U.S. FOOD & DRUG ADMINISTRATION

eCTD Updates

Jonathan Resnick
Project Management Officer
Office of Business Informatics
CDER | US FDA

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Learning Objectives

- Describe updates to eCTD validations
- Locate latest version of eCTD guidance, specifications, and validations
- Review eCTD submission metrics
- List the 5 most common errors made when submitting in eCTD format
- Review most common questions eSub team receives
- Prepare for the next major version of eCTD

eCTD validations: What's new?

Module 1 using DTD 2.01 no longer supported

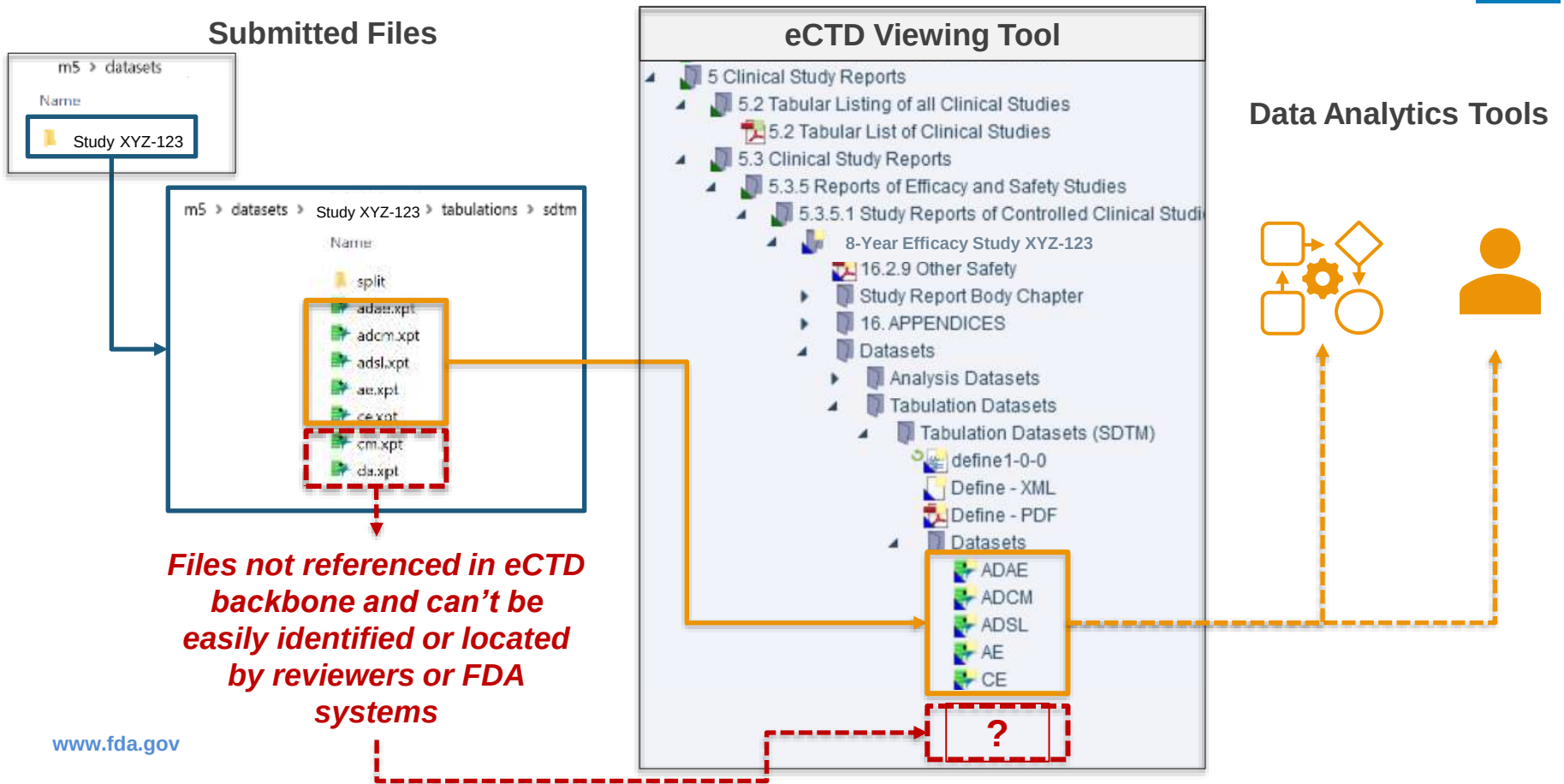
- Older version of eCTD M1, utilizing DTD 2.01, no longer supported
- DTD 3.3 required to pass validation
- For more information, please see Federal Register Notice located here: https://www.regulations.gov/document?D=FDA-2018-D-1216-0017

eCTD validations: What's new?

eCTD validations 1306 and 1323 elevated to high severity errors

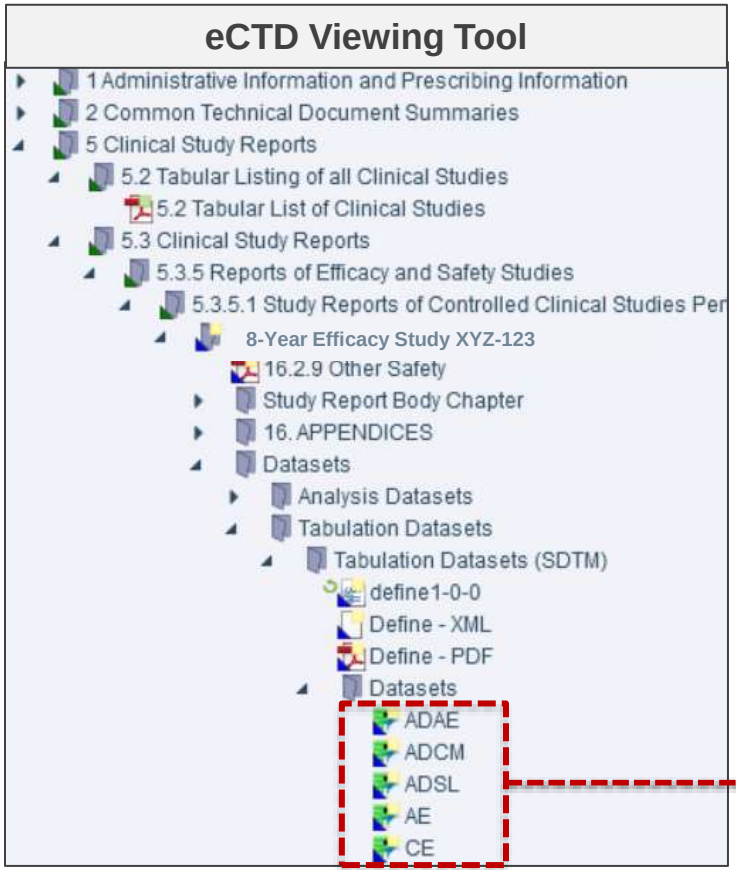
- FDA rejecting submissions which fail eCTD validations 1306 and 1323
- 1306: "No leaf element for file"
- 1323: "No file for leaf element"
- For more information, please see Federal Register Notice located here: https://www.regulations.gov/document?D=FDA-2018-D-1216-0019

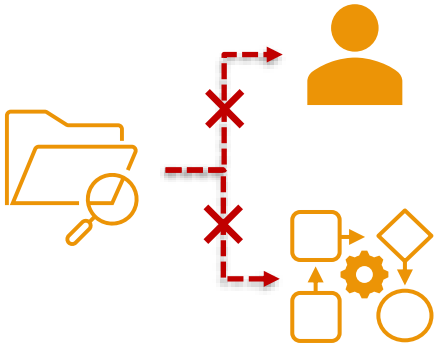
Impacts from 1306 Errors



Impacts from 1323 Errors

Files appear to be in the submission but can't be located by reviewers or FDA systems





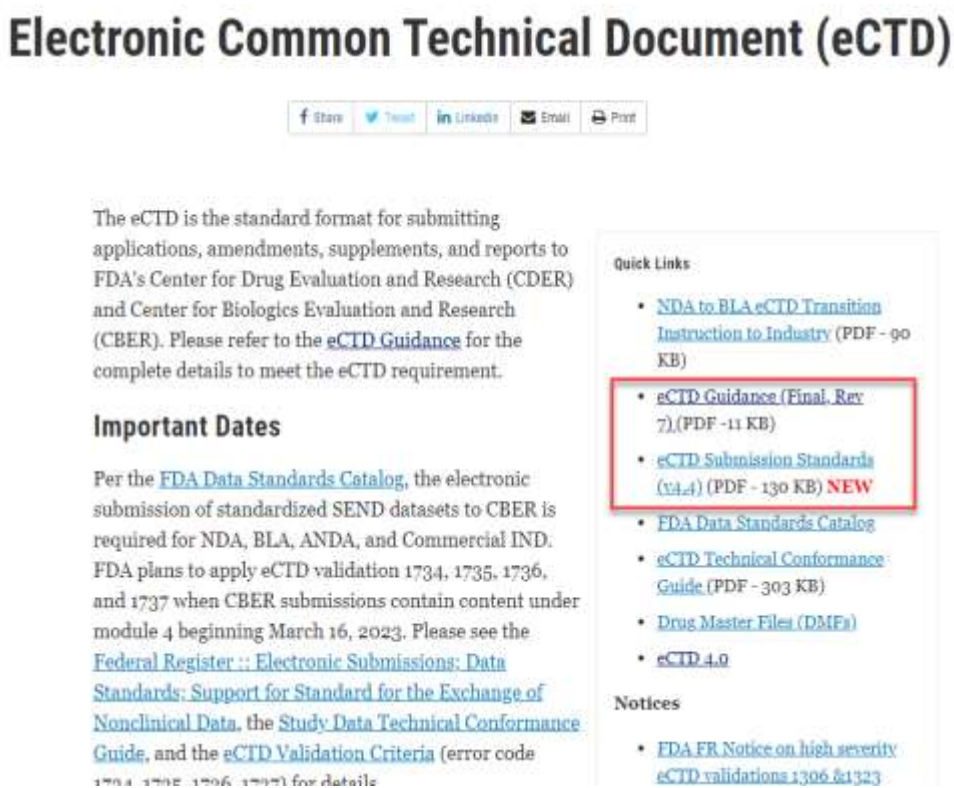
eCTD Viewer Error:

File not found.

Locate latest version of eCTD guidance, specifications, and validations

www.fda.gov/ectd

- Latest Guidance
- eCTD Submission Standards
  - eCTD specifications
  - eCTD validations
- Important Dates, Notices, Past Presentations, and More



Electronic Common Technical Document (eCTD)

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The eCTD is the standard format for submitting applications, amendments, supplements, and reports to FDA's Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER). Please refer to the eCTD Guidance for the complete details to meet the eCTD requirement.

Important Dates

Per the FDA Data Standards Catalog, the electronic submission of standardized SEND datasets to CBER is required for NDA, BLA, ANDA, and Commercial IND. FDA plans to apply eCTD validation 1734, 1735, 1736, and 1737 when CBER submissions contain content under module 4 beginning March 16, 2023. Please see the Federal Register :: Electronic Submissions: Data Standards; Support for Standard for the Exchange of Nonclinical Data, the Study Data Technical Conformance Guide, and the eCTD Validation Criteria (error code 1734, 1735, 1736, 1737) for details.

Quick Links

- NDA to BLA eCTD Transition Instruction to Industry (PDF - 90 KB)
- eCTD Guidance (Final, Rev 7) (PDF - 11 KB)
- eCTD Submission Standards (v4.4) (PDF - 130 KB) **NEW**
- FDA Data Standards Catalog
- eCTD Technical Conformance Guide (PDF - 303 KB)
- Drug Master Files (DMFs)
- eCTD 4.0

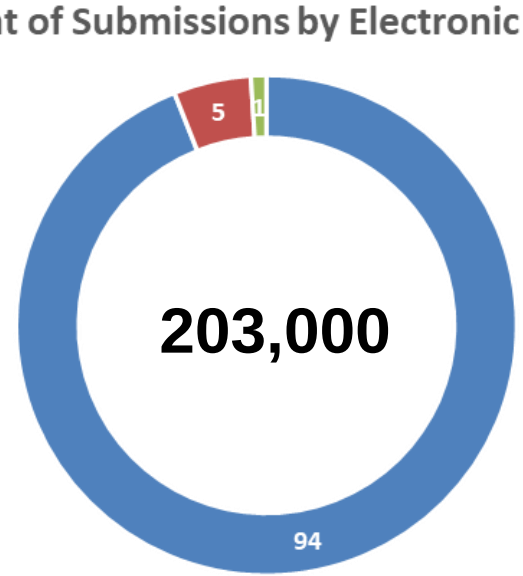
Notices

- FDA FR Notice on high severity eCTD validations 1306 &1323

eCTD Submission Metrics

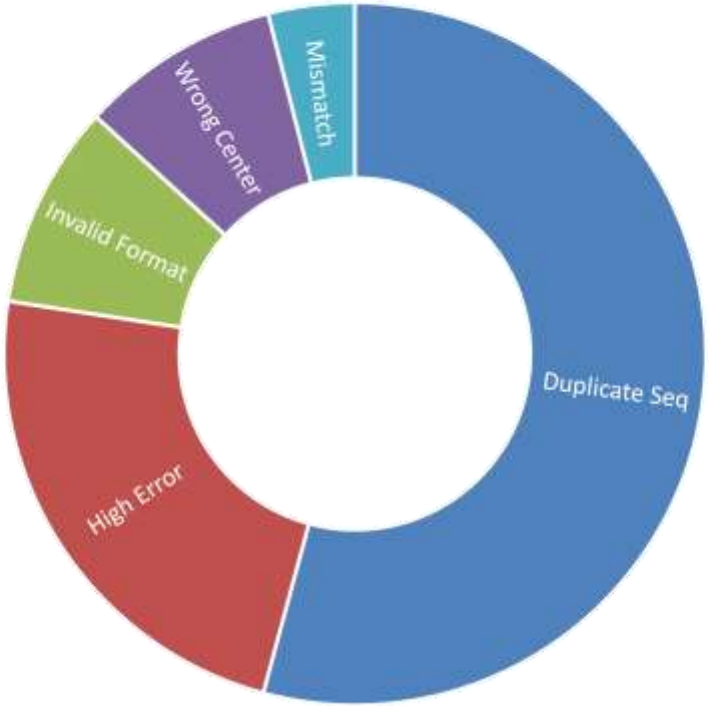
CDER Submissions October 1, 2021 through April 30, 2022

203,000 Total Submissions

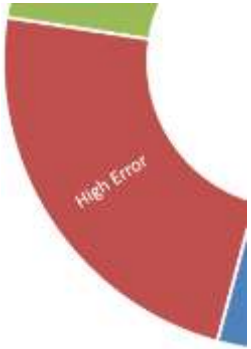


ECTD	94%
NON ECTD	5%
PAPER	1%

Top 5 eCTD Rejection Reasons



Top 5 eCTD Rejection Reasons



Most common High Error Codes

- Code 2034 – Submission Type invalid for Application Type
- Code 2022 – Submission Sub-Type is invalid for Submission Type
- Code 1734 - A dataset named ts.xpt with information on study start date must be present for each study in Module 4, sections 4.2.3.1, 4.2.3.2, 4.2.3.4, and in Module 5, sections 5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2
- Code 1789 - A file has been submitted in a study section without providing an STF file. STFs are not required for 4.3 Literature references, 5.2 Tabular listings, 5.4 Literature references and 5.3.6 Postmarketing reports

Challenge Question #1

Most eCTD submission failures are due to:

A. Duplicate sequence number

B. eCTD validation error

C. Submission sent to wrong Center

D. Mismatch between data included in eCTD message and application form

Top 5 Questions eSub Team Receives

- Where do I place content?
- How do I send ECG waveforms?
- What eCTD Submission Type/Sub-Type should be used?
- How to remove duplicate content?
- What file formats are expected?

Top 5 Questions eSub Team Receives

Where do I place content?

Resources:

- ✓ The Comprehensive Table of Contents Headings and Hierarchy
- ✓ M4 Organization of the Common Technical Document for the Registration of Pharmaceuticals for Human Use Guidance fo Industry
- ✓ FDA Regulatory Project Manager
- ✓ esub@fda.hhs.gov

The Comprehensive Table of Contents Headings and Hierarchy

Module 1 Administrative information

- ***1.1 Forms***
  - Form [form-type]
- ***1.2 Cover letters***
- ***1.3 Administrative information***
  - 1.3.1 Contact/sponsor/applicant information
    - **1.3.1.1 Change of address or corporate name**
    - **1.3.1.2 Change in contact/agent**
    - **1.3.1.3 Change in sponsor**
    - **1.3.1.4 Transfer of obligation**
    - **1.3.1.5 Change in ownership of an application or reissuance of licens**
  - 1.3.2 Field copy certification
  - 1.3.3 Debarment certification
  - 1.3.4 Financial certification and disclosure
  - 1.3.5 Patent and exclusivity
    - **1.3.5.1 Patent information**
    - **1.3.5.2 Patent certification**
    - **1.3.5.3 Exclusivity claim**
  - 1.3.6 Tropical disease priority review voucher
- ***1.4 References***
  - 1.4.1 Letter of authorization
  - 1.4.2 Statement of right of reference
  - 1.4.3 List of authorized persons to incorporate by reference

Top 5 Questions eSub Team Receives

How do I send ECG waveforms?

Resources:

- ✓ eCTD Technical Conformance Guide
- ✓ Interdisciplinary Review Team for Cardiac Safety Studies (formerly QT-IRT)

Top 5 Questions eSub Team Receives

What eCTD Submission Type/Sub-Type should be used?

Resources:

- ✓ The eCTD Backbone Files Specification for Module 1

The eCTD Backbone Files Specification for Module 1
Table 2: Submission Types and Descriptions of Use

Submission Type	Submission Sub-Type	Supplement Effective Date Type (if applicable and *submission-sub-type* = "application")	Valid For Application Types
Original Application	Presubmission Application Amendment Resubmission		IND, NDA, ANDA, BLA, DMF, EUA
Efficacy Supplement	Presubmission		NDA, BLA
	Application	Prior Approval Supplement (PAS)	
	Amendment Resubmission		
Chemistry Manufacturing Controls Supplement	Presubmission		NDA, ANDA, BLA
	Application	Prior Approval Supplement (PAS), Changes Being Effected (CBE-0), or Changes Being Effected 30 (CBE-30)	
	Amendment Resubmission		
Labeling Supplement	Presubmission		NDA, ANDA, BLA
	Application	Prior Approval Supplement (PAS) or Changes Being Effected (CBE-0)	
	Amendment Resubmission		
REMS Supplement	Application	Prior Approval Supplement (PAS) or Changes Being Effected (CBE-30)	NDA, ANDA, BLA
	Amendment Resubmission		
Annual Report	Report		IND, NDA, ANDA

Top 5 Questions eSub Team Receives

How to remove duplicate content?

- ✓ **Remove document**: Use “delete” eCTD lifecycle operator in next eCTD sequence
- ✓ **Remove duplicate heading (e.g., Multiple “3.2.P”):** Remove all documents under the duplicate heading(s) and re-reference under the heading that should remain

Top 5 Questions eSub Team Receives

What file formats are expected?

Resources:

- ✓ Specifications for File Format Types

Specifications for File Format Types
Using eCTD Specifications

File Type	File Format	Format Name	Accepted location in eCTD	Archive Format Copy	Permissible Uses
Documents					
	.pdf	Portable Document Format	M1 – M5		
	.doc	Microsoft Word document	M1.14, 1.16		
			M2.3, M2.7	PDF	ANDA
	.docx	Microsoft Word Open XML document	M1.14, 1.16		
			M2.3, M2.7	PDF	ANDA
	.txt	Text file	M3 - M5		
	.xls	Microsoft Excel document	M3 – M5	PDF	
	.xlsx	Microsoft Excel Open XML document	M3 – M5	PDF	
Images					
	.bmp	Bitmap	M1.15		

Challenge Question #2

Where can I locate valid eCTD Submission Type/Sub-Type combinations?

A. Specifications for File Format Types

B. eCTD Comprehensive Table of Contents Headings and Hierarchy

C. The eCTD Backbone Files Specification for Module 1

D. Interdisciplinary Review Team for Cardiac Safety Studies (formerly QT-IRT)

The Road Ahead

Next Major Version of eCTD is eCTD v4

- Regulatory Authorities started implementations
- ICH eCTD v4 Implementation Package is Published
- FDA Regional eCTD v4 Implementation Package, Technical Conformance Guide, and Validation Specifications are Published
- FDA Timeline to accept eCTD v4 currently planned for late 2023
- Please see FDA's eCTD v4 implementation page for more details

Resources

- Web page for latest version of eCTD guidance, specifications, and validations
- eCTD Comprehensive Table of Contents Headings and Hierarchy
- M4 Organization of the Common Technical Document for the Registration of Pharmaceuticals for Human Use Guidance for Industry
- eCTD Technical Conformance Guide
- Interdisciplinary Review Team for Cardiac Safety Studies (formerly QT-IRT)
- The eCTD Backbone Files Specification for Module 1
- Specifications for File Format Types
- FDA's eCTD v4 implementation page

Summary

- Module 1 DTD v3.3 required to pass validation
- Check FDA's eCTD webpage, www.fda.gov/ectd for announcements and updates
- Most common eCTD submission mistake is using a duplicate sequence number
- FDA is testing the next major version of eCTD (version 4)

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Questions?

Please join us for a live Q&A panel after this presentation

Have questions after the conference? Please send to esub@fda.hhs.gov