Regulatory Submissions, Information, and Document Management Forum
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Disclaimer

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Electronic Submissions
eCTD Submission Metrics and Guidance

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- Guidance
- eCTD Metrics (FY 2018)
- Electronic Submission Processing
- Top 3 Rejections and How to Avoid Them
- Frequently Asked Question
Guidance
The number of submissions to the FDA has significantly increased.

- eCTD guidance became binding:
  - May 5, 2017: NDA, BLA, and ANDA must be in eCTD format.
  - May 5, 2018: Commercial IND and Master Files* must be in eCTD format.

See the following resources for more information:
- eCTD Guidance (Revision 6, posted January 2019)
- eCTD Technical Conformance Guide
- eCTD Website

Have Questions? Contact eSub@fda.hhs.gov

*Type III Master File requirement effective starting May 5, 2020
Study Data Submission Deadlines

- Studies that start after December 17, 2016 must be in standardized format for NDA, BLA and ANDA submissions
- For Commercial IND submissions, the date is December 17, 2017

See the following resources for more information

- Study Data Standards Resources page
- Technical Rejection Criteria for Study Data
- The Study Data Guidance

Have Questions? Contact eData@fda.hhs.gov
Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications

Guidance for Industry

D. The eCTD Specifications

You must submit electronic submissions using the version of eCTD currently supported by FDA. The version of eCTD currently supported is specified in the Data Standards Catalog (available at http://www.fda.gov/downloads/ForIndustry/DataStandards/StudyDataStandards/UCM340684.xls) and is further described in the following technical specification documents:

- ICH<sup>10</sup> Electronic Common Technical Document Specification
- ICH eCTD Backbone File Specification for Study Tagging Files
- FDA eCTD Backbone Files Specification for Module 1

J. Datasets and Study Information

Datasets must only be provided in modules 3, 4, or 5 and not in modules 1 or 2. When providing study information in either module 4 or 5, you must include the Study Tagging File (STF) described in the associated ICH M2 technical specification eCTD Backbone File Specification for Study Tagging Files (see section III.D). Datasets must be referenced in an STF using the appropriate STF file-tag describing the document’s contents.

For further information regarding the submission of study data, see FDA guidance for industry Providing Regulatory Submissions in Electronic Format — Standardized Study Data.
CDER receives approximately 200,000 electronic submissions via ESG annually. Nearly 192,000 were in eCTD in FY 2018.
In FY 2018, nearly 100% of the regulatory submissions for NDA, BLA, and ANDA were in eCTD. For Commercial IND and DMF, 96% and 78% (Type II, IV, V)
Electronic Submission Processing: Current and Future
Current State: Submission Processing

All CDER regulatory submissions received are processed by Document Room.

Current Document Room Process:
Staff reads the Cover Page of every submission (Approx. 850 per day) to categorize and route to correct Review Divisions
Future: Submission Processing

Automate process to identify Submission Category

Process:
1. Determine Submission Category based on structured data in eCTD sequence
2. Route to Review Division based on Submission Category

Benefit:
Reviewer gets submission faster

Document Room continues to process submissions where category cannot be determined automatically and submissions which contain high validation errors
Future: Submission Processing Challenges

- To efficiently and effectively process the increased number of submissions and leverage the submitted structured eCTD and study data, FDA is in the process of automating inbound submissions by using structured data from the eCTD backbone files and FDA Forms. However, data submitted in eCTD backbone files (e.g. us-regional.xml file) and regulatory form (e.g., Form 356h) are not always consistent.

- FDA reviewers use the state-of-the-art review tools (e.g. JMP Clinical) to support analyzing submitted study data. However, study data submitted do not always conform with the published FDA Data Standards Catalog.
The “eCTD Backbone Files Specification for Module 1” explains how to build regulatory activities using M1 elements and attributes such as submission-type, submission-id and submission-sub-type (if DTD version 3.3)
eCTD Data Discrepancy Example 1:

Can you guess the correct regulatory activity in this submission?

**us-regional.xml (DTD V2.01)**

- Indicating “Original Application”

**Form 356h**

- Indicating “Periodic Safety Report”

This submission was a periodic safety report. The appropriate eCTD “submission-type” would have been “other”.
Can you guess the correct regulatory activity in this submission?

**us-regional.xml (DTD V2.01)**

```xml
<application-information application-type="">
  <submission submission-type="amendment">
    <sequence-number"></sequence-number>
    <related-sequence-number"></related-sequence-number>
  </submission>
</application-information>
```

**Form 356h**

This submission was an amendment containing patent information. The appropriate **Submission Sub-Type** on Form 356h would have been **Amendment**.
eCTD Data Discrepancy Example 3:

Can you guess the correct regulatory activity in this submission?

us-regional.xml (DTD V3.3)

```
<submission-information>
  <submission-id submission-type="fdastl">00000</submission-id>
  <sequence-number submission-sub-type="fdasst4">00000</sequence-number>
</submission-information>
```

Form 356h

- Indicating “Amendment”
- Indicating “Initial Submission”

This submission was an amendment to an original application. The appropriate “Submission Sub-Type” on Form 356h would have been “Amendment”
eCTD Data Discrepancy Example 4:

Can you guess the correct regulatory activity in this submission?

**us-regional.xml (DTD V3.3)**

```xml
<submission-information>
    <submission-id submission-type="fdast3" supplement-effective-date-type="fdasedtz"></submission-id>
    <sequence-number submission-sub-type="fasst3"></sequence-number>
</submission-information>
```

**Form 356h**

This submission was an Initial CMC Supplement CBE. The appropriate “**Supplement Category**” on Form 356h would have been “**CBE**”
When data is submitted correctly in eCTD backbone files (e.g. us-regional.xml file) and regulatory form (e.g., Form 356h), submission can be efficiently routed to the assigned review division and/or reviewer(s).

Indicating different Submission Type and/or Submission Sub-Type in us-regional.xml and Form 356h could:

- Impact FDA’s ability to automate the submission process
- Require additional effort to read the Cover Letter in order to resolve the discrepancy
- May require Request(s) for Information that may otherwise not be necessary
Top 3 Rejections and How to Avoid Them
Top 3 Rejections and How to Avoid Them (FY 2018)

Top 3 Rejection Categories

- Sent to Wrong Center
- eCTD Validation Error
- Duplicate Sequence
### Duplicate Sequence Number Received  
(Most Common, Nearly 50% of All Errors)

<table>
<thead>
<tr>
<th>Issue</th>
<th>Resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Submitting revised content under same sequence number (e.g. trying to swap out a sequence)</td>
<td>Content should be updated by submitting changes in the next available sequence</td>
</tr>
<tr>
<td>Transfer of application but new owner is not aware of sequence numbers used</td>
<td>Recommend obtaining full sequence history from prior owner</td>
</tr>
<tr>
<td>Re-using a sequence number if submission has been withdrawn</td>
<td>Even if a submission is withdrawn, FDA continues to keep the sequence</td>
</tr>
</tbody>
</table>
eCTD Validation Error (Most common was 2022)

**Issue**

Validation Code 2022: You have used a submission-sub-type which is not allowed for the submission-type and/or type of application. Ex: Original Application/Correspondence

**Resolution**

See list of valid Submission Type and Sub-Type combinations.

**Resource:** eCTD Backbone Files Specifications for Module 1, Table 2: Submission Types and Descriptions of Use
### Issue
Sequence submitted to wrong FDA Center (e.g., CBER BLA submitted to CDER)

### Resolution
Select appropriate FDA Center in ESG/Webtrader
Frequently Asked Questions
Frequently Asked Questions

Where do I place my 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 for Industry
- FDA Regulatory Project Manager

Note: Do not send empty sections or provide placeholders for files
Frequently Asked Questions

- Can I submit a particular file format? (e.g., .docx, xpt, etc.)
  - When creating content, follow the Specifications for File Format Types Using eCTD Specifications for guidance on file formats FDA expects under the different CTD headings.

- Questions related to PDF files (e.g., hyperlinks, bookmarks, font, etc.)
  - Follow FDA’s PDF Specifications and communicate to vendors the need to follow these specifications.
Frequently Asked Questions

If I receive a successful third acknowledgement, does that mean the review office finds my submission to be complete?

− No, the successful third acknowledgement means the submission has passed technical validation and is now available to the review office to conduct their processing (e.g., Filing review).
What is the relevance of the ESG timestamp?

- The ESG timestamp (e.g., date and time on Official Center Acknowledgment (second acknowledgment)) is used to calculate the official receipt date of the submission.
- If submission arrives through the ESG on a weekend, a federal holiday, or another day on which the FDA office that will review the submission is not open for business, it is deemed to have arrived at FDA on the next day when that office is open for business.
- Please see the FDA Guidance* for complete details

*Guidance for Industry Providing Regulatory Submissions in Electronic Format — Receipt Dates
Frequently Asked Questions

- How to get started with eCTD?
- How to request an application number?
- How to get a gateway account?

These questions and more are answered on the eCTD website:

Electronic Common Technical Document (eCTD)

Submit Using eCTD

Visit our Submit Using eCTD page to learn how to submit an application using eCTD and obtain an ESG account.
To view all eCTD Submission Resources, visit our eCTD Resources page.
WHERE TO GET HELP

Specification documents are posted on www.fda.gov/ectd in the eCTD Submission Standards.

Validation Documents Include:
- eCTD Validation Specifications
- Technical Rejection for Study Data Criteria

CDER submissions, contact:
- EDATA@fda.hhs.gov
- ESUB@fda.hhs.gov
THANK YOU

U.S. FOOD & DRUG ADMINISTRATION