

# Practical Tips on eCTD

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FDA Disclaimer

The views and opinions presented here represent those of the speaker and should not be considered to represent advice or guidance on behalf of the U.S. Food and Drug Administration.



# Poll

How would you characterize your ability to submit your ANDA in proper eCTD format?

- I'm an experienced expert
- I'm pretty good at it
- Somebody else in my company handles the eCTD
- I am a beginner
- Wait. What is eCTD?

# Topics Covered



- Guidance
- eCTD Metrics (FY 2018)
- Electronic Submission Processing
- Preparing to Submit Electronically and Points to Consider



## Guidance – eCTD Required

- **ANDAs, NDAs, BLAs, DMFs\*** and **Commercial INDs** must be in eCTD format
- Paper and/or non-eCTD submissions are no longer accepted for above application types
- Study information in modules 4 or 5 must include the Study Tagging File (STF)
- Please see the eCTD web page [www.fda.gov/ectd](http://www.fda.gov/ectd) for further information and guidance

\*Type III DMFs deadline extended to May 5, 2020

# Guidance - Standardized Study Data in Electronic Format

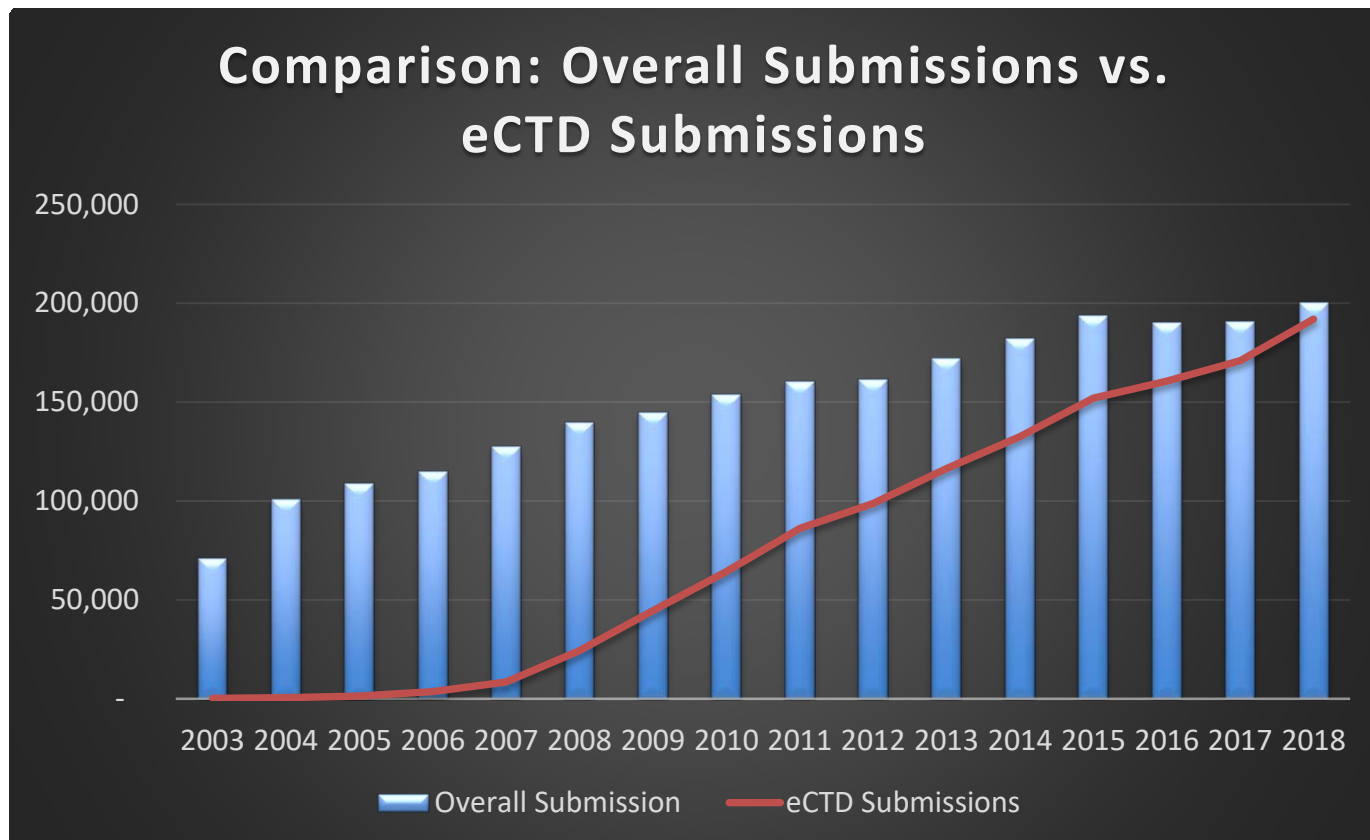


- **What** is the requirement?
  - Studies that start after **December 17, 2016** must be in standardized format for ANDA, NDA, and BLA submissions. *Commercial IND (December 17, 2017)*
  - See the [Study Data for Submission to CDER and CBER](#) website for more information
- **How** will it be enforced?
  - [Technical Rejection Criteria for Study Data](#)
  - [Specifications for eCTD Validation Criteria](#)
- **Where** can I find [The Guidance](#)?

Have Questions? Contact [eData@fda.hhs.gov](mailto:eData@fda.hhs.gov)

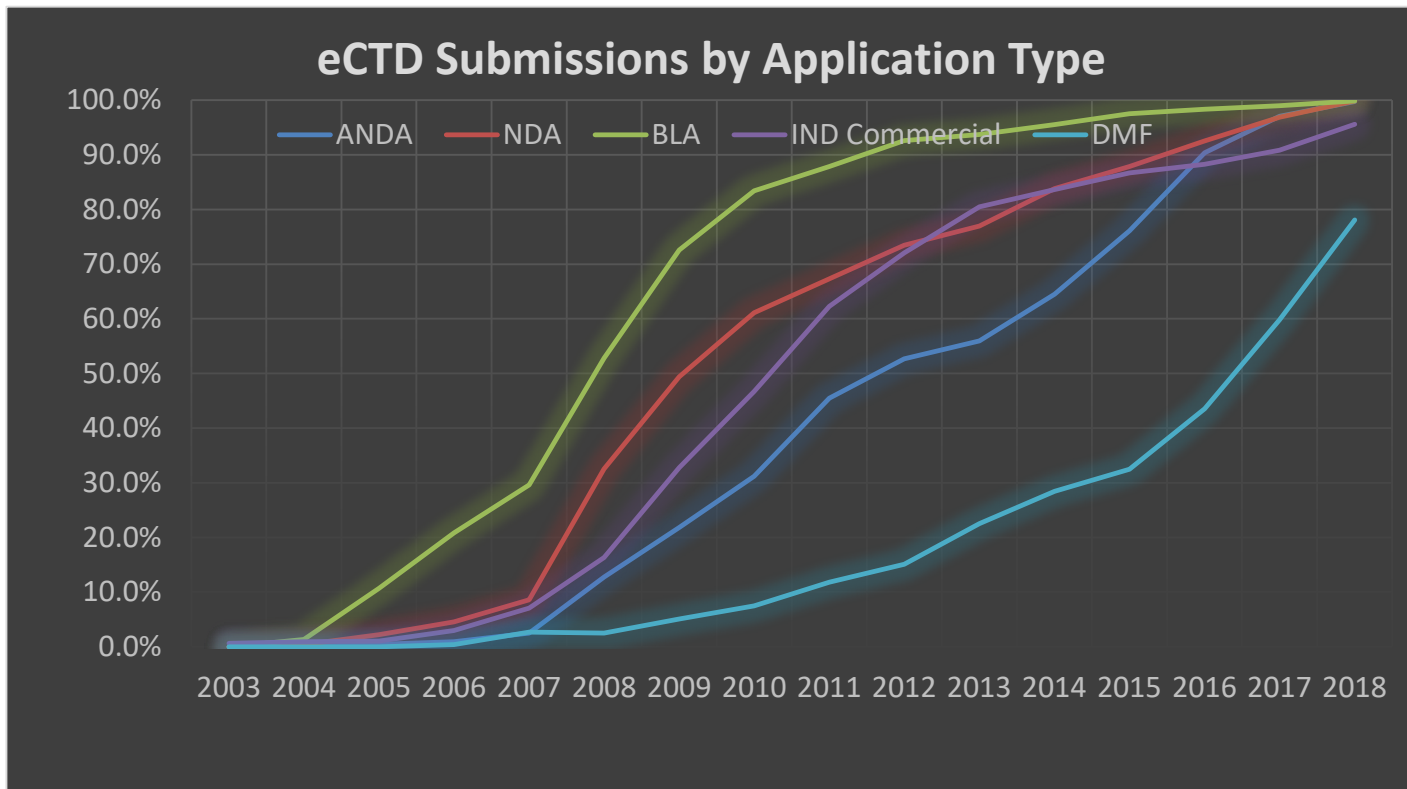
# eCTD Submission Metrics

CDER receives approximately 200,000 electronic submissions via ESG annually. Nearly 192,000 were in eCTD in FY 2018.



# eCTD Submission Metrics

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: Increasing Automation**



# Submission Processing: 2018

All CDER regulatory submissions received are processed by Document Room

## Document Room Process:

Staff reads the Cover Page of every submission (Approx. 850 per day) to categorize and route to correct Review Divisions



# Submission Processing: 2019

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

# 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.**

# eCTD Data Discrepancy Example: 1

Can you guess the correct regulatory activity in this submission?



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

```
<submission submission-type="original-application">  
  <sequence-number>0022</sequence-number>  
</submission>
```

Indicating "Original Application"



**Form 356h**

21. Submission (See instructions)

<input type="checkbox"/> Original	<input type="checkbox"/> Labeling Supplement	<input type="checkbox"/> CMC Supplement	<input type="checkbox"/> Efficacy Supplement	<input type="checkbox"/> Annual Report
<input type="checkbox"/> Product Correspondence	<input type="checkbox"/> REMS Supplement	<input type="checkbox"/> Postmarketing Requirements or Commitments	<input checked="" type="checkbox"/> Periodic Safety Report	
<input type="checkbox"/> Request for Proprietary Name Review	<input type="checkbox"/> Other (Specify): _____			

Indicating "Periodic Safety Report"

This submission was a periodic safety report.  
The appropriate eCTD "submission-type" would have been "other".

# eCTD Data Discrepancy Example: 2

Can you guess the correct regulatory activity in this submission?

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

```
<submission-information>
  <submission-id submission-type="fdast3" supplement-effective-date-type="fdasedt2" [REDACTED] </submission-id>
  <sequence-number submission-sub-type="fdasst3" [REDACTED] </sequence-number>
```

Indicating "CBE"

**Form 356h**



21. Submission (See instructions) <input type="checkbox"/> Original <input type="checkbox"/> Labeling Supplement <input checked="" type="checkbox"/> CMC Supplement <input type="checkbox"/> Efficacy Supplement <input type="checkbox"/> Annual Report		23. If a supplement, identify the appropriate category. <input type="checkbox"/> CBE <input checked="" type="checkbox"/> Prior Approval (PA)
<input type="checkbox"/> Product Correspondence <input type="checkbox"/> REMS Supplement <input type="checkbox"/> Postmarketing Requirements or Commitments <input type="checkbox"/> Periodic Safety Report		
<input type="checkbox"/> Request for Proprietary Name Review <input type="checkbox"/> Other (Specify): _____		<input type="checkbox"/> CBE-30
22. Submission Sub-Type <input type="checkbox"/> Presubmission <input type="checkbox"/> Amendment	<input checked="" type="checkbox"/> Initial Submission <input type="checkbox"/> Resubmission	

Indicating "Prior Approval"

This submission was an Initial CMC Supplement CBE.  
 The appropriate "Supplement Category" on Form 356h would have been "CBE"

# eCTD Data Discrepancy Impact



-  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



# Preparing to Submit Electronically and Points to Consider

# Become familiar with the eCTD website

**Electronic Submissions to CDER**

CDER Data Standards Program

Data Standards in the Drug Lifecycle

**Electronic Common Technical Document (eCTD)**

Electronic Regulatory Submissions and Review Helpful Links

Electronic Submissions Presentations

Study Data for Submission to CDER and CBER

[Source Data Capture from Electronic Health Records \(EHRs\)](#)

Data Standards Manual (monographs)

## Electronic Common Technical Document (eCTD)

SHARE | TWEET | LINKEDIN | PIN IT | EMAIL | PRINT

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).

### Important Dates

After the dates listed below, eCTD requirements for submissions to CDER and CBER will go into effect and submissions that do not use eCTD will not be filed or received.

- May 5, 2017:** New Drug Applications (NDAs), Abbreviated NDAs (ANDAs), and Biologics License Applications (BLAs), must be submitted using eCTD format.
- May 5, 2018:** Commercial Investigational New Drug Applications (INDs) and Master Files must be submitted using eCTD format.
- Please refer to the [eCTD Guidance](#) for the complete details to meet the eCTD requirement.

### Quick Links

- [eCTD Guidance \(PDF -11 KB\)](#)
- [eCTD Submission Standards \(PDF - 91KB\)](#)
- [FDA Data Standards Catalog](#)
- [eCTD Technical Conformance Guide \(PDF - 303KB\)](#)
- [Drug Master Files \(DMFs\)](#)
- [Technical Rejection Criteria for Study Data \(PDF - 921 KB\)](#)
- [eCTD Submission Types and Sub-Types \(PDF - 630 KB\) \*\*NEW\*\*](#)

### Notices

- [Third Acknowledgement for Successful eCTD Submissions \(May 2016\)](#)
- [Past Notices](#)

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.

## Important Dates

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# Submission Hierarchy



- Organize content to follow Common Technical Document (CTD) structure

- 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](#)

*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 license

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

# File Format and PDF Specifications

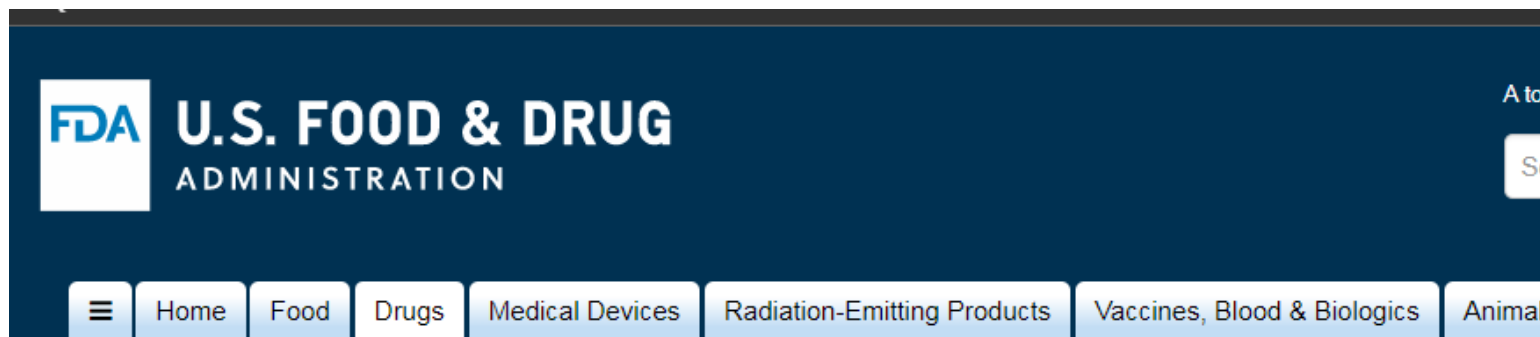
- When creating content, follow the [Specifications for File Format Types Using eCTD Specifications](#) for guidance on file formats FDA expects under the different CTD headings
- Follow FDA's [PDF Specifications](#) and communicate to vendors the need to follow these specifications

# Study Data

- If submitting study data, please see the [Study Data for Submission to CDER and CBER](#) website.
- Key Study Data Resources:
  - [Providing Regulatory Submissions In Electronic Format — Standardized Study Data Guidance for Industry](#)
  - [Technical Rejection Criteria for Study Data](#)
  - [Study Data Technical Conformance Guide](#)
  - [ANDA Forms and Submission Requirements Website](#)

# Prepare for Submission to FDA

- Request an Application Number from FDA
- Register for an Electronic Submission Gateway



[Learn about eCTD](#)

[Review the Electronic Submission Resources](#)

[Submit Fillable Forms and Compliant PDFs](#)

[Request an Application Number](#)



[Register for an Electronic Submissions Gateway Account](#)



[Send a Sample Submission to FDA](#)

[Submit Via the Electronic Submission Gateway](#)

# Generate the eCTD for Submission to FDA

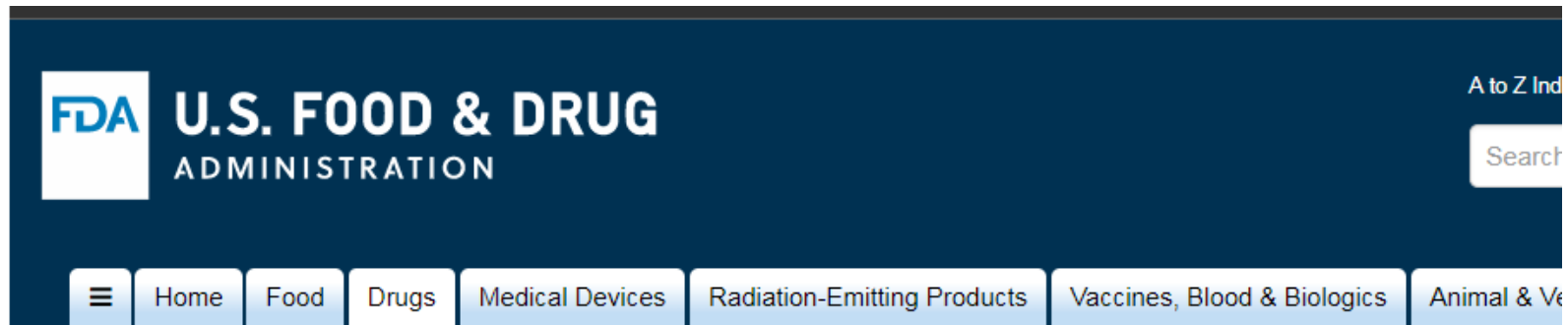


- Publish content into eCTD format via eCTD Publishing Tool or eCTD Tool Vendor
  - Utilize eCTD publishing tool to:
    - Capture administrative information
    - Map submission content to CTD section headings
    - Generate final submission in eCTD format including all required technical files/folder structure

# Validate eCTD (Optional) and/or Request eSub Feedback



- (Optional) Validate via eCTD Validation Tool
- (Optional) Ask [ESUB-Testing@fda.hhs.gov](mailto:ESUB-Testing@fda.hhs.gov) for technical feedback via Sample Submission Process



## Submit an eCTD or Standardized Data Sample to the FDA

Please follow the steps below to submit a sample submission:

### 1. Request a Sample Application Number

To initiate the process of submitting a sample submission, notify the Electronic Submissions Capability Team at [ESUB-Testing@fda.hhs.gov](mailto:ESUB-Testing@fda.hhs.gov) to request a Sample Application Number.

# Summary



- Important Guidance Requirements
  - **ANDAs, NDAs, BLAs, DMFs, and Commercial INDs must be submitted in eCTD**
  - **Technical Rejection Criteria for Study Data**
- Confirm eCTD metadata is consistent with FDA Form
  - **eCTD Submission Type and Subtype align with values on 356h**
- Preparing to Submit Electronically and Points to Consider
  - **Utilize FDA's eCTD Website**
  - **Align Content with CTD**



# Thank You

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CDER Electronic Submission Support Team

[eSub@fda.hhs.gov](mailto:eSub@fda.hhs.gov)

[www.fda.gov/ectd](http://www.fda.gov/ectd)



