eCTD Digital Handbook
Table of Contents

- One section contains all information to perform in-depth clinical pharmacology and clinical/ statistical BLA/NDA review.
- Permits comprehensive clinical pharmacology, clinical, statistical reviews.
- Majority of IND/BLA/NDA clinical content in section 5.3.
- A study report now comes in multiple files (E3) *different from the past.
- Datasets and CRF's organized by study, but still XPT and PDF, respectively.

Section 1.6 eCTDs Quality CMC Issues.

- This section outlines and describes the following issues:
  - Historical FDA e-submission efforts.
  - How to read the eCTD DTDs.
  - Repeated sections.
  - Location issues in Module 3.
  - Topics appearing in multiple sections.
  - Issues to be resolved.

Section 1.7 Prequel Template or Guidance.

- This presentation provides advice on:
  - Background/Motivation.
  - ICH CTD–General guidance on summaries–Annex: granularity document.
  - Module 2: Summaries.
  - Mapping from the CFR .
  - Module 4: Safety.

Part 2 Guidances

Section 02 Guidance for Industry M4 The CTD - Efficacy Questions and Answers.

- This is one in a series of guidances that provide recommendations for applicants preparing the Common Technical Document for the Registration of Pharmaceuticals for Human Use (CTD) for submission to the U.S. Food and Drug Administration (FDA). This guidance provides answers to questions that have arisen since the finalization of the harmonized CTD guidance documents. This guidance specifically addresses questions related to efficacy. Other question and answer (Q &A) guidances are under development to address general questions as well as questions related to quality and safety. The questions and answers provided here reflect the consensus of the ICH parties.

Section 03 Structure and Content of Clinical Study Reports.

- The objective of this guideline is to facilitate the compilation of a single core clinical study report acceptable to all regulatory authorities of the ICH regions. The regulatory authority-specific additions will consist of modules to be considered as appendices, available upon request according to regional regulatory requirements.

Part 3 Submissions

Section 04 Electronic Submission Guidances.

- PowerPoint presentation on providing regulatory submissions in electronic format including:
  - Overview.
  - Available guidances-traditional electronic submissions.
  - Electronic submissions using eCTD specifications.
  - eCTD guidance — changes from eNDA guidance–continuation of eNDA guidance.
  - Submissions 101 references.

Section 05 Providing Regulatory Submissions in Electronic Format Using eCTD Specifications.

- This is one in a series of guidance documents intended to assist applicants making regulatory submissions to the FDA in electronic format using the electronic common technical document (eCTD) specifications. This guidance discusses issues related to the electronic submission of applications for human pharmaceutical products and related submissions, including abbreviated new drug applications (ANDAs), biologics license applications (BLAs), investigational new drug applications (INDs), new drug application (NDAs), master files (e.g., drug master files), advertising material, and promotional labeling. At this time, this does not include applications supporting combination products.

Part 4 Technical Requirements.

Part 4 contains a number of specification, standards, definitions, presentations and checklists for creating and maintaining an eCTD protocol within your company.

Section 6 Comprehensive eCTD Table of Contents Headings and Hierarchy.

- This section includes the complete structure and numbering for content headings and the hierarchy of Modules 1-5

Section 7 Conformance Review Checklist For NDAs.

- This document provides a checklist for
  - General issues.
  - Organization of folders.
  - Organization of the electronic submission.

Section 8 eCTD Backbone Files Specification for Module 1.

- This document provides specifications for creating the electronic common technical document (eCTD) backbone file for Module 1 for use with the guidance to industry: Providing Regulatory Submissions in Electronic Format — Human Pharmaceutical Applications and Related Submissions.

Section 9 eCTD Backbone Files Specification for Modules 2 through 5.

- This document provides specifications for creating the electronic common technical document (eCTD) backbone file for modules 2 to 5 of the common technical document (CTD) for use with the guidance to industry: Providing Regulatory Submissions in Electronic Format - Human Pharmaceutical Applications and Related Submissions.

Section 10 eCTD Backbone Files Study Tagging Files.

- In order to help identify all of the files associated with a study, information is needed on each document including the document title, subject matter (defined by the headings under which the documents are located in the table of contents), relationship to other documents, revision information, the location of the document and information on the submission that included the document. This document outlines the eCTD backbone files which include many of these information items. However, the eCTD backbone files do not contain enough information on the subject matter of several documents (e.g., study report documents) to support certain regulatory business rules. This additional information is provided in the STF. The complete structure and contents of the STF files is presented in this section.

Section 11 eCTD Change Control Process v1.8.

- This document establishes the change control process for the eCTD Specification. Change control for regional eCTD Module 1 specifications is the regional authority's responsibility.

Section 12 eCTD Change Request Form.

- This form should be used to request a change to the ICH eCTD Specification. The change can be to fix a perceived "bug", meet a new requirement or to enhance existing functionality.

Section 13 eCTD Specification v 3.2.

- This document describes the parts of the registration application that are common to all regions and some of the lifecycle 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.

Section 14 eSUBS and eCTDs: Practical Advice and Pitfalls to Avoid.

- PowerPoint presentation outlining the factors to be aware of when submitting an eDoc:
  - Correct use of elements and leaf titles.
  - Always Reference all Files in the XML Backbone(s).
  - Include Module 1 in all eCTD Submissions.
  - Make Sure All Application Numbers are 6 Digits.
  - Make Sure all Sequence Numbers are 4 Digits.
  - Do Not Use Node Extension.
  - Verify That All MD5 Checksums are Correct.
  - All Documents Should Conform to eCTD Granularity.
  - All XML must use standard components.
  - Be Sure All PDF Hyperlinks & Bookmarks are Correct
  - Include TOCs In All PDF Documents.

Section 15 Evaluation and Research ISS/ISE: Where Do They Fit in the CTD-eCTD.

- PowerPoint presentation that provides advice on how to:
  - Differentiate between ICH guidelines and FDA requirements for the CTD/eCTD.
  - Identify the goals of the CTD/eCTD for both industry and regulators.
  - Identify strategies to include the ISS/ISE in the CTD and eCTD submission formats.

Section 16 Future of Case Report Tabulation Submissions.

- PowerPoint presentation on case report tabulations including discussion of:
  - Study data standards.
  - Status of patient profile pilot.
  - Medical review technology for an NDA safety database.

Section 17 Granularity Document Annex M4 Organization of the CTD.

- This is one in a series of guidances that provide recommendations for applicants preparing the Common Technical Document for the Registration of Pharmaceuticals for Human Use (CTD) for submission to the U.S. Food and Drug Administration (FDA). This annex to the M4 guidance on the organization of the CTD was developed by ICH in response to requests for additional information after the harmonized CTD guidance documents were finalized in November 2000.

Section 18 ICH eCTD Specification Document DTD 3.2.

- This section includes code for the XML submission that needs to be created and validated according to the XML eCTD DTD standard.

Section 19 Module 1 Document Type Definition File.

- The ICH eCTD specification calls for a regional Module 1 document type definition file to allow regional information to be submitted along with information from ICH Modules 2 to 5. The section provided sample code for the FDA draft eCTD Module 1 DTD version 2.01 hierarchy.

Section 20 Placement of Integrated Summaries of Safety and Effectiveness (ISS/ISE) in Applications Submitted in the eCTD Format.

- The tables in this document are examples of the various sections of the CTD that contain sum mary and integrated discussions of efficacy and safety and the corresponding FDA regulations, where applicable, that inform the content of those sections.

Section 21 Portable Document Format Specifications.

- These specifications are for submitting documents in Portable Document Format (PDF).

Section 22 Specification for Transmitting Electronic Submissions using eCTD Specifications.

- This document provides specification for transmitting electronic submissions using eCTD specifications. Details are included for transmitting the electronic submission on physical media or electronically.

Section 23 Standards and Successful Document Creation.

- PowerPoint presentation on standards issues including:
  - ISS/ISE placement one of the most frequently asked questions.
  - ISS/ISE Represent Analysis–5.3.5.3 Reports of analyses of data from more than one study–Module 5 provides necessary organization structures through STF.
  - Module 2 Summaries–Critical and Concise Summaries–Page counts do not define what's acceptable.

Section 24 Study Tagging File Workshop.

- PowerPoint presentation that deals with 2 tagging file problems:
  - The maximum of only 256 characters that can be used.
- This is further limited by ICH to 230 characters to permit the ICH regulatory agencies space for server and folders names to organize the submission.
- ICH guidance recommends that folder names not exceed 64 characters.
  - Computer Displays that cannot readily display lengthy path and filenames.
- In many cases some filenames could be the same up to the ending making it difficult for reviewers.

Section 25 Transformation of the Backbone from XML to HTML.

- eCTD the final ICH Step 4 eCTD specifications and draft specifications from the FDA to enable the assembly of submission-ready documents, create the appropriate file/folder structure, assign leaf document attributes, and then build the required XML backbone and regional XML required in eCTD submissions.

Part 5 Training

Section 26 NDA Electronic Data Analysis Training.

- CDER has provided guidance to industry for sponsors to send case report form tabulations and individual animal line listings as datasets. To help Center review staff use these electronic datasets, the Office of Information Technology, in conjunction with review staff, has developed NDA Electronic Data Analysis Training (NEDAT).

Section 27 NDA Electronic Submissions Training.

- In keeping with CDER's Electronic Regulatory Submission and Review (ERSR) goals, electronic submissions are currently being placed on the CDER network for access and review by CDER review staff. Currently, NDAs and their corresponding Amendments and Supplements are the only submissions received in electronic format. Before these submissions can be reviewed, CDER review staff must first be able to access an electronic submission folder on the network save a drive path (map), copy the folders and files pertinent to their discipline, and learn to use the features available in Adobe Acrobat. Reviewer staff then can access these electronic files from their desktop.