Control of Excipients) P.4.1 ข้อกำหนดมาตรฐาน (Specifications) และหนังสือรับรองการวิเคราะห์ (Certificate of Analysis) P.4.2 วิธีการวิเคราะห์ (Analytical Procedure) P.4.3 สารปรุงแต่งที่มีแหล่งกำเนิดจากมนุษย์หรือสัตว์ (Excipients of Human or Animal Origin) P.4.4 สารปรุงแต่งที่เป็นสารชนิดใหม่ (Novel Excipients)

Module 2 eCTD Structure (Based on EU CTD region)	ACTD Structure		
	Part / Section		Content
2.3.P.5 Control of Drug Product	Quality	B	P5 การควบคุมผลิตภัณฑ์สำเร็จรูป (Control of Finished Product) P.5.1 ข้อกำหนดมาตรฐาน (Specification) และหนังสือรับรองการวิเคราะห์ (Certificate of Analysis) P.5.2 วิธีการวิเคราะห์ (Analytical Procedure) P.5.3 การตรวจสอบความถูกต้องของวิธีการวิเคราะห์ (Validation of Analytical Procedures) P.5.4 การวิเคราะห์รุ่นการผลิต (Batch Analyses) P.5.5 การตรวจลักษณะเฉพาะของสารเจือปน (Characterization of Impurities) P.5.6 การชี้แจงเหตุผลของข้อกำหนดมาตรฐาน (Justification of Specifications)
2.3.P.6 Reference Standards or Materials	Quality	B	P6 สารมาตรฐานหรือวัสดุมาตรฐาน (Reference Standards or Materials)
2.3.P.7 Container Closure System	Quality	B	P7 ระบบปิดของภาชนะบรรจุ (Container Closure System)
2.3.P.8 Stability	Quality	B	P8 ความคงสภาพ (Stability)
2.3.A Appendices			
2.3.A.1 Facilities and Equipment	Quality	B	**Optional**
2.3.A.2 Adventitious Agents Safety Evaluation	Quality	B	**Optional**
2.3.A.3 Novel Excipients	Quality	B	**Optional**
2.3.R Regional Information	Quality	B	**Optional**
2.4 Nonclinical Overview	Nonclinical	B	ตอนที่ B (Section B) : ภาพรวมของส่วนข้อมูลที่ไม่ใช่ข้อมูลทางคลินิก (Nonclinical Overview) 1.เกณฑ์โดยทั่วไป (General Aspects) 2.เนื้อหาและรูปแบบโครงสร้าง (Content and Structural Format)
2.5 Clinical Overview	Clinical	B	ตอนที่ B (Section B) : ภาพรวมด้านคลินิก (Clinical Overview) 1.เหตุผลในการพัฒนาผลิตภัณฑ์ (Product Development Rationale) 2.ภาพรวมของชีวเภสัชกรรม (Overview of Biopharmaceutics) 3.ภาพรวมของเภสัชวิทยาทางคลินิก (Overview of Clinical Pharmacology) 4.ภาพรวมด้านประสิทธิภาพในการรักษา (Overview of Efficacy) 5.ภาพรวมด้านความปลอดภัย (Overview of Safety) 6.บทสรุปด้านประโยชน์ที่ได้รับกับความเสี่ยง (Benefits and Risks Conclusions)

Module 2 eCTD Structure (Based on EU CTD region)	ACTD Structure		
	Part / Section		Content
2.6 Nonclinical Written and Tabulated Summaries	Nonclinical	C	C บทสรุปของข้อมูลที่ไม่ใช่ข้อมูลทางคลินิกในลักษณะคำบรรยายและลักษณะตาราง (Nonclinic Summary : Written and Tabulated)
2.6.1 Introduction	Nonclinical	C	1.0 บทสรุปข้อมูลที่ไม่ใช่ข้อมูลทางคลินิก ในลักษณะคำบรรยาย (Nonclinical Written Summary)
2.6.2 Pharmacology Written Summary	Nonclinical	C	1.1 เภสัชวิทยา (Pharmacology) 1.1.1 เภสัชพลศาสตร์ปฐมภูมิ (Primary Pharmacodynamics) 1.1.2 เภสัชพลศาสตร์ทุติยภูมิ (Secondary Pharmacodynamics) 1.1.3 เภสัชวิทยาความปลอดภัย (Safety pharmacology) 1.1.4 อันตรกิริยาของยาในด้านเภสัชพลศาสตร์ (Pharmacodynamic Drug Reactions)
2.6.3 Pharmacology Tabulated Summary	Nonclinical	C	2.บทสรุปของข้อมูลที่ไม่ใช่ข้อมูลทางคลินิก ในลักษณะตาราง (Nonclinical Tabulated Summaries)
2.6.4 Pharmacokinetics Written Summary	Nonclinical	C	1.2 เภสัชจลนศาสตร์ (Pharmacokinetics) 1.2.1 การดูดซึม (Absorption) 1.2.2 การกระจายยา (Distribution) 1.2.3 เมแทบอลิซึม (Metabolism) การเปรียบเทียบภายใน species (inter – species comparison) 1.2.4 การขับถ่ายยา (Excretion) 1.2.5 อันตรกิริยาของยาในด้านเภสัชจลนศาสตร์ (ส่วนที่ไม่ใช่ข้อมูลทางคลินิก) Pharmacokinetic Drug Interaction (Non-clinical) 1.2.6 การศึกษาอื่นๆทางเภสัชจลนศาสตร์ (Other Pharmacokinetics Studies)
2.6.5 Pharmacokinetics Tabulated Summary	Nonclinical	C	2.บทสรุปของข้อมูลที่ไม่ใช่ข้อมูลทางคลินิก ในลักษณะตาราง (Nonclinical Tabulated Summaries)

Module 2 eCTD Structure (Based on EU CTD region)	ACTD Structure		
	Part / Section		Content
2.6.6 Toxicology Written Summary	Nonclinical	C	1. 3 พิษวิทยา (Toxicology) 1.3.1 ความเป็นพิษที่เกิดจากการให้ยาครั้งเดียว (Single Dose Toxicity) 1.3.2 ความเป็นพิษที่เกิดจากการให้ยาซ้ำๆ (Repeat Dose Toxicity) 1.3.3 ความเป็นพิษทางพันธุกรรม (Genotoxicity) 1.3.4 การก่อมะเร็ง(Carcinogenicity) 1.3.5 ความเป็นพิษต่อการสืบพันธุ์และพัฒนาการของตัวอ่อน (Reproductive and developmental Toxicity) 1.3.5.1 ความสามารถในการสืบพันธุ์และ พัฒนาการของตัวอ่อนในระยะแรก (Fertility and Early Embryotic Development) 1.3.5.2 พัฒนาการของเอมบริโอ - ตัวอ่อนในครรภ์ (Embryo-fetal Development) 1.3.5.3 พัฒนาการของตัวอ่อนทั้งก่อนคลอดหรือหลังคลอดรวมทั้งหน้าที่ของตัวแม่ (Pre-Natal and Post-Natal Development including Maternal Function) 1.3.6 ความทนเฉพาะที่ (Local Tolerance) 1.3.7 การศึกษาพิษวิทยาอื่นๆ (Other Toxicity Studies, if available)
2.6.7 Toxicology Tabulated Summary	Nonclinical	C	2.บทสรุปของข้อมูลที่ไม่ใช่ข้อมูลทางคลินิก ในลักษณะตาราง (Nonclinical Tabulated Summaries)
2.7 Clinical Summary	Clinical	C	ตอนที่ C (Section C) : บทสรุปทางคลินิก)Clinical Summary)
2.7.1 Summary of Biophamaceutic Studies and Associated Analytical Methods	Clinical	C	1.บทสรุปของการศึกษาทางชีวเภสัชกรรมและวิธีวิเคราะห์ที่เกี่ยวข้อง (Summary of Biopharmaceutic Studies and Associated Analytical Method) 1.1 ความเป็นมาและภาพรวม (Background and Overview) 1.2 บทสรุปของผลการศึกษาแต่ละการศึกษา (Summary of Results of Individual Studies) 1.3 การเปรียบเทียบและวิเคราะห์ผลของการศึกษาต่างๆ (Comparison and Analyses of Results Across Studies) ภาพผนวก 1 (Appendix 1)
2.7.2 Summary of Clinical Pharmacology Studies	Clinical	C	2.บทสรุปของการศึกษาเภสัชวิทยาทางคลินิก (Summary of Clinical Pharmacology Studies) 2.1 ความเป็นมาและภาพรวม (Background and Overview) 2.2 บทสรุปของผลการศึกษาแต่ละการศึกษา (Summary of Results of Individual Studies) 2.3 การเปรียบเทียบและวิเคราะห์ผลของการศึกษาต่างๆ (Comparison and Analyses of Results Across Studies) 2.4 การศึกษาพิเศษต่างๆ (Special Studies) ภาคผนวก 2 (Appendix 2)

Module 2 eCTD Structure (Based on EU CTD region)	ACTD Structure		
	Part / Section		Content
2.7.3 Summary of Clinical Efficacy - INDICATION	Clinical	C	3.บทสรุปด้านประสิทธิภาพทางคลินิก (Summary of Clinical Efficacy) 3.1 ความเป็นมาและภาพรวมของประสิทธิภาพทางคลินิก (Background and Overview of Clinical Efficacy) 3.2 บทสรุปของผลการศึกษาแต่ละการศึกษา (Summary of Results of Individual Studies) 3.3 การเปรียบเทียบและวิเคราะห์ผลของการศึกษาต่างๆ (Comparison and Analyses of Results Across Studies) 3.4 การวิเคราะห์ข้อมูลทางคลินิกที่สัมพันธ์กับขนาดยาที่แนะนำ (Analysis of Clinical Information Relevant to Dosing Recommendations) 3.5 ความต่อเนื่องของประสิทธิผลและ/หรือ ความทนต่อยา (Persistence of Efficacy and/or Tolerance Effects) ภาคผนวก 3 (Appendix 3)
2.7.4 Summary of Clinical Safety	Clinical	C	4.บทสรุปความปลอดภัยทางคลินิก (Summary of Clinical Safety) 4.1 การได้รับยา (Exposure to the Drug) 4.2 เหตุการณ์ไม่พึงประสงค์ต่างๆ (Adverse Events) 4.3 การประเมินผลทางคลินิกจากห้องปฏิบัติการ (Clinical Laboratory Evaluations) 4.4 สัญญาณชีพ, สิ่งที่พบจากการตรวจร่างกาย, และข้อสังเกตอื่นๆที่เกี่ยวกับความปลอดภัย (Vital Signs, Physical Findings, and Other Observations Related to Safety) 4.5 ความปลอดภัยในกลุ่มพิเศษ และในสถานการณ์พิเศษ (Safety in Special Groups and Situations) 4.6 ข้อมูลหลังจากการจำหน่ายยา (Post-marketing Data) ภาคผนวก 4 (Appendix 4)
2.7.5 Literature- References	Clinical	C	**Optional**
2.7.6 Synopses of Individual Studies	Clinical	C	5.บทความย่อของแต่ละการศึกษา (Synopses of Individual Studies)

3. Module 3 eCTD

Module 3 eCTD Structure (Based on EU CTD region)	ACTD Structure		
	Part / Section		Content
3.1 Table of Contents of Module 3			
3.2 Body of Data			
3.2.S Drug Substance			
3.2.S.1 General Information	Quality	C	S1 ข้อมูลทั่วไป (General Information)
3.2.S.1.1 Nomenclature	Quality	C	S.1.1 ชื่อ (Nomenclature)
3.2.S.1.2 Structure	Quality	C	S.1.2 โครงสร้าง (Structure)
3.2.S.1.3 General Properties	Quality	C	S.1.3 คุณสมบัติทั่วไป (General Properties)
3.2.S.2 Manufacture	Quality	C	S2 การผลิต (Manufacture)
3.2.S.2.1 Manufacturer(s)	Quality	C	S.2.1 ผู้ผลิต (อาจมีมากกว่าหนึ่ง) (Manufacturer(s))
3.2.S.2.2 Description of Manufacturing Process and Process Controls	Quality	C	S.2.2 คำอธิบายกระบวนการผลิตและวิธีควบคุมกระบวนการผลิต (Description of Manufacturing Process and Process Controls)
3.2.S.2.3 Control of Materials	Quality	C	S.2.3 การควบคุมวัตถุดิบ (Control of Materials)
3.2.S.2.4 Controls of Critical Steps and Intermediates	Quality	C	S.2.4 การควบคุมขั้นตอนการผลิตที่สำคัญ และ สารมัธยันตร์ (Controls of Critical Steps and Intermediates)
3.2.S.2.5 Process Validation and/or Evaluation	Quality	C	S.2.5 การตรวจสอบความถูกต้องของกระบวนการผลิตและ/หรือ การประเมินผล (Process Validation and/or Evaluation)
3.2.S.2.6 Manufacturing Process Development	Quality	C	S.2.6 การพัฒนากระบวนการผลิต (Manufacturing Process Development)
3.2.S.3 Characterizations	Quality	C	S3 การตรวจลักษณะเฉพาะ (Characterizations)

Module 3 eCTD Structure (Based on EU CTD region)	ACTD Structure		
	Part / Section		Content
3.2.S.3.1 Elucidation of Structure and Other Characteristics	Quality	C	S.3.1 การแสดงโครงสร้างและลักษณะเฉพาะอื่นๆ (Elucidation of Structure and Other Characteristics)
3.2.S.3.2 Impurities	Quality	C	S.3.2 สารเจือปน (Impurities)
3.2.S.4 Control of Drug Substance	Quality	C	S4 การควบคุมวัตถุดิบตัวยาสำคัญ (Control of Drug Substance)
3.2.S.4.1 Specification	Quality	C	S.4.1 ข้อกำหนดมาตรฐาน)Specification) และหนังสือรับรองการวิเคราะห์ (Certificate of Analysis)
3.2.S.4.2 Analytical Procedures	Quality	C	S.4.2 วิธีการวิเคราะห์ (Analytical Procedure)
3.2.S.4.3 Validation of Analytical Procedures	Quality	C	S.4.3 การตรวจสอบความถูกต้องของวิธีการวิเคราะห์ (Validation of Analytical Procedures)
3.2.S.4.4 Batch Analyses	Quality	C	S.4.4 การวิเคราะห์การผลิตแต่ละรุ่น (Batch Analysis)
3.2.S.4.5 Justification of Specification	Quality	C	S.4.5 การชี้แจงเหตุผลของข้อกำหนดมาตรฐาน (Justification of Specification)
3.2.S.5 Reference Standards of Specification	Quality	C	S5 สารมาตรฐานหรือวัสดุมาตรฐาน (Reference Standards or Materials)
3.2.S.6 Container Closure System	Quality	C	S6 ระบบปิดของภาชนะบรรจุ (Container Closure System)
3.2.S.7 Stability	Quality	C	S7 ความคงสภาพ (Stability)
3.2.S.7.1 Stability Summary and Conclusions	Quality	C	S7 ความคงสภาพ (Stability)
3.2.S.7.2 Post-approval Stability Protocol and Stability Commitment	Quality	C	S7 ความคงสภาพ (Stability)
3.2.S.7.3 Stability Data	Quality	C	S7 ความคงสภาพ (Stability)

Module 3 eCTD Structure (Based on EU CTD region)	ACTD Structure		
	Part / Section		Content
3.2.P Drug Product			
3.2.P.1 Description and Composition of the Drug Product	Quality	C	P1 ลักษณะยาและส่วนประกอบ (Description and Composition)
3.2.P.2 Pharmaceutical Development	Quality	C	P2 การพัฒนาทางเภสัชกรรม (Pharmaceutical Development)
3.2.P.2.1 Components of the Drug Product	Quality	C	P.2.2 ส่วนประกอบของผลิตภัณฑ์ยา (Components of the Drug Product)
3.2.P.2.2 Drug Product	Quality	C	P.2.3 ผลิตภัณฑ์สำเร็จรูป (Finished Product)
3.2.P.2.3 Manufacturing Process Development	Quality	C	P.2.4 การพัฒนากระบวนการผลิต (Manufacturing Process Development)
3.2.P.2.4 Container Closure System	Quality	C	P.2.5 ระบบปิดของภาชนะบรรจุ (Container Closure System)
3.2.P.2.5 Microbiological Attributes	Quality	C	P.2.6 คุณสมบัติทางจุลชีววิทยา (Microbiological Attributes)
3.2.P.2.6 Compatibility	Quality	C	P.2.7ความเข้ากันได้ของผลิตภัณฑ์ (Compatibility)
3.2.P.3 Manufacture	Quality	C	P3 การผลิต (Manufacture)
3.2.P.3.1 Manufacturer(s)	Admin	C	1.2 แบบคำขอขึ้นทะเบียนตำรับยาแบบ ASEAN HARMONIZATION (แบบ ย.1) - Page 1-2
3.2.P.3.2 Batch Formula	Quality	C	P.3.1 สูตรยาต่อรุ่นการผลิต (Batch Formula)
3.2.P.3.3 Description of Manufacturing Process and Process Controls	Quality	C	P.3.2 กระบวนการผลิตและวิธีการควบคุมกระบวนการผลิต (Manufacturing Process and Process Controls)
3.2.P.3.4 Controls of Critical Steps and Intermediates	Quality	C	P.3.3 การควบคุมขั้นตอนการผลิตที่สำคัญ และ สารมัธยันตร์ (Controls of Critical Steps and Intermediates)
3.2.P.3.5 Process Validation and/or Evaluation	Quality	C	P.3.4 การตรวจสอบความถูกต้องของกระบวนการ และหรือ การประเมินผล/ (Process Validation and/or Evaluation)

Module 3 eCTD Structure (Based on EU CTD region)	ACTD Structure		
	Part / Section		Content
3.2.P.4 Control of Excipients - Compendia			
3.2.P.4.1 Specifications	**Quality**	**C**	**Optional**
3.2.P.4 Control of Excipients - Excipient			
3.2.P.4.1 Specifications	Quality	C	P.4.1 ข้อกำหนดมาตรฐาน (Specifications) และหนังสือรับรองการวิเคราะห์ (Certificate of Analysis)
3.2.P.4.2 Analytical Procedures	Quality	C	P.4.2 วิธีการวิเคราะห์ (Analytical Procedure)
3.2.P.4.3 Validation of Analytical Procedures	**Quality**	**C**	**Optional**
3.2.P.4.4 Justification of Specifications	**Quality**	**C**	**Optional**
3.2.P.4 Control of Excipients - Animal-Human-Novel			
3.2.P.4.5 Excipients of Human or Animal Origin	Quality	C	P.4.3 สารปรุงแต่งที่มีแหล่งกำเนิดจากมนุษย์หรือสัตว์ (Excipients of Human or Animal Origin)
3.2.P.4.6 Novel Excipients	Quality	C	P.4.4 สารปรุงแต่งที่เป็นสารชนิดใหม่ (Novel Excipients)
3.2.P.5 Control of Drug Product	Quality	C	P5 การควบคุมผลิตภัณฑ์สำเร็จรูป (Control of Finished Product)
3.2.P.5.1 Specification(s)	Quality	C	P.5.1 ข้อกำหนดมาตรฐาน (Specification) และหนังสือรับรองการวิเคราะห์ (Certificate of Analysis)
3.2.P.5.2 Analytical Procedures	Quality	C	P.5.2 วิธีการวิเคราะห์ (Analytical Procedure)
3.2.P.5.3 Validation of Analytical Procedures	Quality	C	P.5.3 การตรวจสอบความถูกต้องของวิธีการวิเคราะห์ (Validation of Analytical Procedures)

Module 3 eCTD Structure (Based on EU CTD region)	ACTD Structure		
	Part / Section		Content
3.2.P.5.4 Batch Analyses	Quality	C	P.5.4 การวิเคราะห์รุ่นการผลิต (Batch Analyses)
3.2.P.5.5 Characterizations of Impurities	Quality	C	P.5.5 การตรวจลักษณะเฉพาะของสารเจือปน (Characterizations of Impurities)
3.2.P.5.6 Justification of Specifications	Quality	C	P.5.6 การชี้แจงเหตุผลของข้อกำหนดมาตรฐาน (Justification of Specifications)
3.2.P.6 Reference Standards or Materials	Quality	C	P6 สารมาตรฐานหรือวัสดุมาตรฐาน (Reference Standards or Materials)
3.2.P.7 Container Closure System	Quality	C	P7 ระบบปิดของภาชนะบรรจุ (Container Closure System)
3.2.P.8 Stability	Quality	C	P8 ความคงสภาพ (Stability)
3.2.P.8.1 Stability Summary and Conclusion	Quality	C	P8 ความคงสภาพ (Stability)
3.2.P.8.2 Post-approval Stability Protocol and Stability Commitment	Admin	C	- 6.5.1 คำรับรองในการส่งเอกสารเพิ่มเติมในการศึกษาความคงสภาพของยา (Stability Commitment)
3.2.P.8.3 Stability Data	Quality	C	P8 ความคงสภาพ (Stability)
3.2.A Appendices			
3.2.A.1 Facilities and Equipment - MANUFACTURER			**Optional**
3.2.A.2 Adventitious Agents Safety Evaluation - MANUFACTURER			**Optional**
3.2.A.3 Excipients			**Optional**
3.2.A.3.1 EXCIPIENT			**Optional**

Module 3 eCTD Structure (Based on EU CTD region)	ACTD Structure		
	Part / Section		Content
3.2.R Regional Information			**Optional**
3.3 Literature References	Quality	D	เอกสารอ้างอิงที่สำคัญ (ถ้ามี) (Key Literature Reference, if applicable)

4. Module 4 eCTD

Module 4 eCTD Structure (Based on EU CTD region)	ACTD Structure		
	Part / Section		Content
4 Nonclinical Study Reports			
4.1 Table of Contents of Module 4			
4.2 Study Reports	Nonclinical		รายงานการศึกษาที่ไม่ใช่การศึกษาทางคลินิก (ตามที่ต้องการ) (Nonclinical Study Report (As requested))
4.2.1 Pharmacology	Nonclinical	D	2. เภสัชวิทยา (Pharmacology)
4.2.1.1 Primary Pharmacodynamics	Nonclinical	D	2.1 เภสัชพลศาสตร์ปฐมภูมิ (Primary Pharmacodynamics)
4.2.1.2 Secondary Pharmacodynamics	Nonclinical	D	2.2 เภสัชพลศาสตร์ทุติยภูมิ (Secondary Pharmacodynamics)
4.2.1.3 Safety Pharmacology	Nonclinical	D	2.3 เภสัชวิทยาความปลอดภัย (Safety Pharmacology)
4.2.1.4 Pharmacodynamic Drug Interactions	Nonclinical	D	2.4 อันตรกิริยาของยาในด้านเภสัชพลศาสตร์ (Pharmacodynamics Drug Interactions)
4.2.2 Pharmacokinetics	Nonclinical	D	3. เภสัชจลนศาสตร์ (Pharmacokinetics)
4.2.2.1 Analytical Methods and Validation Reports	Nonclinical	D	3.1 วิธีวิเคราะห์และรายงานการตรวจสอบความถูกต้อง (Analytical Methods and Validation Reports)
4.2.2.2Absorption	Nonclinical	D	3.2 การดูดซึม (Absorption)
4.2.2.3 Distribution	Nonclinical	D	3.3 การกระจายยา (Distribution)
4.2.2.4 Metabolism	Nonclinical	D	3.4 เมแทบอลิซึม (Metabolism)
4.2.2.5 Excretion	Nonclinical	D	3.5 การขับถ่ายยา (Excretion)
4.2.2.6 Pharmacokinetic Drug Interactions (nonclinical)	Nonclinical	D	3.6 อันตรกิริยาของยาในด้านเภสัชจลนศาสตร์ (ส่วนที่ไม่ใช่ข้อมูลทางคลินิก (Pharmacokinetics Drug Interaction (non-clinical)
4.2.2.7 Other Pharmacokinetic Studies	Nonclinical	D	3.7 การศึกษาอื่นๆทางเภสัชจลนศาสตร์ (Other Pharmacokinetics studies)
4.2.3 Toxicology	Nonclinical	D	4. พิษวิทยา (Toxicology)
4.2.3.1 Single-Dose Toxicity	Nonclinical	D	4.1 ความเป็นพิษที่เกิดจากการให้ยาครั้งเดียว (Single dose toxicity)
4.2.3.2 Repeat-Dose Toxicity	Nonclinical	D	4.2 ความเป็นพิษที่เกิดจากการให้ยาซ้ำๆ (Repeat dose toxicity)
4.2.3.3 Genotoxicity	Nonclinical	D	4.3 ความเป็นพิษทางพันธุกรรม (Genotoxicity)
4.2.3.3.1 In vitro	Nonclinical	D	4.3.1 การทดลองในหลอดทดลอง (in vitro)
4.2.3.3.2 In vivo	Nonclinical	D	4.3.2 การทดลองในสิ่งมีชีวิต (in vivo)

Module 4 eCTD Structure (Based on EU CTD region)	ACTD Structure		
	Part / Section		Content
4.2.3.4 Carcinogenicity	Nonclinical	D	4.4 การก่อมะเร็ง (Carcinogenicity)
4.2.3.4.1 Long-term studies	Nonclinical	D	4.4.1 การศึกษาในมะเร็ง (Carcinogenicity-term studies)
4.2.3.4.2 Short- or medium-term studies	Nonclinical	D	4.4.2 การศึกษาในระยะสั้นหรือในระยะปานกลาง (Short or medium term studies)
4.2.3.4.3 Other studies	Nonclinical	D	4.4.3 การศึกษาอื่นๆ (Other studies)
4.2.3.5 Reproductive and Developmental Toxicity	Nonclinical	D	4.5 ความเป็นพิษต่อการสืบพันธุ์และพัฒนาการของตัวอ่อน (Reproductive and developmental Toxicity)
4.2.3.5.1 Fertility and early embryonic development	Nonclinical	D	4.5.1 ความสามารถในการสืบพันธุ์และ พัฒนาการของตัวอ่อนในระยะแรก (Fertility and Early Embryotic Development)
4.2.3.5.2 Embryo-fetal development	Nonclinical	D	4.5.2 พัฒนาการของเอมบริโอ - ตัวอ่อนในครรภ์ (Embryo-fetal Development)
4.2.3.5.3 Prenatal and postnatal development, including maternal function	Nonclinical	D	4.5.3 พัฒนาการของตัวอ่อนทั้งก่อนคลอดหรือหลังคลอดรวมทั้งหน้าที่ของตัวแม่ (Pre-Natal and Post-Natal Development including Maternal Function)
4.2.3.5.4 Studies in which the offspring (juvenile animals) are dosed and/or further evaluated	Nonclinical	D	4.5.4 การศึกษาในลูกสัตว์ที่ได้รับยา และ/หรือ ได้รับการประเมินเพิ่มเติม (Studies in which the offspring are dosed and/or further evaluated)
4.2.3.6 Local Tolerance	Nonclinical	D	4.6 ความทนเฉพาะที่ (Local tolerance)
4.2.3.7 Other Toxicity Studies	Nonclinical	D	4.7 การศึกษาอื่นๆทางพิษวิทยา (ถ้ามี) (Other toxicity studies, if available)
4.2.3.7.1 Antigenicity	Nonclinical	D	4.7.1 การก่อภูมิต้านทาน (Antigenicity)
4.2.3.7.2 Immunotoxicity	Nonclinical	D	4.7.2. ต่อระบบภูมิคุ้มกัน (Immuno toxicity)
4.2.3.7.3 Mechanistic studies	Nonclinical		Optional
4.2.3.7.4 Dependence	Nonclinical	D	4.7.3 การติดยา (Dependence)
4.2.3.7.5 Metabolites	Nonclinical	D	4.7.4 เมแทบอไลท์ (Metabolites)
4.2.3.7.6 Impurities	Nonclinical	D	4.7.5 สารเจือปน (Impurities)
4.2.3.7.7 Other	Nonclinical	D	4.7.6 อื่นๆ (Other)
4.3 Literature References	Nonclinical	E	รายการ เอกสารอ้างอิงที่สำคัญ (List of Key Literature Reference)

5. Module 5 eCTD

Module 5 eCTD Structure (Based on EU CTD region)	ACTD Structure		
	Part / Section		Content
5.1 Table of Contents of Module 5			
5.2 Tabular Listing of all Clinical Studies			
5.3 Clinical Study Reports	Clinical	E	รายงานการศึกษาทางคลินิก ถ้ามี (Clinical Study Reports (if applicable)
5.3.1 Reports of Biopharmaceutic Studies	Clinical	E	1.รายงานการศึกษาของชีวเภสัชกรรม (Reports of Biopharmaceutic Studies)
5.3.1.1 Bioavailability (BA) Study Reports	Clinical	E	1.1 รายงานการศึกษา BA (BA Study Reports)
5.3.1.2 Comparative BA and Bioequivalence (BE) Study Reports	Clinical	E	1.2 รายงานการศึกษาเปรียบเทียบ BA หรือ BE (Comparative BA or BE Study Reports)
5.3.1.3 In vitro - In vivo Correlation Study Reports	Clinical	E	1.3 รายงานการศึกษาความสัมพันธ์ของการทดลองในหลอดทดลองและในสิ่งมีชีวิต (In vitro-In vivo Correlation Study Reports)
5.3.1.4 Reports of Bioanalytical and Analitical Methods for Human Studies	Clinical	E	1.4 รายงานการวิเคราะห์โดยชีววิธีและวิธีวิเคราะห์ สำหรับการศึกษาในมนุษย์ (Reports of Bioanalytical and Analytical Methods for Human Studies)
5.3.2 Reports of studies pertinent to Pharmacokinetics using Human Biomaterials	Clinical	E	2.รายงานของการศึกษาที่เกี่ยวข้องกับเภสัชจลนศาสตร์ที่ใช้ชีววัสดุจากมนุษย์ (Reports of Studies Pertinent to Pharmacokinetics using Human Biomaterials)
5.3.2.1 Plasma Protein Binding Study Reports	Clinical	E	2.1 รายงานการศึกษาการจับกับพลาสมาโปรตีน (Plasma Protein Binding Study Reports)
5.3.2.2 Reports of Hepatic Metabolism and Drug Interaction Studies	Clinical	E	2.2 รายงานการศึกษาเกี่ยวกับเมแทบอลิคที่ตับและอันตรกิริยาของยา (Reports of Hepatic Metabolism and Drug Interaction Studies)
5.3.2.3 Reports of Studies Using Other Human Biomaterials	Clinical	E	2.3 รายงานการศึกษาโดยใช้ชีววัสดุอื่นๆของมนุษย์ (Reports of Studies Using Other Human Biomaterials)
5.3.3 Reports of Human Pharmacokinetic (PK) Studies	Clinical	E	3.รายงานการศึกษาเภสัชจลนศาสตร์ในมนุษย์ (Reports of Human Pharmacokinetic (PK) Studies
5.3.3.1 Healthy Subject PK and Initial Tolerability Study Reports	Clinical	E	3.1 รายงานการศึกษา PK ในผู้รับการทดลองสุขภาพดี และการ ทนต่อ ยาระยะแรก (Heatthy Subiect PK and Initial Tolerability Study Reports)
5.3.3.2 Patient PK and Initial Tolerability Study Reports	Clinical	E	3.2 รายงานการศึกษา PK ในผู้ป่วย และ การทนต่อยาระยะแรกเริ่ม (Patient PK and Initial Tolerability Study Reports)

Module 5 eCTD Structure (Based on EU CTD region)	ACTD Structure		
	Part / Section		Content
5.3.3.3 Intrinsic Factor PK Study Reports	Clinical	E	Optional
5.3.3.4 Extrinsic Factor PK Study Reports	Clinical	E	Optional
5.3.3.5 Population PK Study Reports	Clinical	E	3.3 รายงานการศึกษา PK ในกลุ่มประชากรต่างๆ (Population PK Study Reports)
5.3.4 Reports of Human Pharmacodynamic (PD) Studies	Clinical	E	4.รายงานการศึกษาเภสัชพลศาสตร์ในมนุษย์ (Reports of Human Pharmacodynamic (PD) Studies)
5.3.4.1 Healthy Subject PD and PK/PD Study Reports	Clinical	E	4.1 รายงานการศึกษา PD และ PK/PD ในผู้รับการทดลองสุขภาพดี (Healthy Subject PD and PK/PD Study Reports)
5.3.4.2 Patient PD and PK/PD Study Reports	Clinical	E	4.2 รายงานการศึกษา PD และ PK/PD ในผู้ป่วย (Patient PD and PK/PD Study Reports)
5.3.5 Reports of Efficacy and Safety Studies	Clinical	E	5.รายงานการศึกษาด้านประสิทธิภาพและความปลอดภัย (Reports of Efficacy and Safety Studies)
5.3.5.1 Study Reports of Controlled Clinical Studies Pertinent to the Claimed Indication	Clinical	E	5.1 รายงานของการศึกษาทางคลินิกที่มีกลุ่มควบคุมซึ่งเกี่ยวข้องกับข้อบ่งใช้ที่แจ้งไว้ (Study Reports of Controlled Clinical Studies Pertinent to the Claimed Indication)
5.3.5.2 Study Reports of Uncontrolled Clinical Studies	Clinical	E	5.2 รายงานของการศึกษาทางคลินิกต่างๆที่ไม่มีกลุ่มควบคุม (Study Reports of Uncontrolled Clinical Studies
5.3.5.3 Reports of Analyses of Data from More than One Study	Clinical	E	5.3 รายงานการวิเคราะห์ข้อมูลการศึกษาที่มากกว่าหนึ่งการศึกษารวมถึงการวิเคราะห์ผลโดยรวมที่เป็นระเบียบแบบแผนการวิเคราะห์อภิมาน และการวิเคราะห์โดยเชื่อมโยงข้อมูล (Reports of Analyses of Data from More Than One Study ,Including Any Formal Integrated Analyses, Meta-analyses, and Bridging Analyses)
5.3.5.4 Other Study Reports	Clinical	E	5.4 รายงานการศึกษาทางคลินิกอื่นๆ (Other Clinical Study Reports)
5.3.6 Reports of Post-marketing Experience	Clinical	E	6.รายงานของประสบการณ์หลังจากการจำหน่ายยา (Reports of Post-Marketing Experience)
5.3.7 Case Report Forms and Individual Patient Listings	Clinical	E	7.แบบฟอร์มรายงานของผู้รับการทดลองกรณีต่างๆ และผู้ป่วยที่มีการกล่าวถึงแต่ละราย (Case Report Forms and Individual Patient Listing)
5.4 Literature References	Clinical	F	F. รายการของเอกสารอ้างอิงที่สำคัญ (List of Key Literature References)

ภาคผนวก ๓

รายละเอียดและวิธีการในการตรวจสอบ
ความถูกต้องของไฟล์ข้อมูลที่ยื่นคำขอขึ้น
ทะเบียนตำรับยาโดยวิธีทางอิเล็กทรอนิกส์

Version	Date	Component	Change Description
0.90	1-Jul-14	Multiple	Initial release for eCTD pilot launch
0.91	7-Aug-14	Headers and Elements	Numbering for 1.3.1.3.3.1 Updated
		File-Folder Names	Folder for 1.3.5.1 Added
		Defined Lists	Sequence Type updated to lower-case
0.92	7-Oct-14	eCTD Validation	Update specification version in section 3.3,3.4,3.5,6.3

TH Envelope Attributes

XML Element	Description	Constraint	Occurrence	Defined List*
esub-id	eSubmission Identifier	Mandatory	Single	
seq-type	Sequence Type	Mandatory	Single	X
reg-activity-lead	Regulatory Activity Lead	Mandatory	Single	X
licensee	Licensee	Mandatory	Single	
licensee-type	Licensee Type	Mandatory	Single	X
licensee-name	Licensee Name	Mandatory	Single	
inn	INN or Generic Name	Mandatory	Multiple	
product-name	Product Name	Mandatory	Multiple	
sequence	Sequence Number	Mandatory	Single	
related-sequence	Related Sequence Number	Mandatory	Single	
seq-description	Sequence Description	Mandatory	Single	
email	Contact email	Mandatory	Single	

Sequence Type	
List Value	**Description**
a-ph-newce	A: Pharmaceutics - New Chemical Entity
a-ph-newse	A: Pharmaceutics - New Salt or Ester of Existing Active Ingredient
a-ph-newdosage	A: Pharmaceutics - New Dosage Form
a-ph-newroute	A: Pharmaceutics - New Route of Administration
a-ph-newcomb	A: Pharmaceutics - New Combination
a-ph-abridge	A: Pharmaceutics – Abridge application
a-ph-newothers	A: Pharmaceutics - New Medicinal Product (Others)
a-ph-newgen	A: Pharmaceutics - New Generic
a-ph-generic	A: Pharmaceutics - Generic
a-ph-house	A: House Hold Remedies
b-bio-vaccine	B: Biologics - Vaccine
b-bio-blood	B: Biologics - Blood and Plasma Derived Product
b-bio-cell	B: Biologics - Cell- and Tissue- Based Therapy Product
b-bio-biotech	B: Biologics - Biotechnology Product
b-bio-biosimilar	B: Biologics - Biosimilar Product
b-bio-abridge	B: Biologics – Abridge application
b-bio-others	B: Biologics - Others
c-vet-newprod	C: Veterinary - New Medicinal Product
c-vet-newgeneric	C: Veterinary - New Generic Medicinal Product

c-vet-generic	C: Veterinary - Generic Medicinal Product
c-vet-premixed	C: Veterinary - Medicated Premixed
c-vet-bio	C: Veterinary - Biologics
d-traditional	D: Traditional Medicinal Product
f-var-major	F: Variation - Major Variation (MaV)
f-var-minor-pa	F: Variation - Minor Variation (MiV-PA)
f-var-minor-n	F: Variation - Minor Variation (MiV-N)
f-var-others	F: Variation - Others
g-clin-authapp	G: Clinical Trial Authorization Application
g-clin-authamend	G: Clinical Trial Authorization Amendments
h-review-smph	H: Review of SMP Application
h-riskmgtplan	H: Risk Management Plan
h-pv	H: Pharmacovigilance
h-psur	H: Periodic Safety Update Report
i-dmf	I: Drug Master Files
i-pmf	I: Plasma Master Files
i-vamf	I: Vaccine Antigen Master File
i-tmf	I: Tissue Master File
j-suppl	J: Supplementary Information
k-orphan	K: Orphan Drug Application
k-emergency	K: Emergency Used Application

I-consult	L: Consultative Application
z-undefined-regact	Z: Undefined Regulatory Activity

Regulatory Activity Lead	
List Value	**Description**
Biologicals	Biological Product Review
Pharmaceuticals	Pharmaceutical Product Review
Pharmacovigilance	Pharmacovigilance Review
Cosmetic	Cosmetic Review
Medical-Devices	Medical Device Review

Licensee Type	
Importer	Importer
Manufacturer	Manufacturer

Section ID	Business Terminology	XML-Element
1.0	**Cover**	m1-0-cover
1.0.1	Tracking Table	m1-0-1-tracking
1.0.2	Cover Letter	m1-0-2-cover-letter
1.2	**Application Forms**	m1-2-forms
1.2.1	Application Form	m1-2-1-form
1.2.1.1	<Sequence Number> <Description>	leaf-node
1.2.2	Annexes	m1-2-2-annexes
1.2.2.1	<Sequence Number> <Description of Annex>	leaf-node
1.3	**Product Information**	m1-3-pi
1.3.1	SPC, Labelling and Package Leaflet	m1-3-1-spc-label-pl
1.3.1.1	Labelling	m1-3-1-1-label
1.3.1.1.1	<Description of Labelling>	leaf-node
1.3.1.2	SPC	m1-3-1-2-spc
1.3.1.3	Package Leaflet	m1-3-1-3-pl
1.3.1.3.1	Package Leaflet - Thai	m1-3-1-3-pl-th
1.3.1.3.2	Package Leaflet - English	m1-3-1-3-pl-en
1.3.1.3.3	Package Leaflet - Other Language	m1-3-1-3-pl-ot
1.3.1.3.3.1	<Language> <Description>	leaf-node
1.3.2	Mock-up	m1-3-2-mockup
1.3.3	Specimen	m1-3-3-specimen
1.3.4	Consultation with Target Patient Groups	m1-3-4-consultation
1.3.5	Product Information already approved in Other States	m1-3-5-approved
1.3.5.1	Foreign Regulatory Status	m1-3-5-1-status
1.3.5.2	Foreign Product Information	m1-3-5-2-pi
1.3.5.2.1	<Country> <Product Information Type>	leaf-node
1.3.5.3	Data Similarities and Differences	m1-3-5-3-smilarities
1.3.6	Braille	m1-3-6-braille
1.4	**Information about the Experts**	m1-4-expert
1.4.1	Quality	m1-4-1-quality
1.4.2	Non-Clinical	m1-4-2-non-clinical
1.4.3	Clinical	m1-4-3-clinical
1.5	**Specific Requirements for Different Types of**	m1-5-specific
1.5.1	Information for Bibliographical Applications	m1-5-1-bibliographic
1.5.2	Information for Generic, 'Hybrid' or Bio-similar Applications	m1-5-2-generic-hybrid-bio-similar
1.5.2.1	Information for Generic Application	m1-5-2-1-generic
1.5.2.2	Information for 'Hybrid' Applications	m1-5-2-2-hybrid
1.5.2.3	Information for Bio-similar Applications	m1-5-2-3-bio-similar
1.5.3	(Extended) Data/Market Exclusivity	m1-5-3-data-market-exclusivity
1.5.4	Exceptional Circumstances	m1-5-4-exceptional-circumstances
1.5.5	Conditional Marketing Authorisation	m1-5-5-conditional-ma
1.5.6	Additional Trade Name Declarations	m1-5-6-trade-name
1.5.7	Co-marketed Medicines Declarations	m1-5-7-co-marketed
1.6	**Environmental Risk Assessment**	m1-6-environrisk
1.6.1	Non-GMO	m1-6-1-non-gmo

Section ID	Business Terminology	XML-Element
1.6.2	GMO	m1-6-2-gmo
1.7	**Product Interchangeability Equivalence Evidence**	m1-7-productinter
1.7.1	BE Protocol	m1-7-1-beprotocol
1.7.2	BE study report	m1-7-2-bestudy
1.7.3	Comparative in vitro dissolution/release studies	m1-7-3-beinvitro
1.7.4	Comparative clinical studies	m1-7-4-beclinic
1.7.5	Comparative pharmacodynamics studies	m1-7-5-bepharmaco
1.7.6	Other	m1-7-6-beother
1.8	**Information relating to Pharmacovigilance**	m1-8-pharmacovigilance
1.8.1	Pharmacovigilance System	m1-8-1-pharmacovigilance-system
1.8.2	Risk-management System	m1-8-2-risk-management-system
1.8.3	SMP Protocol	m1-8-3-smp
1.9	**Information relating to Clinical Trials**	m1-9-clinical-trials
1.10	**Information relating to Paediatrics**	m1-10-paediatrics
1.R	**Responses to Questions**	m1-responses
1.R.1	<Sequence Number> <Sequence Description>	leaf-node
1.A	**Additional Data**	m1-additional-data
1.A.1	Assessment report from other regulatory agency	m1-a-1-assessment-report
1.A.2	Checklist Form /Self Assessment Report	m1-a-2-self-assessment
1.A.3	Information on Development Studies	m1-a-3-development-studies
1.A.4	COA from Institute of Biological Product	m1-a-4-coa-biologic
1.A.5	Comparison Table	m1-a-5-comparison-table
1.A.6	Information of Exportation	m1-a-6-exportation
1.A.7	Declaration from applicant	m1-a-7-declaration
1.A.8	Template of Database entering	m1-a-8-database-entering
1.A.99	Other	m1-a-99-other

Number	Validation Criterion	Type of check	Lifecycle needed? "YES" (Y) *	Comments
Type of	**Description of Type of check**			
P/F	**Pass/Fail** These are validation criteria that can either be passed or failed. eCTDs that fail to meet one or more of these criteria will be returned to the applicant for fixing and resubmission as the same sequence number. The pass/fail category has been introduced for the possibility of future automation of eCTD validation.			
BP	**Best Practices** Any deviation from the criterion should always be reported by the validating tool. These are validation criteria that it is considered good practice to ensure are correct in the submitted eCTD. The applicant should make every effort to address these areas before the eCTD is submitted to the agency. - eCTDs that fail to meet one or more of these criteria will still be accepted by the agency during technical validation and it is possible that agencies may not even check these criteria during technical validation. These criteria assess factors that affect the overall ease of use of the eCTD. All tool vendors should include these criteria in their validation tools so that applicants can produce eCTDs that are easier to use. Users of the validation tool should also be able to check the eCTD without checking for the Best Practice criteria.			
Info	**Information** Data is collected for Information purposes only. Findings will not influence the acceptance of the application.			
*	**"Y"- Criteria** Test marked with “Y” needs the relevant former sequences for the specific criterion to be present for the result to be fully reliable. If these sequences are not present when testing, any FAIL results for these criteria should be interpreted carefully. When reporting a 'Fail' for these 'Y' criteria, validation tools should also report the specific missing sequences that are related to the 'Fail'.			

Number	Validation Criterion	Type of check	Lifecycle needed? "YES" (Y) *	Comments
1 - ICH DTD				
1.1	The specified filename is used	P/F		File is named ich-ectd-3-2.dtd
1.2	The file is placed in the correct folder	P/F		In the folder /XXXX/util/dtd
1.3	A currently acceptable version of the DTD is used (checksum matches the published value)	P/F		Currently acceptable versions are described in the current ICH eCTD Specification. (The checksum for the DTD in eCTD v3.2 (ich-ectd-3-2.dtd) is 1d6f631cc6b6357f0f4fe378e5f79a27)
1.4	The version number of the DTD/specification used in the sequence being tested is higher than or equal to the version of the DTD used in the sequence numerically preceding the incoming sequence in the eCTD lifecycle.	P/F	Y	With reference to any transition guidance, going back to an earlier version is not allowed when a newer version has already been used for that eCTD. 'The sequence numerically preceding the incoming sequence in the eCTD lifecycle' refers to the highest numbered sequence that is numerically lower than the incoming sequence. The criterion should only be tested if there are sequences with lower sequence numbers present.
1.5	The version number of the DTD/specification used in the sequence being tested is lower than or equal to the version of the DTD used in the sequence numerically succeeding the incoming sequence in the eCTD lifecycle.	P/F	Y	This rule specifically tests in situations where sequences have been submitted out of order. 'The sequence numerically succeeding the incoming sequence in the eCTD lifecycle' refers to the lowest numbered sequence that is numerically higher than the incoming sequence. The criterion should only be tested if there are sequences with higher sequence numbers present.

Number	Validation Criterion	Type of check	Lifecycle needed? "YES" (Y) *	Comments
2 - ICH Style-Sheet				
2.1	The specified filename is used	P/F		File is named ectd-2-0.xsl
2.2	The file is placed in the correct folder	P/F		In the folder /XXXX/util/style
2.3	The checksum for the stylesheet used must match the published checksum for the stylesheet associated with the DTD used for the sequence	P/F		For example, the checksum corresponding to the stylesheet from eCTD specification v3.2 (ectd-2-0.xsl) is 3a07a202455e954a2eb203c5bb443f77
3 - TH M1 Schema				
3.1	The specified filename is used	P/F		File is named th-regional.xsd
3.2	The file is placed in the correct folder	P/F		In the folder /XXXX/util/dtd
3.3	A currently acceptable version of the Schema is used (checksum matches the published value)	P/F		Currently acceptable with reference to any transition guidance The checksum for the Schema for TH m1 v0.92 is c6c0c9dcb64cc267c2985e793ebaa456
3.4	The version number of the Schema/specification used in the sequence being tested is higher than or equal to the version of the Schema used in the sequence numerically preceding the incoming sequence in the eCTD lifecycle.	P/F	Y	With reference to any transition guidance, going back to an earlier version is not allowed when a newer version has already been used for that eCTD. 'The sequence numerically preceding the incoming sequence in the eCTD lifecycle' refers to the highest numbered sequence that is numerically lower than the incoming sequence. For example if 0109 used Schema 0.92, 0110 was Schema 1.0, and 0111 is not present, then 0112 must be built in either Schema 1.0 or higher. The criterion should only be tested if there are sequences with lower sequence numbers present.

Number	Validation Criterion	Type of check	Lifecycle needed? "YES" (Y) *	Comments
3.5	The version number of the Schema/specification used in the sequence being tested is lower than or equal to the version of the Schema used in the sequence numerically succeeding the incoming sequence in the eCTD lifecycle.	P/F	Y	This rule specifically tests in situations where sequences have been submitted out of order. 'The sequence numerically succeeding the incoming sequence in the eCTD lifecycle' refers to the lowest numbered sequence that is numerically higher than the incoming sequence. For example if 0010 used Schema 0.92, and 0012 was Schema 1.0, then 0011 must be built in either Schema 1.0 or 0.92. The criterion should only be tested if there are sequences with higher sequence numbers present. Note: This cannot be checked properly in an offline scenario (validation tools may not necessarily know what has alredy been submitted). It is recommended that sponsors check the highest available sequence against criterion number 3.4 instead.
4 - EU M1 Leaf MOD File				
	VALIDATION SECTION NOT APPLICABLE FOR THAILAND			
5 - EU M1 Envelope MOD File				
	VALIDATION SECTION NOT APPLICABLE FOR THAILAND			
6 - TH M1 Style-sheet				
6.1	The specified filename is used	P/F		File is named th-regional.xsl
6.2	The file is placed in the correct folder	P/F		In the folder /XXXX/util/style
6.3	The checksum for the stylesheet used must match the published checksum for the stylesheet associated with the DTD used for the sequence	P/F		For example, the checksum for the stylesheet from TH eCTD Module 1 v0.92 is cb3d43ac42bb6f653360cc3695bea1c9.

Number	Validation Criterion	Type of check	Lifecycle needed? "YES" (Y) *	Comments
7 - Index XML				
7.1	The file is placed in the correct folder	P/F		The root folder /XXXX
7.2	The file is named correctly	P/F		File is named index.xml
7.3	The file is well formed	P/F		Well formed with respect to the rules of the XML specification
7.4	The file is valid	P/F		Valid with respect to the ICH eCTD DTD file included in the util/dtd folder
7.5	The reference to the DTD in index.xml is directed to the DTD provided in the util folder.	P/F		This is the ICH DTD in /XXXX/util/dtd, and tested for validity by rules 1.1 - 1.5. A valid reference means a URI - see http://www.w3.org/TR/xml/ and http://www.ietf.org/rfc/rfc3986.txt (version 2005 page 22, section 3.3)
7.6	The reference to the stylesheet in index.xml is directed to the stylesheet provided in the util folder.	P/F		This is the ICH stylesheet in /XXXX/util/style and tested for validity by rules 2.1 - 2.3. A valid reference means a URI - see http://www.w3.org/TR/xml/ and http://www.ietf.org/rfc/rfc3986.txt (version 2005 page 22, section 3.3)
8 - Index MD5 txt				
8.1	The file is placed in the correct folder	P/F		The root folder /XXXX
8.2	The file is named correctly	P/F		The file is named index-md5.txt
8.3	The regenerated checksum for the index.xml matches the value in the file index-md5.txt.	P/F		

Number	Validation Criterion	Type of check	Lifecycle needed? "YES" (Y) *	Comments
9 - TH Regional XML				
9.1	The file is placed in the correct folder	P/F		The folder /XXXX/m1/th
9.2	The file is named correctly	P/F		File is named th-regional.xml
9.3	The file is well formed	P/F		Well formed with respect to the rules of the XML specification
9.4	The file is valid	P/F		Valid with respect to the TH Module 1 Schema file included in the util/dtd folder
9.5	The reference to the Schema in th-regional.xml is directed to the Schema provided in the util folder.	P/F		This is the TH Regional Schema in /XXXX/util/dtd, and tested for validity by rules 3.1-3.5. A valid reference means a URI - see http://www.w3.org/TR/xml/ and http://www.ietf.org/rfc/rfc3986.txt (version 2005 page 22, section 3.3)
9.6	The reference to the stylesheet in th-regional.xml is directed to the stylesheet provided in the util folder.	P/F		This is the stylesheet in /XXXX/util/style, and tested for validity by rules 6.1-6.3. A valid reference means a URI - see http://www.w3.org/TR/xml/ and http://www.ietf.org/rfc/rfc3986.txt (version 2005 page 22, section 3.3)
10 - Submission Structure				
10.1	All the lowest level heading elements in the XML (including node-extensions) included in the submission contain at least one leaf	P/F		

Number	Validation Criterion	Type of check	Lifecycle needed? "YES" (Y) *	Comments
11 - Leaf Attributes				
11.1	The leaf attribute "checksum-type" has a value of md5 or MD5	P/F		Note that this value is not case sensitive
11.2	The regenerated checksum for each file matches the value in the leaf attribute "checksum"	P/F	Y	Note that if the content file is in an earlier sequence within the same eCTD application then the checksum can only be regenerated if access to this file is available. The MD5 checksum is not case sensitive.
11.3	For every leaf the "title" attribute is not empty	P/F		
11.4	All leaves with an operation attribute value of new, replace or append must have a value for the cross reference (xlink:href)	P/F		The value for the cross reference (xlink:href) should be valid, and not contain any illegal characters. (Legal characters are lower case characters a-z, digits 0-9 and hyphens, as documented in the ICH eCTD specification). A valid reference means a URI - see http://www.w3.org/TR/xml/ and http://www.ietf.org/rfc/rfc3986.txt (version 2005 page 22, section 3.3)
11.5	All leaves with an operation attribute value of delete must have no value for the cross reference (xlink:href)	P/F		The attribute does not need to be included, or can be declared but with a null value
11.6	The file referenced by the cross reference (xlink:href) must exist in the same or a previously submitted sequence within the same eCTD application	P/F	Y	The link within the XML leaf element is valid, i.e the target exists
11.7	All leaves with an operation attribute value of replace, delete or append must have a value for modified-file	P/F		
11.8	All leaves with an operation attribute value of new must have no value for modified-file	P/F		The attribute does not need to be included, or can be declared but with a null value
11.9	The leaf referenced by the modified file must exist in a previously submitted sequence within the same eCTD application	P/F	Y	If a <leaf> has the 'modified-file' attribute set, the referenced <leaf> must exist in a previously submitted sequence.

Number	Validation Criterion	Type of check	Lifecycle needed? "YES" (Y) *	Comments
11.10	For all leaves with an operation attribute value of replace, delete or append, the modified file must be present in the same CTD section of the dossier. Using the operation attribute 'delete' to remove content in sections in EU m1 which are no longer used, due to updates of the CTD, should be exempt from this rule.	P/F		'Same CTD section' refers to the position in the table of contents. Sections are defined by the CTD and also by attributes in the eCTD. For example, applicants cannot replace content in the application form section with revised content that is being provided in the cover letter section. eCTD attributes also create applicant defined sections. For example, each 'substance' or 'manufacturer' attribute in m3-2-s-drug-substance, or 'product-name' attribute in m3-2-p–drug-product will create a new CTD section, and lifecycle between these sections is also not allowed.
12 - Node Extensions				
12.1	For every node-extension the "title" attribute is not empty	P/F		If node-extensions are used, the 'title' attribute must be set.
13 - Sequence Number				
13.1	The sequence folder name is a 4 digit number	P/F		i.e. numbers between 0000 and 9999
13.2	The sequence number (folder name) has not already been used	P/F	Y	The sequence number must not have been used in a previous sequence of the same submission. The program will not only check the folder names but also the sequence numbers in the TH regional backbones of previous sequences.
13.3	The sequence folder name matches the sequence number in each envelope in th-regional.xml	P/F		The sequence folder name and the sequence numbers given in the TH envelopes must be identical.

Number	Validation Criterion	Type of check	Lifecycle needed? "YES" (Y) *	Comments
14 - Envelope Attributes				
14.BP1	If the sequence type is supplemental information (j-suppl) then the related-sequence attribute must have a value.	**BP**		If the envelope element 'sequence-type' has the value 'j-suppl' , the 'related-sequence' element value must be specified.
14.BP2	If the sequence type is not supplemental information (j-suppl) then there must not be related sequence attribute	**BP**		Refer to TH M1 speciifcation. If the envelope element 'sequence-type' does not have the value 'j-suppl' the 'related sequence' element must be empty or not present.
15 - Files/Folders				
15.1	The files provided in the folders for Module 1 are in acceptable formats	**P/F**		Refer to table in TH Module 1 specification. : this is XML (where a specification exists), PDF, JPEG/JPG, PNG, SVG and GIF.
15.2	The files provided in the folders for Module 2-5 are in acceptable formats	**P/F**		Refer to ICH eCTD specification. This is XML, PDF, JPEG/JPG, PNG, SVG and GIF.
15.3	Total file folder path length must not exceed 180 characters	**P/F**		Counting starts from the first digit of the sequence number in the sequence number folder name, and includes the filename.
15.4	File names, including the extension, must not exceed 64 characters	**P/F**		
15.5	Folder names must not exceed 64 characters	**P/F**		
15.6	Only valid characters are used in file names	**P/F**		Lower case characters a-z, digits 0-9 and hyphens are allowed (as documented in the ICH eCTD specification). This test should only be applied to the file names in the file system, for checks on the XML see test 11.4.
15.7	Only valid characters are used in folder names	**P/F**		Lower case characters a-z, digits 0-9 and hyphens are allowed (as documented in the ICH eCTD specification). This test should only be applied to the folder names in the file system, for checks on the XML see test 11.4.
15.8	There are no unreferenced files in M1, M2, M3, M4 and M5 folders	**P/F**		Including all subfolders within the m1-m5 folders but excluding ‘util’ folder and subfolders
15.9	The only files in the sequence folder (/XXXX/...) are the index.xml and index-md5.txt	**P/F**		

Number	Validation Criterion	Type of check	Lifecycle needed? "YES" (Y) *	Comments
15.10	There are no empty folders	P/F		
15.11	The tracking table file is present in the correct location	P/F		The folder /XXXX/m1/th/10-cover/101-tracking
15.12	The tracking table file is correctly named	P/F		File is named tracking-var.pdf
15.BP1	Individual files do not exceed 100 MB in size	BP		Any deviation should always be reported by the validating tool. Files larger than 100 MB should be avoided due to potential archiving issues and to make the assessment easier.
15.BP2	The recommended folder structure and folder names in the ICH and TH specifications are used	Info		Although navigation of an eCTD is typically carried out via the XML backbone, it is also helpful if the underlying files and folders follow the ICHand TH naming guidance.
15.BP3	The recommended file names from the ICH and TH specifications are used for all files	Info		Although navigation of an eCTD is typically carried out via the XML backbone, it is also helpful if the underlying files and folders follow the ICH and TH naming guidance.

Number	Validation Criterion	Type of check	Lifecycle needed? "YES" (Y) *	Comments
16 - PDF Files				
16.1	No PDF has been created and saved as version 1.3 or earlier	P/F		PDF 1.3 or earlier is not acceptable for technical reasons. No exceptions will be made. For example, if a literature reference is received in PDF 1.3 or earlier, then the applicant must provide it in PDF 1.4, 1.5, 1.6 or 1.7, even if this means copying the full text into a new document or even getting a paper copy and scanning it. Further guidance is provided about the best ways to check the PDF version in the comment to rule 16.BP1.
16.2	There is no security setting to open any individual file	P/F		This includes passwords, certificate security, or adobe policy server settings. This test should not be used to test for corrupted files, instead see 16.5.
16.3	There are no further security settings applied to any individual file (except for files in Modules 1.2, 3.3, 4.3 and 5.4)	P/F		All "restrictions" should be "allowed" when viewing the Document Preferences > Security settings. This includes any of the following document restrictions: printing, changing the document, document assembly, content copying, content copying for accessibility, page extraction, filling of form fields, signing, creation of template pages. Specific security settings of files in m1.2 are tested in criterion 16.4.
16.4	Individual files in section 1.2 have no security settings except for the following, which are allowed: Changing the document Document assembly Page extraction Creation of template pages.	P/F		These limiited security settings are allowable for the application form, because they are necessary for the functioning of the eAF.

Number	Validation Criterion	Type of check	Lifecycle needed? "YES" (Y) *	Comments
16.5	The submission does not contain corrupted files	P/F		This can be achieved by opening a PDF file in software which is compliant to ISO 32000-1; if the file opens without error, the PDF file is considered to be conformant. Absence of detection of conformance means corrupted PDF.
16.BP1	Files have been created and saved as PDF 1.4, 1.5, 1.6, or PDF 1.7	BP		For PDF files with apparent versions of 1.3 or earlier, the version information should be taken from the first eight characters from the first line of the header in the file. For versions 1.4 and higher, the version should be taken from the document catalogue dictionary, if present. If both the header information and the catalogue information are present, then the document catalogue dictionary information takes precedent, see PDF 32000-1:2008 specification, chapter 7.5.2 for further details. Only the PDF versions specified are recommended by ICH. This test is important due to archiving and also that PDF files can be correctly open and read by assessors.
16.BP2	Hyperlinks and bookmarks within documents, or between documents within the same sequence, have a valid target.	BP		Only links that open in the same software application are tested. Other links (e.g. web links and e-mail addresses) are not considered to link to essential content and should not be tested. If this BP criterion is not met, the assessor might not be able to conveniently find the relevant documents and read the submission as intended by the applicant.

Number	Validation Criterion	Type of check	Lifecycle needed? "YES" (Y) *	Comments
16.BP3	Hyperlinks and bookmarks to destinations in a different sequence in the same eCTD have a valid target.	BP	Y	Only links that open in the same software application are tested. Other links (e.g. web links and e-mail addresses) are not considered to link to essential content and should not be tested. If this BP criterion is not met, the assessor might not be able to conveniently find the relevant documents and read the submission as intended by the applicant.
16.BP4	All hyperlinks and bookmarks are set to "inherit zoom"	BP		Using 'inherit zoom' ensures that assessors do not need to spend time repeatedly setting the view when using the links for navigation to new documents.
16.BP5	PDFs must have "Fast Web View" active	BP		The use of 'Fast Web View' helps ensure optimum performance of the review system.
16.BP6	PDF Document Properties for the Initial View are set for "Page Layout = Default" and "Magnification = Default"	BP		Setting page layout and magnification to default allows the assessor to set his/her own preferences to define how the PDF is displayed, rather than the settings being taken from each individual PDF file.
16.BP7	All PDF hyperlinks and bookmarks are relative	BP		Relative links and bookmarks will continue to work when the submission is copied and loaded into new a environment at the agency side. Absolute (rooted) links and bookmarks will not.
16.BP8	The bookmarks pane should be visible if bookmarks are included within a PDF document	BP		Fulfilling this BP criterion make it more convenient for the assessor in knowing there are bookmarks without opening the pane.
16.BP9	The bookmarks pane should not be visible if there are no bookmarks included within a PDF document	BP		Fulfilling this BP criterion makes it more convenient for the assessor in knowing there are no bookmarks without opening the pane to check.

Number	Validation Criterion	Type of check	Lifecycle needed? "YES" (Y) *	Comments
16.BP10	All hyperlinks and bookmarks between two PDFs must be configured as specified in ISO 32000-1:2008	BP		Consult the PDF specifications as in ISO 32000-1:2008 for section 7.11.2.3 on how the paths need to be written in PDF. The paths cannot contain back slashes, only forward slashes. See also 12.6.4.3 for the remote goto action. The link to another PDF cannot be made with javascript code in the PDF. Please note, not all PDF tools display the path for the link with forward slashes. However, the presence of a backslash in a link as displayed in a PDF viewer or editor does not necessarily mean that the link is NOT according to the ISO specifications. Therefore, tests for backslashes must be performed in eCTD validation software. This BP criterion is important because links who are not according to section 7.11.2.3 may not work on certain devices, such as non-Windows operating systems or tablets.
17 - Study Tagging Files (STFs)				
17.1	Check Index Reference	P/F		The files from the xlink:href references must exist. Corresponds to US FDA criterion 1833.
17.2	Check Index Reference (title match)	BP		The titles from the doc-content elements must match the corresponding leaf title values from the ICH backbone.See FDA criterion 3001.
17.3	Content Block are not accepted	BP		Using content-block elements must be avoided. Corresponds to US FDA criterion 3029.
17.4	No backslash in xlink:href reference	P/F		The xlink:href values must not contain backslashes
17.5	Study Identifier category must not be empty	BP		The value of the study-identifier/category element must not be empty.
17.6	Study Identifier study-id must not be empty	BP		The value of the study-identifier/study-id element must not be empty.

Number	Validation Criterion	Type of check	Lifecycle needed? "YES" (Y) *	Comments
17.7	Study Identifier title must not be empty	BP		The value of the study-identifier/title element must not be empty. Corresponds to US FDA criterion 1985.
17.8	Categories and file tags	BP		Checks file tag values and category values against definitions in valid-values.xml file
17.9	STF leaf elements must reference other STF leaf upon append	P/F		Such leaf elements must not reference PDF files as modified files.
17.10	Category information must be provided for certain STFs	BP		ICH eCTD STF Specification V 2.6.1 3-June-2008: The category element provides an additional level of study organization not currently provided by the eCTD DTD. This element is only relevant for studies provided in the specific CTD sections cited below. - 4.2.3.1 Single dose toxicity (grouped by species and route of administration) - 4.2.3.2 Repeat dose toxicity (grouped by species, route of administration, and duration if applicable) - 4.2.3.4.1 Long term [carcinogenicity] studies (grouped by species) - 5.3.5.1 Study reports of controlled clinical studies pertinent to the claimed indication (grouped by type of control)
17.11	STF cannot reference another STF	BP		Leaf references in STFs must always target content files, not STFs. Corresponds to US FDA criterion 1789.
17.12	STF files must reference at least one leaf	BP		Any STF that does not relate to any leaf elements will be reported here. Corresponds to US FDA criterion 1816.
17.13	Study ID for STF must remain constant	BP		The STF study IDs must not change in the application life cycle. Corresponds to US FDA criterion 1850.
17.14	Invalid STF TOC location	BP		STFs should only be associated with certain headings under Modules 4 or 5. Corresponds to US FDA criterion 1901.
17.15	STF doc-content file tag count	BP		There should be one and only one file tag for each doc-content. Corresponds to US FDA criteria 1918 and 1935.

Number	Validation Criterion	Type of check	Lifecycle needed? "YES" (Y) *	Comments
17.16	STF XML title and leaf element title do not match	BP		For all leaf elements in the STF, the leaf title must be identical to the title of the corresponding leaf in the ICH backbone. Corresponds to US FDA criterion 1953.
17.17	Detect invalid life cycle pattern: Append operations not appending to most recent STF leaf	BP		For STF leaf elements the append operation should not reference the leaf where the STF has been added initially but the most recent update to this file.
STF_INFO	Informational output about the number and total size of non E3 documents.	Info		Sample: Non E3 study files Total size (KB): 133.76 Number of 16.3 files: 3 Number of US files: 4 Number of JP files: 1

LEGEND

Bold	Fixed Folder Name
Regular	Fixed File Name
Black	Fixed Component
Red	Variable Component
	Consistent with EU
	Thailand Specific

Suggested TH eCTD Naming Conventions

Content	Correlating eCTD Section	
eSubmission Identifier		
0000		
index.xml		
index-md5.txt		
m1		
th		
th-regional.xml		
10-cover	1.0	Cover
101-tracking	1.0.1	Tracking Table
tracking-var.pdf		
102-cover-letter	1.0.2	Cover Letter
cover-var.pdf		
12-forms	1.2	Application Forms
121-form	1.2.1	Application Form
form-var.pdf		
122-annex	1.2.2	Annexes
annex-var.pdf		
13-pi	1.3	Product Information
131-spclabelpl	1.3.1	SPC, Labelling and Package Leaflet
1311-labelling	1.3.1.1	Labelling
labelling-var.pdf		
1312-spc	1.3.1.2	SPC
spc-var.pdf		
1313-pl	1.3.1.3	Package Leaflet
pl-en-var.pdf	1.3.1.3.1	Package Leaflet - Thai
pl-th-var.pdf	1.3.1.3.2	Package Leaflet - English
pl-other-var.pdf	1.3.1.3.3	Package Leaflet - Other Language
132-mockup	1.3.2	Mock-up
mockup-var.pdf		
mockup-var.jpg		
mockup-var.jpeg		
mockup-var.gif		
mockup-var.png		
mockup-var.svg		
133-specimen	1.3.3	Specimen
specimen-var.pdf		
134-consultation	1.3.4	Consultation with Target Patient Groups
consultation-var.pdf		
135-approved	1.3.5	Product Information already approved in Other States
1351-status	1.3.5.1	Foreign Regulatory Status
status-var.pdf	1.3.5.1	
1352-pi	1.3.5.2	Foreign Product Information
pi-var.pdf		
1353-similarities	1.3.5.3	Data Similarities and Differences
similarities-var.pdf		
136-braille	1.3.6	Braille
braille-var.pdf		
14-expert	1.4	Information about the Experts
141-quality	1.4.1	Quality
quality-var.pdf		
142-nonclinical	1.4.2	Non-Clinical
nonclinical-var.pdf		
143-clinical	1.4.3	Clinical
clinical-var.pdf		
15-specific	1.5	Specific Requirements for Different Types of Applications
151-bibliographic	1.5.1	Information for Bibliographical Applications
bibliographic-var.pdf		
152-generic-hybrid-bio-similar	1.5.2	Information for Generic, 'Hybrid' or Bio-similar Applications
generic-var.pdf	1.5.2.1	Information for Generic Application
hybrid-var.pdf	1.5.2.2	Information for 'Hybrid' Applications
biosimilar-var.pdf	1.5.2.3	Information for Bio-similar Applications
153-data-market-exclusivity	1.5.3	(Extended) Data/Market Exclusivity
datamarketexclusivity-var.pdf		

LEGEND

Bold	Fixed Folder Name
Regular	Fixed File Name
Black	Fixed Component
Red	Variable Component
	Consistent with EU
	Thailand Specific

Suggested TH eCTD Naming Conventions

Content	Correlating eCTD Section	
154-exceptional	1.5.4	Exceptional Circumstances
exceptional-var.pdf		
155-conditional-ma	1.5.5	Conditional Marketing Authorisation
conditionalma-var.pdf		
156-add-tradename	1.5.6	Additional Trade Name Declarations
add-tradename-var.pdf		
157-co-marketed	1.5.7	Co-marketed Medicines Declarations
co-marketed-var.pdf		
16-environrisk	1.6	Environmental Risk Assessment
161-nongmo	1.6.1	Non-GMO
nongmo-var.pdf		
162-gmo	1.6.2	GMO
gmo-var.pdf		
17-productinter	1.7	Product Interchangeability Equivalence Evidence
171-beprotocol	1.7.1	BE Protocol
beprotocol-var.pdf		
172-bestudy	1.7.2	BE study report
bestudy-var.pdf		
173-beinvitro	1.7.3	Comparative in vitro dissolution/release studies
beinvitro-var.pdf		
174-beclinic	1.7.4	Comparative clinical studies
beclinic-var.pdf		
175-bepharmaco	1.7.5	Comparative pharmacodynamics studies
bepharmaco-var.pdf		
176-beother	1.7.6	Other
beother-var.pdf		
18-pharmacovigilance	1.8	Information relating to Pharmacovigilance
181-phvig-system	1.8.1	Pharmacovigilance System
phvigsystem-var.pdf		
182-riskmgt-system	1.8.2	Risk-management System
riskmgtsystem-var.pdf		
183-smp	1.8.3	SMP Protocol
smp-var.pdf		
19-clinical-trials	1.9	Information relating to Clinical Trials
clinicaltrials-var.pdf		
110-paediatrics	1.10	Information relating to Paediatrics
paediatrics-var.pdf		
1R-responses	1.R	Responses to Questions
responses-var.pdf		
1A-additional-data	1.A	Additional Data
1A1-assessment-report	1.A.1	Assessment report from other regulatory agency
assessment-report-var.pdf		
1A2-self-assessment	1.A.2	Checklist Form /Self Assessment Report
self-assessment-var.pdf		
1A3-development-studies	1.A.3	Information on Development Studies
development-studies-var.pdf		
1A4-coa-biologic	1.A.4	COA from Institute of Biological Product
coa-biologic-var.pdf		
1A5-comparison-table	1.A.5	Comparison Table
comparison-table-var.pdf		
1A6-exportation	1.A.6	Information of Exportation
exportation-var.pdf		
1A7-declaration	1.A.7	Declaration from applicant
declaration-var.pdf		
1A8-database-entering	1.A.8	Template of Database entering
database-entering-var.pdf		
1A99-other	1.A.99	Other
other-var.pdf		
additionaldata-var.pdf		
util		
dtd		
th-regional.xsd		
xlink.xsd		

LEGEND

Bold	Fixed Folder Name
Regular	Fixed File Name
Black	Fixed Component
Red	Variable Component
	Consistent with EU
	Thailand Specific

Suggested TH eCTD Naming Conventions

Content	Correlating eCTD Section
xml.xsd	
ich-ectd-3-2.dtd	
style	
ectd-2-0.xsl	
th-regional.xsl	

ภาคผนวก ๔

- มาตรฐานตามไอซีเอช อีซีทีดี (ICH eCTD)

INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE

ICH M2 EWG

Electronic Common Technical Document Specification

This specification has been developed by the ICH M2 Expert Working Group and maintained by the eCTD Implementation Working Group in accordance with the ICH Process as pertains to the M2 EWG and eCTD change control as it pertains to the eCTD IWG.

Document Change History

Version Number	Date	Description
Version 3.0	October 2003	Initial Step 4 Document
Version 3.1	November 2003	Incorporated approved change requests 00020, 00030, 00090, 00110, 00190, 00200, 00240, 00260, 00290, 00310, 00380, 00400, 00420, 00450, 00480, 00500, 00510, 00520, 00530
Version 3.2	February 2004	Editorial Corrections and Changes to Align with the M4 Organisation Document : Granularity Annex
Version 3.2.1	June 2008	Incorporated approved change requests 0120, 0130, 0140, 0210, 0270, 0300, 0390, 0560, 0590, 0600, 0620, 0640, 0670, 0700, 0710, 0720, 0730, 0750, 0760, 0770, 0780, 0810, 0820, 0940, 0960, 1030, 1080, 01170, 1250, 1280, 1310, 1320, 1360, 1370, 1400, 1450, 1580, 1660, 1680. Incorporated eCTD Q&As 1-3, 5-7, 9-11, 13, 15, 17-19, 21, 23, 24, 28-34, 37-39 and 41-47. Provided clarity on Operation Attribute use. Converted all instances of 'leafs' to 'leaf elements'. Removed numbering not defined by CTD (e.g., 4.2.1.1.1). Introduced allowance for 'append' leaf to modify leaf in same sequence. Corrected typos and other wording issues.
Version 3.2.2	July 2008	Minor editorial corrections after Step 4 approval and sign-off

ICH eCTD Specification

Introduction

The ICH M4 Expert Working Group (EWG) has defined the Common Technical Document (CTD). The ICH M2 EWG has defined, in the current document, the specification for the Electronic Common Technical Document (eCTD). The eCTD is defined as an interface for industry to agency transfer of regulatory information while at the same time taking into consideration the facilitation of the creation, review, life cycle management and archiving of the electronic submission. The eCTD specification lists the criteria that will make an electronic submission technically valid. The focus of the specification is to provide the ability to transfer the registration application electronically from industry to a regulatory authority. Industry to industry and agency to agency transfer is not addressed.

Background

The specification for the eCTD is based upon content defined within the CTD issued by the ICH M4 EWG. The CTD describes the organization of modules, sections and documents. The structure and level of detail specified in the CTD have been used as the basis for defining the eCTD structure and content but, where appropriate, additional details have been developed within the eCTD specification.

The philosophy of the eCTD is to use open standards. Open standards, including proprietary standards which through their widespread use can be considered *de facto* standards, are deemed to be appropriate in general.

Scope

The CTD as defined by the M4 EWG does not cover the full submission that is to be made in a region. It describes only modules 2 to 5, which are common across all regions. The CTD does not describe the content of module 1, the Regional Administrative Information and Prescribing Information, nor does it describe documents that can be submitted as amendments or variations to the initial application.

The value of producing a specification for the creation of an electronic submission based only upon the modules described in the CTD would be limited. Therefore, the M2 EWG has produced a specification for the eCTD that is applicable to all modules of initial registration applications and for other submissions of information throughout the life cycle of the product, such as variations and amendments.

This document describes the parts of the registration application that are common to all regions and some of the life cycle requirements for products. The parts of the registration application that are specific to a region will be covered by regional guidance. However, this backbone has been developed to handle both the regional and common parts of submissions.

Technical Requirements

The specification is designed to support high-level functional requirements such as the following:

- Copy and paste
- Viewing and printing of documents
- Annotation of documentation
- Facilitate the exporting of information to databases
- Searching within and across applications
- Navigation throughout the eCTD and its subsequent amendments/variations

Change Control

The specification for the eCTD is likely to change with time. Factors that could affect the content of the specification include, but are not limited to:

- Change in the content of the CTD, either through the amendment of information, at the same level of detail, or by provision of more detailed definition of content and structure
- Change to the regional requirements for applications that are outside the scope of the CTD
- Updating standards that are already in use within the eCTD
- Identification of new standards that provide additional value for the creation and/or usage of the eCTD
- Identification of new functional requirements
- Experience of use of the eCTD by all parties

Details of the change control management are described in an external ICH document.

Appendix 1: Overall Architecture

Guiding Design Principles

This appendix defines the basic principles that drove the design and architecture of the eCTD. Detailed specifications are defined in appendices 2 and 6.

Business Model

The business process to be supported can be described as follow:

Industry <-----> Message <------> Agency

The business process defines specific requirements for the message. The eCTD Specification currently provides only a transport mechanism for one-way traffic from applicant to agency.

The primary focus of the eCTD is to provide a data interchange message between industry and agencies. Industry initiates the process by creating the initial submission in terms of an electronic CTD. Throughout the life cycle of this process, additional information will be submitted to update or modify the information contained in the initial submission (e.g., supplement, amendment, variation.) The agency can submit acknowledgements, queries and requests to industry. These are considered simple messages using electronic mail or other transport formats. The overall architecture of the eCTD is designed to provide a commonly agreed upon submission and submission structure that imposes minimal restriction to the industry and agencies.

Modular Structure of the eCTD

The structure of the electronic submission in terms of organization and navigation should be consistent with the modular structure of the Common Technical Document. The goal of this design principle is to standardize the electronic format of the common parts of the eCTD.

XML Based eCTD

The XML eCTD DTD (Document Type Definition) defines the overall structure of the submission. The purpose of the XML backbone is two-fold: (1) to manage meta-data for the entire submission and each document within the submission and (2) to constitute a comprehensive table of contents and provide corresponding navigation aids. Meta-data on submission level include information about submitting and receiving organization, manufacturer, publisher, ID and kind of the submission, and related data items. Examples for meta-data on document level are versioning information, language, descriptive information such as document names and checksums. Details are defined in appendix 6.

The XML instance of any submission should be created and validated according to the XML eCTD DTD as defined in appendix 8.

The XML eCTD DTD describes the hierarchical structure according to the CTD as defined by the ICH M4 Expert Working Group. It includes multiple hierarchical levels depending on the specific module as defined in the CTD. The actual submission can include more hierarchical levels below those defined in the CTD. The XML eCTD instance covers the entire submission including all hierarchical levels and includes references to each individual file.

The submission should include a Stylesheet that supports presentation of the XML instance, navigation according to the table of contents, and provides access to all documents within the submission. A standard Stylesheet for viewing the eCTD submission is defined and provided by the ICH M2 EWG. Presentation and navigation via other Stylesheets on the receiving side should be possible. Consult regional authorities on the acceptability of submitting non-ICH stylesheets.

Multiple Region Support

The scope of each submission is global according to the Common Technical Document, meaning that modules 2 through 5 of a submission are intended for all regions with the exception of selected documents (e.g., in the quality module), which have a regional scope. Module 1 of a submission is regional in nature.

The DTD as defined by the ICH M2 expert working group specifies the structure of the common parts of the eCTD primarily focusing on module 2 through 5. It enables linking to regional XML index files for module 1 which will be defined by the authorities in each region. Due to the significant differences in documentation requirements across regions it is not expected that a single, global eCTD submission could be constructed and transmitted to multiple regions with each regional authority ignoring or deleting other regions' submission material.

Life Cycle Management

The applicant creates a submission that is stored in a local repository. The applicant submits the initial submission to the agency, which imports the submission into another local repository. The nature and kind of the local repositories is not within the scope of the eCTD. The initial submission should be self-contained, meaning that it includes all documents and no references to other submissions. Regional guidance should be consulted if references to other submissions are needed.

Following the initial submission, the applicant can submit incremental updates such as amendments and variations. Updates can refer to documents in the previous submissions. Updates should be designed in a way that they can be loaded into the repository by fully preserving the initial or previous submission via version control. The XML backbone should include meta-data identifying the update and providing navigation aids to filter for different submission types.

It is preferred that when a Common Technical Document is submitted electronically, the entire submission be in electronic form with the exception of certain regional forms that currently require written signatures. See appendix 5 for regional requirements. See appendix 6 for a description of how to submit a CTD containing both paper and electronic components.

Appendix 2: The eCTD Submission

Introduction

This appendix specifies the Information Technology aspect of the eCTD submission. Informally, the eCTD submission is a directory structure with files including the XML eCTD instance, reports, data and other submission information. The eCTD submission supports multilingual and multi-region aspects.

The eCTD Submission

- An eCTD submission is a collection of data objects that follows the eCTD specification. The main function of the eCTD submission is data exchange. Information systems would need to be developed to process the eCTD submission. The biggest benefits are expected when the eCTD submission is loaded into an information system that supports the review process. However, one can view an eCTD submission with a Web browser as it is Web ready.

The eCTD submission is composed of the following:

- Directory structure
- XML eCTD instance
- Content files

Directory Structure

The directory structure is a structure of directories and files. There should be a reasonable maximum number of entries (directories and files) per directory. The directory structure should follow the rules below. The files could be in several formats as specified below.

The name of the files and directories are identifiers. They should be short. The file names are not intended to convey meta-data, though some meaning in the names helps (i.e., no random names.)

Recommended, but optional, names for directories and files are provided in Appendix 4. Any directory names and file names that are added to the eCTD submission by the applicant should be descriptive, logical and brief.

XML eCTD Instance

The instance is in the submission sequence number directory (see appendix 6). The submission sequence number directory should contain at least two files and one or more directories. One of the files in the submission sequence directory should be the instance and the other should be the MD5 checksum of the instance. The instance is the starting file for the processing by an XML processor.

The intention is to have links from the leaf elements of the instance to the files in the eCTD submission as opposed to creating a single XML document that contains the entire eCTD submission. The instance also contains meta-data at the leaf level.

eCTD Template

The ICH Web site (http://estri.ich.org/eCTD) includes an empty eCTD folder template as an example of an eCTD submission folder structure. It shows all of the possible Module 2-5 folders as defined in Appendix 4 and can be populated with the applicant data and edited as appropriate (i.e., adding additional subfolders or removing unnecessary folders). The applicant should still add the relevant regional Module 1 folders and content, add the appropriate utility folders and content, and create the XML index files to complete a valid eCTD submission.

Formats

Formats should be readable at least for as long as it is needed for the regulatory process. This process could be very long (e.g., 50 years). This points to the advantage of neutral formats: formal standard, industrial

standard, vendor independent, and text-like. The format should be adapted to the type of data. Appendix 7 describes the way in which these files should be constructed.

The list of agreed to formats will be updated as technology evolves and new requirements arise. XML will be the preferred format for all types of data.

Common Formats

The common formats that can be included in an eCTD submission are:

- Narrative: Portable Document Format (PDF)
- Structured: Extensible Markup Language (XML)
- Graphic: Whenever possible, use PDF. When appropriate or when PDF is not possible, use Joint Photographic Experts Group (JPEG), Portable Network Graphics (PNG), Scalable Vector Graphics (SVG), and Graphics Interchange Format (GIF). Special formats for very high resolutions could be appropriate on a case-by-case basis.

Regional Use of Other Formats

Regulatory authorities and applicants could agree to use other formats regionally (i.e., non-common formats or uses of the common formats in a different way from above). The use of other formats is discouraged and the intention is to use as much as possible the common formats. The intention of the use of other formats is for transition.

There are two classes of transitions:

- Legacy Transition: from the past to the present (i.e., old formats to present formats.)
- Future Transition: from the present to the future (i.e., from present formats to new formats.) The new formats would normally be candidates for common formats.

Links

CTD cross-references can be supported in the eCTD through the use of hyperlinks. Links among objects in the eCTD submission should be relative. The intention is to make the eCTD submission self-contained. All literature references introduced by the applicant should be included in the submission.

One can always point to a file. The capacity to point to a specific location within a file depends on the linking technology. Different formats allow for the use of different linking technology. See Appendix 7.

Presentation

Presentation is closely associated with formats. To associate a Stylesheet with a file usually one has to use a linking technology. The linking between Stylesheet (which could be in a separate file) and a data file should be relative. In addition, there is the dimension of media. One file could have several Stylesheets; the one used depends on the media. For example, there could be one presentation for the screen and another for paper.

Checksums

The eCTD submission should contain checksums for each individual file including a checksum file for the eCTD XML instance. Initially, the MD5 Message-Digest Algorithm (MD5) should be used for this purpose. Including a checksum for each individual file provides a number of benefits including:

- The integrity of each file can be verified by comparing the checksum submitted with the file and the computed checksum.
- The checksum can be used to verify that the file has not been altered in the historical archive of the regulatory authority. This is especially useful as the files are migrated from one storage medium to another, as in the case of backup to magnetic tape storage.

Element to File Directory Mapping

The following rules are recommended:

- The rules below for the file and directories take precedence.
- Add the corresponding extension to the file.
- If appropriate, use a reasonable abbreviation.

File Extension

All files should have one and only one file extension. The file extension should be used to indicate the format of the file. For example:

hello.pdf	PDF
hello.rtf	RTF

The mapping between formats and extensions are:

IANA nomenclature	
text/css	css
text/html	html or htm
text/xml	xml
application/pdf	pdf
application/rtf	rtf
application/vnd.ms-excel	xls
image/jpeg	jpg
image/png	png
image/gif	gif

Non IANA nomenclature	
DTD	dtd
XPT (SAS)	xpt
XSL	xsl

The eCTD submission could use formats not registered with the Internet Assigned Numbers Authority (IANA).

The presence of a format in this list does not imply that it would be considered an acceptable format. For formats absent from this list, widely used mapping between the formats and the extensions should be used.

Future direction: if a mechanism (e.g., standard) becomes available that associates the formats with file extension, it should be considered for this specification.

Name

Name is a token composed of the following characters:

- Letters "a" to "z" [U+0061 to U+007A].
- Digits "0" to "9" [U+0030 to U+0039].
- "-" [HYPHEN-MINUS, U+002D].

The notation "U+" refers to the Unicode [UNICODE] notation.

This Specification does not provide for Japanese characters in file and folder names.

Examples of correct names (only the name without the extension):

part-b
myfile
hello

Examples of incorrect names (only the name without the extension):

part a (' ' ; SPACE is not allowed)

myfile.xml	('.' ; FULL STOP is not allowed)
hello:pdf	(':' ; COLON is not allowed)
part_a	('_', LOW LINE is not allowed)
Parta	(UPPERCASE is not allowed)

Directory name is a name.

File name is one name followed by one name separated by a '.' (FULL STOP, U+002E).

Correct file names (with the extension):

myfile.pdf
hello.cml

Incorrect file names (with the extension)::

a part.pdf	(' '; SPACE is not allowed)
hello	(missing extension)
hello:xml	(':'; COLON is not allowed)

The maximum length of the name of a single folder or file is 64 characters including the extension. Only lower case letters should be used in all file and directory names. The maximum length of a path is 230 characters, including file name, and extension. This allows regulators 26 characters to add to the path in their review environments. Consult regional guidance for further restrictions on the maximum path length. If the path exceeds the 230 character limit or the regionally-defined limit, then folder and file names created by the applicant should be abbreviated. If further reduction is still called for, the file and folder names recommended in Appendix 4 should be abbreviated. Applicants should also consult regional media formats and M2 EWG recommendations for possible folder limits imposed by the media.

Document name is the first name in the file name. For example, “docname” in the file name “docname.ext”.

Character encoding

The character encoding (charset) in order of preference is:

- Unicode UTF-8, Unicode 16 bits [ISO-10646].
- ISO-8859-1 (Latin-1) or appropriate ISO-8859-x; e.g., ISO-8859-7 for Greek.
- The appropriate SHIFT_JIS.
- Other character encoding agreed upon regionally by the regulatory authority and applicant.

References

[CML] *Chemical Markup Language*
http://cml.sourceforge.net

[CSS2] *Cascading Style Sheets, level 2*
http://www.w3.org/TR/REC-CSS2

[ECMAScript] *ECMAScript Language Specification*, 3rd edition. ECMA- 262
http://www.ecma-international.org/publications/standards/Ecma-262.htm

[EXCEL] Microsoft Excel
http://www.microsoft.com/office/excel/default.htm

[GIF] *Graphics Interchange Format*
http://tronche.com/computer-graphics/gif/gif89a.html

[HTML] *HTML 4.01 Specification*
http://www.w3.org/TR/html4

[IANA] Internet Assigned Numbers Authority
http://www.iana.org

[IMT] Internet Media Types
http://www.iana.org/assignments/media-types/

[ISO-10646] Information Technology -- Universal Multiple-Octet Coded Character Set (UCS) -- Part 1: Architecture and Basic Multilingual Plane, ISO/IEC 10646-1:1993

[ISO-639] *Codes for the representation of names of languages*
ISO 639:1988.
http://www.oasis-open.org/cover/iso639a.html

[JPEG] Joint Photographic Experts Group
http://www.jpeg.org/public/wg1n1807.txt

[MD5] *The MD5 Message-Digest Algorithm*
http://ietf.org/rfc/rfc1321.txt

[PDF] *Portable Document Format*
http://www.adobe.com/devnet/pdf/pdf_reference.html

[PNG] *PNG (Portable Network Graphics) Specification Version 1.0*
http://www.w3.org/TR/REC-png.html

[RTF] *Rich Text Format (RTF) Specification, version 1.6*
http://msdn.microsoft.com/library/specs/rtfspec.htm

[SVG] *Scalable Vector Graphics (SVG) 1.0 Specificatio*n (work in progress)
http://www.w3.org/TR/1999/WD-SVG-19991203

[UNICODE] Unicode Consortium
http://www.unicode.org

[XHTML] *XHTML 1.0: The Extensible HyperText Markup Language*
http://www.w3.org/TR/WD-html-in-xml

[XML] *Extensible Markup Language (XML) 1.0 (Second Edition)*
http://www.w3.org/TR/REC-xml.html

[XSL] *Extensible Stylesheet Language (XSL)*
Version 1.0 W3C Recommendation 15 October 2001
http://www.w3.org/TR/WD-xsl

[XSLT] *XSL Transformations*
http://www.w3.org/TR/xslt.html

Appendix 3: General Considerations for the CTD Modules

Introduction

Documents that are provided in the different modules should be formatted as defined by the ICH Common Technical Document. There should also be consistency in the way navigational aids are provided. Within each document, bookmarks and hypertext links from the table of contents should be provided to all tables, figures, publications, and appendices.

Hypertext links should be provided throughout the body of these documents to aid efficient navigation to annotations, related sections, publications, appendices, tables, and figures that are not located on the same page. CTD cross-references can be supported in the eCTD through the use of hyperlinks. If a list of references is included at the end of a document, there should be hypertext links to the appropriate publication.

Documents should be generated from electronic source documents and not from scanned material, except where access to the source electronic file is unavailable or where a signature is called for.

Folder and File Naming Conventions

Recommended, but optional, folder and file names are presented in this specification. These could be used in most cases, however applicants can modify this specification where appropriate.[1] For example, it is generally acceptable to include an additional folder for information where an appropriate folder name is unavailable in the eCTD specification or to provide for additional file organization where the recommended foldering is inadequate. It is recommended that applicants maintain folder names listed in this specification. This should not be interpreted to mean that the actual eCTD XML DTD should be changed or altered in any way.

The maximum length of the name of a single folder or file is 64 characters including the extension. Folder or file names should be written in lower case only. All files should have one and only one file extension. The file extension should be used to indicate the format of the file. More details on the naming conventions are given in Appendix 2, and examples in Appendix 4.

Filenames provided in the eCTD are optional. To assist the reviewer when several similar files are open at the same time, it can be appropriate to consider alternative naming conventions that could provide unique, understandable filenames. The general provisions for naming of files are in Appendix 2 of the Specification.

Typically, the file name would be the applicant's internal numbering or naming convention for the studies. The following table gives an example of how files could be named.

[1] Regulatory authorities should be notified of additions and changes to the folder structure according to regional guidance.

Table 3-1

Description	File Name
Study Report 1	*study-report-1.pdf*
Study Report 2	*study-report-2.pdf*
…	…
Study Report n	*study-report-n.pdf*

Screenshots and Folder Hierarchy

Screenshots are provided in the following chapters for all modules down to the level of hierarchy as described in this appendix. The representation in module 3 is in alphabetical order due to the nature of the computer operating system and is therefore not entirely consistent with the sequence of the CTD. In a Web browser the content will appear in the order of the CTD table of contents.

Detailed options on the folders and files are provided in Appendix 4 in case the applicant chooses to submit more granular documents. It is not mandatory to use the full folder hierarchy. Empty directories can be omitted; however, when the content is expected, justification should be provided as to why it is missing in accordance with regional guidance.

Module 1 Administrative Information and Prescribing Information

The name of the folder for module 1 should be *m1*.

This module contains administrative information that is unique for each region. Regional guidance will provide the specific instructions on how to provide the administrative forms and detailed prescribing information. Please refer to Appendix 5 when preparing module 1.

Module 2 Summaries

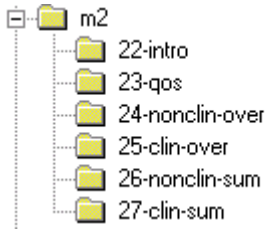
The files in this module should be provided as PDF text with the exception of a few embedded images, when needed. The name of the folder for module 2 should be *m2*. The folders in module 2 should be named as follows but can be further reduced or omitted to minimize path length issues.

Table 3-2

Section in CTD	Description	Folder Name
2.2	Introduction	*22-intro*
2.3	Quality overall summary	*23-qos*
2.4	Nonclinical Overview	*24-nonclin-over*
2.5	Clinical Overview	*25-clin-over*
2.6	Nonclinical Written and Tabulated Summaries	*26-nonclin-sum*
2.7	Clinical summary	*27-clin-sum*

A representative folder hierarchy for module 2 is presented in the screenshot in figure 3-1.

Figure 3-1 Screenshot representation of the folder structure of module 2



Module 3 Quality

The name of the folder for module 3 should be *m3*. The folders in module 3 should be named as follows but can be further reduced or omitted to minimize path length issues.

Table 3-3

Section in CTD	Description	Folder Name
3.2	Body of Data	*32-body-data*
3.2.S	Drug Substance	*32s-drug-sub*
3.2.S	Drug Substance [Drug Substance Name] [Manufacturer][2]	*substance-1-manufacturer-1*
3.2.S.1	General Information (name, manufacturer)	*32s1-gen-info*
3.2.S.2	Manufacture (name, manufacturer)	*32s2-manuf*
3.2.S.3	Characterisation (name, manufacturer)	*32s3-charac*
3.2.S.4	Control of Drug Substance (name, manufacturer)	*32s4-contr-drug-sub*
3.2.S.4.1	Specification (name, manufacturer)	*32s41-spec*
3.2.S.4.2	Analytical Procedures (name, manufacturer)	*32s42- analyt-proc*
3.2.S.4.3	Validation of Analytical Procedures (name, manufacturer)	*32s43-val-analyt-proc*
3.2.S.4.4	Batch Analyses (name, manufacturer)	*32s44-batch-analys*
3.2.S.4.5	Justification of Specification (name, manufacturer)	*32s45-justif-spec*
3.2.S.5	Reference Standards or Materials (name, manufacturer)	*32s5-ref-stand*
3.2.S.6	Container Closure System (name, manufacturer)	*32s6-cont-closure-sys*
3.2.S.7	Stability (name, manufacturer)	*32s7-stab*
3.2.P	Drug Product (name, dosage form)[3]	*32p-drug-prod*
3.2.P	Drug Product (name, dosage form) - *Name*	*product-1*
3.2.P.1	Description and Composition of the Drug Product (name, dosage form)	*32p1-desc-comp*
3.2.P.2	Pharmaceutical Development (name, dosage form)	*32p2-pharm-dev*

[2]Each drug substance-manufacturer should be placed in a separate subordinate folder. Folders and files should be created for each drug substance-manufacturer section included in the submission in accordance with the hierarchy identified in the following chapters.

[3] Each drug product should be placed in a separate subordinate folder. Folders and files should be created for each drug product section included in the submission in accordance with the hierarchy identified in the following chapters. Reference should be made to regional guidance to determine whether the inclusion of multiple products within a single application is considered appropriate.

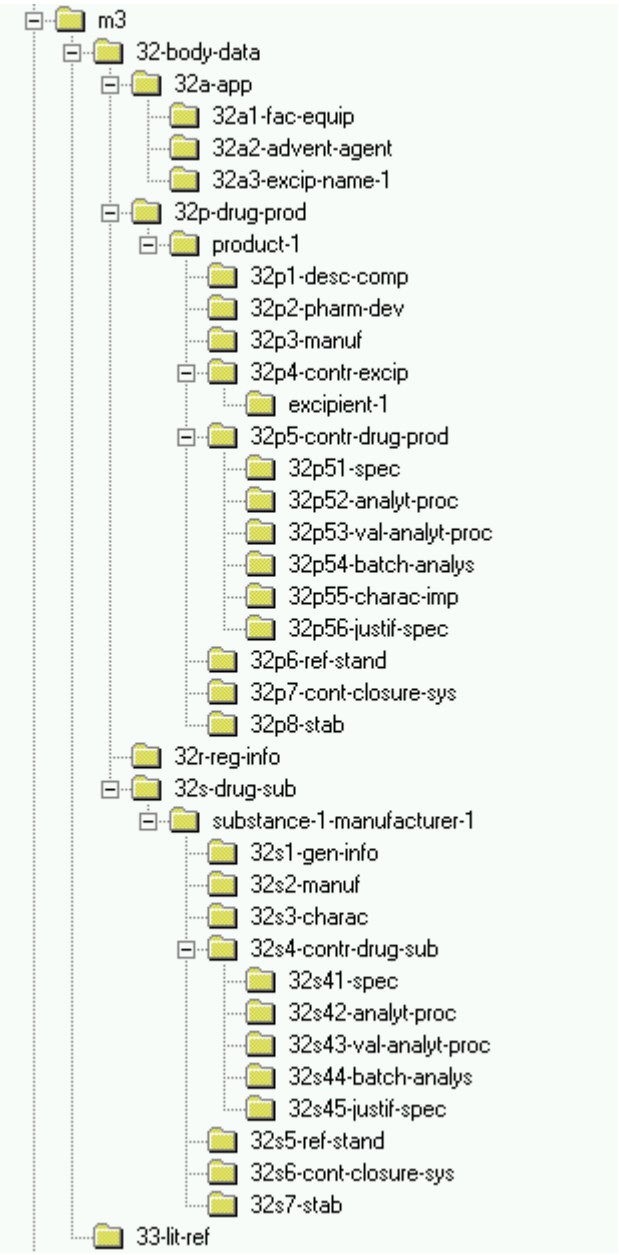
Section in CTD	Description	Folder Name
3.2.P.3	Manufacture (name, dosage form)	*32p3-manuf*
3.2.P.4	Control of Excipients (name, dosage form)	*32p4-contr-excip*
3.2.P.4	Control of Excipients (name, dosage form) - *Excipient 1*	*excipient-1*
3.2.P.5	Control of Drug Product (name, dosage form)	*32p5-contr-drug-prod*
3.2.P.5.1	Specification(s) (name, dosage form)	*32p51-spec*
3.2.P.5.2	Analytical Procedures (name, dosage form)	*32p52-analyt-proc*
3.2.P.5.3	Validation of Analytical Procedures (name, dosage form)	*32p53-val-analyt-proc*
3.2.P.5.4	Batch Analyses (name, dosage form)	*32p54-batch-analys*
3.2.P.5.5	Characterisation of Impurities (name, dosage form)	*32p55-charac-imp*
3.2.P.5.6	Justification of Specifications (name, dosage form)	*32p56-justif-spec*
3.2.P.6	Reference Standards or Materials (name, dosage form)	*32p6-ref-stand*
3.2.P.7	Container Closure System (name, dosage form)	*32p7-cont-closure-sys*
3.2.P.8	Stability (name, dosage form)	*32p8-stab*
3.2.A	Appendices	*32a-app*
3.2.A.1	Facilities and Equipment (name, manufacturer)	*32a1-fac-equip*
3.2.A.2	Adventitious Agents Safety Evaluation (name, dosage form, manufacturer)	*32a2-advent-agent*
3.2.A.3	Excipients- *Name* [4]	*32a3-excip-name-1*
3.2.R	Regional Information[5]	*32r-reg-info*
3.3	Literature References	*33-lit-ref*

[4] The folder name should include the name of the excipient, abbreviated as necessary to remain within the 64 character limit.

[5] This folder should be included where regional information is appropriate. Reference should be made to regional guidance for the types of information to be included in this section.

A representative folder hierarchy for module 3 is presented in the screenshot in figure 3-2.

Figure 3-2 Screenshot representation of the folder structure of module 3



Module 4 Nonclinical Study Reports

The name of the folder for module 4 should be *m4*. The folders in module 4 should be named as follows but can be further reduced or omitted to minimize path length issues.

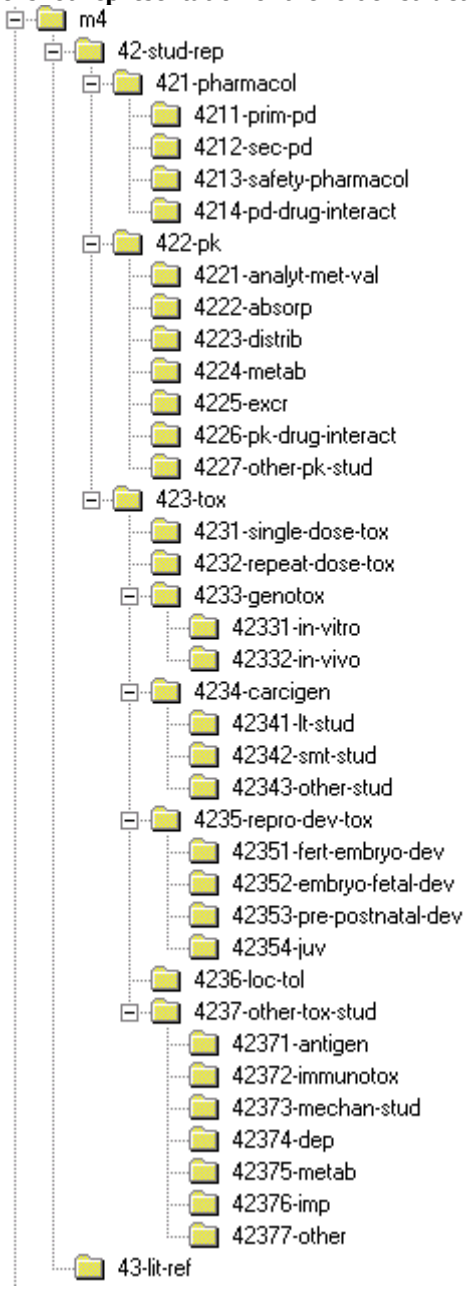
Table 3-4

Section in CTD	Description	Folder Name
4.2	Study Reports	*42-stud-rep*
4.2.1	Pharmacology	*421-pharmacol*
4.2.1.1	Primary Pharmacodynamics	*4211-prim-pd*
4.2.1.2	Secondary Pharmacodynamics	*4212-sec-pd*
4.2.1.3	Safety Pharmacology	*4213-safety-pharmacol*
4.2.1.4	Pharmacodynamic Drug Interactions	*4214-pd-drug-interact*
4.2.2	Pharmacokinetics	*422-pk*
4.2.2.1	Analytical Methods and Validation Reports (if separate reports are available)	*4221-analyt-met-val*
4.2.2.2	Absorption	*4222-absorp*
4.2.2.3	Distribution	*4223-distrib*
4.2.2.4	Metabolism	*4224-metab*
4.2.2.5	Excretion	*4225-excr*
4.2.2.6	Pharmacokinetic Drug Interactions (nonclinical)	*4226-pk-drug-interact*
4.2.2.7	Other Pharmacokinetic Studies	*4227-other-pk-stud*
4.2.3	Toxicology	*423-tox*
4.2.3.1	Single-Dose Toxicity (in order by species, by route)	*4231-single-dose-tox*
4.2.3.2	Repeat-Dose Toxicity (in order by species, by route, by duration, including supportive toxicokinetics evaluations)	*4232-repeat-dose-tox*
4.2.3.3	Genotoxicity	*4233-genotox*
4.2.3.3.1	In vitro	*42331-in-vitro*
4.2.3.3.2	In vivo (including supportive toxicokinetics evaluations)	*42332-in-vivo*
4.2.3.4	Carcinogenicity (including supportive toxicokinetics evaluations)	*4234-carcigen*
4.2.3.4.1	Long-term studies (in order by species, including range-finding studies that cannot be appropriately included under repeat-dose toxicity or pharmacokinetics)	*42341-lt-stud*

Section in CTD	Description	Folder Name
4.2.3.4.2	Short-or medium-term studies (including range-finding studies that cannot be appropriately included under repeat-dose toxicity or pharmacokinetics)	*42342-smt-stud*
4.2.3.4.3	Other studies	*42343-other-stud*
4.2.3.5	Reproductive and Developmental Toxicity (including range-finding studies and supportive toxicokinetics evaluations)	*4235-repro-dev-tox*
4.2.3.5.1	Fertility and early embryonic development	*42351-fert-embryo-dev*
4.2.3.5.2	Embryo-fetal development	*42352-embryo-fetal-dev*
4.2.3.5.3	Prenatal and postnatal development, including maternal function	*42353-pre-postnatal-dev*
4.2.3.5.4	Studies in which the offspring (juvenile animals) are dosed and/or further evaluated	*42354-juv*
4.2.3.6	Local Tolerance	*4236-loc-tol*
4.2.3.7	Other Toxicity Studies (if available)	*4237-other-tox-stud*
4.2.3.7.1	Antigenicity	*42371-antigen*
4.2.3.7.2	Immunotoxicity	*42372-immunotox*
4.2.3.7.3	Mechanistic studies (if not included elsewhere)	*42373-mechan-stud*
4.2.3.7.4	Dependence	*42374-dep*
4.2.3.7.5	Metabolites	*42375-metab*
4.2.3.7.6	Impurities	*42376-imp*
4.2.3.7.7	Other	*42377-other*
4.3	Literature References	*43-lit-ref*

A representative folder hierarchy for module 4 is presented in the screenshot in figure 3-3.

Figure 3-3 Screenshot representation of the folder structure of module 4



Module 5 Clinical Study Reports

The name of the folder for module 5 should be *m5*. The folders in module 5 should be named as follows but can be further reduced or omitted to minimize path length issues.

Table 3-5

Section in CTD	Description	Folder Name
5.2	Tabular Listing of all Clinical Studies	*52-tab-list*
5.3	Clinical Study Reports	*53-clin-stud-rep*
5.3.1	Reports of Biopharmaceutic Studies	*531-rep-biopharm-stud*
5.3.1.1	Bioavailability (BA) Study Reports	*5311-ba-stud-rep*
	"Study Report 1"	*study-report-1*
	"Study Report 2"	*study-report-2*
	"Study Report 3"	*study-report-3*
5.3.1.2	Comparative BA and Bioequivalence (BE) Study Reports	*5312-compar-ba-be-stud-rep*
	"Study Report 1"	*study-report-1*
	"Study Report 2"	*study-report-2*
	"Study Report 3"	*study-report-3*
5.3.1.3	In vitro – In vivo Correlation Study Reports	*5313-in-vitro-in-vivo-corr-stud-rep*
	"Study Report 1"	*study-report-1*
	"Study Report 2"	*study-report-2*
	"Study Report 3"	*study-report-3*
5.3.1.4	Reports of Bioanalytical and Analytical Methods for Human Studies	*5314-bioanalyt-analyt-met*
	"Study Report 1"	*study-report-1*
	"Study Report 2"	*study-report-2*
	"Study Report 3"	*study-report-3*
5.3.2	Reports of Studies Pertinent to Pharmacokinetics using Human Biomaterials	*532-rep-stud-pk-human-biomat*
5.3.2.1	Plasma Protein Binding Study Reports	*5321-plasma-prot-bind-stud-rep*
	"Study Report 1"	*study-report-1*
	"Study Report 2"	*study-report-2*
	"Study Report 3"	*study-report-3*

Section in CTD	Description	Folder Name
5.3.2.2	Reports of Hepatic Metabolism and Drug Interaction Studies	*5322-rep-hep-metab-interact-stud*
	"Study Report 1"	*study-report-1*
	"Study Report 2"	*study-report-2*
	"Study Report 3"	*study-report-3*
5.3.2.3	Reports of Studies Using Other Human Biomaterials	*5323-stud-other-human-biomat*
	"Study Report 1"	*study-report-1*
	"Study Report 2"	*study-report-2*
	"Study Report 3"	*study-report-3*
5.3.3	Reports of Human Pharmacokinetic (PK) Studies	*533-rep-human-pk-stud*
5.3.3.1	Healthy Subject PK and Initial Tolerability Study Reports	*5331-healthy-subj-pk-init-tol-stud-rep*
	"Study Report 1"	*study-report-1*
	"Study Report 2"	*study-report-2*
	"Study Report 3"	*study-report-3*
5.3.3.2	Patient PK and Initial Tolerability Study Reports	*5332-patient-pk-init-tol-stud-rep*
	"Study Report 1"	*study-report-1*
	"Study Report 2"	*study-report-2*
	"Study Report 3"	*study-report-3*
5.3.3.3	Intrinsic Factor PK Study Reports	*5333-intrin-factor-pk-stud-rep*
	"Study Report 1"	*study-report-1*
	"Study Report 2"	*study-report-2*
	"Study Report 3"	*study-report-3*
5.3.3.4	Extrinsic Factor PK Study Reports	*5334-extrin-factor-pk-stud-rep*
	"Study Report 1"	*study-report-1*
	"Study Report 2"	*study-report-2*
	"Study Report 3"	*study-report-3*
5.3.3.5	Population PK Study Reports	*5335-popul-pk-stud-rep*
	"Study Report 1"	*study-report-1*

Section in CTD	Description	Folder Name
	"Study Report 2"	*study-report-2*
	"Study Report 3"	*study-report-3*
5.3.4	Reports of Human Pharmacodynamic (PD) Studies	*534-rep-human-pd-stud*
5.3.4.1	Healthy Subject PD and PK/PD Study Reports	*5341-healthy-subj-pd-stud-rep*
	"Study Report 1"	*study-report-1*
	"Study Report 2"	*study-report-2*
	"Study Report 3"	*study-report-3*
5.3.4.2	Patient PD and PK/PD Study Reports	*5342-patient-pd-stud-rep*
	"Study Report 1"	*study-report-1*
	"Study Report 2"	*study-report-2*
	"Study Report 3"	*study-report-3*
5.3.5	Reports of Efficacy and Safety Studies	*535-rep-effic-safety-stud*
5.3.5	Reports of Efficacy and Safety Studies – *Indication Name*	*indication-1*
5.3.5.1	Study Reports of Controlled Clinical Studies Pertinent to the Claimed Indication	*5351-stud-rep-contr*
	"Study Report 1"	*study-report-1*
	"Study Report 2"	*study-report-2*
	"Study Report 3"	*study-report-3*
5.3.5.2	Study Reports of Uncontrolled Clinical Studies	*5352-stud-rep-uncontr*
	"Study Report 1"	*study-report-1*
	"Study Report 2"	*study-report-2*
	"Study Report 3"	*study-report-3*
5.3.5.3	Reports of Analyses of Data from More than One Study	*5353-rep-analys-data-more-one-stud*
	"Study Report 1"	*study-report-1*
	"Study Report 2"	*study-report-2*
	"Study Report 3"	*study-report-3*
5.3.5.4	Other Study Reports	*5354-other-stud-rep*
	"Study Report 1"	*study-report-1*

Section in CTD	Description	Folder Name
	"Study Report 2"	*study-report-2*
	"Study Report 3"	*study-report-3*
5.3.6	Reports of Postmarketing Experience	*536-postmark-exp*
5.3.7	Case Report Forms and Individual Patient Listings[6]	*537-crf-ipl*
	“Study Report 1”	*study-report-1*
	“Study Report 2”	*study-report-2*
	“Study Report 3”	*study-report-3*
5.4	Literature References	*54-lit-ref*

The CTD organization provides locations for case report forms and individual patient data listings in Module 5.3.7 and for literature references in Module 5.4.

In the eCTD, files for publications and literature references should be located in the folder for Module 5.4. However, in the index.xml file the leaf elements for these publications and literature references should be included under the same heading as the other study report files with additional information included through use of the study tagging file, if applicable in that region. In addition, a repeat of the leaf element should be placed under the heading for 5.4 Literature References.

Case report forms, data sets and individual patient data listings should be organized according to regional guidance.

[6] The content of this folder should follow regional guidance.

A representative folder hierarchy for module 5 is presented in the screenshot in figure 3-4.

Figure 3-4 Screenshot representation of the folder structure of module 5

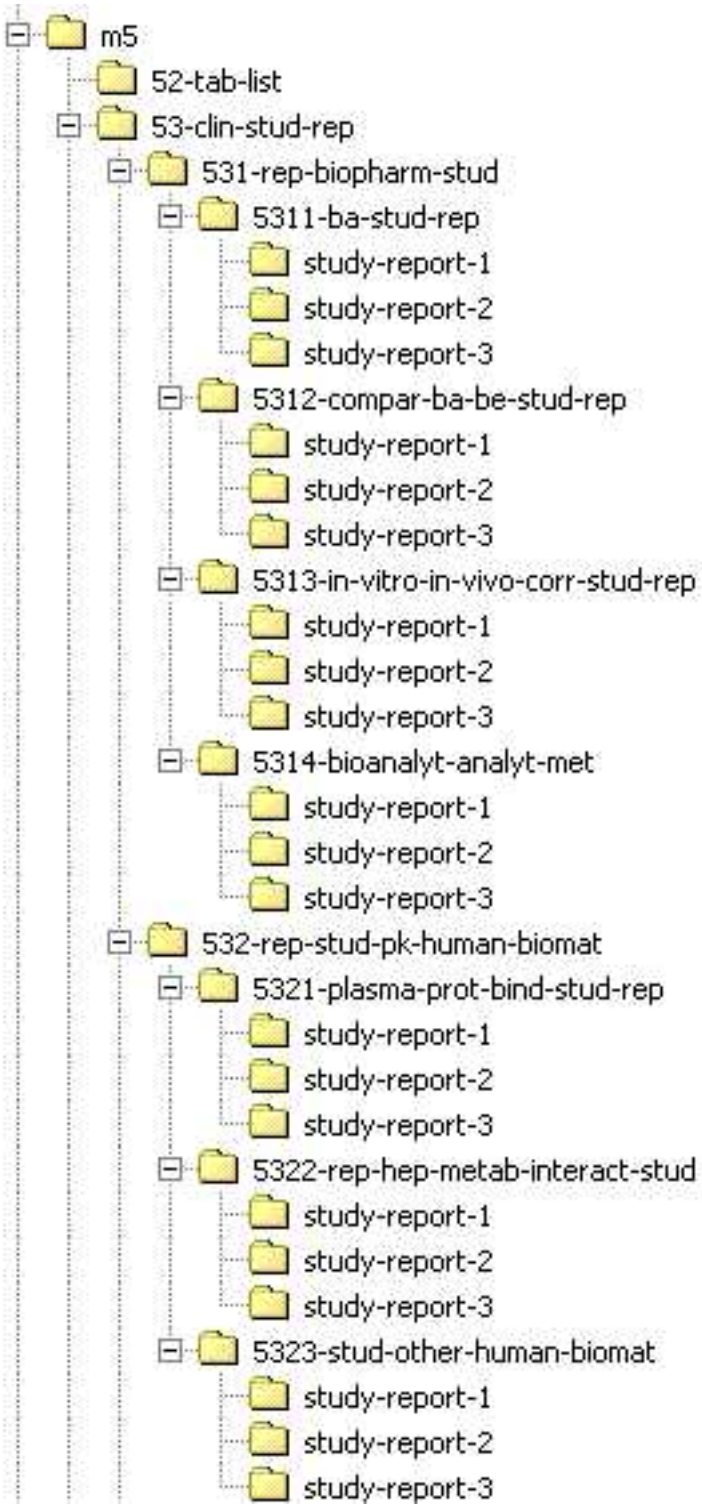


Figure 3-4 Screenshot representation of the folder structure of module 5 (cont)

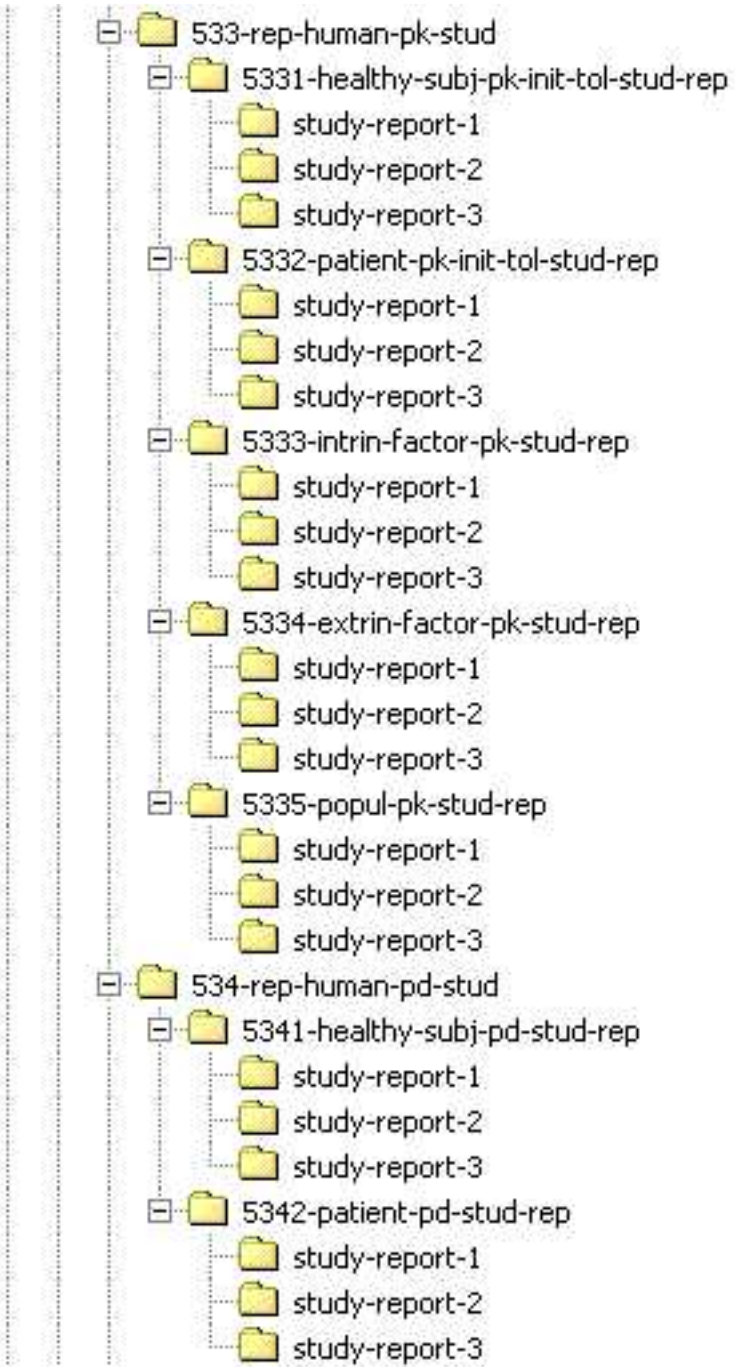
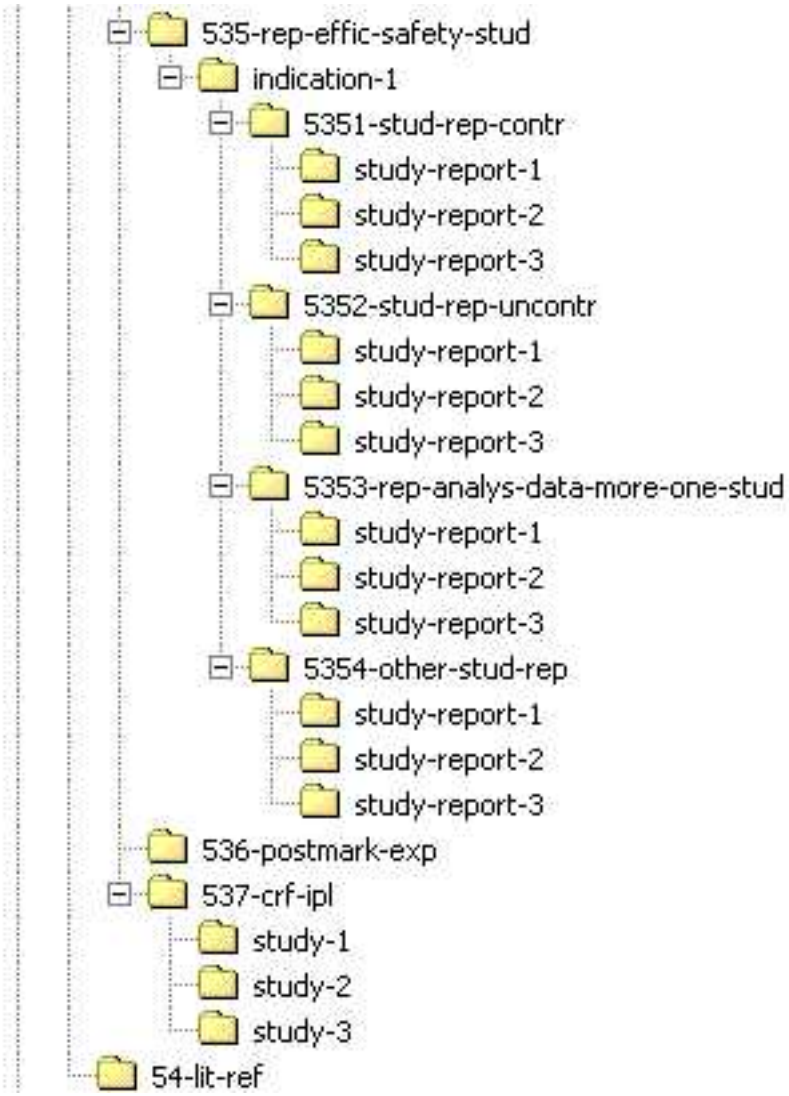


Figure 3-4 Screenshot representation of the folder structure of module 5 (cont)



Appendix 4: File Organization for the eCTD

Each item in the file organization table that is listed in this appendix includes the information outlined below:

Sequential number		Each item in the table has a unique sequentially assigned reference number. These reference numbers can change with each version of this appendix.
	Number	CTD section number
	Title	CTD title
	Element	Element name in the Backbone
	File/Directory	Relative path of the File/Directory. The file extension corresponds to the file type; i.e., the “pdf” extension is only illustrative. Refer to Table 6.1, Appendix 6, for details for the head of the path name
	Comment	Comments

The file organization table covers files that constitute the backbone itself plus any additional files to make the submission complete, readable and processable. The file and folder names shown within modules 2-5 are not mandatory, but recommended, and can be further reduced or omitted to avoid path length issues. Refer to the M4 Organisation Document: Granularity Annex in the ICH guidance on 'Organisation of the Common Technical Document for the Registration of Pharmaceuticals for Human Use' for information on where multiple documents/files are appropriate in each section or subsection of the eCTD. This describes what is considered to be the appropriate granularity for each section of the CTD and hence the eCTD. Where there is no definition provided in the organisation document, applicants are free to construct the dossier as they see fit with respect to document granularity.

Where file and folder names are presented in italics applicants would substitute these with appropriate file names in accordance with their own naming conventions.

Table 4-1

1	Number	
	Title	
	Element	
	File	index.xml
	Comment	This is the Backbone
2	Number	
	Title	
	Element	
	File	index-md5.txt
	Comment	The MD5 of the Backbone

3	Number	1
	Title	Administrative Information and Prescribing Information
	Element	m1-administrative-information-and-prescribing-information
	Directory	m1
	Comment	Only one of the regional directories is needed
4	Number	
	Title	
	Element	
	Directory	m1/eu
	Comment	EU directory: In addition to the appropriate regional documents, the regional xml instance should be located in this folder. Refer to regional guidance for details
5	Number	
	Title	
	Element	
	Directory	m1/jp
	Comment	Japan directory: In addition to the appropriate regional documents, the regional xml instance should be located in this folder. Refer to regional guidance for details
6	Number	
	Title	
	Element	
	Directory	m1/us
	Comment	US directory: In addition to the appropriate regional documents, the regional xml instance should be located in this folder. Refer to regional guidance for details
7	Number	
	Title	
	Element	
	Directory	m1/xx
	Comment	xx directory; where xx is a two character country code from ISO-3166-1. In addition to the appropriate regional documents, the regional xml instance should be located in this folder. Refer to regional guidance for details

8	Number	2
	Title	Common Technical Document Summaries
	Element	m2-common-technical-document-summaries
	Directory	m2
	Comment	
9	Number	2.2
	Title	Introduction
	Element	m2-2-introduction
	Directory	m2/22-intro
	Comment	
10	Number	2.2
	Title	Introduction
	Element	m2-2-introduction
	File	m2/22-intro/introduction.pdf
	Comment	
11	Number	2.3
	Title	Quality Overall Summary
	Element	m2-3-quality-overall-summary
	Directory	m2/23-qos
	Comment	Refer to the Granularity Annex of the M4 Organisation Document for guidance on the flexibility of multiple documents for the Quality Overall Summary
12	Number	2.3
	Title	Introduction
	Element	m2-3-introduction
	File	m2/23-qos/introduction.pdf
	Comment	
13	Number	2.3.S
	Title	Drug Substance - *Name* - *Manufacturer*
	Element	m2-3-s-drug-substance
	File	m2/23-qos/drug-substance.pdf

	Comment	Refer to the Granularity Annex of the M4 Organisation Document for guidance on the flexibility of multiple documents for the Quality Overall Summary Where there are more than one drug substance and/or manufacturer, separate files can be provided for each.
14	Number	2.3.P
	Title	Drug Product -*Name*
	Element	m2-3-p-drug-product
	File	m2/23-qos/drug-product-*name*.pdf
	Comment	Refer to the Granularity Annex of the M4 Organisation Document for guidance on the flexibility of multiple documents for the Quality Overall Summary Refer to regional guidance for definition of what constitutes a drug product and the acceptability of more than one drug product in an application. Where more than one drug product is acceptable in an application, a separate file can be provided for each drug product.
15	Number	2.3.A
	Title	Appendices
	Element	m2-3-a-appendices
	File	m2/23-qos/appendices.pdf
	Comment	Refer to the Granularity Annex of the M4 Organisation Document for guidance on the flexibility of multiple documents for the Quality Overall Summary
16	Number	2.3.R
	Title	Regional Information
	Element	m2-3-r-regional-information
	File	m2/23-qos/regional-information.pdf
	Comment	Refer to the Granularity Annex of the M4 Organisation Document for guidance on the flexibility of multiple documents for the Quality Overall Summary
17	Number	2.4
	Title	Nonclinical Overview
	Element	m2-4-nonclinical-overview
	Directory	m2/24-nonclin-over
	Comment	
18	Number	2.4
	Title	Nonclinical Overview
	Element	m2-4-nonclinical-overview
	File	m2/24-nonclin-over/nonclinical-overview.pdf
	Comment	Typically, this document should consist of a single file. The CTD defines further heading levels and navigation should be provided within the document to these sub-headings.

19	Number	2.5
	Title	Clinical Overview
	Element	m2-5-clinical-overview
	Directory	m2/25-clin-over
	Comment	
20	Number	2.5
	Title	Clinical Overview
	Element	m2-5-clinical-overview
	File	m2/25-clin-over/clinical-overview.pdf
	Comment	Typically, this document should consist of a single file. The CTD defines further heading levels and navigation should be provided within the document to these sub-headings.
21	Number	2.6
	Title	Nonclinical Written and Tabulated Summaries
	Element	m2-6-nonclinical-written-and-tabulated-summaries
	Directory	m2/26-nonclin-sum
	Comment	
22	Number	2.6.1
	Title	Introduction
	Element	m2-6-1-introduction
	File	m2/26-nonclin-sum/introduction.pdf
	Comment	
23	Number	2.6.2
	Title	Pharmacology Written Summary
	Element	m2-6-2-pharmacology-written-summary
	File	m2/26-nonclin-sum/pharmacol-written-summary.pdf
	Comment	Typically, this document should consist of a single file. The CTD defines further heading levels and navigation should be provided within the document to these sub-headings.
24	Number	2.6.3
	Title	Pharmacology Tabulated Summary
	Element	m2-6-3-pharmacology-tabulated-summary
	File	m2/26-nonclin-sum/pharmacol-tabulated-summary.pdf
	Comment	Should have further navigation via bookmarks
25	Number	2.6.4

	Title	Pharmacokinetics Written Summary
	Element	m2-6-4-pharmacokinetics-written-summary
	File	m2/26-nonclin-sum/pharmkin-written-summary.pdf
	Comment	Typically, this document should consist of a single file. The CTD defines further heading levels and navigation should be provided within the document to these sub-headings.
26	Number	2.6.5
	Title	Pharmacokinetics Tabulated Summary
	Element	m2-6-5-pharmacokinetics-tabulated-summary
	File	m2/26-nonclin-sum/pharmkin-tabulated-summary.pdf
	Comment	Should have further navigation via bookmarks
27	Number	2.6.6
	Title	Toxicology Written Summary
	Element	m2-6-6-toxicology-written-summary
	File	m2/26-nonclin-sum/toxicology-written-summary.pdf
	Comment	Typically, this document should consist of a single file. The CTD defines further heading levels and navigation should be provided within the document to these sub-headings.
28	Number	2.6.7
	Title	Toxicology Tabulated Summary
	Element	m2-6-7-toxicology-tabulated-summary
	File	m2/26-nonclin-sum/toxicology-tabulated-summary.pdf
	Comment	Should have further navigation via bookmarks
29	Number	2.7
	Title	Clinical Summary
	Element	m2-7-clinical-summary
	Directory	m2/27-clin-sum
	Comment	
30	Number	2.7.1
	Title	Summary of Biopharmaceutic Studies and Associated Analytical Methods
	Element	m2-7-1-summary-of-biopharmaceutic-studies-and-associated-analytical-methods
	File	m2/27-clin-sum/summary-biopharm.pdf
	Comment	Typically, this document should consist of a single file. The CTD defines further heading levels and navigation should be provided within the document to these sub-headings.
31	Number	2.7.2
	Title	Summary of Clinical Pharmacology Studies

	Element	m2-7-2-summary-of-clinical-pharmacology-studies
	File	m2/27-clin-sum/summary-clin-pharm.pdf
	Comment	Typically, this document should consist of a single file. The CTD defines further heading levels and navigation should be provided within the document to these sub-headings.
32	Number	2.7.3
	Title	Summary of Clinical Efficacy – *Indication*
	Element	m2-7-3-summary-of-clinical-efficacy
	File	m2/27-clin-sum/summary-clin-efficacy-*indication.pdf*
	Comment	The file name should always include the indication being claimed (abbreviated if appropriate) e.g., 'summary-clin-efficacy-asthma.pdf'. Where there is more than one indication (e.g., asthma & migraine) then the first indication has a file name 'summary-clin-efficacy-asthma.pdf' and the second 'summary-clin-efficacy-migraine.pdf'. Typically, this document should consist of a single file. The CTD defines further heading levels and navigation should be provided within the document to these sub-headings. The 'indication' attribute in the backbone should be consistent with that used in the filename but can be different. For example, an 'indication' attribute value of 'Non-Small Cell Lung Cancer' could be expressed as 'NSCLC' in the filename for that document (i.e., summclineff-nsclc.pdf). There is currently no standard terminology list for 'indication' and applicants should choose these attributes carefully as they can not be easily changed during the life cycle of the application. The only way this can be accomplished currently is to delete all the leaf elements with the incorrect attribute value and provide new leaf elements for those files with the modified attribute value. Applicants should consult with the regional authority before attempting to modify these attributes to discuss the appropriateness of, and approach to be taken for, this type of change.
33	Number	2.7.4
	Title	Summary of Clinical Safety
	Element	m2-7-4-summary-of-clinical-safety
	File	m2/27-clin-sum/summary-clin-safety.pdf
	Comment	Typically, this document should consist of a single file. The CTD defines further heading levels and navigation should be provided within the document to these sub-headings.
34	Number	2.7.5
	Title	Literature References
	Element	m2-7-5-literature-references
	File	m2/27-clin-sum/literature-references.pdf
	Comment	
35	Number	2.7.6
	Title	Synopses of Individual Studies
	Element	m2-7-6-synopses-of-individual-studies

	File	m2/27-clin-sum/synopses-indiv-studies.pdf
	Comment	These synopses should already be located in the Clinical Study Reports in Module 5 and should not, therefore, be repeated in Module 2. It is considered sufficient to provide hyperlinks from the listing of the studies, located here, to the locations of the synopses in Module 5.

36	Number	3
	Title	Quality
	Element	m3-quality
	Directory	m3
	Comment	Refer to the Granularity Annex of the M4 Organisation Document for guidance on the flexibility of multiple documents for Module 3
37	Number	3.2
	Title	Body of Data
	Element	m3-2-body-of-data
	Directory	m3/32-body-data
	Comment	
38	Number	3.2.S
	Title	Drug Substance
	Element	m3-2-s-drug-substance
	Directory	m3/32-body-data/32s-drug-sub
	Comment	
39	Number	3.2.S
	Title	Drug Substance - *Drug Substance Name - Manufacturer*
	Element	m3-2-s-drug-substance
	Directory	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*
	Comment	In this section, it can be helpful if the folder name includes the name of the drug substance and manufacturer. This applies particularly when there are multiple drug substances and/or manufacturers. When naming folders, attention should be paid to the length of the name of the folder on the overall length of the full path. Abbreviations can help control the length of the path. The 'substance' and 'manufacturer' attribute values in the backbone should be consistent with that used in the folder name but can be different. For example, a 'manufacturer' attribute value of 'Company XXX, City Name, Country Name' could be expressed as 'xxx' in the folder name. There is currently no standard terminology list for these attributes and applicants should choose these attributes carefully as they can not be easily changed during the life cycle of the application. The only way this can be accomplished currently is to delete all the leaf elements with the incorrect attribute value and provide new leaf elements for those files with the modified attribute value. Applicants should consult with the regional authority before attempting to modify these attributes to discuss the appropriateness of, and approach to be taken for, this type of change.
40	Number	3.2.S.1
	Title	General Information (name, manufacturer)

	Element	m3-2-s-1-general-information
	Directory	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s1-gen-info
	Comment	
41	Number	3.2.S.1.1
	Title	Nomenclature (name, manufacturer)
	Element	m3-2-s-1-1-nomenclature
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s1-gen-info/nomenclature.pdf
	Comment	
42	Number	3.2.S.1.2
	Title	Structure (name, manufacturer)
	Element	m3-2-s-1-2-structure
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s1-gen-info/structure.pdf
	Comment	
43	Number	3.2.S.1.3
	Title	General Properties (name, manufacturer)
	Element	m3-2-s-1-3-general-properties
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s1-gen-info/general-properties.pdf
	Comment	
44	Number	3.2.S.2
	Title	Manufacture (name, manufacturer)
	Element	m3-2-s-2-manufacture
	Directory	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s2-manuf
	Comment	
45	Number	3.2.S.2.1
	Title	Manufacturer(s) (name, manufacturer)
	Element	m3-2-s-2-1-manufacturer
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s2-manuf/manufacturer.pdf
	Comment	For this document there should be only information regarding one manufacturer
46	Number	3.2.S.2.2
	Title	Description of Manufacturing Process and Process Controls (name, manufacturer)
	Element	m3-2-s-2-2-description-of-manufacturing-process-and-process-controls
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s2-manuf/manuf-process-and-controls.pdf
	Comment	

47	Number	3.2.S.2.3
	Title	Control of Materials (name, manufacturer)
	Element	m3-2-s-2-3-control-of-materials
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s2-manuf/control-of-materials.pdf
	Comment	
48	Number	3.2.S.2.4
	Title	Controls of Critical Steps and Intermediates (name, manufacturer)
	Element	m3-2-s-2-4-controls-of-critical-steps-and-intermediates
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s2-manuf/control-critical-steps.pdf
	Comment	
49	Number	3.2.S.2.5
	Title	Process Validation and/or Evaluation (name, manufacturer)
	Element	m3-2-s-2-5-process-validation-and-or-evaluation
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s2-manuf/process-validation.pdf
	Comment	
50	Number	3.2.S.2.6
	Title	Manufacturing Process Development (name, manufacturer)
	Element	m3-2-s-2-6-manufacturing-process-development
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s2-manuf/manuf-process-development.pdf
	Comment	
51	Number	3.2.S.3
	Title	Characterisation (name, manufacturer)
	Element	m3-2-s-3-characterisation
	Directory	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s3-charac
	Comment	
52	Number	3.2.S.3.1
	Title	Elucidation of Structure and Other Characteristics (name, manufacturer)
	Element	m3-2-s-3-1-elucidation-of-structure-and-other-characteristics
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s3-charac/elucidation-of-structure.pdf
	Comment	
53	Number	3.2.S.3.2
	Title	Impurities (name, manufacturer)
	Element	m3-2-s-3-2-impurities

	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s3-charac/impurities.pdf
	Comment	
54	Number	3.2.S.4
	Title	Control of Drug Substance (name, manufacturer)
	Element	m3-2-s-4-control-of-drug-substance
	Directory	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s4-contr-drug-sub
	Comment	
55	Number	3.2.S.4.1
	Title	Specification (name, manufacturer)
	Element	m3-2-s-4-1-specification
	Directory	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s4-contr-drug-sub/32s41-spec
	Comment	
56	Number	3.2.S.4.1
	Title	Specification (name, manufacturer)
	Element	m3-2-s-4-1-specification
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s4-contr-drug-sub/32s41-spec/specification.pdf
	Comment	
57	Number	3.2.S.4.2
	Title	Analytical Procedures (name, manufacturer)
	Element	m3-2-s-4-2-analytical-procedures
	Directory	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s4-contr-drug-sub/32s42-analyt-proc
	Comment	The example below shows how a multiple file approach, where a separate file is provided for each analytical procedure, can be organized. CTD numbering is not defined below this level (e.g., 3.2.S.4.2.1).
58	Number	
	Title	*Analytical Procedure-1*
	Element	m3-2-s-4-2-analytical-procedures
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s4-contr-drug-sub/32s42-analyt-proc/*analytical-procedure-1.pdf*
	Comment	
59	Number	
	Title	*Analytical Procedure-2*
	Element	m3-2-s-4-2-analytical-procedures
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s4-contr-drug-sub/32s42-analyt-proc/*analytical-procedure-2.pdf*
	Comment	

60	Number	
	Title	*Analytical Procedure-3*
	Element	m3-2-s-4-2-analytical-procedures
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s4-contr-drug-sub/32s42-analyt-proc/*analytical-procedure-3.pdf*
	Comment	
61	Number	3.2.S.4.3
	Title	Validation of Analytical Procedures
	Element	m3-2-s-4-3-validation-of-analytical-procedures (name, manufacturer)
	Directory	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s4-contr-drug-sub/32s43-val-analyt-proc
	Comment	The example below shows how a multiple file approach, where a separate file is provided for each analytical procedure, can be organized. CTD numbering is not defined below this level (e.g., 3.2.S.4.3.1).
62	Number	
	Title	*Validation of Analytical Procedure-1*
	Element	m3-2-s-4-3-validation-of-analytical-procedures
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s4-contr-drug-sub/32s43-val-analyt-proc/*validation-analyt-procedure-1.pdf*
	Comment	
63	Number	
	Title	*Validation of Analytical Procedure-2*
	Element	m3-2-s-4-3-validation-of-analytical-procedures
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s4-contr-drug-sub/32s43-val-analyt-proc/*validation-analyt-procedure-2.pdf*
	Comment	
64	Number	
	Title	*Validation of Analytical Procedure-3*
	Element	m3-2-s-4-3-validation-of-analytical-procedures
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s4-contr-drug-sub/32s43-val-analyt-proc/*validation-analyt-procedure-3.pdf*
	Comment	
65	Number	3.2.S.4.4
	Title	Batch Analyses (name, manufacturer)
	Element	m3-2-s-4-4-batch-analyses
	Directory	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s4-contr-drug-sub/32s44-batch-analys
	Comment	
66	Number	3.2.S.4.4

	Title	Batch Analyses (name, manufacturer)
	Element	m3-2-s-4-4-batch-analyses
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s4-contr-drug-sub/32s44-batch-analys/batch-analyses.pdf
	Comment	
67	Number	3.2.S.4.5
	Title	Justification of Specification (name, manufacturer)
	Element	m3-2-s-4-5-justification-of-specification
	Directory	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s4-contr-drug-sub/32s45-justif-spec
	Comment	
68	Number	3.2.S.4.5
	Title	Justification of Specification (name, manufacturer)
	Element	m3-2-s-4-5-justification-of-specification
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s4-contr-drug-sub/32s45-justif-spec/justification-of-specification.pdf
	Comment	
69	Number	3.2.S.5
	Title	Reference Standards or Materials (name, manufacturer)
	Element	m3-2-s-5-reference-standards-or-materials
	Directory	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s5-ref-stand
	Comment	
70	Number	3.2.S.5
	Title	Reference Standards or Materials (name, manufacturer)
	Element	m3-2-s-5-reference-standards-or-materials
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s5-ref-stand/reference-standards.pdf
	Comment	Where a multiple file approach is taken for this section, the file names should indicate which reference standard is covered in the document.
71	Number	3.2.S.6
	Title	Container Closure System (name, manufacturer)
	Element	m3-2-s-6-container-closure-system
	Directory	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s6-cont-closure-sys
	Comment	
72	Number	3.2.S.6
	Title	Container Closure System (name, manufacturer)
	Element	m3-2-s-6-container-closure-system
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s6-cont-closure-sys/container-closure-system.pdf

	Comment	
73	Number	3.2.S.7
	Title	Stability (name, manufacturer)
	Element	m3-2-s-7-stability
	Directory	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s7-stab
	Comment	
74	Number	3.2.S.7.1
	Title	Stability Summary and Conclusions (name, manufacturer)
	Element	m3-2-s-7-1-stability-summary-and-conclusions
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s7-stab/stability-summary.pdf
	Comment	
75	Number	3.2.S.7.2
	Title	Post-approval Stability Protocol and Stability Commitment (name, manufacturer)
	Element	m3-2-s-7-2-post-approval-stability-protocol-and-stability-commitment
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s7-stab/postapproval-stability.pdf
	Comment	
76	Number	3.2.S.7.3
	Title	Stability Data (name, manufacturer)
	Element	m3-2-s-7-3-stability-data
	File	m3/32-body-data/32s-drug-sub/*substance-1-manufacturer-1*/32s7-stab/stability-data.pdf
	Comment	
77	Number	3.2.P
	Title	Drug Product (name, dosage form)
	Element	m3-2-p-drug-product
	Directory	m3/32-body-data/32p-drug-prod
	Comment	
78	Number	3.2.P
	Title	Drug Product (name, dosage form) – *Name*
	Element	m3-2-p-drug-product
	Directory	m3/32-body-data/32p-drug-prod/*product-1*

	Comment	In this section, it can be helpful if the folder name includes the name of the drug product. This applies particularly where there is more than one drug product (e.g., powder for reconstitution and diluent); the first drug product would have a folder 'powder-for-reconstitution' and the second, 'diluent'. Refer to regional guidance for definition of what constitutes a drug product and the acceptability of more than one drug product in an application. The 'product-name' attribute value in the backbone should be consistent with that used in the folder name but can be different. For example, a 'product-name' attribute value of 'Lyophilized Powder for Reconstitution' could be expressed as 'powder' in the folder name. There is currently no standard terminology list for these attributes and applicants should choose these attributes carefully as they can not be easily changed during the life cycle of the application. The only way this can be accomplished currently is to delete all the leaf elements with the incorrect attribute value and provide new leaf elements for those files with the modified attribute value. Applicants should consult with the regional authority before attempting to modify these attributes to discuss the appropriateness of, and approach to be taken for, this type of change.
79	Number	3.2.P.1
	Title	Description and Composition of the Drug Product (name, dosage form)
	Element	m3-2-p-1-description-and-composition-of-the-drug-product
	Directory	m3/32-body-data/32p-drug-prod/*product-1*/32p1-desc-comp
	Comment	
80	Number	3.2.P.1
	Title	Description and Composition of the Drug Product (name, dosage form)
	Element	m3-2-p-1-description-and-composition-of-the-drug-product
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p1-desc-comp/description-and-composition.pdf
	Comment	
81	Number	3.2.P.2
	Title	Pharmaceutical Development (name, dosage form)
	Element	m3-2-p-2-pharmaceutical-development
	Directory	m3/32-body-data/32p-drug-prod*/product-1*/32p2-pharm-dev
	Comment	Refer to the M4 Organisation Document: Granularity Annex for guidance on the flexibility of multiple documents for the Pharmaceutical Development section.
82	Number	3.2.P.2
	Title	Pharmaceutical Development (name, dosage form)
	Element	m3-2-p-2-pharmaceutical-development
	File	m3/32-body-data/32p-drug-prod*/product-1*/32p2-pharm-dev/pharmaceutical-development.pdf

	Comment	Refer to the M4 Organisation Document: Granularity Annex for guidance on the flexibility of multiple documents for the Pharmaceutical Development section.
83	Number	3.2.P.3
	Title	Manufacture (name, dosage form)
	Element	m3-2-p-3-manufacture
	Directory	m3/32-body-data/32p-drug-prod/*product-1*/32p3-manuf
	Comment	
84	Number	3.2.P.3.1
	Title	Manufacturer(s) (name, dosage form)
	Element	m3-2-p-3-1-manufacturers
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p3-manuf/manufacturers.pdf
	Comment	
85	Number	3.2.P.3.2
	Title	Batch Formula (name, dosage form)
	Element	m3-2-p-3-2-batch-formula
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p3-manuf/batch-formula.pdf
	Comment	
86	Number	3.2.P.3.3
	Title	Description of Manufacturing Process and Process Controls (name, dosage form)
	Element	m3-2-p-3-3-description-of-manufacturing-process-and-process-controls
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p3-manuf/manuf-process-and-controls.pdf
	Comment	
87	Number	3.2.P.3.4
	Title	Controls of Critical Steps and Intermediates (name, dosage form)
	Element	m3-2-p-3-4-controls-of-critical-steps-and-intermediates
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p3-manuf/control-critical-steps.pdf
	Comment	
88	Number	3.2.P.3.5
	Title	Process Validation and/or Evaluation (name, dosage form)
	Element	m3-2-p-3-5-process-validation-and-or-evaluation
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p3-manuf/process-validation.pdf
	Comment	The applicant has the option to submit one or multiple files, one for each validation or evaluation.

89	Number	3.2.P.4
	Title	Control of Excipients (name, dosage form)
	Element	m3-2-p-4-control-of-excipients
	Directory	m3/32-body-data/32p-drug-prod/*product-1*/32p4-contr-excip
	Comment	
90	Number	3.2.P.4
	Title	Control of Excipients (name, dosage form) – *Excipient*
	Element	m3-2-p-4-control-of-excipients
	Directory	m3/32-body-data/32p-drug-prod/*product-1*/32p4-contr-excip/*excipient-1*
	Comment	For a drug product containing more than one excipient, the information requested for sections 3.2.P.4.1 – 3.2.P.4.4 should be provided in its entirety for each excipient. Refer to the ICH eCTD QA and Change Requests document, Q&A No.4 for additional suggestions on structuring this section. For compendial excipient(s) without additional specification tests, it is appropriate to have all information in one file, making sure to introduce a folder for each of new documents to avoid mixing files and folders at the same level. Non-compendial excipients should follow the structure outlined below. The 'excipient' attribute value in the backbone should be consistent with that used in the folder name but can be different. There is currently no standard terminology list for these attributes and applicants should choose these attributes carefully as they can not be easily changed during the life cycle of the application. The only way this can be accomplished currently is to delete all the leaf elements with the incorrect attribute value and provide new leaf elements for those files with the modified attribute value. Applicants should consult with the regional authority before attempting to modify these attributes to discuss the appropriateness of, and approach to be taken for, this type of change.
91	Number	3.2.P.4.1
	Title	Specifications (name, dosage form)
	Element	m3-2-p-4-1-specifications
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p4-contr-excip/*excipient-1*/specifications.pdf
	Comment	See comment under 3.2.P.4.
92	Number	3.2.P.4.2
	Title	Analytical Procedures (name, dosage form)
	Element	m3-2-p-4-2-analytical-procedures
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p4-contr-excip/*excipient-1*/analytical-procedures.pdf
	Comment	See comment under 3.2.P.4.
93	Number	3.2.P.4.3
	Title	Validation of Analytical Procedures (name, dosage form)
	Element	m3-2-p-4-3-validation-of-analytical-procedures

	File	m3/32-body-data/32p-drug-prod/*product-1*/32p4-contr-excip/*excipient-1*/validation-analyt-procedures.pdf
	Comment	See comment under 3.2.P.4.
94	Number	3.2.P.4.4
	Title	Justification of Specifications (name, dosage form)
	Element	m3-2-p-4-4-justification-of-specifications
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p4-contr-excip/*excipient-1*/justification-of-specifications.pdf
	Comment	See comment under 3.2.P.4.
95	Number	3.2.P.4.5
	Title	Excipients of Human or Animal Origin (name, dosage form)
	Element	m3-2-p-4-5-excipients-of-human-or-animal-origin
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p4-contr-excip/excipients-human-animal.pdf
	Comment	
96	Number	3.2.P.4.6
	Title	Novel Excipients (name, dosage form)
	Element	m3-2-p-4-6-novel-excipients
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p4-contr-excip/novel-excipients.pdf
	Comment	
97	Number	3.2.P.5
	Title	Control of Drug Product (name, dosage form)
	Element	m3-2-p-5-control-of-drug-product
	Directory	m3/32-body-data/32p-drug-prod/*product-1*/32p5-contr-drug-prod
	Comment	
98	Number	3.2.P.5.1
	Title	Specification(s) (name, dosage form)
	Element	m3-2-p-5-1-specifications
	Directory	m3/32-body-data/32p-drug-prod/*product-1*/32p5-contr-drug-prod/32p51-spec
	Comment	
99	Number	3.2.P.5.1
	Title	Specification(s) (name, dosage form)
	Element	m3-2-p-5-1-specifications
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p5-contr-drug-prod/32p51-spec/specifications.pdf
	Comment	
100	Number	3.2.P.5.2

	Title	Analytical Procedures (name, dosage form)
	Element	m3-2-p-5-2-analytical-procedures
	Directory	m3/32-body-data/32p-drug-prod/*product-1*/32p5-contr-drug-prod/32p52-analyt-proc
	Comment	The example below shows how a multiple file approach, where a separate file is provided for each analytical procedure, may be organized. CTD numbering is not defined below this level (e.g., 3.2.P.5.2.1).
101	Number	
	Title	*Analytical Procedure – 1*
	Element	m3-2-p-5-2-analytical-procedures
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p5-contr-drug-prod/32p52-analyt-proc/*analytical-procedure-1.pdf*
	Comment	
102	Number	
	Title	*Analytical Procedure – 2*
	Element	m3-2-p-5-2-analytical-procedures
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p5-contr-drug-prod/32p52-analyt-proc/*analytical-procedure-2.pdf*
	Comment	
103	Number	
	Title	*Analytical Procedure – 3*
	Element	m3-2-p-5-2-analytical-procedures
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p5-contr-drug-prod/32p52-analyt-proc/*analytical-procedure-3.pdf*
	Comment	
104	Number	3.2.P.5.3
	Title	Validation of Analytical Procedures (name, dosage form)
	Element	m3-2-p-5-3-validation-of-analytical-procedures
	Directory	m3/32-body-data/32p-drug-prod/*product-1*/32p5-contr-drug-prod/32p53-val-analyt-proc
	Comment	The example below shows how a multiple file approach, where a separate file is provided for each analytical procedure, may be organized. CTD numbering is not defined below this level (e.g., 3.2.P.5.3.1).
105	Number	
	Title	*Validation of Analytical Procedures – 1*
	Element	m3-2-p-5-3-validation-of-analytical-procedures
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p5-contr-drug-prod/32p53-val-analyt-proc/*validation-analytical-procedures-1.pdf*
	Comment	
106	Number	
	Title	*Validation of Analytical Procedures – 2*

	Element	m3-2-p-5-3-validation-of-analytical-procedures
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p5-contr-drug-prod/32p53-val-analyt-proc/*validation-analytical-procedures-2.pdf*
	Comment	
107	Number	
	Title	*Validation of Analytical Procedures – 3*
	Element	m3-2-p-5-3-validation-of-analytical-procedures
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p5-contr-drug-prod/32p53-val-analyt-proc/*validation-analytical-procedures-3.pdf*
	Comment	
108	Number	3.2.P.5.4
	Title	Batch Analyses (name, dosage form)
	Element	m3-2-p-5-4-batch-analyses
	Directory	m3/32-body-data/32p-drug-prod/*product-1*/32p5-contr-drug-prod/32p54-batch-analys
	Comment	
109	Number	3.2.P.5.4
	Title	Batch Analyses (name, dosage form)
	Element	m3-2-p-5-4-batch-analyses
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p5-contr-drug-prod/32p54-batch-analys/batch-analyses.pdf
	Comment	
110	Number	3.2.P.5.5
	Title	Characterisation of Impurities (name, dosage form)
	Element	m3-2-p-5-5-characterisation-of-impurities
	Directory	m3/32-body-data/32p-drug-prod/*product-1*/32p5-contr-drug-prod/32p55-charac-imp
	Comment	
111	Number	3.2.P.5.5
	Title	Characterisation of Impurities (name, dosage form)
	Element	m3-2-p-5-5-characterisation-of-impurities
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p5-contr-drug-prod/32p55-charac-imp/characterisation-impurities.pdf
	Comment	
112	Number	3.2.P.5.6
	Title	Justification of Specifications (name, dosage form)
	Element	m3-2-p-5-6-justification-of-specifications
	Directory	m3/32-body-data/32p-drug-prod/*product-1*/32p5-contr-drug-prod/32p56-justif-spec
	Comment	

113	Number	3.2.P.5.6
	Title	Justification of Specifications (name, dosage form)
	Element	m3-2-p-5-6-justification-of-specifications
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p5-contr-drug-prod/32p56-justif-spec/justification-of-specifications.pdf
	Comment	
114	Number	3.2.P.6
	Title	Reference Standards or Materials (name, dosage form)
	Element	m3-2-p-6-reference-standards-or-materials
	Directory	m3/32-body-data/32p-drug-prod/*product-1*/32p6-ref-stand
	Comment	
115	Number	3.2.P.6
	Title	Reference Standards or Materials (name, dosage form)
	Element	m3-2-p-6-reference-standards-or-materials
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p6-ref-stand/reference-standards.pdf
	Comment	When a multiple file approach is taken for this section, the file names should indicate which reference standard is covered in the document.
116	Number	3.2.P.7
	Title	Container Closure System (name, dosage form)
	Element	m3-2-p-7-container-closure-system
	Directory	m3/32-body-data/32p-drug-prod/*product-1*/32p7-cont-closure-sys
	Comment	
117	Number	3.2.P.7
	Title	Container Closure System (name, dosage form)
	Element	m3-2-p-7-container-closure-system
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p7-cont-closure-sys/container-closure-system.pdf
	Comment	
118	Number	3.2.P.8
	Title	Stability (name, dosage form)
	Element	m3-2-p-8-stability
	Directory	m3/32-body-data/32p-drug-prod/*product-1*/32p8-stab
	Comment	
119	Number	3.2.P.8.1
	Title	Stability Summary and Conclusion (name, dosage form)
	Element	m3-2-p-8-1-stability-summary-and-conclusion

	File	m3/32-body-data/32p-drug-prod/*product-1*/32p8-stab/stability-summary.pdf
	Comment	
120	Number	3.2.P.8.2
	Title	Post-approval Stability Protocol and Stability Commitment (name, dosage form)
	Element	m3-2-p-8-2-post-approval-stability-protocol-and-stability-commitment
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p8-stab/postapproval-stability.pdf
	Comment	
121	Number	3.2.P.8.3
	Title	Stability Data (name, dosage form)
	Element	m3-2-p-8-3-stability-data
	File	m3/32-body-data/32p-drug-prod/*product-1*/32p8-stab/stability-data.pdf
	Comment	
122	Number	3.2.A
	Title	Appendices
	Element	m3-2-a-appendices
	Directory	m3/32-body-data/32a-app
	Comment	
123	Number	3.2.A.1
	Title	Facilities and Equipment (name, manufacturer)
	Element	m3-2-a-1-facilities-and-equipment
	Directory	m3/32-body-data/32a-app/32a1-fac-equip
	Comment	Several reports are likely to be included in this appendix. The organisation is left to the applicant to define. However, where there is more than one manufacturer a folder should be created for each manufacturer and the identity of the manufacturer included in the directory name. CTD numbering is not defined below this level (e.g., 3.2.A.1.1).
124	Number	
	Title	*Facilities and Equipment Report 1*
	Element	m3-2-a-1-facilities-and-equipment
	File	m3/32-body-data/32a-app/32a1-fac-equip*/facilities-and-equipment-report-1.pdf*
	Comment	
125	Number	
	Title	*Facilities and Equipment Report 2*
	Element	m3-2-a-1-facilities-and-equipment
	File	m3/32-body-data/32a-app/32a1-fac-equip/*facilities-and-equipment-report-2.pdf*

	Comment	
126	Number	
	Title	*Facilities and Equipment Report 3*
	Element	m3-2-a-1-facilities-and-equipment
	File	m3/32-body-data/32a-app/32a1-fac-equip/*facilities-and-equipment-report-3.pdf*
	Comment	
127	Number	3.2.A.2
	Title	Adventitious Agents Safety Evaluation (name, dosage form, manufacturer)
	Element	m3-2-a-2-adventitious-agents-safety-evaluation
	Directory	m3/32-body-data/32a-app/32a2-advent-agent
	Comment	Nonviral adventitious agents reports should be placed in this folder. For viral adventitious agents the following sub-folder structure should be used. However, where there is more than one drug substance, drug product, manufacturer etc., a directory should be created for each option and its identity included in the directory name. CTD numbering is not defined below this level (e.g., 3.2.A.2.1).
128	Number	
	Title	*Adventitious Agents Safety Evaluation Report 1*
	Element	m3-2-a-2-adventitious-agents-safety-evaluation
	File	m3/32-body-data/32a-app/32a2-advent-agent/*adventitious-agents-report-1.pdf*
	Comment	
129	Number	
	Title	*Adventitious Agents Safety Evaluation Report 2*
	Element	m3-2-a-2-adventitious-agents-safety-evaluation
	File	m3/32-body-data/32a-app/32a2-advent-agent/*adventitious-agents-report-2.pdf*
	Comment	
130	Number	
	Title	*Adventitious Agents Safety Evaluation Report 3*
	Element	m3-2-a-2-adventitious-agents-safety-evaluation
	File	m3/32-body-data/32a-app/32a2-advent-agent/*adventitious-agents-report-3.pdf*
	Comment	
131	Number	3.2.A.3
	Title	Excipients – *Name*
	Element	m3-2-a-3-excipients
	Directory	m3/32-body-data/32a-app/32a3-excip-*name-1*

	Comment	The name of any novel excipient should be included in the folder name. If there is more than one novel excipient then each folder should have unique identification through the use of different names e.g., '32a3-excip-*name-1'* and '32a3-excip-*name-2'*. The directory/file structure would typically follow that of the drug substance section in Module 3.2.S. Refer to regional guidances for the need for such information to be included in the submission directly as opposed to its inclusion in a Drug Master File.
132	Number	3.2.R
	Title	Regional Information
	Element	m3-2-r-regional-information
	Directory	m3/32-body-data/32r-reg-info
	Comment	Refer to the M4 Organisation Document: Granularity Annex for the approach to take with this section.
133	Number	3.3
	Title	Literature References
	Element	m3-3-literature-references
	Directory	m3/33-lit-ref
	Comment	Copies of literature references should ordinarily be submitted as individual files (i.e., one for each reference). CTD numbering is not defined below this level (e.g., 3.3.1).
134	Number	
	Title	*Reference 1*
	Element	m3-3-literature-references
	File	m3/33-lit-ref/*reference-1.pdf*
	Comment	
135	Number	
	Title	*Reference 2*
	Element	m3-3-literature-references
	File	m3/33-lit-ref/*reference-2.pdf*
	Comment	
136	Number	
	Title	*Reference 3*
	Element	m3-3-literature-references
	File	m3/33-lit-ref/*reference-3.pdf*
	Comment	

137	Number	4
	Title	Nonclinical Study Reports
	Element	m4-nonclinical-study-reports
	Directory	m4
	Comment	
138	Number	4.2
	Title	Study Reports
	Element	m4-2-study-reports
	Directory	m4/42-stud-rep
	Comment	
139	Number	4.2.1
	Title	Pharmacology
	Element	m4-2-1-pharmacology
	Directory	m4/42-stud-rep/421-pharmacol
	Comment	
140	Number	4.2.1.1
	Title	Primary Pharmacodynamics
	Element	m4-2-1-1-primary-pharmacodynamics
	Directory	m4/42-stud-rep/421-pharmacol/4211-prim-pd
	Comment	
141	Number	
	Title	*Study Report 1*
	Element	m4-2-1-1-primary-pharmacodynamics
	File	m4/42-stud-rep/421-pharmacol/4211-prim-pd/*study-report-1.pdf*

	Comment	This comment is applicable to all study reports in Module 4. A single file can be provided for each study report document in Module 4. However, where the study report is large (e.g., a carcinogenicity study) the applicant can choose to submit the report as more than one file. In this case the text portion of the report should be one file and the appendices can be one or more files. In choosing the level of granularity for these reports, the applicant should consider that, when relevant information is changed at any point in the product's life cycle, replacements of complete files should be provided. Where submission as a collection of multiple files is used it is recommended that a directory is created at the study report level and the relevant files included within the directory. It is possible to have the additional graphical file(s) inserted directly into the PDF file, thus making management of the file easier. Alternatively, the applicant can choose to manage graphical files independently. Individual studies and files do not have specific CTD numbers.
142	Number	
	Title	*Study Report 2*
	Element	m4-2-1-1-primary-pharmacodynamics
	File	m4/42-stud-rep/421-pharmacol/4211-prim-pd/*study-report-2.pdf*
	Comment	
143	Number	
	Title	*Study Report 3*
	Element	m4-2-1-1-primary-pharmacodynamics
	File	m4/42-stud-rep/421-pharmacol/4211-prim-pd/*study-report-3.pdf*
	Comment	
144	Number	4.2.1.2
	Title	Secondary Pharmacodynamics
	Element	m4-2-1-2-secondary-pharmacodynamics
	Directory	m4/42-stud-rep/421-pharmacol/4212-sec-pd
	Comment	
145	Number	
	Title	*Study Report 1*
	Element	m4-2-1-2-secondary-pharmacodynamics
	File	m4/42-stud-rep/421-pharmacol/4212-sec-pd/*study-report-1.pdf*
	Comment	
146	Number	

	Title	*Study Report 2*
	Element	m4-2-1-2-secondary-pharmacodynamics
	File	m4/42-stud-rep/421-pharmacol/4212-sec-pd/*study-report-2.pdf*
	Comment	
	Number	
	Title	*Study Report 3*
147	Element	m4-2-1-2-secondary-pharmacodynamics
	File	m4/42-stud-rep/421-pharmacol/4212-sec-pd/*study-report-3.pdf*
	Comment	
	Number	4.2.1.3
	Title	Safety Pharmacology
148	Element	m4-2-1-3-safety-pharmacology
	Directory	m4/42-stud-rep/421-pharmacol/4213-safety-pharmacol
	Comment	
	Number	
	Title	*Study Report 1*
149	Element	m4-2-1-3-safety-pharmacology
	File	m4/42-stud-rep/421-pharmacol/4213-safety-pharmacol/*study-report-1.pdf*
	Comment	
	Number	
	Title	*Study Report 2*
150	Element	m4-2-1-3-safety-pharmacology
	File	m4/42-stud-rep/421-pharmacol/4213-safety-pharmacol/*study-report-2.pdf*
	Comment	
	Number	
	Title	*Study Report 3*
151	Element	m4-2-1-3-safety-pharmacology
	File	m4/42-stud-rep/421-pharmacol/4213-safety-pharmacol/*study-report-3.pdf*
	Comment	
152	Number	4.2.1.4
	Title	Pharmacodynamic Drug Interactions
	Element	m4-2-1-4-pharmacodynamic-drug-interactions
	Directory	m4/42-stud-rep/421-pharmacol/4214-pd-drug-interact

	Comment	
153	Number	
	Title	*Study Report 1*
	Element	m4-2-1-4-pharmacodynamic-drug-interactions
	File	m4/42-stud-rep/421-pharmacol/4214-pd-drug-interact/*study-report-1.pdf*
	Comment	
154	Number	
	Title	*Study Report 2*
	Element	m4-2-1-4-pharmacodynamic-drug-interactions
	File	m4/42-stud-rep/421-pharmacol/4214-pd-drug-interact/*study-report-2.pdf*
	Comment	
155	Number	
	Title	*Study Report 3*
	Element	m4-2-1-4-pharmacodynamic-drug-interactions
	File	m4/42-stud-rep/421-pharmacol/4214-pd-drug-interact/*study-report-3.pdf*
	Comment	
156	Number	4.2.2
	Title	Pharmacokinetics
	Element	m4-2-2-pharmacokinetics
	Directory	m4/42-stud-rep/422-pk
	Comment	
157	Number	4.2.2.1
	Title	Analytical Methods and Validation Reports (if separate reports are available)
	Element	m4-2-2-1-analytical-methods-and-validation-reports
	Directory	m4/42-stud-rep/422-pk/4221-analyt-met-val
	Comment	
158	Number	
	Title	*Study Report 1*
	Element	m4-2-2-1-analytical-methods-and-validation-reports
	File	m4/42-stud-rep/422-pk/4221-analyt-met-val/*study-report-1.pdf*
	Comment	
159	Number	
	Title	*Study Report 2*

	Element	m4-2-2-1-analytical-methods-and-validation-reports
	File	m4/42-stud-rep/422-pk/4221-analyt-met-val/*study-report-2.pdf*
	Comment	
160	Number	
	Title	*Study Report 3*
	Element	m4-2-2-1-analytical-methods-and-validation-reports
	File	m4/42-stud-rep/422-pk/4221-analyt-met-val/*study-report-3.pdf*
	Comment	
161	Number	4.2.2.2
	Title	Absorption
	Element	m4-2-2-2-absorption
	Directory	m4/42-stud-rep/422-pk/4222-absorp
	Comment	
162	Number	
	Title	*Study Report 1*
	Element	m4-2-2-2-absorption
	File	m4/42-stud-rep/422-pk/4222-absorp/*study-report-1.pdf*
	Comment	
163	Number	
	Title	*Study Report 2*
	Element	m4-2-2-2-absorption
	File	m4/42-stud-rep/422-pk/4222-absorp/*study-report-2.pdf*
	Comment	
164	Number	
	Title	*Study Report 3*
	Element	m4-2-2-2-absorption
	File	m4/42-stud-rep/422-pk/4222-absorp/*study-report-3.pdf*
	Comment	
165	Number	4.2.2.3
	Title	Distribution
	Element	m4-2-2-3-distribution
	Directory	m4/42-stud-rep/422-pk/4223-distrib
	Comment	

166	Number	
	Title	*Study Report 1*
	Element	m4-2-2-3-distribution
	File	m4/42-stud-rep/422-pk/4223-distrib/*study-report-1.pdf*
	Comment	
167	Number	
	Title	*Study Report 2*
	Element	m4-2-2-3-distribution
	File	m4/42-stud-rep/422-pk/4223-distrib/*study-report-2.pdf*
	Comment	
168	Number	
	Title	*Study Report 3*
	Element	m4-2-2-3-distribution
	File	m4/42-stud-rep/422-pk/4223-distrib/*study-report-3.pdf*
	Comment	
169	Number	4.2.2.4
	Title	Metabolism
	Element	m4-2-2-4-metabolism
	Directory	m4/42-stud-rep/422-pk/4224-metab
	Comment	
170	Number	
	Title	*Study Report 1*
	Element	m4-2-2-4-metabolism
	File	m4/42-stud-rep/422-pk/4224-metab/*study-report-1.pdf*
	Comment	
171	Number	
	Title	*Study Report 2*
	Element	m4-2-2-4-metabolism
	File	m4/42-stud-rep/422-pk/4224-metab/*study-report-2.pdf*
	Comment	
172	Number	
	Title	*Study Report 3*
	Element	m4-2-2-4-metabolism

	File	m4/42-stud-rep/422-pk/4224-metab/*study-report-3.pdf*
	Comment	
173	Number	4.2.2.5
	Title	Excretion
	Element	m4-2-2-5-excretion
	Directory	m4/42-stud-rep/422-pk/4225-excr
	Comment	
174	Number	
	Title	*Study Report 1*
	Element	m4-2-2-5-excretion
	File	m4/42-stud-rep/422-pk/4225-excr/*study-report-1.pdf*
	Comment	
175	Number	
	Title	*Study Report 2*
	Element	m4-2-2-5-excretion
	File	m4/42-stud-rep/422-pk/4225-excr/*study-report-2.pdf*
	Comment	
176	Number	
	Title	*Study Report 3*
	Element	m4-2-2-5-excretion
	File	m4/42-stud-rep/422-pk/4225-excr/*study-report-3.pdf*
	Comment	
177	Number	4.2.2.6
	Title	Pharmacokinetic Drug Interactions (nonclinical)
	Element	m4-2-2-6-pharmacokinetic-drug-interactions
	Directory	m4/42-stud-rep/422-pk/4226-pk-drug-interact
	Comment	
178	Number	
	Title	*Study Report 1*
	Element	m4-2-2-6-pharmacokinetic-drug-interactions
	File	m4/42-stud-rep/422-pk/4226-pk-drug-interact/*study-report-1.pdf*
	Comment	
179	Number	

	Title	*Study Report 2*
	Element	m4-2-2-6-pharmacokinetic-drug-interactions
	File	m4/42-stud-rep/422-pk/4226-pk-drug-interact/*study-report-2.pdf*
	Comment	
	Number	
	Title	*Study Report 3*
180	Element	m4-2-2-6-pharmacokinetic-drug-interactions
	File	m4/42-stud-rep/422-pk/4226-pk-drug-interact/*study-report-3.pdf*
	Comment	
	Number	4.2.2.7
	Title	Other Pharmacokinetic Studies
181	Element	m4-2-2-7-other-pharmacokinetic-studies
	Directory	m4/42-stud-rep/422-pk/4227-other-pk-stud
	Comment	
	Number	
	Title	*Study Report 1*
182	Element	m4-2-2-7-other-pharmacokinetic-studies
	File	m4/42-stud-rep/422-pk/4227-other-pk-stud/*study-report-1.pdf*
	Comment	
	Number	
	Title	*Study Report 2*
183	Element	m4-2-2-7-other-pharmacokinetic-studies
	File	m4/42-stud-rep/422-pk/4227-other-pk-stud/*study-report-2.pdf*
	Comment	
	Number	
	Title	*Study Report 3*
184	Element	m4-2-2-7-other-pharmacokinetic-studies
	File	m4/42-stud-rep/422-pk/4227-other-pk-stud/*study-report-3.pdf*
	Comment	
185	Number	4.2.3
	Title	Toxicology
	Element	m4-2-3-toxicology
	Directory	m4/42-stud-rep/423-tox

	Comment	
186	Number	4.2.3.1
	Title	Single-Dose Toxicity (in order by species, by route)
	Element	m4-2-3-1-single-dose-toxicity
	Directory	m4/42-stud-rep/423-tox/4231-single-dose-tox
	Comment	
187	Number	
	Title	*Study Report 1*
	Element	m4-2-3-1-single-dose-toxicity
	File	m4/42-stud-rep/423-tox/4231-single-dose-tox/*study-report-1.pdf*
	Comment	
188	Number	
	Title	*Study Report 2*
	Element	m4-2-3-1-single-dose-toxicity
	File	m4/42-stud-rep/423-tox/4231-single-dose-tox/*study-report-2.pdf*
	Comment	
189	Number	
	Title	*Study Report 3*
	Element	m4-2-3-1-single-dose-toxicity
	File	m4/42-stud-rep/423-tox/4231-single-dose-tox/*study-report-3.pdf*
	Comment	
190	Number	4.2.3.2
	Title	Repeat-Dose Toxicity (in order by species, by route, by duration, including supportive toxicokinetics evaluations)
	Element	m4-2-3-2-repeat-dose-toxicity
	Directory	m4/42-stud-rep/423-tox/4232-repeat-dose-tox
	Comment	
191	Number	
	Title	*Study Report 1*
	Element	m4-2-3-2-repeat-dose-toxicity
	File	m4/42-stud-rep/423-tox/4232-repeat-dose-tox/*study-report-1.pdf*
	Comment	
192	Number	
	Title	*Study Report 2*

	Element	m4-2-3-2-repeat-dose-toxicity
	File	m4/42-stud-rep/423-tox/4232-repeat-dose-tox/*study-report-2.pdf*
	Comment	
193	Number	
	Title	*Study Report 3*
	Element	m4-2-3-2-repeat-dose-toxicity
	File	m4/42-stud-rep/423-tox/4232-repeat-dose-tox/*study-report-3.pdf*
	Comment	
194	Number	4.2.3.3
	Title	Genotoxicity
	Element	m4-2-3-3-genotoxicity
	Directory	m4/42-stud-rep/423-tox/4233-genotox
	Comment	
195	Number	4.2.3.3.1
	Title	In vitro
	Element	m4-2-3-3-1-in-vitro
	Directory	m4/42-stud-rep/423-tox/4233-genotox/42331-in-vitro
	Comment	
196	Number	
	Title	*Study Report 1*
	Element	m4-2-3-3-1-in-vitro
	File	m4/42-stud-rep/423-tox/4233-genotox/42331-in-vitro/*study-report-1.pdf*
	Comment	
197	Number	
	Title	*Study Report 2*
	Element	m4-2-3-3-1-in-vitro
	File	m4/42-stud-rep/423-tox/4233-genotox/42331-in-vitro/*study-report-2.pdf*
	Comment	
198	Number	
	Title	*Study Report 3*
	Element	m4-2-3-3-1-in-vitro
	File	m4/42-stud-rep/423-tox/4233-genotox/42331-in-vitro/*study-report-3.pdf*
	Comment	

199	Number	4.2.3.3.2
	Title	In vivo (including supportive toxicokinetics evaluations)
	Element	m4-2-3-3-2-in-vivo
	Directory	m4/42-stud-rep/423-tox/4233-genotox/42332-in-vivo
	Comment	
200	Number	
	Title	*Study Report 1*
	Element	m4-2-3-3-2-in-vivo
	File	m4/42-stud-rep/423-tox/4233-genotox/42332-in-vivo/*study-report-1.pdf*
	Comment	
201	Number	
	Title	*Study Report 2*
	Element	m4-2-3-3-2-in-vivo
	File	m4/42-stud-rep/423-tox/4233-genotox/42332-in-vivo/*study-report-2.pdf*
	Comment	
202	Number	
	Title	*Study Report 3*
	Element	m4-2-3-3-2-in-vivo
	File	m4/42-stud-rep/423-tox/4233-genotox/42332-in-vivo/*study-report-3.pdf*
	Comment	
203	Number	4.2.3.4
	Title	Carcinogenicity (including supportive toxicokinetics evaluations)
	Element	m4-2-3-4-carcinogenicity
	Directory	m4/42-stud-rep/423-tox/4234-carcigen
	Comment	
204	Number	4.2.3.4.1
	Title	Long-term studies (in order by species, including range-finding studies that cannot be appropriately included under repeat-dose toxicity or pharmacokinetics)
	Element	m4-2-3-4-1-long-term-studies
	Directory	m4/42-stud-rep/423-tox/4234-carcigen/42341-lt-stud
	Comment	
205	Number	
	Title	*Study Report 1*

	Element	m4-2-3-4-1-long-term-studies
	File	m4/42-stud-rep/423-tox/4234-carcigen/42341-lt-stud/*study-report-1.pdf*
	Comment	
206	Number	
	Title	*Study Report 2*
	Element	m4-2-3-4-1-long-term-studies
	File	m4/42-stud-rep/423-tox/4234-carcigen/42341-lt-stud/*study-report-2.pdf*
	Comment	
207	Number	
	Title	*Study Report 3*
	Element	m4-2-3-4-1-long-term-studies
	File	m4/42-stud-rep/423-tox/4234-carcigen/42341-lt-stud/*study-report-3.pdf*
	Comment	
208	Number	4.2.3.4.2
	Title	Short- or medium-term studies (including range-finding studies that cannot be appropriately included under repeat-dose toxicity or pharmacokinetics)
	Element	m4-2-3-4-2-short-or-medium-term-studies
	Directory	m4/42-stud-rep/423-tox/4234-carcigen/42342-smt-stud
	Comment	
209	Number	
	Title	*Study Report 1*
	Element	m4-2-3-4-2-short-or-medium-term-studies
	File	m4/42-stud-rep/423-tox/4234-carcigen/42342-smt-stud/*study-report-1.pdf*
	Comment	
210	Number	
	Title	*Study Report 2*
	Element	m4-2-3-4-2-short-or-medium-term-studies
	File	m4/42-stud-rep/423-tox/4234-carcigen/42342-smt-stud/*study-report-2.pdf*
	Comment	
211	Number	
	Title	*Study Report 3*
	Element	m4-2-3-4-2-short-or-medium-term-studies
	File	m4/42-stud-rep/423-tox/4234-carcigen/42342-smt-stud/*study-report-3.pdf*

	Comment	
212	Number	4.2.3.4.3
	Title	Other studies
	Element	m4-2-3-4-3-other-studies
	Directory	m4/42-stud-rep/423-tox/4234-carcigen/42343-other-stud
	Comment	
213	Number	
	Title	*Study Report 1*
	Element	m4-2-3-4-3-other-studies
	File	m4/42-stud-rep/423-tox/4234-carcigen/42343-other-stud/*study-report-1.pdf*
	Comment	
214	Number	
	Title	*Study Report 2*
	Element	m4-2-3-4-3-other-studies
	File	m4/42-stud-rep/423-tox/4234-carcigen/42343-other-stud/*study-report-2.pdf*
	Comment	
215	Number	
	Title	*Study Report 3*
	Element	m4-2-3-4-3-other-studies
	File	m4/42-stud-rep/423-tox/4234-carcigen/42343-other-stud/*study-report-3.pdf*
	Comment	
216	Number	4.2.3.5
	Title	Reproductive and Developmental Toxicity (including range-finding studies and supportive toxicokinetics evaluations) (If modified study designs are used, the following subheadings should be modified accordingly)
	Element	m4-2-3-5-reproductive-and-developmental-toxicity
	Directory	m4/42-stud-rep/423-tox/4235-repro-dev-tox
	Comment	
217	Number	4.2.3.5.1
	Title	Fertility and early embryonic development
	Element	m4-2-3-5-1-fertility-and-early-embryonic-development
	Directory	m4/42-stud-rep/423-tox/4235-repro-dev-tox/42351-fert-embryo-dev
	Comment	
218	Number	

	Title	*Study Report 1*
	Element	m4-2-3-5-1-fertility-and-early-embryonic-development
	File	m4/42-stud-rep/423-tox/4235-repro-dev-tox/42351-fert-embryo-dev/*study-report-1.pdf*
	Comment	
219	Number	
	Title	*Study Report 2*
	Element	m4-2-3-5-1-fertility-and-early-embryonic-development
	File	m4/42-stud-rep/423-tox/4235-repro-dev-tox/42351-fert-embryo-dev/*study-report-2.pdf*
	Comment	
220	Number	
	Title	*Study Report 3*
	Element	m4-2-3-5-1-fertility-and-early-embryonic-development
	File	m4/42-stud-rep/423-tox/4235-repro-dev-tox/42351-fert-embryo-dev/*study-report-3.pdf*
	Comment	
221	Number	4.2.3.5.2
	Title	Embryo-fetal development
	Element	m4-2-3-5-2-embryo-fetal-development
	Directory	m4/42-stud-rep/423-tox/4235-repro-dev-tox/42352-embryo-fetal-dev
	Comment	
222	Number	
	Title	*Study Report 1*
	Element	m4-2-3-5-2-embryo-fetal-development
	File	m4/42-stud-rep/423-tox/4235-repro-dev-tox/42352-embryo-fetal-dev/*study-report-1.pdf*
	Comment	
223	Number	
	Title	*Study Report 2*
	Element	m4-2-3-5-2-embryo-fetal-development
	File	m4/42-stud-rep/423-tox/4235-repro-dev-tox/42352-embryo-fetal-dev/*study-report-2.pdf*
	Comment	
224	Number	
	Title	*Study Report 3*
	Element	m4-2-3-5-2-embryo-fetal-development
	File	m4/42-stud-rep/423-tox/4235-repro-dev-tox/42352-embryo-fetal-dev/*study-report-3.pdf*

	Comment	
225	Number	4.2.3.5.3
	Title	Prenatal and postnatal development, including maternal function
	Element	m4-2-3-5-3-prenatal-and-postnatal-development-including-maternal-function
	Directory	m4/42-stud-rep/423-tox/4235-repro-dev-tox/42353-pre-postnatal-dev
	Comment	
226	Number	
	Title	*Study Report 1*
	Element	m4-2-3-5-3-prenatal-and-postnatal-development-including-maternal-function
	File	m4/42-stud-rep/423-tox/4235-repro-dev-tox/42353-pre-postnatal-dev/*study-report-1.pdf*
	Comment	
227	Number	
	Title	*Study Report 2*
	Element	m4-2-3-5-3-prenatal-and-postnatal-development-including-maternal-function
	File	m4/42-stud-rep/423-tox/4235-repro-dev-tox/42353-pre-postnatal-dev/*study-report-2.pdf*
	Comment	
228	Number	
	Title	*Study Report 3*
	Element	m4-2-3-5-3-prenatal-and-postnatal-development-including-maternal-function
	File	m4/42-stud-rep/423-tox/4235-repro-dev-tox/42353-pre-postnatal-dev/*study-report-3.pdf*
	Comment	
229	Number	4.2.3.5.4
	Title	Studies in which the offspring (juvenile animals) are dosed and/or further evaluated
	Element	m4-2-3-5-4-studies-in-which-the-offspring-juvenile-animals-are-dosed-and-or-further-evaluated
	Directory	m4/42-stud-rep/423-tox/4235-repro-dev-tox/42354-juv
	Comment	
230	Number	
	Title	*Study Report 1*
	Element	m4-2-3-5-4-studies-in-which-the-offspring-juvenile-animals-are-dosed-and-or-further-evaluated
	File	m4/42-stud-rep/423-tox/4235-repro-dev-tox/42354-juv/*study-report-1.pdf*
	Comment	
231	Number	
	Title	*Study Report 2*

	Element	m4-2-3-5-4-studies-in-which-the-offspring-juvenile-animals-are-dosed-and-or-further-evaluated
	File	m4/42-stud-rep/423-tox/4235-repro-dev-tox/42354-juv/*study-report-2.pdf*
	Comment	
232	Number	
	Title	*Study Report 3*
	Element	m4-2-3-5-4-studies-in-which-the-offspring-juvenile-animals-are-dosed-and-or-further-evaluated
	File	m4/42-stud-rep/423-tox/4235-repro-dev-tox/42354-juv/*study-report-3.pdf*
	Comment	
233	Number	4.2.3.6
	Title	Local Tolerance
	Element	m4-2-3-6-local-tolerance
	Directory	m4/42-stud-rep/423-tox/4236-loc-tol
	Comment	
234	Number	
	Title	*Study Report 1*
	Element	m4-2-3-6-local-tolerance
	File	m4/42-stud-rep/423-tox/4236-loc-tol/*study-report-1.pdf*
	Comment	
235	Number	
	Title	*Study Report 2*
	Element	m4-2-3-6-local-tolerance
	File	m4/42-stud-rep/423-tox/4236-loc-tol/*study-report-2.pdf*
	Comment	
236	Number	
	Title	*Study Report 3*
	Element	m4-2-3-6-local-tolerance
	File	m4/42-stud-rep/423-tox/4236-loc-tol/*study-report-3.pdf*
	Comment	
237	Number	4.2.3.7
	Title	Other Toxicity Studies (if available)
	Element	m4-2-3-7-other-toxicity-studies
	Directory	m4/42-stud-rep/423-tox/4237-other-tox-stud
	Comment	

238	Number	4.2.3.7.1
	Title	Antigenicity
	Element	m4-2-3-7-1-antigenicity
	Directory	m4/42-stud-rep/423-tox/4237-other-tox-stud/42371-antigen
	Comment	
239	Number	
	Title	*Study Report 1*
	Element	m4-2-3-7-1-antigenicity
	File	m4/42-stud-rep/423-tox/4237-other-tox-stud/42371-antigen/*study-report-1.pdf*
	Comment	
240	Number	
	Title	*Study Report 2*
	Element	m4-2-3-7-1-antigenicity
	File	m4/42-stud-rep/423-tox/4237-other-tox-stud/42371-antigen/*study-report-2.pdf*
	Comment	
241	Number	
	Title	*Study Report 3*
	Element	m4-2-3-7-1-antigenicity
	File	m4/42-stud-rep/423-tox/4237-other-tox-stud/42371-antigen/*study-report-3.pdf*
	Comment	
242	Number	4.2.3.7.2
	Title	Immunotoxicity
	Element	m4-2-3-7-2-immunotoxicity
	Directory	m4/42-stud-rep/423-tox/4237-other-tox-stud/42372-immunotox
	Comment	
243	Number	
	Title	*Study Report 1*
	Element	m4-2-3-7-2-immunotoxicity
	File	m4/42-stud-rep/423-tox/4237-other-tox-stud/42372-immunotox/*study-report-1.pdf*
	Comment	
244	Number	
	Title	*Study Report 2*
	Element	m4-2-3-7-2-immunotoxicity

	File	m4/42-stud-rep/423-tox/4237-other-tox-stud/42372-immunotox/*study-report-2.pdf*
	Comment	
245	Number	
	Title	*Study Report 3*
	Element	m4-2-3-7-2-immunotoxicity
	File	m4/42-stud-rep/423-tox/4237-other-tox-stud/42372-immunotox/*study-report-3.pdf*
	Comment	
246	Number	4.2.3.7.3
	Title	Mechanistic studies (if not included elsewhere)
	Element	m4-2-3-7-3-mechanistic-studies
	Directory	m4/42-stud-rep/423-tox/4237-other-tox-stud/42373-mechan-stud
	Comment	
247	Number	
	Title	*Study Report 1*
	Element	m4-2-3-7-3-mechanistic-studies
	File	m4/42-stud-rep/423-tox/4237-other-tox-stud/42373-mechan-stud/*study-report-1.pdf*
	Comment	
248	Number	
	Title	*Study Report 2*
	Element	m4-2-3-7-3-mechanistic-studies
	File	m4/42-stud-rep/423-tox/4237-other-tox-stud/42373-mechan-stud/*study-report-2.pdf*
	Comment	
249	Number	
	Title	*Study Report 3*
	Element	m4-2-3-7-3-mechanistic-studies
	File	m4/42-stud-rep/423-tox/4237-other-tox-stud/42373-mechan-stud/*study-report-3.pdf*
	Comment	
250	Number	4.2.3.7.4
	Title	Dependence
	Element	m4-2-3-7-4-dependence
	Directory	m4/42-stud-rep/423-tox/4237-other-tox-stud/42374-dep
	Comment	
251	Number	

	Title	*Study Report 1*
	Element	m4-2-3-7-4-dependence
	File	m4/42-stud-rep/423-tox/4237-other-tox-stud/42374-dep/*study-report-1.pdf*
	Comment	
252	Number	
	Title	*Study Report 2*
	Element	m4-2-3-7-4-dependence
	File	m4/42-stud-rep/423-tox/4237-other-tox-stud/42374-dep/*study-report-2.pdf*
	Comment	
253	Number	
	Title	*Study Report 3*
	Element	m4-2-3-7-4-dependence
	File	m4/42-stud-rep/423-tox/4237-other-tox-stud/42374-dep/*study-report-3.pdf*
	Comment	
254	Number	4.2.3.7.5
	Title	Metabolites
	Element	m4-2-3-7-5-metabolites
	Directory	m4/42-stud-rep/423-tox/4237-other-tox-stud/42375-metab
	Comment	
255	Number	
	Title	*Study Report 1*
	Element	m4-2-3-7-5-metabolites
	File	m4/42-stud-rep/423-tox/4237-other-tox-stud/42375-metab/*study-report-1.pdf*
	Comment	
256	Number	
	Title	*Study Report 2*
	Element	m4-2-3-7-5-metabolites
	File	m4/42-stud-rep/423-tox/4237-other-tox-stud/42375-metab/*study-report-2.pdf*
	Comment	
257	Number	
	Title	*Study Report 3*
	Element	m4-2-3-7-5-metabolites
	File	m4/42-stud-rep/423-tox/4237-other-tox-stud/42375-metab/*study-report-3.pdf*

	Comment	
258	Number	4.2.3.7.6
	Title	Impurities
	Element	m4-2-3-7-6-impurities
	Directory	m4/42-stud-rep/423-tox/4237-other-tox-stud/42376-imp
	Comment	
259	Number	
	Title	*Study Report 1*
	Element	m4-2-3-7-6-impurities
	File	m4/42-stud-rep/423-tox/4237-other-tox-stud/42376-imp/*study-report-1.pdf*
	Comment	
260	Number	
	Title	*Study Report 2*
	Element	m4-2-3-7-6-impurities
	File	m4/42-stud-rep/423-tox/4237-other-tox-stud/42376-imp/*study-report-2.pdf*
	Comment	
261	Number	
	Title	*Study Report 3*
	Element	m4-2-3-7-6-impurities
	File	m4/42-stud-rep/423-tox/4237-other-tox-stud/42376-imp/*study-report-3.pdf*
	Comment	
262	Number	4.2.3.7.7
	Title	Other
	Element	m4-2-3-7-7-other
	Directory	m4/42-stud-rep/423-tox/4237-other-tox-stud/42377-other
	Comment	
263	Number	
	Title	*Study Report 1*
	Element	m4-2-3-7-7-other
	File	m4/42-stud-rep/423-tox/4237-other-tox-stud/42377-other/*study-report-1.pdf*
	Comment	
264	Number	
	Title	*Study Report 2*

	Element	m4-2-3-7-7-other
	File	m4/42-stud-rep/423-tox/4237-other-tox-stud/42377-other/*study-report-2.pdf*
	Comment	
265	Number	
	Title	*Study Report 3*
	Element	m4-2-3-7-7-other
	File	m4/42-stud-rep/423-tox/4237-other-tox-stud/42377-other/*study-report-3.pdf*
	Comment	
266	Number	4.3
	Title	Literature References
	Element	m4-3-literature-references
	Directory	m4/43-lit-ref
	Comment	Copies of literature references should ordinarily be submitted as individual files (i.e., one for each reference).
267	Number	
	Title	*Reference 1*
	Element	m4-3-literature-references
	File	m4/43-lit-ref/*reference-1.pdf*
	Comment	
268	Number	
	Title	*Reference 2*
	Element	m4-3-literature-references
	File	m4/43-lit-ref/*reference-2.pdf*
	Comment	
269	Number	
	Title	*Reference 3*
	Element	m4-3-literature-references
	File	m4/43-lit-ref/*reference-3.pdf*
	Comment	

270	Number	5
	Title	Clinical Study Reports
	Element	m5-clinical-study-reports
	Directory	m5
	Comment	
271	Number	5.2
	Title	Tabular Listing of all Clinical Studies
	Element	m5-2-tabular-listing-of-all-clinical-studies
	Directory	m5/52-tab-list
	Comment	
272	Number	5.2
	Title	Tabular Listing of all Clinical Studies
	Element	m5-2-tabular-listing-of-all-clinical-studies
	File	m5/52-tab-list/tabular-listing.pdf
	Comment	
273	Number	5.3
	Title	Clinical Study Reports
	Element	m5-3-clinical-study-reports
	Directory	m5/53-clin-stud-rep
	Comment	
274	Number	5.3.1
	Title	Reports of Biopharmaceutic Studies
	Element	m5-3-1-reports-of-biopharmaceutic-studies
	Directory	m5/53-clin-stud-rep/531-rep-biopharm-stud
	Comment	
275	Number	5.3.1.1
	Title	Bioavailability (BA) Study Reports
	Element	m5-3-1-1-bioavailability-study-reports
	Directory	m5/53-clin-stud-rep/531-rep-biopharm-stud/5311-ba-stud-rep
	Comment	
276	Number	
	Title	*Study Report 1*

	Element	m5-3-1-1-bioavailability-study-reports
	Directory	m5/53-clin-stud-rep/531-rep-biopharm-stud/5311-ba-stud-rep/*study-report-1*
	Comment	This comment is applicable to all study reports in Module 5. The applicants should ordinarily provide the study reports as multiple files (a synopsis, a main body and appropriate appendices). Appendices should be organized in accordance with the ICH E3 guideline, which describes the content and format of the clinical study report. In choosing the level of granularity for reports the applicant should consider that, when relevant information is changed at any point in the product's life cycle, replacements of complete files should be provided. A directory should be created for each study and the files associated with the study report should be organized within the directory. Individual studies and files do not have specific CTD numbers.
277	Number	
	Title	*Study Report 2*
	Element	m5-3-1-1-bioavailability-study-reports
	Directory	m5/53-clin-stud-rep/531-rep-biopharm-stud/5311-ba-stud-rep/*study-report-2*
	Comment	
278	Number	
	Title	*Study Report 3*
	Element	m5-3-1-1-bioavailability-study-reports
	Directory	m5/53-clin-stud-rep/531-rep-biopharm-stud/5311-ba-stud-rep/*study-report-3*
	Comment	
279	Number	5.3.1.2
	Title	Comparative BA and Bioequivalence (BE) Study Reports
	Element	m5-3-1-2-comparative-ba-and-bioequivalence-study-reports
	Directory	m5/53-clin-stud-rep/531-rep-biopharm-stud/5312-compar-ba-be-stud-rep
	Comment	
280	Number	
	Title	*Study Report 1*
	Element	m5-3-1-2-comparative-ba-and-bioequivalence-study-reports
	Directory	m5/53-clin-stud-rep/531-rep-biopharm-stud/5312-compar-ba-be-stud-rep/*study-report-1*
	Comment	
281	Number	
	Title	*Study Report 2*
	Element	m5-3-1-2-comparative-ba-and-bioequivalence-study-reports
	Directory	m5/53-clin-stud-rep/531-rep-biopharm-stud/5312-compar-ba-be-stud-rep/*study-report-2*

	Comment	
282	Number	
	Title	*Study Report 3*
	Element	m5-3-1-2-comparative-ba-and-bioequivalence-study-reports
	Directory	m5/53-clin-stud-rep/531-rep-biopharm-stud/5312-compar-ba-be-stud-rep/*study-report-3*
	Comment	
283	Number	5.3.1.3
	Title	In vitro – In vivo Correlation Study Reports
	Element	m5-3-1-3-in-vitro-in-vivo-correlation-study-reports
	Directory	m5/53-clin-stud-rep/531-rep-biopharm-stud/5313-in-vitro-in-vivo-corr-stud-rep
	Comment	
284	Number	
	Title	*Study Report 1*
	Element	m5-3-1-3-in-vitro-in-vivo-correlation-study-reports
	Directory	m5/53-clin-stud-rep/531-rep-biopharm-stud/5313-in-vitro-in-vivo-corr-stud-rep/*study-report-1*
	Comment	
285	Number	
	Title	*Study Report 2*
	Element	m5-3-1-3-in-vitro-in-vivo-correlation-study-reports
	Directory	m5/53-clin-stud-rep/531-rep-biopharm-stud/5313-in-vitro-in-vivo-corr-stud-rep/*study-report-2*
	Comment	
286	Number	
	Title	*Study Report 3*
	Element	m5-3-1-3-in-vitro-in-vivo-correlation-study-reports
	Directory	m5/53-clin-stud-rep/531-rep-biopharm-stud/5313-in-vitro-in-vivo-corr-stud-rep/*study-report-3*
	Comment	
287	Number	5.3.1.4
	Title	Reports of Bioanalytical and Analytical Methods for Human Studies
	Element	m5-3-1-4-reports-of-bioanalytical-and-analytical-methods-for-human-studies
	Directory	m5/53-clin-stud-rep/531-rep-biopharm-stud/5314-bioanalyt-analyt-met
	Comment	
288	Number	
	Title	*Study Report 1*

	Element	m5-3-1-4-reports-of-bioanalytical-and-analytical-methods-for-human-studies
	Directory	m5/53-clin-stud-rep/531-rep-biopharm-stud/5314-bioanalyt-analyt-met/*study-report-1*
	Comment	
289	Number	
	Title	*Study Report 2*
	Element	m5-3-1-4-reports-of-bioanalytical-and-analytical-methods-for-human-studies
	Directory	m5/53-clin-stud-rep/531-rep-biopharm-stud/5314-bioanalyt-analyt-met/*study-report-2*
	Comment	
290	Number	
	Title	*Study Report 3*
	Element	m5-3-1-4-reports-of-bioanalytical-and-analytical-methods-for-human-studies
	Directory	m5/53-clin-stud-rep/531-rep-biopharm-stud/5314-bioanalyt-analyt-met/*study-report-3*
	Comment	
291	Number	5.3.2
	Title	Reports of Studies Pertinent to Pharmacokinetics using Human Biomaterials
	Element	m5-3-2-reports-of-studies-pertinent-to-pharmacokinetics-using-human-biomaterials
	Directory	m5/53-clin-stud-rep/532-rep-stud-pk-human-biomat
	Comment	
292	Number	5.3.2.1
	Title	Plasma Protein Binding Study Reports
	Element	m5-3-2-1-plasma-protein-binding-study-reports
	Directory	m5/53-clin-stud-rep/532-rep-stud-pk-human-biomat/5321-plasma-prot-bind-stud-rep
	Comment	
293	Number	
	Title	*Study Report 1*
	Element	m5-3-2-1-plasma-protein-binding-study-reports
	Directory	m5/53-clin-stud-rep/532-rep-stud-pk-human-biomat/5321-plasma-prot-bind-stud-rep/*study-report-1*
	Comment	
294	Number	
	Title	*Study Report 2*
	Element	m5-3-2-1-plasma-protein-binding-study-reports
	Directory	m5/53-clin-stud-rep/532-rep-stud-pk-human-biomat/5321-plasma-prot-bind-stud-rep/*study-report-2*
	Comment	

295	Number	
	Title	*Study Report 3*
	Element	m5-3-2-1-plasma-protein-binding-study-reports
	Directory	m5/53-clin-stud-rep/532-rep-stud-pk-human-biomat/5321-plasma-prot-bind-stud-rep/*study-report-3*
	Comment	
296	Number	5.3.2.2
	Title	Reports of Hepatic Metabolism and Drug Interaction Studies
	Element	m5-3-2-2-reports-of-hepatic-metabolism-and-drug-interaction-studies
	Directory	m5/53-clin-stud-rep/532-rep-stud-pk-human-biomat/5322-rep-hep-metab-interact-stud
	Comment	
297	Number	
	Title	*Study Report 1*
	Element	m5-3-2-2-reports-of-hepatic-metabolism-and-drug-interaction-studies
	Directory	m5/53-clin-stud-rep/532-rep-stud-pk-human-biomat/5322-rep-hep-metab-interact-stud/*study-report-1*
	Comment	
298	Number	
	Title	*Study Report 2*
	Element	m5-3-2-2-reports-of-hepatic-metabolism-and-drug-interaction-studies
	Directory	m5/53-clin-stud-rep/532-rep-stud-pk-human-biomat/5322-rep-hep-metab-interact-stud/*study-report-2*
	Comment	
299	Number	
	Title	*Study Report 3*
	Element	m5-3-2-2-reports-of-hepatic-metabolism-and-drug-interaction-studies
	Directory	m5/53-clin-stud-rep/532-rep-stud-pk-human-biomat/5322-rep-hep-metab-interact-stud/*study-report-3*
	Comment	
300	Number	5.3.2.3
	Title	Reports of Studies Using Other Human Biomaterials
	Element	m5-3-2-3-reports-of-studies-using-other-human-biomaterials
	Directory	m5/53-clin-stud-rep/532-rep-stud-pk-human-biomat/5323-stud-other-human-biomat
	Comment	
301	Number	
	Title	*Study Report 1*
	Element	m5-3-2-3-reports-of-studies-using-other-human-biomaterials

	Directory	m5/53-clin-stud-rep/532-rep-stud-pk-human-biomat/5323-stud-other-human-biomat/*study-report-1*
	Comment	
302	Number	
	Title	*Study Report 2*
	Element	m5-3-2-3-reports-of-studies-using-other-human-biomaterials
	Directory	m5/53-clin-stud-rep/532-rep-stud-pk-human-biomat/5323-stud-other-human-biomat/*study-report-2*
	Comment	
303	Number	
	Title	*Study Report 3*
	Element	m5-3-2-3-reports-of-studies-using-other-human-biomaterials
	Directory	m5/53-clin-stud-rep/532-rep-stud-pk-human-biomat/5323-stud-other-human-biomat/*study-report-3*
	Comment	
304	Number	5.3.3
	Title	Reports of Human Pharmacokinetic (PK) Studies
	Element	m5-3-3-reports-of-human-pharmacokinetics-pk-studies
	Directory	m5/53-clin-stud-rep/533-rep-human-pk-stud
	Comment	
305	Number	5.3.3.1
	Title	Healthy Subject PK and Initial Tolerability Study Reports
	Element	m5-3-3-1-healthy-subject-pk-and-initial-tolerability-study-reports
	Directory	m5/53-clin-stud-rep/533-rep-human-pk-stud/5331-healthy-subj-pk-init-tol-stud-rep
	Comment	
306	Number	
	Title	*Study Report 1*
	Element	m5-3-3-1-healthy-subject-pk-and-initial-tolerability-study-reports
	Directory	m5/53-clin-stud-rep/533-rep-human-pk-stud/5331-healthy-subj-pk-init-tol-stud-rep/*study-report-1*
	Comment	
307	Number	
	Title	*Study Report 2*
	Element	m5-3-3-1-healthy-subject-pk-and-initial-tolerability-study-reports
	Directory	m5/53-clin-stud-rep/533-rep-human-pk-stud/5331-healthy-subj-pk-init-tol-stud-rep/*study-report-2*
	Comment	
308	Number	

	Title	*Study Report 3*
	Element	m5-3-3-1-healthy-subject-pk-and-initial-tolerability-study-reports
	Directory	m5/53-clin-stud-rep/533-rep-human-pk-stud/5331-healthy-subj-pk-init-tol-stud-rep/*study-report-3*
	Comment	
309	Number	5.3.3.2
	Title	Patient PK and Initial Tolerability Study Reports
	Element	m5-3-3-2-patient-pk-and-initial-tolerability-study-reports
	Directory	m5/53-clin-stud-rep/533-rep-human-pk-stud/5332-patient-pk-init-tol-stud-rep
	Comment	
310	Number	
	Title	*Study Report 1*
	Element	m5-3-3-2-patient-pk-and-initial-tolerability-study-reports
	Directory	m5/53-clin-stud-rep/533-rep-human-pk-stud/5332-patient-pk-init-tol-stud-rep/*study-report-1*
	Comment	
311	Number	
	Title	*Study Report 2*
	Element	m5-3-3-2-patient-pk-and-initial-tolerability-study-reports
	Directory	m5/53-clin-stud-rep/533-rep-human-pk-stud/5332-patient-pk-init-tol-stud-rep/*study-report-2*
	Comment	
312	Number	
	Title	*Study Report 3*
	Element	m5-3-3-2-patient-pk-and-initial-tolerability-study-reports
	Directory	m5/53-clin-stud-rep/533-rep-human-pk-stud/5332-patient-pk-init-tol-stud-rep/*study-report-3*
	Comment	
313	Number	5.3.3.3
	Title	Intrinsic Factor PK Study Reports
	Element	m5-3-3-3-intrinsic-factor-pk-study-reports
	Directory	m5/53-clin-stud-rep/533-rep-human-pk-stud/5333-intrin-factor-pk-stud-rep
	Comment	
314	Number	
	Title	*Study Report 1*
	Element	m5-3-3-3-intrinsic-factor-pk-study-reports
	Directory	m5/53-clin-stud-rep/533-rep-human-pk-stud/5333-intrin-factor-pk-stud-rep/*study-report-1*

	Comment	
315	Number	
	Title	*Study Report 2*
	Element	m5-3-3-3-intrinsic-factor-pk-study-reports
	Directory	m5/53-clin-stud-rep/533-rep-human-pk-stud/5333-intrin-factor-pk-stud-rep/*study-report-2*
	Comment	
316	Number	
	Title	*Study Report 3*
	Element	m5-3-3-3-intrinsic-factor-pk-study-reports
	Directory	m5/53-clin-stud-rep/533-rep-human-pk-stud/5333-intrin-factor-pk-stud-rep/*study-report-3*
	Comment	
317	Number	5.3.3.4
	Title	Extrinsic Factor PK Study Reports
	Element	m5-3-3-4-extrinsic-factor-pk-study-reports
	Directory	m5/53-clin-stud-rep/533-rep-human-pk-stud/5334-extrin-factor-pk-stud-rep
	Comment	
318	Number	
	Title	*Study Report 1*
	Element	m5-3-3-4-extrinsic-factor-pk-study-reports
	Directory	m5/53-clin-stud-rep/533-rep-human-pk-stud/5334-extrin-factor-pk-stud-rep/*study-report-1*
	Comment	
319	Number	
	Title	*Study Report 2*
	Element	m5-3-3-4-extrinsic-factor-pk-study-reports
	Directory	m5/53-clin-stud-rep/533-rep-human-pk-stud/5334-extrin-factor-pk-stud-rep/*study-report-2*
	Comment	
320	Number	
	Title	*Study Report 3*
	Element	m5-3-3-4-extrinsic-factor-pk-study-reports
	Directory	m5/53-clin-stud-rep/533-rep-human-pk-stud/5334-extrin-factor-pk-stud-rep/*study-report-3*
	Comment	
321	Number	5.3.3.5
	Title	Population PK Study Reports

	Element	m5-3-3-5-population-pk-study-reports
	Directory	m5/53-clin-stud-rep/533-rep-human-pk-stud/5335-popul-pk-stud-rep
	Comment	
322	Number	
	Title	*Study Report 1*
	Element	m5-3-3-5-population-pk-study-reports
	Directory	m5/53-clin-stud-rep/533-rep-human-pk-stud/5335-popul-pk-stud-rep/*study-report-1*
	Comment	
323	Number	
	Title	*Study Report 2*
	Element	m5-3-3-5-population-pk-study-reports
	Directory	m5/53-clin-stud-rep/533-rep-human-pk-stud/5335-popul-pk-stud-rep/*study-report-2*
	Comment	
324	Number	
	Title	*Study Report 3*
	Element	m5-3-3-5-population-pk-study-reports
	Directory	m5/53-clin-stud-rep/533-rep-human-pk-stud/5335-popul-pk-stud-rep/*study-report-3*
	Comment	
325	Number	5.3.4
	Title	Reports of Human Pharmacodynamic (PD) Studies
	Element	m5-3-4-reports-of-human-pharmacodynamics-pd-studies
	Directory	m5/53-clin-stud-rep/534-rep-human-pd-stud
	Comment	
326	Number	5.3.4.1
	Title	Healthy Subject PD and PK/PD Study Reports
	Element	m5-3-4-1-healthy-subject-pd-and-pk-pd-study-reports
	Directory	m5/53-clin-stud-rep/534-rep-human-pd-stud/5341-healthy-subj-pd-stud-rep
	Comment	
327	Number	
	Title	*Study Report 1*
	Element	m5-3-4-1-healthy-subject-pd-and-pk-pd-study-reports
	Directory	m5/53-clin-stud-rep/534-rep-human-pd-stud/5341-healthy-subj-pd-stud-rep/*study-report-1*
	Comment	

328	Number	
	Title	*Study Report 2*
	Element	m5-3-4-1-healthy-subject-pd-and-pk-pd-study-reports
	Directory	m5/53-clin-stud-rep/534-rep-human-pd-stud/5341-healthy-subj-pd-stud-rep/*study-report-2*
	Comment	
329	Number	
	Title	*Study Report 3*
	Element	m5-3-4-1-healthy-subject-pd-and-pk-pd-study-reports
	Directory	m5/53-clin-stud-rep/534-rep-human-pd-stud/5341-healthy-subj-pd-stud-rep/*study-report-3*
	Comment	
330	Number	5.3.4.2
	Title	Patient PD and PK/PD Study Reports
	Element	m5-3-4-2-patient-pd-and-pk-pd-study-reports
	Directory	m5/53-clin-stud-rep/534-rep-human-pd-stud/5342-patient-pd-stud-rep
	Comment	
331	Number	
	Title	*Study Report 1*
	Element	m5-3-4-2-patient-pd-and-pk-pd-study-reports
	Directory	m5/53-clin-stud-rep/534-rep-human-pd-stud/5342-patient-pd-stud-rep/*study-report-1*
	Comment	
332	Number	
	Title	*Study Report 2*
	Element	m5-3-4-2-patient-pd-and-pk-pd-study-reports
	Directory	m5/53-clin-stud-rep/534-rep-human-pd-stud/5342-patient-pd-stud-rep/*study-report-2*
	Comment	
333	Number	
	Title	*Study Report 3*
	Element	m5-3-4-2-patient-pd-and-pk-pd-study-reports
	Directory	m5/53-clin-stud-rep/534-rep-human-pd-stud/5342-patient-pd-stud-rep/*study-report-3*
	Comment	
334	Number	5.3.5
	Title	Reports of Efficacy and Safety Studies
	Element	m5-3-5-reports-of-efficacy-and-safety-studies

	Directory	m5/53-clin-stud-rep/535-rep-effic-safety-stud
	Comment	
335	Number	5.3.5
	Title	Reports of Efficacy and Safety Studies - *Indication Name*
	Element	m5-3-5-reports-of-efficacy-and-safety-studies
	Directory	m5/53-clin-stud-rep/535-rep-effic-safety-stud/*indication-1*
	Comment	The folder name should always include the indication being claimed, for example, 'asthma' (abbreviated if appropriate). Where there is more than one indication (e.g., asthma and migraine), then the first indication has a folder 'asthma' and the second 'migraine'. The 'indication' attribute in the backbone should be consistent with that used in the folder name but can be different. For example, an 'indication' attribute value of 'Non-Small Cell Lung Cancer' could be expressed as 'NSCLC' in the folder name. There is currently no standard terminology list for 'indication' and applicants should choose the 'indication' attributes carefully as they can not be easily changed during the life cycle of the application. The only way this can be accomplished currently is to delete all the leaf elements with the incorrect attribute value and provide new leaf elements for those files with the modified attribute value. Applicants should consult with the regional authority before attempting to modify these attributes to discuss the appropriateness of, and approach to be taken for, this type of change.
336	Number	5.3.5.1
	Title	Study Reports of Controlled Clinical Studies Pertinent to the Claimed Indication
	Element	m5-3-5-1-study-reports-of-controlled-clinical-studies-pertinent-to-the-claimed-indication
	Directory	m5/53-clin-stud-rep/535-rep-effic-safety-stud/*indication-1*/5351-stud-rep-contr
	Comment	
337	Number	
	Title	*Study Report 1*
	Element	m5-3-5-1-study-reports-of-controlled-clinical-studies-pertinent-to-the-claimed-indication
	Directory	m5/53-clin-stud-rep/535-rep-effic-safety-stud/*indication-1*/5351-stud-rep-contr/*study-report-1*
	Comment	
338	Number	
	Title	*Study Report 2*
	Element	m5-3-5-1-study-reports-of-controlled-clinical-studies-pertinent-to-the-claimed-indication
	Directory	m5/53-clin-stud-rep/535-rep-effic-safety-stud/*indication-1*/5351-stud-rep-contr/*study-report-2*
	Comment	
339	Number	
	Title	*Study Report 3*
	Element	m5-3-5-1-study-reports-of-controlled-clinical-studies-pertinent-to-the-claimed-indication
	Directory	m5/53-clin-stud-rep/535-rep-effic-safety-stud/*indication-1*/5351-stud-rep-contr/*study-report-3*

	Comment	
340	Number	5.3.5.2
	Title	Study Reports of Uncontrolled Clinical Studies
	Element	m5-3-5-2-study-reports-of-uncontrolled-clinical-studies
	Directory	m5/53-clin-stud-rep/535-rep-effic-safety-stud/*indication-1*/5352-stud-rep-uncontr
	Comment	
341	Number	
	Title	*Study Report 1*
	Element	m5-3-5-2-study-reports-of-uncontrolled-clinical-studies
	Directory	m5/53-clin-stud-rep/535-rep-effic-safety-stud/*indication-1*/5352-stud-rep-uncontr/*study-report-1*
	Comment	
342	Number	
	Title	*Study Report 2*
	Element	m5-3-5-2-study-reports-of-uncontrolled-clinical-studies
	Directory	m5/53-clin-stud-rep/535-rep-effic-safety-stud/*indication-1*/5352-stud-rep-uncontr/*study-report-2*
	Comment	
343	Number	
	Title	*Study Report 3*
	Element	m5-3-5-2-study-reports-of-uncontrolled-clinical-studies
	Directory	m5/53-clin-stud-rep/535-rep-effic-safety-stud/*indication-1*/5352-stud-rep-uncontr/*study-report-3*
	Comment	
344	Number	5.3.5.3
	Title	Reports of Analyses of Data from More than One Study
	Element	m5-3-5-3-reports-of-analyses-of-data-from-more-than-one-study
	Directory	m5/53-clin-stud-rep/535-rep-effic-safety-stud/*indication-1*/5353-rep-analys-data-more-one-stud
	Comment	
345	Number	
	Title	*Study Report 1*
	Element	m5-3-5-3-reports-of-analyses-of-data-from-more-than-one-study
	Directory	m5/53-clin-stud-rep/535-rep-effic-safety-stud/*indication-1*/5353-rep-analys-data-more-one-stud/*study-report-1*
	Comment	
346	Number	
	Title	*Study Report 2*

	Element	m5-3-5-3-reports-of-analyses-of-data-from-more-than-one-study
	Directory	m5/53-clin-stud-rep/535-rep-effic-safety-stud/*indication-1*/5353-rep-analys-data-more-one-stud/*study-report-2*
	Comment	
347	Number	
	Title	*Study Report 3*
	Element	m5-3-5-3-reports-of-analyses-of-data-from-more-than-one-study
	Directory	m5/53-clin-stud-rep/535-rep-effic-safety-stud/*indication-1*/5353-rep-analys-data-more-one-stud/*study-report-3*
	Comment	
348	Number	5.3.5.4
	Title	Other Study Reports
	Element	m5-3-5-4-other-study-reports
	Directory	m5/53-clin-stud-rep/535-rep-effic-safety-stud/*indication-1*/5354-other-stud-rep
	Comment	
349	Number	
	Title	*Study Report 1*
	Element	m5-3-5-4-other-study-reports
	Directory	m5/53-clin-stud-rep/535-rep-effic-safety-stud/*indication-1*/5354-other-stud-rep/*study-report-1*
	Comment	
350	Number	
	Title	*Study Report 2*
	Element	m5-3-5-4-other-study-reports
	Directory	m5/53-clin-stud-rep/535-rep-effic-safety-stud/*indication-1*/5354-other-stud-rep/*study-report-2*
	Comment	
351	Number	
	Title	*Study Report 3*
	Element	m5-3-5-4-other-study-reports
	Directory	m5/53-clin-stud-rep/535-rep-effic-safety-stud/*indication-1*/5354-other-stud-rep/*study-report-3*
	Comment	
352	Number	5.3.6
	Title	Reports of Postmarketing Experience
	Element	m5-3-6-reports-of-postmarketing-experience
	Directory	m5/53-clin-stud-rep/536-postmark-exp
	Comment	

353	Number	5.3.7
	Title	Case Report Forms and Individual Patient Listings
	Element	m5-3-7-case-report-forms-and-individual-patient-listings
	Directory	m5/53-clin-stud-rep/537-crf-ipl
	Comment	
354	Number	
	Title	*Study 1*
	Element	m5-3-7-case-report-forms-and-individual-patient-listings
	Directory	m5/53-clin-stud-rep/537-crf-ipl/*study-1*
	Comment	
355	Number	
	Title	*Document/Dataset 1*
	Element	m5-3-7-case-report-forms-and-individual-patient-listings
	File	m5/53-clin-stud-rep/537-crf-ipl/*study-1*/*filename-1.pdf*
	Comment	The filename and extension should include the description of the file and appropriate file extension according to Appendix 2. Reference should be made to regional guidance for the acceptability of submission of datasets
356	Number	
	Title	*Document/Dataset 2*
	Element	m5-3-7-case-report-forms-and-individual-patient-listings
	File	m5/53-clin-stud-rep/537-crf-ipl/*study-1/filename-2.pdf*
	Comment	
357	Number	
	Title	*Document/Dataset 3*
	Element	m5-3-7-case-report-forms-and-individual-patient-listings
	File	m5/53-clin-stud-rep/537-crf-ipl/*study-1*/*filename-3.pdf*
	Comment	
358	Number	
	Title	*Study 2*
	Element	m5-3-7-case-report-forms-and-individual-patient-listings
	Directory	m5/53-clin-stud-rep/537-crf-ipl/*study-2*
	Comment	define element
359	Number	
	Title	*Document/Dataset 1*

	Element	m5-3-7-case-report-forms-and-individual-patient-listings
	File	m5/53-clin-stud-rep/537-crf-ipl/*study-2/filename-1.pdf*
	Comment	
360	Number	
	Title	*Document/Dataset 2*
	Element	m5-3-7-case-report-forms-and-individual-patient-listings
	File	m5/53-clin-stud-rep/537-crf-ipl/*study-2/filename-2.pdf*
	Comment	
361	Number	
	Title	*Document/Dataset 3*
	Element	m5-3-7-case-report-forms-and-individual-patient-listings
	File	m5/53-clin-stud-rep/537-crf-ipl/*study-2/filename-3.pdf*
	Comment	
362	Number	
	Title	*Study 3*
	Element	m5-3-7-case-report-forms-and-individual-patient-listings
	Directory	m5/53-clin-stud-rep/537-crf-ipl/*study-3*
	Comment	define element
363	Number	
	Title	*Document/Dataset 1*
	Element	m5-3-7-case-report-forms-and-individual-patient-listings
	File	m5/53-clin-stud-rep/537-crf-ipl/*study-3/filename-1.pdf*
	Comment	
364	Number	
	Title	*Document/Dataset 2*
	Element	m5-3-7-case-report-forms-and-individual-patient-listings
	File	m5/53-clin-stud-rep/537-crf-ipl/*study-3/filename-2.pdf*
	Comment	
365	Number	
	Title	*Document/Dataset 3*
	Element	m5-3-7-case-report-forms-and-individual-patient-listings
	File	m5/53-clin-stud-rep/537-crf-ipl/*study-3/filename-3.pdf*
	Comment	

366	Number	5.4
	Title	Literature References
	Element	m5-4-literature-references
	Directory	m5/54-lit-ref
	Comment	Copies of literature references should ordinarily be submitted as individual files (i.e,. one for each reference).
367	Number	
	Title	*Reference 1*
	Element	m5-4-literature-references
	File	m5/54-lit-ref/*reference-1.pdf*
	Comment	
368	Number	
	Title	*Reference 2*
	Element	m5-4-literature-references
	File	m5/54-lit-ref/*reference-2.pdf*
	Comment	
369	Number	
	Title	*Reference 3*
	Element	m5-4-literature-references
	File	m5/54-lit-ref/*reference-3.pdf*
	Comment	

370	Number	
	Title	
	Element	
	Directory	util
	Comment	utilities
371	Number	
	Title	
	Element	
	Directory	util/dtd
	Comment	DTDs/Schemas – it is not necessary to include regional DTDs/Schemas other than the one for the region to which the application is being made. File names in rows 372 - 379 are illustrative only. Please consult regional guidance for the current name and version of the files.
372	Number	
	Title	
	Element	
	File	util/dtd/ich-ectd-n.dtd
	Comment	DTD for the instance – the version used to create the eCTD submission must be included. “n” denotes the specific version (e.g., 3-2).
373	Number	
	Title	
	Element	
	File	util/dtd/eu-regional-n.dtd
	Comment	DTD for the EU specific documentation. “n” denotes the specific version (e.g., 1-1).
374	Number	
	Title	
	Element	
	File	util/dtd/jp-regional-n.xsd
	Comment	Schema for the Japan specific documentation. “n” denotes the specific version (e.g., 1-0).
375	Number	
	Title	
	Element	
	File	util/dtd/us-regional-n.dtd
	Comment	DTD for the US specific documentation. “n” denotes the specific version (e.g., 1-0).

376	Number	
	Title	
	Element	
	File	util/dtd/xx-regional-n.dtd
	Comment	DTD for the xx specific documentation, where xx is a two character country code from ISO-3166-1. “n” denotes the specific version (e.g., 1-0).
377	Number	
	Title	
	Element	
	Directory	util/style
	Comment	Directory for style sheets – ICH and regional stylesheets
378	Number	
	Title	
	Element	
	File	util/style/ectd-n.xsl
	Comment	The specific version of the eCTD stylesheet used by the applicant as a reference during the creation of the submission should be included. “n” denotes the specific version (e.g., 1-0).
379	Number	
	Title	
	Element	
	File	util/style/xx-regional-n.xsl
	Comment	Stylesheet for the xx specific documentation, where xx is a two character country code from ISO-3166-1. “n” denotes the specific version (e.g., 1-0).

Appendix 5: Region Specific Information Including Transmission and Receipt

Introduction

This section describes region specific information for content that is not explicitly included in the Common Technical Document and logistical details appropriate for the transmission and receipt of submissions using the electronic Common Technical Document.

Region Specific Information: Module 1

This module contains administrative information that is unique for each region. There will be local requirements for both the content and electronic component of module 1. The eCTD backbone was developed to enable the transfer of the regional information included in a regulatory dossier.

Regional guidance will provide the specific instructions on how to provide the administrative forms and detailed prescribing information. Please refer to this information and appendix 6 when preparing module 1. Module 1 includes all administrative documents (e.g., forms and certifications) and labeling, including the documents described in regional guidance.

Not all regionally specific documents are included in module 1. Technical reports required for a specific region should be placed in modules 2 to 5. These reports should be included in the module most appropriate for the content of the information provided.

Each region provides specific guidance on the format and content of the regional requirements of each module. Table 5-1 provides contact information for each region.

Table 5-1

Region	Internet Address	Electronic Mail Contact
European Union	http://www.emea.europa.eu	esubmission@emea.europa.eu
Food And Drug Administration, USA	www.fda.gov/cber www.fda.gov/cder	esubprep@fda.hhs.gov esub@fda.hhs.gov
Ministry of Health, Labour and Welfare, Japan	http://www.mhlw.go.jp http://www.pmda.go.jp	ectd@pmda.go.jp
Health Canada	http://www.hc-sc.gc.ca	ereview@hc-sc.gc.ca

Submission Addresses

Submissions should be sent directly to the appropriate regulatory authority. Information on how to send submissions to each regulatory authority can be found at the reference location in Table 5-2.

Table 5-2

Regulatory Authority	Reference location
EMEA, European Union or national agencies	http://www.emea.europa.eu http://www.hma.eu/
Ministry of Health, Labour and Welfare, Japan	http://www.mhlw.go.jp http://www.pmda.go.jp
Food and Drug Administration, United States of America	http://www.fda.gov/
Health Canada, Health Protection Branch, Canada	http://www.hc-sc.gc.ca

Media

Refer to regional guidance for appropriate media types.

Cover Letter

Applicants should provide a cover letter as a PDF file (e.g., cover.pdf). A paper cover letter should also be included with non-electronic portions of the submission (such as forms with signatures or seals, and certifications). The cover letter should include:

- A description of the submission including appropriate regulatory information.
- A listing of the sections of the submission filed as paper, electronic, or both paper and electronic.
- A description of the electronic submission including type and number of electronic media, approximate size of the submission, and if appropriate, characteristics concerning the media (e.g., format used for DLT tapes) based on regional guidance.
- A statement that the submission is virus free with a description of the software used to check the files for viruses.
- The regulatory and information technology points of contact for the submission.

Transport

Secure data exchange over the Internet is the recommended means for transporting submissions. However, until the regulatory authorities can develop secure electronic gateways, submissions should continue to be physically transported by courier or registered mail.

Security

An MD5 checksum should be included for each physical file in the eCTD. The checksum enables the recipient to verify the integrity of each of the content files in the submission. Each leaf of the XML eCTD instance contains the location and calculated checksum of each of the files.

A checksum of the XML eCTD instance should also be included. Applicants should name this checksum file index-md5.txt and include it as a file in the same directory as the XML eCTD instance. Applicants should print the contents of the index-md5.txt file and include the paper copy with the paper cover letter for the submission. A separate file containing the checksum of the regional index file is unnecesary as that file (and its MD5 checksum) is referenced by a leaf element in the index.xml file.

An applicant can provide the eCTD as an encrypted file in accordance with the ICH M2 Recommendation 4.1, if the regulatory body has implemented it. This solution enables the eCTD to be encrypted and transferred over the Internet (if Internet receipt is implemented regionally) or to be encrypted on one of the approved physical media standards. The purpose of encryption is to protect the privacy of the confidential information and to ensure it is only available to the authorized receiver. Encryption is always appropriate when the eCTD is sent via the Internet.

Encryption is not considered necessary if the information is sent using a physical media, although encryption is an option. The applicant should assume all liability for the media until it is delivered to the regulatory authority.

Applicants should not include any file level security settings or password protection for individual files in the eCTD. Applicants should allow printing, changes to the document, selecting text and graphics, and adding or changing notes and form fields. Internal security and access control processes in the regulatory authority should maintain the integrity of the submitted files.

Receipt

Upon arrival at the regulatory authority, the submission is archived according to local regulations. A read-only copy of the submission is then made available to the review community in the regulatory authority. This is typically done by placing the copy on a network server.

Acknowledgment

Each regulatory authority should acknowledge the receipt of the eCTD submission according to the policy and procedure of the individual regulatory authority. Applicants should use the address in Table 5-1 to find guidance regarding acknowledgments.

Appendix 6: The eCTD XML Submission

Background

Many factors have influenced the design of the eCTD. Factors that have had a significant impact on the design are listed below:

- The submissions should accommodate full regulatory dossiers, supplements, amendments, and variations.
- The submissions should be able to accommodate regional requirements that are represented in regional guidance documents, regulations, and statutes.
- The technology should be extensible so that as technology changes, the new electronic solutions can be accommodated.

The eCTD is designed around the concept of a backbone. The backbone is similar to a container that holds pointers (called leaf elements) to the files that are part of the submission. The backbone is based on an XML Document Type Definition (DTD). There is a close relationship between the documents defined in the CTD and the elements defined in the eCTD DTD. The leaf elements in the backbone will provide the navigation links to the various files and information that make up the submission.

The file that is produced based on the XML eCTD DTD is the eCTD XML instance or XML backbone. The XML backbone allows more than one leaf element to point to the same physical file. This should be done with caution since managing the life cycle of that file can be more difficult for the regulatory authority if there is more than one pointer to the file.

File Names and Directory Structure

Recipients of the eCTD should be able to directly navigate through the submission at the folder and file level (i.e., without benefit of a customized end user application.) The structure of the eCTD and instructions for how to create folder names facilitate this type of navigation.

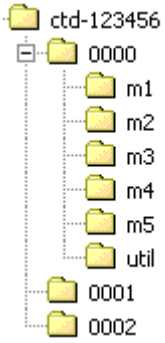
In order to preserve the navigational linkages that can be present in the documents contained in the eCTD, the directory structure will be preserved by the agencies. The navigational links should be relative links within a module.

Specific folder and file names have been defined in appendix 4. The top level of the directory structure will vary by region. The identification of the top-level folder uniquely identifies the application in a region. Consult regional guidance for specific requirements on top-level folder naming conventions. The original submission and subsequent amendments and variations should use the same top-level folder name. Submissions should be differentiated by a subfolder named according to the sequence number of the submission in that region. For all regions, sequence numbers should be unique within the overall application. For Japanese submissions, sequential numbering is required. For all other regions, it is preferred, but not required. Table 6-1 and Figure 6-1 illustrate this naming convention.

Table 6-1

Example top level folder name	Sequence number	Type of submission
ctd-123456	0000	Original Submission
ctd-123456	0001	First amendment, supplement or variation
ctd-123456	0002	Second amendment, supplement or variation
…		
ctd-123456	Nnnn	Nth amendment, supplement or variation

Figure 6-1



You should submit the XML backbone as a single file named *index.xml*, which should be placed in the submission sequence number folder for that submission. In the example shown in Figure 6-1, there should be an *index.xml* file in folder "0000", folder "0001" and folder "0002". The MD5 checksum file, *index-md5.txt*, should be in each folder with the corresponding *index.xml* file. The DTD for *index.xml* should be in the "util" folder for each submission.

The regional administrative XML backbone file should be in the region specific module 1 folder for each submission. For each sequence, the operation attribute of the leaf element referencing this file is always 'new'. A separate file containing the checksum of the regional index file is unnecessary as that file (and its MD5 checksum) is referenced by the index.xml file. The DTD for the regional XML backbone file should be in the util folder for each submission.

Table 6-2 presents the file locations for the example in Figure 6-1.

Table 6-2

Submission Folder	Files
ctd-123456/0000	index.xml index-md5.txt
ctd-123456/0000/m1/us	us-regional.xml
ctd-123456/0000/util/dtd	ich-ectd-3-x.dtd us-regional-vx-x.dtd
ctd-123456/0001	index.xml index-md5.txt
ctd-123456/0001/m1/us	us-regional.xml
ctd-123456/0001/util/dtd	ich-ectd-3-x.dtd us-regional-vx-x.dtd
ctd-123456/0002	index.xml index-md5.txt
ctd-123456/0002/m1/us	us-regional.xml
ctd-123456/0002/util/dtd	ich-ectd-3-x.dtd us-regional-vx-x.dtd

Life Cycle Management

It is important for the recipients of an eCTD to be able to establish the location of the submission in the life cycle of a product.

The eCTD is capable of containing initial submissions, supplements, amendments, and variations. There are no uniform definitions for these terms in the three regions, but amendments and supplements are terms used in the United States. Variations apply in Europe. The variations, supplements, and amendments are used to provide additional information to an original regulatory dossier. For example, if a new manufacturer for the drug substance were being proposed, this would result in submission of an amendment or supplement to the FDA and a variation to Europe. When regulatory authorities request additional information, the information is also provided as a variation, supplement, or amendment to the original submission. Therefore, the regulatory agencies need a way to manage the life cycle of the submission. This function will be provided by each regulatory authority in the form of guidance that can include regional DTDs and specifications. The relevant regional DTD should be referenced in the eCTD DTD by the applicant.

The eCTD DTD provides some facilities for life cycle management at the leaf element level but does not fully support the life cycle at the submission level. When revisions are sent to a regulatory authority, the new leaf element should be submitted in the same location in the backbone as the leaf element being appended, replaced or deleted. The "modified-file" attribute of the leaf element should contain the leaf ID of the leaf being appended, replaced, or deleted. This will allow the regulatory authority to accurately locate the original leaf and update the original leaf's status. A detailed description of modified-file is provided in the next section.

Operation Attribute

The operation attribute is a key to managing each individual leaf element in a submission. The applicant uses the operation attribute to tell the regulatory authority how the applicant intends the leaf elements in the submission to be used. The operation attribute describes the relation between leaf elements in subsequent submissions during the life cycle of a medicinal product. In the very first submission all the leaf elements would typically be new. In the second, third, and subsequent submissions, all the newly submitted leaf elements can have different operation attributes due to having or not having a relation with previously submitted leaf elements. Table 6-3 describes the meaning of each allowed value of the operation attribute.

Table 6-3: Understanding the Operation Attribute

Operation attribute value	Meaning	What the reviewer might see when using the Agency review software	
		This leaf	Previous leaf
New	The leaf element has no relationship with leaf elements submitted previously. It is acceptable for multiple leaf elements in a single eCTD element to have the operation attribute of new, either in the same sequence or during the life cycle of the application.	Current	
Append	This means there is an existing leaf element to which this new leaf element should be associated. (e.g., providing missing or new information to that leaf element). It is recommended that append not be used to associate two leaf elements in the same submission (e.g., splitting a file due to size restrictions). However, use of append could be appropriate when leaf elements which normally would be submitted with the append relationship are provided in the same sequence (e.g., a document and its amendment). Consult with the regulatory authority before using append to associate two leaf elements in the same sequence.	Current	Current - Appended
Replace	This means there is an existing leaf element that this	Current	Replaced

Operation attribute value	Meaning	What the reviewer might see when using the Agency review software	
		This leaf	Previous leaf
	new leaf element replaces.		
Delete	There is no new file submitted in this case. Instead, the leaf element has the operation of "delete" and the "modified-file" attribute identifies the leaf element in a previous submission that is to be considered no longer relevant to the review. As there is no file being submitted, the checksum attribute value will be empty i.e., double quotation marks with no entry between ("").		No longer relevant to the review

The purpose of the modified-file attribute is to provide the location of a leaf element that is being modified (i.e. replaced, appended or deleted) by the subsequent leaf element. The modified-file attribute should have a value when the operation attribute has a value of *append*, *replace* or *delete*. The modified-file attribute points to the "index.xml" file and the leaf ID of the leaf element being altered. The modified-file attribute can only target a single leaf element. Furthermore, once a leaf element has been replaced or deleted by another leaf element, it is no longer current and can no longer be targeted by any subsequent leaf elements through the modified-file attribute.

An example of a modified-file attribute value is provided below:

modified-file="../0001/index.xml#a1234567"

This would provide the information needed to locate the file with the leaf element ID assigned as "a1234567" and provided in the sequence folder numbered "0001".

If a modified-file attribute is presented with no value (i.e. no characters or spaces between the quotation marks, modified-file="") it will be the same as not including the attribute in the leaf element.

The following case examples show the use of each of the operation attribute values. These examples do not cover all possible situations. Consult the appropriate regulatory authority if you have specific questions about the use of the operation attribute. When actually populating the XML instance, use the leaf ID to refer to files.

Case 1 – The first submission of a dossier.

Table 6-4

Submission sequence #	File name	Operation	File Being Modified	Sample logical display in a review tool
0000	0000\…\structure.pdf	New		structure.pdf (current)

Case 2 – Two submissions. Submission 0000 is the first submission of a dossier. Submission 0001 is a subsequent amendment or variation in which the applicant intends to completely replace the structure.pdf file in submission 0000. The intent is to keep the original structure.pdf for historical purposes but to consider only the contents of the 0001\…\structure2.pdf as relevant to the review. These two submissions could be described as follows:

- Submission 0000 is the first submission of the file structure.pdf, and this file is the current version of this file.
- Submission 0001, which is submitted at a later time, is the submission of the file structure2.pdf, which is now current and replaces the file structure.pdf in submission 0000.

There is no requirement to preserve file names during life cycle changes; in fact, logical differences in file names can be helpful during review when both files are open simultaneously for comparative or other purposes.

Table 6-5

Submission sequence #	File name	Operation	File Being Modified	Sample logical display in a review tool
0000	0000\…\structure.pdf	New		structure.pdf (current)
0001	0001\…\structure2.pdf	Replace	0000\…\structure.pdf	*structure.pdf (replaced)* structure2.pdf (current)

Case 3 – Two submissions. Submission 0000 is the first submission of a dossier. Submission 0001 is an amendment or variation where the applicant intends to add new information to the original structure.pdf file, which was submitted in submission 0000. The intent is to have the reviewer consider the contents of both files relevant to the submission. These two submissions could be described as follows:

- Submission 0000 is the first submission of the file structure.pdf, and this file is the current version of this file.
- Submission 0001, submitted at a later time, is the submission of the file structure2.pdf, which is the current file but contains information that should be appended to file structure.pdf in submission 0000. Both files should be considered relevant to the review of the dossier.

There is no requirement to preserve file names during life cycle changes; in fact, logical differences in file names can be helpful during review when both files are open simultaneously for comparative or other purposes.

Table 6-6

Submission sequence #	File name	Operation	File Being Modified	Sample logical display in a review tool
0000	0000\…\structure.pdf	New		structure.pdf (current)
0001	0001\…\structure2.pdf	Append	0000\...\structure.pdf	structure.pdf (current - appended) structure2.pdf (current)

Case 4 – Two submissions. Submission 0000 is the first submission of a dossier. Submission 0001 is an amendment or variation where the applicant intends to delete a file in the previous submission. The intent is to have the reviewer disregard the contents of the original file, possibly because it should not have been submitted with the original dossier. These two submissions could be described as follows:

- Submission 0000 is the first submission of the file structure.pdf and this file is the current version of this file.
- Submission 0001, submitted at a later time, requests that the file structure.pdf in submission 0000 be deleted and no longer considered relevant to the review of the dossier.

Table 6-7

Submission sequence #	File name	Operation	File Being Modified	Sample logical display in a review tool
0000	0000\...\structure.pdf	New		structure.pdf (current)
0001		Delete	0000\...\structure.pdf	**structure.pdf (no longer relevant to the review)**

File Reuse

It is important to the successful utilization of the eCTD to clearly understand the differences between a file and a leaf element. When reviewing an eCTD sequence, either through the stylesheet or an eCTD viewing tool, the presentation of the organization of the content files is based on the organization of the leaf elements in the index.xml files. The underlying file and folder structure is not critical to the view of the organization of the files referenced in the XML backbone. This aspect of the eCTD provides users the ability to provide a file once and display it in multiple locations of the eCTD by providing multiple leaf

elements referencing that file. Users of the eCTD Specification are encouraged to provide files once in a sequence and provide as many leaf elements referencing that file as necessary. The location of the file is not critical and should only be included once in an appropriate place in the folder structure. Suppliers of eCTD viewing tools are encouraged to develop a visual way of displaying when this occurs so reviewers can readily identify files which are referenced multiple times.

This capability can also be extended across sequences and even applications as long as the location of the file is accurately cited in the xlink:href attribute for the leaf element referencing that file. Suppliers of eCTD viewing tools are encouraged to develop a visual way of displaying the difference between a leaf element referring to a file in the current sequence and a leaf element referring to a file in a previous sequence. In these situations, validation checks for the presence of files referenced by the XML backbone should allow for the xlink:href to refer to files in other sequences and not prevent viewing of the eCTD by another applicant/regulator. Users of the eCTD Specification should consult with the regulatory authority before referencing content across sequences and/or applications.

DTD Content Model

The content model of the eCTD is derived from the organization of the Common Technical Document. The graphic representation of a portion of the content model is shown below. The content model is hierarchical starting at the "ectd" and going down to a specific item to be included in the submission.

Figure 6-2

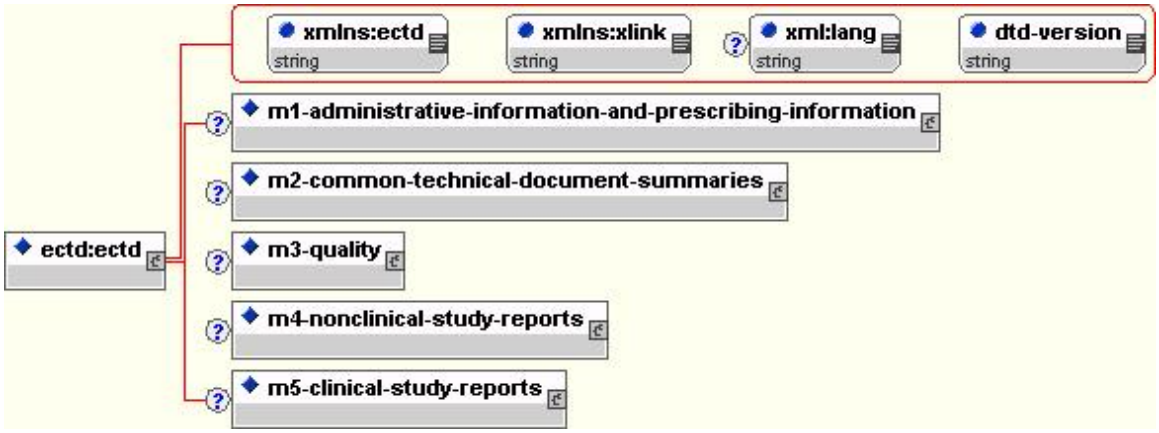
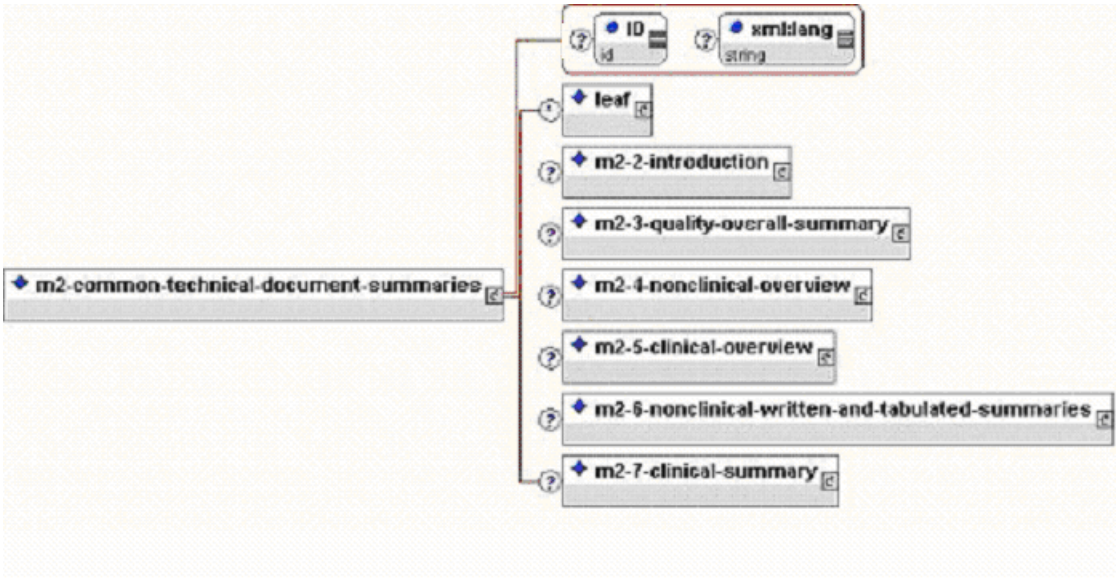


Figure 6-3 shows how the section of the CTD containing summaries is structured.

Figure 6-3



Once the appropriate element has been selected (e.g., Figure 6-4), you should use the <leaf> element and attributes (Figure 6-5) to specify a file in the submission. See "eCTD Element/Attribute Instructions" in this appendix for details.

Figure 6-4

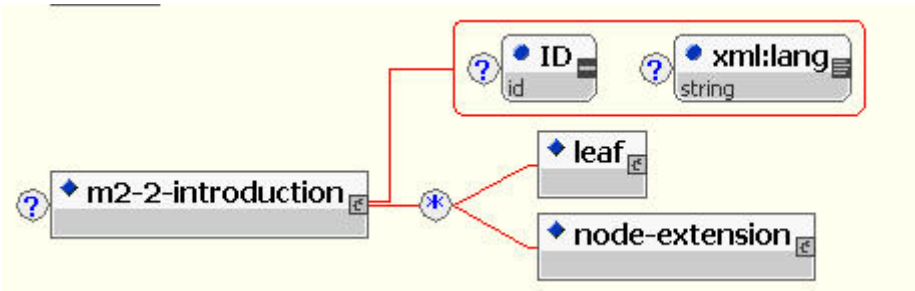
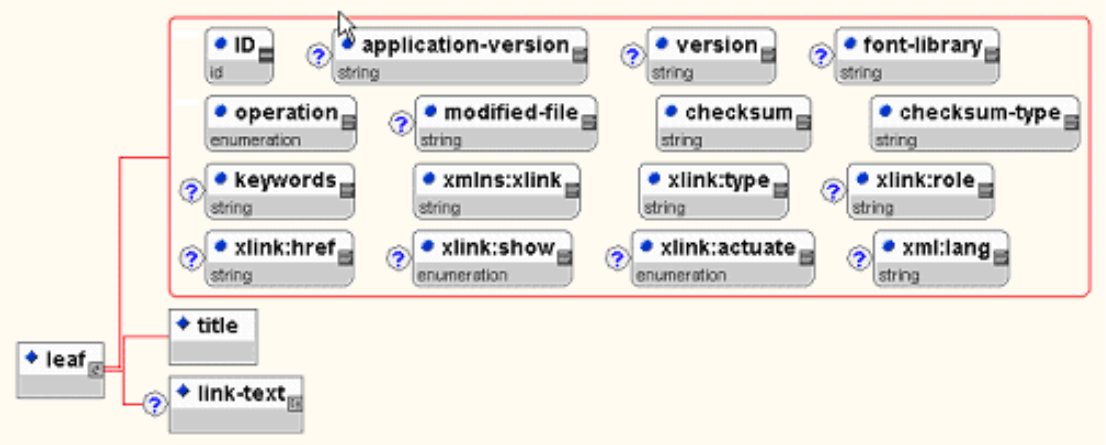


Figure 6-5



eCTD Element/Attribute Instructions

The eCTD consists of 5 primary modules:

- m1-administrative-information-and-prescribing-information
- m2-common-technical-document-summaries
- m3-quality
- m4-nonclinical-study-reports
- m5-clinical-study-reports

Each of the 5 modules is divided into one or more elements, each with a distinct element identifier that represents a CTD table of contents location. The steps should be completed as shown in the following example, where all files are submitted for modules 1 through 5:

1. Select an element that best corresponds to the CTD table of contents location for a document or file being submitted. For example, select the element <m2-7-3-summary-of-clinical-efficacy> to submit the summary of clinical efficacy document.
2. Specify any additional element attribute as appropriate; in this example, specify the 'indication' attribute to identify the subject of the efficacy summary in 2.7.3.
3. Create a child <leaf> element within the <m2-7-3-summary-of-clinical-efficacy> element.
4. Provide the relative location and file name of the actual file in the "xlink:href" attribute for the leaf element.
5. Provide a descriptive and concise title for the file in the <title> element of the leaf element.
6. Provide information for the appropriate attributes of the leaf element as described in Table 6-8.

Table 6-8 describes each of these elements and attributes in further detail.

Table 6-8

Element	Attribute	Description/Instructions	Example
Any table of contents element such as <m2-4-nonclinical-overview>		A table of contents element represents a grouping of one or more files related to a specific section of the Common Technical Document. A number of TOC elements can be further defined by the use of attributes. The eCTD DTD defines the following attributes at various places in the eCTD: substance, manufacturer, product-name, indication, excipient, dosage-form (e.g., 2.3.S and 3.2.S have two 'free text' attributes: substance and manufacturer; 5.3.5 has the additional 'free text' attribute, indication). To be consistent with the CTD General Q&A, values for these attributes should be included where specified as is appropriate. There is currently no standard terminology list for any of these attributes and applicants should carefully choose the text of these attributes as they can not be easily changed during the life cycle of the application. One or more child <leaf> elements can be declared for a parent table of contents element. It is possible to extend a table of contents element by providing a <node-extension> element. Node extensions should only be added at the lowest level of the defined table of contents elements. Using node extensions is discouraged and should be done only when unavoidable. Please refer to regional guidance before using node extensions. See the section "Instructions for extending XML eCTD DTD elements" in this appendix (Example 6-5).	
	ID	A unique identifier for this location in the XML instance.	id403 (note: At this level, ID is optional)
	xml:lang	The primary language used by the files in this entire section of the submission. Use ISO-639 standard language abbreviations	en

Element	Attribute	Description/Instructions	Example
<leaf>		A leaf element is a reference to a file. One or more leaf elements can be declared for a table of contents element.	
	application-version	This is the version of the file format produced by the software application that was used to create this file.	PDF 1.4
	font-library	Reserved for Future Use	
	ID	The ID attribute is intended to be a unique reference within the submission that can be used to reference the item from another item within the XML document. An XML ID value begins with an alphabetic character or underscore. If an applicant is using an internal ID generator that uses only numbers, appending this generated number to a leading alphabetic character or underscore will create a valid ID value.	id050520 NOTE: See the XML-ID recommendations on the W3C website for info on the composition of this attribute value (http://www.w3.org/TR/xml-id/#processing)
	checksum	The checksum value for the file being submitted.	e854d3002c02a61fe5cbe926fd97b001
	checksum-type	The checksum algorithm used.	MD5
	modified-file	The purpose of the modified-file attribute is to provide the location of the leaf that is being modified (i.e. replaced, appended or deleted) by the leaf element. The modified-file attribute should have a value when the operation attribute has a value of append, replace or delete. The modified-file attribute points to the "index.xml" file and the leaf ID of the leaf being altered.	../0001/index.xml#a1234567
	operation	Indicates the action to be performed. You should select one of the following valid values: • new • replace • append • delete See the section Operation Attribute in this appendix for details on the meaning of these values.	new
	version	The file submitter's internal version number or version identification for the file.	V23.5
	xlink:actuate	Reserved for Future Use	

Element	Attribute	Description/Instructions	Example
	xlink:href	Provides the reference to the actual content file. You should use the relative path to the file and the file name. The content file does not need to be in the same sequence as the leaf element that refers to it.	0000/m2/27-clin-sum/literature-references.pdf
	xlink:role	Reserved for Future Use	
	xlink:show	Reserved for Future Use	
	xlink:type	Fixed value of "simple"	simple
	keywords	Reserved for Future Use	
<title>		As part of the leaf element, this element contains a practical name for the file being referenced by the leaf.	Study Report 1234 NOTE: Leaf titles should be concise; 1024 bytes (512 characters) are proposed as the maximum length
	ID	Unique identifier for this location in the XML instance. Leaf ID starts with an alphabetic character or underscore.	a1234567 NOTE 1: See the XML-ID recommendations on the W3C website for info on the composition of this attribute value (http://www.w3.org/TR/xml-id/#processing) NOTE 2: At this level, ID is optional
<link-text>		Reserved for Future Use	
<xref>		Reserved for Future Use	

Example 6-1: Instructions for a Simple New Submission[7]

The following XML fragment demonstrates the submission of a clinical overview of efficacy as a single PDF document.

```
<?xml version = "1.0" encoding = "UTF-8"?>
<!DOCTYPE ectd:ectd SYSTEM "util/dtd/ich-ectd-3-x.dtd">
<?xml-stylesheet type="text/xsl" href="util/style/ectd-2-1-x.xsl"?>
<ectd:ectd xmlns:ectd = "http://www.ich.org/ectd" xmlns:xlink = "http://www.w3c.org/1999/xlink">
        <m2-common-technical-document-summaries>
                <m2-5-clinical-overview xml:lang = "en">
                        <leaf ID="s123456" operation = "new" xlink:type = "simple" checksum-type="md5"
                        checksum = "e854d3002c02a61fe5cbe926fd973401" xlink:href = "m2/25-clin-
                        over/clinical-overview.pdf" application-version = "PDF 1.4">
                        <title>Clinical Overview</title>
                        </leaf>
                </m2-5-clinical-overview>
        </m2-common-technical-document-summaries>
</ectd:ectd>
```

This submission includes the file "clinical-overview.pdf" in the relative directory "m2/25-clin-over/" (i.e. the one starting below the dossier number directory). The file is "new" and has a descriptive name of "Clinical Overview"

The regional review application should treat this as a new submission to be associated with the submission identified in CTD module 1, which is region specific.

[7] Note that these XML examples are examples only and do not necessarily contain all of the elements and attributes that you should use when preparing an eCTD submission.

If this is the first submission for Dossier CTD 123456, all the files in this submission would typically be in the ctd-123456\0000 directory and below.

Example 6-2: Instructions for an Amendment, Supplement, or Variation

In the previous example, a clinical overview was submitted. In this example, it is replaced by an updated version.

To replace a file, add the replacement <leaf> element under the same element as the original file.
If this is the second submission for Dossier CTD 123456, all the files in this submission would typically be in the ctd-123456\0001 directory and below.

```
<?xml version = "1.0" encoding = "UTF-8"?>
<!DOCTYPE ectd:ectd SYSTEM "util/dtd/ich-ectd-3-x.dtd">
<?xml-stylesheet type="text/xsl" href="util/style/ectd-2-1-x.xsl"?>
<ectd:ectd xmlns:ectd = "http://www.ich.org/ectd" xmlns:xlink = "http://www.w3c.org/1999/xlink">
<m2-common-technical-document-summaries>
        <m2-5-clinical-overview xml:lang = "en">
                <leaf ID="a123457" operation = "replace"  xlink:type = "simple" checksum-type="md5" checksum =
                "502e9ab5827431f077340cea3b5e465a" xlink:href = "m2/25-clin-over/clinical-overview-revised.pdf"
                application-version = "PDF 1.4" modified-file = "../0000/index.xml#s123456">
                   <title>Clinical Overview</title>
                </leaf>
        </m2-5-clinical-overview>
</m2-common-technical-document-summaries>
</ectd:ectd>
```

Example 6-3: Instructions for Multiple Indications

Multiple therapeutic indications use an additional attribute associated with the <m2-7-3-summary-of-clinical-efficacy> and the <m5-3-5-reports-of-efficacy-and-safety-studies> elements to allow multiple indications to be submitted. There is currently no standard terminology list for 'indication'. Applicants should choose these attributes carefully as they can not be easily changed during the life cycle of the application. The only way this can be accomplished currently is to delete all the leaf elements with the incorrect attribute value and provide new leaf elements for those files with the modified attribute value. Applicants should consult with the regional authority before attempting to modify these attributes to discuss the appropriateness of, and approach to be taken for, this type of change. The following table shows the use of these attributes.

Table 6-9

Element	Attribute	Description/Instructions	Example
<m2-7-3-summary-of-clinical-efficacy>	indication	Name of the indication	Pain
<m5-3-5-reports-of-efficacy-and-safety-studies>	indication	Name of the indication.	Pain

Note that the indication attribute is used by the regulatory authority to apply to all the table of contents elements beneath the <m2-7-3-summary-of-clinical-efficacy> and <m5-3-5-reports-of-efficacy-and-safety-studies> elements. The following example expands on the instance showing the submission of information about two indications (pain and nausea).

```
<?xml version = "1.0" encoding = "UTF-8"?>
<!DOCTYPE ectd:ectd SYSTEM "util/dtd/ich-ectd-3-x.dtd">
<?xml-stylesheet type="text/xsl" href="util/style/ectd-2-1-x.xsl"?>
```

```
<ectd:ectd xmlns:ectd = "http://www.ich.org/ectd" xmlns:xlink = "http://www.w3c.org/1999/xlink">
    <m2-common-technical-document-summaries>
        <m2-7-clinical-summary>
        <m2-7-3-summary-of-clinical-efficacy indication = "pain">
            <leaf ID="s123456"operation = "new" xlink:type = "simple" checksum-type="md5" checksum =
            "5aa5c0e630a700af869e4c72535fc922" xlink:href = "m2/27-clin-sum/summary-clin-efficacy-
            pain.pdf">
                <title>pain efficacy summary</title>
            </leaf>
        </m2-7-3-summary-of-clinical-efficacy>
        <m2-7-3-summary-of-clinical-efficacy indication = "nausea">
            <leaf ID="a123457" operation = "new" xlink:type = "simple" checksum-type="md5" checksum =
            "bde4d34dc80678a266352daf450c3962" xlink:href = "m2/27-clin-summ/summary-clin-efficacy-
            nausea.pdf">
                <title>nausea efficacy summary</title>
            </leaf>
        </m2-7-3-summary-of-clinical-efficacy>
        </m2-7-clinical-summary>
    </m2-common-technical-document-summaries>
    <m5-clinical-study-reports>
        <m5-3-clinical-study-reports>
        <m5-3-5-reports-of-efficacy-and-safety-studies indication = "pain">
            <m5-3-5-1-study-reports-of-controlled-clinical-studies-pertinent-to-the-claimed-indication>
                <leaf ID="a123458" operation = "new" xlink:type = "simple" checksum-type="md5" checksum =
                    "a4529c4a257f07f8a0ec591dde854578" xlink:href = "m5/53-clin-stud-rep/535-rep-eff-safety-
                    stud/pain/pain-sr1.pdf">
                    <title>pain study report 1</title>
                </leaf>
            </m5-3-5-1-study-reports-of-controlled-clinical-studies-pertinent-to-the-claimed-indication>
        </m5-3-5-reports-of-efficacy-and-safety-studies>
        <m5-3-5-reports-of-efficacy-and-safety-studies indication = "nausea">
            <m5-3-5-1-study-reports-of-controlled-clinical-studies-pertinent-to-the-claimed-indication>
                <leaf ID="a123459" operation = "new" xlink:type = "simple" checksum-type="md5" checksum =
                    "c5c39f594b2070a57bea66e58860efcf" xlink:href = "m5/53-clin-stud-rep/535-rep-eff-safety-
                    stud/nausea/nausea-sr15.pdf" >
                    <title>nausea study report 15</title>
                </leaf>
                <leaf ID = "a123460" operation = "new" xlink:type = "simple" checksum-type = "md5" checksum
                    = "15faf198015f3599acabb7755c2d6b0c" xlink:href = "m5/53-clin-stud-rep/535-rep-eff-
                    safety-stud/nausea/5351-stud-rep-contr/xyz0015/nausea-sr15.pdf">
                        <title>nausea study report 15</title>
                </leaf>
            </m5-3-5-1-study-reports-of-controlled-clinical-studies-pertinent-to-the-claimed-indication>
        </m5-3-5-reports-of-efficacy-and-safety-studies>
        </m5-3-clinical-study-reports>
    </m5-clinical-study-reports>
</ectd:ectd>
```

Example 6-4: Instructions for Multiple Drug Substances, Manufacturers, and Products

Multiple drug substances use additional attributes associated with the <m3-2-s-drug-substance> element to allow unique combinations of the drug substance name and manufacturer to be submitted. There are currently no standard terminology lists for these attributes. Applicants should choose these attributes carefully as they can not be easily changed during the life cycle of the application. The only way this can be accomplished currently is to delete all the leaf elements with the incorrect attribute value and provide new leaf elements for those files with the modified attribute value.Applicants should consult with the regional authority before attempting to modify these attributes to discuss the appropriateness of, and approach to be taken for, this type of change. The following table shows the use of these attributes in 3.2.S.

Table 6-10

Element	Attribute	Description/Instructions	Example
<m3-2-s-drug-substance>	substance	Name of one of the drug substances	Acetaminophen
	manufacturer	Name of the manufacturer of the drug substance	My Supplier

Example 6-4A:
This is an example of a section of the instance showing the submission of information about two drug substances (acetominophen and codeine), one of which is supplied by two manufacturers:

```
<m3-2-body-of-data>
        <m3-2-s-drug-substance substance = "Acetaminophen" manufacturer = "My Supplier">
                <leaf  ID="a123456" operation = "new" xlink:type = "simple" checksum-type="md5" checksum =
                "b002e4544c02361fe54be926ae777012" xlink:href = "m3/32-body-data/32s-drug-
                sub/acetaminophen-my-supplier/acetaminophen.pdf">
                        <title>Acetaminophen - My Supplier Data</title>
                </leaf>
        </m3-2-s-drug-substance>
        <m3-2-s-drug-substance substance = "Acetaminophen" manufacturer = "Bulk Company 2">
                <leaf ID="a123457" operation = "new" xlink:type = "simple" checksum-type="md5" checksum =
                "0000cdfa05b1e995f88057150414a783" xlink:href = "m3/32-body-data/32s-drug-
                sub/acetaminophen-bulk-company-2/acetaminophen2.pdf">
                        <title>Acetaminophen - bulk company 2 data</title>
                </leaf>
        </m3-2-s-drug-substance>
        <m3-2-s-drug-substance substance = "Codeine" manufacturer = "Drug company 2">
                <leaf ID="a123458" operation = "new" xlink:type = "simple" checksum-type="md5" checksum =
                "f555a3234f65623fe54be926ee435354" xlink:href = "m3/32-body-data/32s-drug-sub/codeine-
                drug-company-2/codeine-quality-data.pdf">
                        <title>codeine - drug company 2 data</title>
                </leaf>
        </m3-2-s-drug-substance>
</m3-2-body-of-data>
```

Multiple drug products use additional attributes associated with the <m3-2-p-drug-product> element to allow unique combinations of the drug product name and dosage form to be submitted. Applicants should choose these attributes carefully as they can not be easily changed during the life cycle of the application. The only way this can be accomplished currently is to delete all the leaf elements with the incorrect attribute value and provide new leaf elements for those files with the modified attribute value. Applicants should consult with the regional authority before attempting to modify these attributes to discuss the appropriateness of, and approach to be taken for, this type of change. The following table shows the use of these attributes in 3.2.P.

Table 6-11

Element	Attribute	Description/Instructions	Example
<m3-2-p-drug-product>	product-name	Name of one of the drug products	Wonder drug
	dosageform	Dosage form	Capsule
	manufacturer	Manufacturer of the drug product	Company A

Example 6-4B
This is an example of a section of the instance showing the submission of information about two drug products (a capsule and a tablet):

```
<m3-2-body-of-data>
        <m3-2-p-drug-product product-name = "Wonder drug" dosageform="Capsule" manufacturer="Company
        A">
```

```
                <leaf ID="a123456" operation = "new" xlink:type = "simple" checksum-type="md5" checksum =
                "f27cd9e659d8acf7baab10cc753d733c" xlink:href = "m3/32-body-data/32p-drug-prod/capsule-
                5mg/32p1-desc-comp/description-and-composition.pdf">
                        <title>Wonder drug capsule product information</title>
                </leaf>
        </m3-2-p-drug-product>
        <m3-2-p-drug-product product-name = "Wonder drug" dosageform="Tablet" manufacturer="Company A">
                <leaf ID="a123457" operation = "new" xlink:type = "simple" checksum-type="md5" checksum =
                "7490d74c3d5e442ad57daa155253eb16" xlink:href = "m3/32-body-data/32p-drug-prod/tablet-
                5mg/32p1-desc-comp/description-and-composition.pdf">
                        <title>Wonder drug tablet product data</title>
                </leaf>
        </m3-2-p-drug-product>
</m3-2-body-of-data>
```

Example 6-5: Instructions for Extending XML eCTD DTD Elements

An applicant can extend the definition of an element by creating node extensions beneath a defined table of contents element. Using node extensions is discouraged and should be done only when unavoidable. Please refer to regional guidance before using node extensions. The child element <node-extension> should be used for each new table of contents node created. The <title> element value is inherited from the parent element. You should only extend the lowest level of defined elements. For example you can extend the <m2-3-r-regional-information> element but not the <m2-3-quality-overall-summary> element since the latter is not the lowest element defined in the table of contents.

The following is an example of a section of an eCTD instance in which the applicant extends the <m2-3-r-regional-information> to provide specific regional information as requested by a regulatory authority. The title element associated with the <node-extension> describes the extension. Alternatively, the regional information in this example could have been provided as a <leaf> element under the <m2-3-r-regional-information> element without the use of a "node extension".

```
<m2-common-technical-document-summaries>
        <m2-3-quality-overall-summary>
        <m2-3-r-regional-information>
        <node-extension>
                <title>special-summary</title>
                <leaf ID="a123456" operation = "new" xlink:type = "simple" xlink:href = "m2/23-qos/extra-
                quality-sum.pdf" checksum-type="md5" checksum = "7490d74c3d5e442ad57daa155253eb16">
                        <title>Extra Quality Summary </title>
                </leaf>
        </node-extension>
        </m2-3-r-regional-information>
        </m2-3-quality-overall-summary>
</m2-common-technical-document-summaries>
```

To update a file that has been submitted as an extended node, you should submit the replacement file using exactly the same element and "node extension" information, including the <title> element for the <node-extension>. This makes it possible for the regulatory authority to locate the original file and update its status.

Example 6-6: Instructions for Submitting Sections as Paper

During the transition to fully electronic submissions of the CTD, some regions will accept that some sections can be submitted as paper only. Please refer to regional guidance. These sections should be identified in the XML eCTD instance by including a PDF file in the instance that describes the content and location of the paper section. For example, the PDF file might consist of only one page with the name of the CTD document and the physical volume number and tab identifier. The <title> element in the XML eCTD instance could indicate that this is a paper submission.

This is an example of the instance showing the submission of a paper efficacy overview document.

```
<m2-common-technical-document-summaries>
        <m2-5-clinical-overview xml:lang = "en">
        <leaf ID=“a123456” operation = "new" xlink:type = "simple" checksum-type=“md5” checksum =
        "e854d3002c02a61fe5cbe926fd973401" xlink:href = "m2/25-clin-over/clinical-overview.pdf" application-
        version = "PDF 1.4">
                <title>Paper Submission </title>
        </leaf>
        </m2-5-clinical-overview>
</m2-common-technical-document-summaries>
```

Appendix 7: Specification for Submission Formats

Introduction

This appendix describes the way files should be constructed for inclusion in the eCTD. This section includes file formats that are commonly used in electronic submissions. Other formats can be used according to guidance published in each region.

PDF

Adobe Portable Document Format (PDF) is a published format created by Adobe Systems Incorporated (http://www.adobe.com). It is not necessary to use a product from Adobe or from any specific company to produce PDF documents. PDF is accepted as a standard for documents defined in this specification. The following recommendations support the creation of PDF files that agencies can review effectively. For any specification of the Japanese version of Adobe Acrobat, or where Japanese characters will be in the file, please refer to the regional guidance.

To ensure that PDF files can be accessed efficiently, PDF files should be no larger than 100 megabytes. Optimize PDF files for fast web view.

Version

All ICH Regional Health Authorities are able to read and have agreed to accept PDF files saved as PDF version 1.4. Agencies should not need any additional software to read and navigate the PDF files. PDF/A-1 (an ISO standard - ISO 19005-1:2005) is an archive format and does not meet the ICH review needs for use with an eCTD. Please consult regional guidance to submit other versions of PDF.

Fonts

PDF viewing software automatically substitutes a font to display text if the font used to create the text is unavailable on the reviewer's computer. Font substitution can affect a document's appearance and structure, and, in some cases, the information conveyed by a document. Agencies cannot guarantee the availability of any fonts except Times New Roman, Arial, and Courier and fonts supported in the Acrobat product set itself. Therefore, all additional fonts used in the PDF files should be embedded to ensure that those fonts would always be available to the reviewer. When embedding fonts, all characters for the font should be embedded, not just a subset of the fonts being used in the document

Embedding fonts requires additional computer storage space. Three techniques to help limit the storage space taken by embedding fonts include:

- Limiting the number of fonts used in each document
- Using only True Type or Adobe Type 1 fonts
- Avoiding customized fonts

Japanese fonts (2-byte fonts) are larger than Roman fonts (1-byte fonts), therefore, the specification allows a subset to be embedded for all Japanese fonts. The purpose of embedding fonts to is to enable the receiver of the document to use a personal computer to display and print the document correctly without having the same fonts installed in the computer. Therefore, it is not necessary to embed all Japanese fonts. Embedding a subset of Japanese fonts should work satisfactorily.

Definition of Subset

A subset means to embed only those characters used in the document. Embedding a full-set means all characters that comprise the font are embedded, even characters that are not used in the document. All two-byte fonts such as Japanese should be embedded as a sub-set.

Notes on Embedding Japanese Fonts:
The following should be considered when embedding fonts:

Advantages:
- Embedding fonts allows the PDF file to be correctly displayed and printed on any receiving PC environment.
- The computer does not need the original fonts installed.

Disadvantages:
- The file size increases when fonts are embedded.
- When document contains many pages, this can make the document slower to print.
- Many eCTD documents contain a large number of pages. Printing time in such cases becomes a concern.
- When using Japanese fonts, rules of operation should be established between the sender and receiver. (See regional guidance)
- The use of popular fonts only would allow the sender and receiver to view and print the document correctly without embedding fonts.

Font Size
Resizing a document because the contents are too small to read is inefficient. Times New Roman, 12-point font, the font used for this document, is adequate in size for narrative text and should be used whenever possible. It is sometimes tempting to use fonts which are smaller than 12 point in tables and charts but this should be avoided whenever possible. When choosing a font size for tables, a balance should be sought between providing sufficient information on a single page to facilitate data comparisons for the reviewer while maintaining a font size that remains legible. The corollary of this is that in using larger font size, more tables might be necessary, which can complicate data comparisons since data might now be included in separate tables. Generally, Times New Roman font sizes 9-10 or an equivalent size of other recommended fonts are considered acceptable in tables but smaller font sizes should be avoided.

Use of Color Fonts
The use of a black font color is recommended. Blue can be used for hypertext links. Light colors that do not print well on grayscale printers should be avoided. Color reproduction can be tested prior to submission by printing sample pages from the document using a gray scale printer. The use of background shadowing should be avoided.

Page Orientation
Pages should be properly oriented so that all portrait pages are presented in portrait and all landscape pages are presented in landscape. To achieve this, the page orientation of landscape pages should be set to landscape prior to saving the PDF document in final form.

Page Size and Margins
The print area for pages should fit on a sheet of A4 (210 x 297 mm) and Letter (8.5” x 11”) paper. A sufficient margin (at least 2.5 cm) on the left side of each page should be provided to avoid obscuring information if the reviewer subsequently prints and binds the pages for temporary use. For pages in landscape orientation (typically tables and publications), smaller margins (at least 2.0 cm at the top and 0.8 cm left and right) allow more information to be displayed legibly on the page (see Fonts). Header and footer information can appear within these margins but should not appear so close to the page edge to risk being lost upon printing.

Headers and Footers
The M4 Granularity document specifies that all pages of a document should include a unique header or footer that briefly identifies its subject matter. With the eCTD there is a significant amount of metadata

available to the reviewer to allow easy identification of the document but it is still appropriate to have a unique identifier on each page (header or footer) of the document (e.g., when the document is printed or multiple documents are viewed on screen at the same time). The unique identifier does not necessarily have to contain the CTD section identifier or other metadata. It should be sufficient to identify the general subject matter of the document (e.g., study identifier, batch number).

Source of Electronic Document

PDF documents produced by scanning paper documents are usually inferior to those produced from an electronic source document. Scanned documents saved as image files are more difficult to read and do not allow reviewers to search or copy and paste text for editing. Scanning should be avoided where possible.

Methods for Creating PDF Documents and Images

The method used for creating PDF documents should produce the best replication of a paper document. To ensure that the paper and PDF version of the document are the same, the document should be printed from the PDF version. Documents that are available only in paper should be scanned at resolutions that will ensure the pages are legible both on the computer screen and when printed. At the same time, the file size should be limited. It is recommended that scanning be undertaken at a resolution of 300 dots per inch (dpi) to balance legibility and file size. The use of grayscale or color is discouraged because of file size. After scanning, resampling to a lower resolution should be avoided.

When creating PDF files containing images, the images should not be downsampled. Downsampling does not preserve all of the pixels in the original. For PDF images, one of the following lossless compression techniques should be used:

- For lossless compression of color and grayscale images, use Zip/Flate (one technique with two names). This is specified in Internet RFC 1950 and RFC 1951 (http://www.ietf.org/rfc/rfc1950.txt).
- For lossless compression of black and white images, use the CCITT Group 4 Fax compression technique. It is specified as CCITT recommendations T.6 (1988) - *Facsimile coding schemes and coding control functions for Group 4 facsimile apparatus*.

Paper documents containing hand-written notes should be scanned at a resolution of at least 300 dpi. Hand-written notes should be done in black ink for clarity. Higher resolution is specifically requested when scanning documents containing non-Western characters (e.g. Kanji); 600 dpi is recommended.

For photographs, the image should be obtained with a resolution of 600 dpi. If black and white photos are submitted, 8-bit grayscale images should be considered. If color photos are submitted, 24-bit RGB images should be considered. A captured image should not be subjected to non-uniform scaling (i.e., sizing).

Gels and karyotypes should be scanned directly, rather than from photographs. Scanning should be at 600 dpi and 8-bit grayscale depth.

Plotter output graphics should be scanned or captured digitally at 300 dpi.

High-pressure liquid chromatography or similar images should be scanned at 300 dpi.
Applicants should validate the quality of the renditions.

Hypertext Linking and Bookmarks

Hypertext links and bookmarks improve navigation through PDF documents. Hypertext links can be designated by rectangles using thin lines or by blue text as appropriate.

In general, for documents with a table of contents, bookmarks for each item listed in the table of contents should be provided including all tables, figures, publications, other references, and appendices. Bookmarks should follow hierarchical level and order of table of contents. These bookmarks are essential for the efficient navigation through documents. The bookmark hierarchy should be identical to the table of contents with no additional bookmark levels beyond those present in the table of contents. Each additional

level increases the need for space to read the bookmarks. The use of no more than 4 levels in the hierarchy is recommended.

Hypertext links throughout the document to support annotations, related sections, references, appendices, tables, or figures that are not located on the same page are helpful and improve navigation efficiency. Relative paths should be used when creating hypertext links to minimize the loss of hyperlink functionality when folders are moved between disk drives. Absolute links that reference specific drives and root directories will no longer work once the submission is loaded onto the Agency's network servers.

When creating bookmarks and hyperlinks, the magnification setting *Inherit Zoom* should be used so that the destination page displays at the same magnification level that the reviewer is using for the rest of the document.

Insufficient experience is available across agencies to provide any formal guidance on whether bookmarks should be presented expanded or collapsed. It might not be considered appropriate to have all the bookmarks open since, in some instances, these can be so numerous that they are not useful to the review and can affect 'refresh' time in a web-browser. Equally, it is probably not useful to have the bookmarks fully closed, since the reviewer would always have to open them. It is recommended, therefore, that the applicant consider the usefulness to the reviewers of how to present bookmarks and have some level of consistency across similar document types within the submission.

Page Numbering

Only the internal page numbers of the document are expected (1-n). No additional page/volume numbers running across documents are expected. It is easier to navigate through an electronic document if the page numbers for the document and the PDF file are the same. To accomplish this, the first page of the document should be numbered page 1, and all subsequent pages (including appendices and attachments) should be numbered consecutively with Arabic numerals. Roman numerals should not be used to number pages (e.g., title pages, tables of contents) and pages should not be left unnumbered (e.g., title page.) Numbering in this manner keeps the Acrobat numbering in synchrony with the internal document page numbers.

The only exception should be where a document is split because of its size (e.g., >100 MB); the second or subsequent file should be numbered consecutively to that of the first or preceding file.

Document Information Fields

Recommendations for the document information fields will be provided in the regional guidance for the specific submission type.

Open Dialog Box

The open dialog box sets the document view when the file is opened. The initial view of the PDF files should be set as *Bookmarks* and *Page*. If there are no bookmarks, the initial view as *Page* only should be set. The *Magnification* and *Page Layout* should be set as default.

Security

No security settings or password protection for PDF files should be included. Security fields should be set to allow printing, changes to the document, selecting text and graphics, and adding or changing notes and form fields.

Indexing PDF Documents

There are no current plans in the ICH regions to use full text indexes.

Use of Acrobat Plug-Ins

It is appropriate to use plug-ins to assist in the creation of a submission. However, the review of the submission should not call for the use of any plug-ins in addition to those provided with Adobe Acrobat because agencies will not necessarily have access to the additional plug-in functionality.

XML Files

A working group at the World Wide Web Consortium (W3C) developed XML. It is a nonproprietary language developed to improve on previous markup languages including standard generalized markup language (SGML) and hypertext markup language (HTML).

Information in an XML file is divided into specific pieces. These pieces are called objects or element types. The element type identifies the piece of information. For example, the name of the company submitting a registration application in eCTD format for review is identified with the element type <applicant>. All element type names are bracketed using the special characters <>. Inside the XML document, the element type name is placed just prior to the piece of information and after the information. This is called tagging. So, in the XML file, the applicant could be tagged as follows: <applicant>Worldwide Pharmaceuticals Inc.</applicant>. The "/" prior to the element type denotes that this is the end of the information about the applicant.

It is recognized that there is a general trend towards describing the contents of documents with XML. However, the current specification supports only the use of XML for structured information. It can be interpreted from this that the submission of summaries, reports and other narrative documents in XML format is not currently supported by the specification. Regulatory authorities and applicants could agree to use other formats regionally (including uses of the common formats in a different way from the above). Thus, if an applicant wishes to use XML for narrative documents, the applicant should contact the applicant's own regional regulatory authority, understanding that other regulatory authorities may not accept these XML files.

By using a hierarchical structure, XML allows you to relate two or more elements. This is accomplished by nesting one element within another.

Additional information about the element type is provided by attributes. Attributes are placed within the element types and are surrounded by quotation marks (" ".) For example, if you wanted to show that the applicant name is presented in the English language, you could add this piece of information as an attribute. This could be represented in the XML file as <applicant XML:LANG="EN"> Worldwide Pharmaceuticals Inc.</applicant>.

XML files are read by a parser found in Internet browsers. Stylesheets provide the browser with the information to create tables, fonts, and colors for display.

The specific names of the element types and attributes as well as the valid syntax, structure and format for defining the XML elements are included in a file called document type definition (DTD). If the XML document does not follow the DTD, then the file will not be able to be used properly.

The top three lines of the XML file should include the XML version, the stylesheet type and address, and the DTD name and address.

Additional information about the XML standard can be found at the W3C Web site at www.w3.org.

SVG Files

SVG is a language for describing two-dimensional graphics in XML. SVG allows for three types of graphic objects: vector graphic shapes (e.g., paths consisting of straight lines and curves), images, and text. Graphical objects can be grouped, styled, transformed and composited into previously rendered objects. Text can be in any XML namespace suitable to the application, which enhances searchability

and accessibility of the SVG graphics. The feature set includes nested transformations, clipping paths, alpha masks, filter effects, template objects, and extensibility.

SVG drawings can be dynamic and interactive. The Document Object Model (DOM) for SVG, which includes the full XML DOM, allows for straightforward and efficient vector graphics animation via scripting. A rich set of event handlers such as onmouseover and onclick can be assigned to any SVG graphical object. Because of its compatibility and leveraging of other Web standards, features like scripting can be done on SVG elements and other XML elements from different namespaces simultaneously within the same Web page. [8]

The specific use of SVG in a submission should be discussed with the regulatory authority.

[8] This description of SVG is from w3c Web page http://www.w3.org/graphics/svg

Appendix 8: XML eCTD DTD

```
<?xml version="1.0" encoding="UTF-8"?>
<!-- Changes prior to Version 1.00 captured in file
      "Historical Changes.txt

    ICH eCTD DTD
    Version 1.0 - March 6, 2002
    Version 3.0 - Sept 11, 2002
    Version 3.0 - Oct 1, 2002
    Version 3.0 - Oct 8, 2002
    Version 3.1 - Nov 11, 2003
          Version 3.2 - Nov 21, 2003

Changes in version 3.1
-         ID was changed to REQUIRED in the following four locations:
                  <!ENTITY % att " ID      ID     #REQUIRED
          xml:lang CDATA  #IMPLIED">

        <!ELEMENT leaf (title, link-text?)>
                        <!ATTLIST leaf
                                ID ID #REQUIRED  <attlist continues>

                  <!ELEMENT xref EMPTY>
                        <!ATTLIST xref
                                ID ID #REQUIRED  <attlist continues>

                  <!ELEMENT node-extension (title, (leaf | node-extension)+)>
                        <!ATTLIST node-extension
                                ID ID #REQUIRED
                                xml:lang CDATA #IMPLIED>


Changes in version 3.2

-         Indication attribute was changed to REQUIRED in the following two locations:
                  <!ATTLIST m2-7-3-summary-of-clinical-efficacy
                  %att;
                  indication CDATA #REQUIRED

                  <!ATTLIST m5-3-5-reports-of-efficacy-and-safety-studies
                  %att;
                  indication CDATA #REQUIRED

-         Since ID is only needed for files referenced in a LEAF, changed ID back to IMPLIED for:
                  <!ENTITY % att " ID      ID     #REQUIRED
                        xml:lang CDATA  #IMPLIED">

                  <!ELEMENT node-extension (title, (leaf | node-extension)+)>
                  <!ATTLIST node-extension
                        ID ID #REQUIRED
                        xml:lang CDATA #IMPLIED>



End of changes
-->
<!ENTITY % att " ID      ID     #IMPLIED
  xml:lang CDATA  #IMPLIED">
<!-- ========================================================== -->
<!-- Top-level element -->
```

```
<!-- ============================================================= -->
<!ELEMENT ectd:ectd (m1-administrative-information-and-prescribing-information?, m2-common-technical-
document-summaries?, m3-quality?, m4-nonclinical-study-reports?, m5-clinical-study-reports?)>
<!ATTLIST ectd:ectd
        xmlns:ectd CDATA #FIXED "http://www.ich.org/ectd"
        xmlns:xlink CDATA #FIXED "http://www.w3c.org/1999/xlink"
        xml:lang CDATA #IMPLIED
        dtd-version CDATA #FIXED "3.2"
>
<!-- ============================================================= -->
<!-- Leaf content -->
<!-- ============================================================= -->
<!ELEMENT leaf (title, link-text?)>
<!ATTLIST leaf
        ID ID #REQUIRED
        application-version CDATA #IMPLIED
        version CDATA #IMPLIED
        font-library CDATA #IMPLIED
        operation (new | append | replace | delete) #REQUIRED
        modified-file CDATA #IMPLIED
        checksum CDATA #REQUIRED
        checksum-type CDATA #REQUIRED
        keywords CDATA #IMPLIED
        xmlns:xlink CDATA #FIXED "http://www.w3c.org/1999/xlink"
        xlink:type CDATA #FIXED "simple"
        xlink:role CDATA #IMPLIED
        xlink:href CDATA #IMPLIED
        xlink:show (new | replace | embed | other | none) #IMPLIED
        xlink:actuate (onLoad | onRequest | other | none) #IMPLIED
        xml:lang CDATA #IMPLIED
>
<!ELEMENT title (#PCDATA)>
<!ATTLIST title
        ID ID #IMPLIED
>
<!ELEMENT link-text (#PCDATA | xref)*>
<!ATTLIST link-text
        ID ID #IMPLIED
>
<!ELEMENT xref EMPTY>
<!ATTLIST xref
        ID ID #REQUIRED
        xmlns:xlink CDATA #FIXED "http://www.w3c.org/1999/xlink"
        xlink:type CDATA #FIXED "simple"
        xlink:role CDATA #IMPLIED
        xlink:title CDATA #REQUIRED
        xlink:href CDATA #REQUIRED
        xlink:show (new | replace | embed | other | none) #IMPLIED
        xlink:actuate (onLoad | onRequest | other | none) #IMPLIED
>
<!ELEMENT node-extension (title, (leaf | node-extension)+)>
<!ATTLIST node-extension
        ID ID #IMPLIED
        xml:lang CDATA #IMPLIED
>
<!-- ============================================================= -->
<!-- CTD Backbone structures -->
<!-- ============================================================= -->
<!ELEMENT m1-administrative-information-and-prescribing-information (leaf*)>
<!ATTLIST m1-administrative-information-and-prescribing-information
        %att;
>
```

```
<!ELEMENT m2-common-technical-document-summaries (leaf*, m2-2-introduction?, m2-3-quality-overall-summary?, m2-4-nonclinical-overview?, m2-5-clinical-overview?, m2-6-nonclinical-written-and-tabulated-summaries?, m2-7-clinical-summary?)>
<!ATTLIST m2-common-technical-document-summaries
        %att;
>
<!ELEMENT m2-2-introduction ((leaf | node-extension)*)>
<!ATTLIST m2-2-introduction
        %att;
>
<!ELEMENT m2-3-quality-overall-summary (leaf*, m2-3-introduction?, m2-3-s-drug-substance*, m2-3-p-drug-product*, m2-3-a-appendices?, m2-3-r-regional-information?)>
<!ATTLIST m2-3-quality-overall-summary
        %att;
>
<!ELEMENT m2-3-introduction ((leaf | node-extension)*)>
<!ATTLIST m2-3-introduction
        %att;
>
<!ELEMENT m2-3-s-drug-substance ((leaf | node-extension)*)>
<!ATTLIST m2-3-s-drug-substance
        %att;
        substance CDATA #REQUIRED
        manufacturer CDATA #REQUIRED
>
<!ELEMENT m2-3-p-drug-product ((leaf | node-extension)*)>
<!ATTLIST m2-3-p-drug-product
        %att;
        product-name CDATA #IMPLIED
        dosageform CDATA #IMPLIED
        manufacturer CDATA #IMPLIED
>
<!ELEMENT m2-3-a-appendices ((leaf | node-extension)*)>
<!ATTLIST m2-3-a-appendices
        %att;
>
<!ELEMENT m2-3-r-regional-information ((leaf | node-extension)*)>
<!ATTLIST m2-3-r-regional-information
        %att;
>
<!ELEMENT m2-4-nonclinical-overview ((leaf | node-extension)*)>
<!ATTLIST m2-4-nonclinical-overview
        %att;
>
<!ELEMENT m2-5-clinical-overview ((leaf | node-extension)*)>
<!ATTLIST m2-5-clinical-overview
        %att;
>
<!ELEMENT m2-6-nonclinical-written-and-tabulated-summaries (leaf*, m2-6-1-introduction?, m2-6-2-pharmacology-written-summary?, m2-6-3-pharmacology-tabulated-summary?, m2-6-4-pharmacokinetics-written-summary?, m2-6-5-pharmacokinetics-tabulated-summary?, m2-6-6-toxicology-written-summary?, m2-6-7-toxicology-tabulated-summary?)>
<!ATTLIST m2-6-nonclinical-written-and-tabulated-summaries
        %att;
>
<!ELEMENT m2-6-1-introduction ((leaf | node-extension)*)>
<!ATTLIST m2-6-1-introduction
        %att;
>
<!ELEMENT m2-6-2-pharmacology-written-summary ((leaf | node-extension)*)>
<!ATTLIST m2-6-2-pharmacology-written-summary
        %att;
```

```
>
<!ELEMENT m2-6-3-pharmacology-tabulated-summary ((leaf | node-extension)*)>
<!ATTLIST m2-6-3-pharmacology-tabulated-summary
        %att;
>
<!ELEMENT m2-6-4-pharmacokinetics-written-summary ((leaf | node-extension)*)>
<!ATTLIST m2-6-4-pharmacokinetics-written-summary
        %att;
>
<!ELEMENT m2-6-5-pharmacokinetics-tabulated-summary ((leaf | node-extension)*)>
<!ATTLIST m2-6-5-pharmacokinetics-tabulated-summary
        %att;
>
<!ELEMENT m2-6-6-toxicology-written-summary ((leaf | node-extension)*)>
<!ATTLIST m2-6-6-toxicology-written-summary
        %att;
>
<!ELEMENT m2-6-7-toxicology-tabulated-summary ((leaf | node-extension)*)>
<!ATTLIST m2-6-7-toxicology-tabulated-summary
        %att;
>
<!ELEMENT m2-7-clinical-summary (leaf*, m2-7-1-summary-of-biopharmaceutic-studies-and-associated-analytical-
methods?, m2-7-2-summary-of-clinical-pharmacology-studies?, m2-7-3-summary-of-clinical-efficacy*, m2-7-4-
summary-of-clinical-safety?, m2-7-5-literature-references?, m2-7-6-synopses-of-individual-studies?)>
<!ATTLIST m2-7-clinical-summary
        %att;
>
<!ELEMENT m2-7-1-summary-of-biopharmaceutic-studies-and-associated-analytical-methods ((leaf | node-
extension)*)>
<!ATTLIST m2-7-1-summary-of-biopharmaceutic-studies-and-associated-analytical-methods
        %att;
>
<!ELEMENT m2-7-2-summary-of-clinical-pharmacology-studies ((leaf | node-extension)*)>
<!ATTLIST m2-7-2-summary-of-clinical-pharmacology-studies
        %att;
>
<!ELEMENT m2-7-3-summary-of-clinical-efficacy ((leaf | node-extension)*)>
<!ATTLIST m2-7-3-summary-of-clinical-efficacy
        %att;
        indication CDATA #REQUIRED
>
<!ELEMENT m2-7-4-summary-of-clinical-safety ((leaf | node-extension)*)>
<!ATTLIST m2-7-4-summary-of-clinical-safety
        %att;
>
<!ELEMENT m2-7-5-literature-references ((leaf | node-extension)*)>
<!ATTLIST m2-7-5-literature-references
        %att;
>
<!ELEMENT m2-7-6-synopses-of-individual-studies ((leaf | node-extension)*)>
<!ATTLIST m2-7-6-synopses-of-individual-studies
        %att;
>
<!ELEMENT m3-quality (leaf*, m3-2-body-of-data?, m3-3-literature-references?)>
<!ATTLIST m3-quality
        %att;
>
<!ELEMENT m3-2-body-of-data (leaf*, m3-2-s-drug-substance*, m3-2-p-drug-product*, m3-2-a-appendices?, m3-2-r-
regional-information?)>
<!ATTLIST m3-2-body-of-data
        %att;
>
```

```
<!ELEMENT m3-2-s-drug-substance (leaf*, m3-2-s-1-general-information?, m3-2-s-2-manufacture?, m3-2-s-3-characterisation?, m3-2-s-4-control-of-drug-substance?, m3-2-s-5-reference-standards-or-materials?, m3-2-s-6-container-closure-system?, m3-2-s-7-stability?)>
<!ATTLIST m3-2-s-drug-substance
        %att;
        substance CDATA #REQUIRED
        manufacturer CDATA #REQUIRED
>
<!ELEMENT m3-2-s-1-general-information (leaf*, m3-2-s-1-1-nomenclature?, m3-2-s-1-2-structure?, m3-2-s-1-3-general-properties?)>
<!ATTLIST m3-2-s-1-general-information
        %att;
>
<!ELEMENT m3-2-s-1-1-nomenclature ((leaf | node-extension)*)>
<!ATTLIST m3-2-s-1-1-nomenclature
        %att;
>
<!ELEMENT m3-2-s-1-2-structure ((leaf | node-extension)*)>
<!ATTLIST m3-2-s-1-2-structure
        %att;
>
<!ELEMENT m3-2-s-1-3-general-properties ((leaf | node-extension)*)>
<!ATTLIST m3-2-s-1-3-general-properties
        %att;
>
<!ELEMENT m3-2-s-2-manufacture (leaf*, m3-2-s-2-1-manufacturer?, m3-2-s-2-2-description-of-manufacturing-process-and-process-controls?, m3-2-s-2-3-control-of-materials?, m3-2-s-2-4-controls-of-critical-steps-and-intermediates?, m3-2-s-2-5-process-validation-and-or-evaluation?, m3-2-s-2-6-manufacturing-process-development?)>
<!ATTLIST m3-2-s-2-manufacture
        %att;
>
<!ELEMENT m3-2-s-2-1-manufacturer ((leaf | node-extension)*)>
<!ATTLIST m3-2-s-2-1-manufacturer
        %att;
>
<!ELEMENT m3-2-s-2-2-description-of-manufacturing-process-and-process-controls ((leaf | node-extension)*)>
<!ATTLIST m3-2-s-2-2-description-of-manufacturing-process-and-process-controls
        %att;
>
<!ELEMENT m3-2-s-2-3-control-of-materials ((leaf | node-extension)*)>
<!ATTLIST m3-2-s-2-3-control-of-materials
        %att;
>
<!ELEMENT m3-2-s-2-4-controls-of-critical-steps-and-intermediates ((leaf | node-extension)*)>
<!ATTLIST m3-2-s-2-4-controls-of-critical-steps-and-intermediates
        %att;
>
<!ELEMENT m3-2-s-2-5-process-validation-and-or-evaluation ((leaf | node-extension)*)>
<!ATTLIST m3-2-s-2-5-process-validation-and-or-evaluation
        %att;
>
<!ELEMENT m3-2-s-2-6-manufacturing-process-development ((leaf | node-extension)*)>
<!ATTLIST m3-2-s-2-6-manufacturing-process-development
        %att;
>
<!ELEMENT m3-2-s-3-characterisation (leaf*, m3-2-s-3-1-elucidation-of-structure-and-other-characteristics?, m3-2-s-3-2-impurities?)>
<!ATTLIST m3-2-s-3-characterisation
        %att;
>
<!ELEMENT m3-2-s-3-1-elucidation-of-structure-and-other-characteristics ((leaf | node-extension)*)>
<!ATTLIST m3-2-s-3-1-elucidation-of-structure-and-other-characteristics
```

```
        %att;
>
<!ELEMENT m3-2-s-3-2-impurities ((leaf | node-extension)*)>
<!ATTLIST m3-2-s-3-2-impurities
        %att;
>
<!ELEMENT m3-2-s-4-control-of-drug-substance (leaf*, m3-2-s-4-1-specification?, m3-2-s-4-2-analytical-procedures?, m3-2-s-4-3-validation-of-analytical-procedures?, m3-2-s-4-4-batch-analyses?, m3-2-s-4-5-justification-of-specification?)>
<!ATTLIST m3-2-s-4-control-of-drug-substance
        %att;
>
<!ELEMENT m3-2-s-4-1-specification ((leaf | node-extension)*)>
<!ATTLIST m3-2-s-4-1-specification
        %att;
>
<!ELEMENT m3-2-s-4-2-analytical-procedures ((leaf | node-extension)*)>
<!ATTLIST m3-2-s-4-2-analytical-procedures
        %att;
>
<!ELEMENT m3-2-s-4-3-validation-of-analytical-procedures ((leaf | node-extension)*)>
<!ATTLIST m3-2-s-4-3-validation-of-analytical-procedures
        %att;
>
<!ELEMENT m3-2-s-4-4-batch-analyses ((leaf | node-extension)*)>
<!ATTLIST m3-2-s-4-4-batch-analyses
        %att;
>
<!ELEMENT m3-2-s-4-5-justification-of-specification ((leaf | node-extension)*)>
<!ATTLIST m3-2-s-4-5-justification-of-specification
        %att;
>
<!ELEMENT m3-2-s-5-reference-standards-or-materials ((leaf | node-extension)*)>
<!ATTLIST m3-2-s-5-reference-standards-or-materials
        %att;
>
<!ELEMENT m3-2-s-6-container-closure-system ((leaf | node-extension)*)>
<!ATTLIST m3-2-s-6-container-closure-system
        %att;
>
<!ELEMENT m3-2-s-7-stability (leaf*, m3-2-s-7-1-stability-summary-and-conclusions?, m3-2-s-7-2-post-approval-stability-protocol-and-stability-commitment?, m3-2-s-7-3-stability-data?)>
<!ATTLIST m3-2-s-7-stability
        %att;
>
<!ELEMENT m3-2-s-7-1-stability-summary-and-conclusions ((leaf | node-extension)*)>
<!ATTLIST m3-2-s-7-1-stability-summary-and-conclusions
        %att;
>
<!ELEMENT m3-2-s-7-2-post-approval-stability-protocol-and-stability-commitment ((leaf | node-extension)*)>
<!ATTLIST m3-2-s-7-2-post-approval-stability-protocol-and-stability-commitment
        %att;
>
<!ELEMENT m3-2-s-7-3-stability-data ((leaf | node-extension)*)>
<!ATTLIST m3-2-s-7-3-stability-data
        %att;
>
<!ELEMENT m3-2-p-drug-product (leaf*, m3-2-p-1-description-and-composition-of-the-drug-product?, m3-2-p-2-pharmaceutical-development?, m3-2-p-3-manufacture?, m3-2-p-4-control-of-excipients*, m3-2-p-5-control-of-drug-product?, m3-2-p-6-reference-standards-or-materials?, m3-2-p-7-container-closure-system?, m3-2-p-8-stability?)>
<!ATTLIST m3-2-p-drug-product
        %att;
```

```
        product-name CDATA #IMPLIED
        dosageform CDATA #IMPLIED
        manufacturer CDATA #IMPLIED
>
<!ELEMENT m3-2-p-1-description-and-composition-of-the-drug-product ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-1-description-and-composition-of-the-drug-product
        %att;
>
<!ELEMENT m3-2-p-2-pharmaceutical-development ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-2-pharmaceutical-development
        %att;
>
<!ELEMENT m3-2-p-3-manufacture (leaf*, m3-2-p-3-1-manufacturers?, m3-2-p-3-2-batch-formula?, m3-2-p-3-3-
description-of-manufacturing-process-and-process-controls?, m3-2-p-3-4-controls-of-critical-steps-and-intermediates?,
m3-2-p-3-5-process-validation-and-or-evaluation?)>
<!ATTLIST m3-2-p-3-manufacture
        %att;
>
<!ELEMENT m3-2-p-3-1-manufacturers ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-3-1-manufacturers
        %att;
>
<!ELEMENT m3-2-p-3-2-batch-formula ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-3-2-batch-formula
        %att;
>
<!ELEMENT m3-2-p-3-3-description-of-manufacturing-process-and-process-controls ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-3-3-description-of-manufacturing-process-and-process-controls
        %att;
>
<!ELEMENT m3-2-p-3-4-controls-of-critical-steps-and-intermediates ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-3-4-controls-of-critical-steps-and-intermediates
        %att;
>
<!ELEMENT m3-2-p-3-5-process-validation-and-or-evaluation ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-3-5-process-validation-and-or-evaluation
        %att;
>
<!ELEMENT m3-2-p-4-control-of-excipients (leaf*, m3-2-p-4-1-specifications?, m3-2-p-4-2-analytical-procedures?,
m3-2-p-4-3-validation-of-analytical-procedures?, m3-2-p-4-4-justification-of-specifications?, m3-2-p-4-5-excipients-
of-human-or-animal-origin?, m3-2-p-4-6-novel-excipients?)>
<!ATTLIST m3-2-p-4-control-of-excipients
        %att;
        excipient CDATA #IMPLIED
>
<!ELEMENT m3-2-p-4-1-specifications ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-4-1-specifications
        %att;
>
<!ELEMENT m3-2-p-4-2-analytical-procedures ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-4-2-analytical-procedures
        %att;
>
<!ELEMENT m3-2-p-4-3-validation-of-analytical-procedures ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-4-3-validation-of-analytical-procedures
        %att;
>
<!ELEMENT m3-2-p-4-4-justification-of-specifications ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-4-4-justification-of-specifications
        %att;
>
<!ELEMENT m3-2-p-4-5-excipients-of-human-or-animal-origin ((leaf | node-extension)*)>
```

```
<!ATTLIST m3-2-p-4-5-excipients-of-human-or-animal-origin
	%att;
>
<!ELEMENT m3-2-p-4-6-novel-excipients ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-4-6-novel-excipients
	%att;
>
<!ELEMENT m3-2-p-5-control-of-drug-product (leaf*, m3-2-p-5-1-specifications?, m3-2-p-5-2-analytical-
procedures?, m3-2-p-5-3-validation-of-analytical-procedures?, m3-2-p-5-4-batch-analyses?, m3-2-p-5-5-
characterisation-of-impurities?, m3-2-p-5-6-justification-of-specifications?)>
<!ATTLIST m3-2-p-5-control-of-drug-product
	%att;
>
<!ELEMENT m3-2-p-5-1-specifications ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-5-1-specifications
	%att;
>
<!ELEMENT m3-2-p-5-2-analytical-procedures ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-5-2-analytical-procedures
	%att;
>
<!ELEMENT m3-2-p-5-3-validation-of-analytical-procedures ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-5-3-validation-of-analytical-procedures
	%att;
>
<!ELEMENT m3-2-p-5-4-batch-analyses ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-5-4-batch-analyses
	%att;
>
<!ELEMENT m3-2-p-5-5-characterisation-of-impurities ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-5-5-characterisation-of-impurities
	%att;
>
<!ELEMENT m3-2-p-5-6-justification-of-specifications ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-5-6-justification-of-specifications
	%att;
>
<!ELEMENT m3-2-p-6-reference-standards-or-materials ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-6-reference-standards-or-materials
	%att;
>
<!ELEMENT m3-2-p-7-container-closure-system ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-7-container-closure-system
	%att;
>
<!ELEMENT m3-2-p-8-stability (leaf*, m3-2-p-8-1-stability-summary-and-conclusion?, m3-2-p-8-2-post-approval-
stability-protocol-and-stability-commitment?, m3-2-p-8-3-stability-data?)>
<!ATTLIST m3-2-p-8-stability
	%att;
>
<!ELEMENT m3-2-p-8-1-stability-summary-and-conclusion ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-8-1-stability-summary-and-conclusion
	%att;
>
<!ELEMENT m3-2-p-8-2-post-approval-stability-protocol-and-stability-commitment ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-8-2-post-approval-stability-protocol-and-stability-commitment
	%att;
>
<!ELEMENT m3-2-p-8-3-stability-data ((leaf | node-extension)*)>
<!ATTLIST m3-2-p-8-3-stability-data
	%att;
>
```

```
<!ELEMENT m3-2-a-appendices (leaf*, m3-2-a-1-facilities-and-equipment*, m3-2-a-2-adventitious-agents-safety-evaluation*, m3-2-a-3-excipients?)>
<!ATTLIST m3-2-a-appendices
        %att;
>
<!ELEMENT m3-2-a-1-facilities-and-equipment ((leaf | node-extension)*)>
<!ATTLIST m3-2-a-1-facilities-and-equipment
        %att;
        manufacturer CDATA #IMPLIED
        substance CDATA #IMPLIED
        dosageform CDATA #IMPLIED
        product-name CDATA #IMPLIED
>
<!ELEMENT m3-2-a-2-adventitious-agents-safety-evaluation ((leaf | node-extension)*)>
<!ATTLIST m3-2-a-2-adventitious-agents-safety-evaluation
        %att;
        manufacturer CDATA #IMPLIED
        substance CDATA #IMPLIED
        dosageform CDATA #IMPLIED
        product-name CDATA #IMPLIED
>
<!ELEMENT m3-2-a-3-excipients ((leaf | node-extension)*)>
<!ATTLIST m3-2-a-3-excipients
        %att;
>
<!ELEMENT m3-2-r-regional-information ((leaf | node-extension)*)>
<!ATTLIST m3-2-r-regional-information
        %att;
>
<!ELEMENT m3-3-literature-references ((leaf | node-extension)*)>
<!ATTLIST m3-3-literature-references
        %att;
>
<!ELEMENT m4-nonclinical-study-reports (leaf*, m4-2-study-reports?, m4-3-literature-references?)>
<!ATTLIST m4-nonclinical-study-reports
        %att;
>
<!ELEMENT m4-2-study-reports (leaf*, m4-2-1-pharmacology?, m4-2-2-pharmacokinetics?, m4-2-3-toxicology?)>
<!ATTLIST m4-2-study-reports
        %att;
>
<!ELEMENT m4-2-1-pharmacology (leaf*, m4-2-1-1-primary-pharmacodynamics?, m4-2-1-2-secondary-pharmacodynamics?, m4-2-1-3-safety-pharmacology?, m4-2-1-4-pharmacodynamic-drug-interactions?)>
<!ATTLIST m4-2-1-pharmacology
        %att;
>
<!ELEMENT m4-2-1-1-primary-pharmacodynamics ((leaf | node-extension)*)>
<!ATTLIST m4-2-1-1-primary-pharmacodynamics
        %att;
>
<!ELEMENT m4-2-1-2-secondary-pharmacodynamics ((leaf | node-extension)*)>
<!ATTLIST m4-2-1-2-secondary-pharmacodynamics
        %att;
>
<!ELEMENT m4-2-1-3-safety-pharmacology ((leaf | node-extension)*)>
<!ATTLIST m4-2-1-3-safety-pharmacology
        %att;
>
<!ELEMENT m4-2-1-4-pharmacodynamic-drug-interactions ((leaf | node-extension)*)>
<!ATTLIST m4-2-1-4-pharmacodynamic-drug-interactions
        %att;
>
```

```
<!ELEMENT m4-2-2-pharmacokinetics (leaf*, m4-2-2-1-analytical-methods-and-validation-reports?, m4-2-2-2-absorption?, m4-2-2-3-distribution?, m4-2-2-4-metabolism?, m4-2-2-5-excretion?, m4-2-2-6-pharmacokinetic-drug-interactions?, m4-2-2-7-other-pharmacokinetic-studies?)>
<!ATTLIST m4-2-2-pharmacokinetics
        %att;
>
<!ELEMENT m4-2-2-1-analytical-methods-and-validation-reports ((leaf | node-extension)*)>
<!ATTLIST m4-2-2-1-analytical-methods-and-validation-reports
        %att;
>
<!ELEMENT m4-2-2-2-absorption ((leaf | node-extension)*)>
<!ATTLIST m4-2-2-2-absorption
        %att;
>
<!ELEMENT m4-2-2-3-distribution ((leaf | node-extension)*)>
<!ATTLIST m4-2-2-3-distribution
        %att;
>
<!ELEMENT m4-2-2-4-metabolism ((leaf | node-extension)*)>
<!ATTLIST m4-2-2-4-metabolism
        %att;
>
<!ELEMENT m4-2-2-5-excretion ((leaf | node-extension)*)>
<!ATTLIST m4-2-2-5-excretion
        %att;
>
<!ELEMENT m4-2-2-6-pharmacokinetic-drug-interactions ((leaf | node-extension)*)>
<!ATTLIST m4-2-2-6-pharmacokinetic-drug-interactions
        %att;
>
<!ELEMENT m4-2-2-7-other-pharmacokinetic-studies ((leaf | node-extension)*)>
<!ATTLIST m4-2-2-7-other-pharmacokinetic-studies
        %att;
>
<!ELEMENT m4-2-3-toxicology (leaf*, m4-2-3-1-single-dose-toxicity?, m4-2-3-2-repeat-dose-toxicity?, m4-2-3-3-genotoxicity?, m4-2-3-4-carcinogenicity?, m4-2-3-5-reproductive-and-developmental-toxicity?, m4-2-3-6-local-tolerance?, m4-2-3-7-other-toxicity-studies?)>
<!ATTLIST m4-2-3-toxicology
        %att;
>
<!ELEMENT m4-2-3-1-single-dose-toxicity ((leaf | node-extension)*)>
<!ATTLIST m4-2-3-1-single-dose-toxicity
        %att;
>
<!ELEMENT m4-2-3-2-repeat-dose-toxicity ((leaf | node-extension)*)>
<!ATTLIST m4-2-3-2-repeat-dose-toxicity
        %att;
>
<!ELEMENT m4-2-3-3-genotoxicity (leaf*, m4-2-3-3-1-in-vitro?, m4-2-3-3-2-in-vivo?)>
<!ATTLIST m4-2-3-3-genotoxicity
        %att;
>
<!ELEMENT m4-2-3-3-1-in-vitro ((leaf | node-extension)*)>
<!ATTLIST m4-2-3-3-1-in-vitro
        %att;
>
<!ELEMENT m4-2-3-3-2-in-vivo ((leaf | node-extension)*)>
<!ATTLIST m4-2-3-3-2-in-vivo
        %att;
>
<!ELEMENT m4-2-3-4-carcinogenicity (leaf*, m4-2-3-4-1-long-term-studies?, m4-2-3-4-2-short-or-medium-term-studies?, m4-2-3-4-3-other-studies?)>
```

```
<!ATTLIST m4-2-3-4-carcinogenicity
	%att;
>
<!ELEMENT m4-2-3-4-1-long-term-studies ((leaf | node-extension)*)>
<!ATTLIST m4-2-3-4-1-long-term-studies
	%att;
>
<!ELEMENT m4-2-3-4-2-short-or-medium-term-studies ((leaf | node-extension)*)>
<!ATTLIST m4-2-3-4-2-short-or-medium-term-studies
	%att;
>
<!ELEMENT m4-2-3-4-3-other-studies ((leaf | node-extension)*)>
<!ATTLIST m4-2-3-4-3-other-studies
	%att;
>
<!ELEMENT m4-2-3-5-reproductive-and-developmental-toxicity (leaf*, m4-2-3-5-1-fertility-and-early-embryonic-development?, m4-2-3-5-2-embryo-fetal-development?, m4-2-3-5-3-prenatal-and-postnatal-development-including-maternal-function?, m4-2-3-5-4-studies-in-which-the-offspring-juvenile-animals-are-dosed-and-or-further-evaluated?)>
<!ATTLIST m4-2-3-5-reproductive-and-developmental-toxicity
	%att;
>
<!ELEMENT m4-2-3-5-1-fertility-and-early-embryonic-development ((leaf | node-extension)*)>
<!ATTLIST m4-2-3-5-1-fertility-and-early-embryonic-development
	%att;
>
<!ELEMENT m4-2-3-5-2-embryo-fetal-development ((leaf | node-extension)*)>
<!ATTLIST m4-2-3-5-2-embryo-fetal-development
	%att;
>
<!ELEMENT m4-2-3-5-3-prenatal-and-postnatal-development-including-maternal-function ((leaf | node-extension)*)>
<!ATTLIST m4-2-3-5-3-prenatal-and-postnatal-development-including-maternal-function
	%att;
>
<!ELEMENT m4-2-3-5-4-studies-in-which-the-offspring-juvenile-animals-are-dosed-and-or-further-evaluated ((leaf | node-extension)*)>
<!ATTLIST m4-2-3-5-4-studies-in-which-the-offspring-juvenile-animals-are-dosed-and-or-further-evaluated
	%att;
>
<!ELEMENT m4-2-3-6-local-tolerance ((leaf | node-extension)*)>
<!ATTLIST m4-2-3-6-local-tolerance
	%att;
>
<!ELEMENT m4-2-3-7-other-toxicity-studies (leaf*, m4-2-3-7-1-antigenicity?, m4-2-3-7-2-immunotoxicity?, m4-2-3-7-3-mechanistic-studies?, m4-2-3-7-4-dependence?, m4-2-3-7-5-metabolites?, m4-2-3-7-6-impurities?, m4-2-3-7-7-other?)>
<!ATTLIST m4-2-3-7-other-toxicity-studies
	%att;
>
<!ELEMENT m4-2-3-7-1-antigenicity ((leaf | node-extension)*)>
<!ATTLIST m4-2-3-7-1-antigenicity
	%att;
>
<!ELEMENT m4-2-3-7-2-immunotoxicity ((leaf | node-extension)*)>
<!ATTLIST m4-2-3-7-2-immunotoxicity
	%att;
>
<!ELEMENT m4-2-3-7-3-mechanistic-studies ((leaf | node-extension)*)>
<!ATTLIST m4-2-3-7-3-mechanistic-studies
	%att;
>
<!ELEMENT m4-2-3-7-4-dependence ((leaf | node-extension)*)>
<!ATTLIST m4-2-3-7-4-dependence
```

```
        %att;
>
<!ELEMENT m4-2-3-7-5-metabolites ((leaf | node-extension)*)>
<!ATTLIST m4-2-3-7-5-metabolites
        %att;
>
<!ELEMENT m4-2-3-7-6-impurities ((leaf | node-extension)*)>
<!ATTLIST m4-2-3-7-6-impurities
        %att;
>
<!ELEMENT m4-2-3-7-7-other ((leaf | node-extension)*)>
<!ATTLIST m4-2-3-7-7-other
        %att;
>
<!ELEMENT m4-3-literature-references ((leaf | node-extension)*)>
<!ATTLIST m4-3-literature-references
        %att;
>
<!ELEMENT m5-clinical-study-reports (leaf*, m5-2-tabular-listing-of-all-clinical-studies?, m5-3-clinical-study-
reports?, m5-4-literature-references?)>
<!ATTLIST m5-clinical-study-reports
        %att;
>
<!ELEMENT m5-2-tabular-listing-of-all-clinical-studies ((leaf | node-extension)*)>
<!ATTLIST m5-2-tabular-listing-of-all-clinical-studies
        %att;
>
<!ELEMENT m5-3-clinical-study-reports (leaf*, m5-3-1-reports-of-biopharmaceutic-studies?, m5-3-2-reports-of-
studies-pertinent-to-pharmacokinetics-using-human-biomaterials?, m5-3-3-reports-of-human-pharmacokinetics-pk-
studies?, m5-3-4-reports-of-human-pharmacodynamics-pd-studies?, m5-3-5-reports-of-efficacy-and-safety-studies*,
m5-3-6-reports-of-postmarketing-experience?, m5-3-7-case-report-forms-and-individual-patient-listings?)>
<!ATTLIST m5-3-clinical-study-reports
        %att;
>
<!ELEMENT m5-3-1-reports-of-biopharmaceutic-studies (leaf*, m5-3-1-1-bioavailability-study-reports?, m5-3-1-2-
comparative-ba-and-bioequivalence-study-reports?, m5-3-1-3-in-vitro-in-vivo-correlation-study-reports?, m5-3-1-4-
reports-of-bioanalytical-and-analytical-methods-for-human-studies?)>
<!ATTLIST m5-3-1-reports-of-biopharmaceutic-studies
        %att;
>
<!ELEMENT m5-3-1-1-bioavailability-study-reports ((leaf | node-extension)*)>
<!ATTLIST m5-3-1-1-bioavailability-study-reports
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<!ELEMENT m5-3-1-2-comparative-ba-and-bioequivalence-study-reports ((leaf | node-extension)*)>
<!ATTLIST m5-3-1-2-comparative-ba-and-bioequivalence-study-reports
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<!ELEMENT m5-3-1-3-in-vitro-in-vivo-correlation-study-reports ((leaf | node-extension)*)>
<!ATTLIST m5-3-1-3-in-vitro-in-vivo-correlation-study-reports
        %att;
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<!ELEMENT m5-3-1-4-reports-of-bioanalytical-and-analytical-methods-for-human-studies ((leaf | node-extension)*)>
<!ATTLIST m5-3-1-4-reports-of-bioanalytical-and-analytical-methods-for-human-studies
        %att;
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<!ELEMENT m5-3-2-reports-of-studies-pertinent-to-pharmacokinetics-using-human-biomaterials (leaf*, m5-3-2-1-
plasma-protein-binding-study-reports?, m5-3-2-2-reports-of-hepatic-metabolism-and-drug-interaction-studies?, m5-3-
2-3-reports-of-studies-using-other-human-biomaterials?)>
<!ATTLIST m5-3-2-reports-of-studies-pertinent-to-pharmacokinetics-using-human-biomaterials
        %att;
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<!ELEMENT m5-3-2-1-plasma-protein-binding-study-reports ((leaf | node-extension)*)>
<!ATTLIST m5-3-2-1-plasma-protein-binding-study-reports
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<!ELEMENT m5-3-2-2-reports-of-hepatic-metabolism-and-drug-interaction-studies ((leaf | node-extension)*)>
<!ATTLIST m5-3-2-2-reports-of-hepatic-metabolism-and-drug-interaction-studies
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<!ELEMENT m5-3-2-3-reports-of-studies-using-other-human-biomaterials ((leaf | node-extension)*)>
<!ATTLIST m5-3-2-3-reports-of-studies-using-other-human-biomaterials
        %att;
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<!ELEMENT m5-3-3-reports-of-human-pharmacokinetics-pk-studies (leaf*, m5-3-3-1-healthy-subject-pk-and-initial-
tolerability-study-reports?, m5-3-3-2-patient-pk-and-initial-tolerability-study-reports?, m5-3-3-3-intrinsic-factor-pk-
study-reports?, m5-3-3-4-extrinsic-factor-pk-study-reports?, m5-3-3-5-population-pk-study-reports?)>
<!ATTLIST m5-3-3-reports-of-human-pharmacokinetics-pk-studies
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>
<!ELEMENT m5-3-3-1-healthy-subject-pk-and-initial-tolerability-study-reports ((leaf | node-extension)*)>
<!ATTLIST m5-3-3-1-healthy-subject-pk-and-initial-tolerability-study-reports
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>
<!ELEMENT m5-3-3-2-patient-pk-and-initial-tolerability-study-reports ((leaf | node-extension)*)>
<!ATTLIST m5-3-3-2-patient-pk-and-initial-tolerability-study-reports
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<!ELEMENT m5-3-3-3-intrinsic-factor-pk-study-reports ((leaf | node-extension)*)>
<!ATTLIST m5-3-3-3-intrinsic-factor-pk-study-reports
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>
<!ELEMENT m5-3-3-4-extrinsic-factor-pk-study-reports ((leaf | node-extension)*)>
<!ATTLIST m5-3-3-4-extrinsic-factor-pk-study-reports
        %att;
>
<!ELEMENT m5-3-3-5-population-pk-study-reports ((leaf | node-extension)*)>
<!ATTLIST m5-3-3-5-population-pk-study-reports
        %att;
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<!ELEMENT m5-3-4-reports-of-human-pharmacodynamics-pd-studies (leaf*, m5-3-4-1-healthy-subject-pd-and-pk-
pd-study-reports?, m5-3-4-2-patient-pd-and-pk-pd-study-reports?)>
<!ATTLIST m5-3-4-reports-of-human-pharmacodynamics-pd-studies
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<!ELEMENT m5-3-4-1-healthy-subject-pd-and-pk-pd-study-reports ((leaf | node-extension)*)>
<!ATTLIST m5-3-4-1-healthy-subject-pd-and-pk-pd-study-reports
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>
<!ELEMENT m5-3-4-2-patient-pd-and-pk-pd-study-reports ((leaf | node-extension)*)>
<!ATTLIST m5-3-4-2-patient-pd-and-pk-pd-study-reports
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<!ELEMENT m5-3-5-reports-of-efficacy-and-safety-studies (leaf*, m5-3-5-1-study-reports-of-controlled-clinical-
studies-pertinent-to-the-claimed-indication?, m5-3-5-2-study-reports-of-uncontrolled-clinical-studies?, m5-3-5-3-
reports-of-analyses-of-data-from-more-than-one-study?, m5-3-5-4-other-study-reports?)>
<!ATTLIST m5-3-5-reports-of-efficacy-and-safety-studies
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        indication CDATA #REQUIRED
>
<!ELEMENT m5-3-5-1-study-reports-of-controlled-clinical-studies-pertinent-to-the-claimed-indication ((leaf | node-
extension)*)>
<!ATTLIST m5-3-5-1-study-reports-of-controlled-clinical-studies-pertinent-to-the-claimed-indication
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<!ELEMENT m5-3-5-2-study-reports-of-uncontrolled-clinical-studies ((leaf | node-extension)*)>
<!ATTLIST m5-3-5-2-study-reports-of-uncontrolled-clinical-studies
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<!ELEMENT m5-3-5-3-reports-of-analyses-of-data-from-more-than-one-study ((leaf | node-extension)*)>
<!ATTLIST m5-3-5-3-reports-of-analyses-of-data-from-more-than-one-study
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<!ELEMENT m5-3-5-4-other-study-reports ((leaf | node-extension)*)>
<!ATTLIST m5-3-5-4-other-study-reports
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>
<!ELEMENT m5-3-6-reports-of-postmarketing-experience ((leaf | node-extension)*)>
<!ATTLIST m5-3-6-reports-of-postmarketing-experience
        %att;
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<!ELEMENT m5-3-7-case-report-forms-and-individual-patient-listings ((leaf | node-extension)*)>
<!ATTLIST m5-3-7-case-report-forms-and-individual-patient-listings
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<!ELEMENT m5-4-literature-references ((leaf | node-extension)*)>
<!ATTLIST m5-4-literature-references
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