Regulatory Submissions, Information, and Document Management Forum

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General Updates

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Session 7: FDA Electronic Submissions Update
February 8, 2017
Agenda

1. Important Submission Deadlines
2. Submission Metrics
3. Updates on eCTD Website in 2016
4. CDER Gateway Third Acknowledgement
5. Study Data Standards Resources and Validation
6. Lessons Learned When Implementing eCTD
   • Rejections
   • Submission Errors with M1 (DTD 3.3)
Deadlines for Required eCTD Submission

• **May 5, 2017:** NDA, BLA, ANDA and DMFs must be in eCTD format

• **May 5, 2018:** Commercial INDs must be in eCTD format

• Do not send Paper and/or non-eCTD submissions after these deadlines!
Deadlines for Required eCTD Submission

• Exemptions are outlined in the guidance

• Submissions that do not adhere to the requirements stated in the eCTD Guidance will be **not be filed or received**

• Please see the eCTD web page [www.fda.gov/ectd](http://www.fda.gov/ectd) for further information
What else?

✓ Must use Fillable Forms & Electronic Signatures within those forms

✓ Must use correct Lifecycle operators
  ✓ Do not send the same study data over and over
What else?

✓ Must use Gateway for submissions 10GB and smaller – no more CD/DVDs

✓ Submissions larger than 10GB may come via the Gateway or USB drive

*See Transmission Specification for additional details
Deadlines for standardized study data

• Studies that start after December 17, 2016 must be in standardized format for NDA, BLA and ANDA submissions

• For IND submissions, the date is December 17, 2017
Submission Metrics & Milestones

CDER Incoming Submissions in eCTD Format

EXCLUDES PROMOTIONAL ADVERTISING & LABELING SUBMISSIONS
Submission Metrics & Milestones

M1 (DTD 3.3) Submissions in 2016

- Jan: 300
- Feb: 1100
- Mar: 1500
- Apr: 1600
- May: 1800
- Jun: 2000
- Jul: 2000
- Aug: 2600
- Sep: 2700
- Oct: 2800
- Nov: 3450
- Dec: 3500
Updates on eCTD Website in 2016

- Third Acknowledgement
- Update to the eCTD Technical Conformance Guide
- Update to PDF Specifications
- Technical Rejection for Study Data
- And more..
CDER Gateway THIRD ACKNOWLEDGEMENT

• Began May 31, 2016

• Applies only to NDA, ANDA, BLA, IND or DMF submissions

• Sent to you when your submission has successfully completed validation and processing, and is available to the assigned review division
New: CDER GATEWAY THIRD ACKNOWLEDGEMENT
CDER Gateway THIRD ACKNOWLEDGEMENT

• This is in addition to the ESG Message Delivery Notification acknowledgement (first acknowledgement) and the Official Center acknowledgement (second acknowledgement)

• May be delayed if your submission fails validation and needs manual processing (e.g., Mismatch between your form and your eCTD XML)
NEW: STUDY Data Standards Resources

• What’s New
  – Studies that start after **December 17, 2016** must be in standardized format for NDA, BLA and ANDA submissions
  – Study Data Technical Conformance Guide v3.2.1
    [http://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards/default.htm](http://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards/default.htm)

• Validation Codes
  – Technical Rejection Criteria for Study Data
  – Specifications for eCTD Validation Criteria
    [http://www.fda.gov/ectd](http://www.fda.gov/ectd)

• When
  CDER will start using the new validation criteria - TBD
Study Data Standards Validation
Using the eCTD Validation Criteria

Sponsor
NDAs, BLAs, INDs, ANDAs

Study Data Conformance Validation

Study Data Quality Validation

Data Repositories

Analytic Tools

Review Decisions
Conformance Validation…

How will it work?

Sponsor NDAs, BLAs, INDs, ANDAs

Do study data conform to required standards?

YES

Acknowledgement sent via ESG on successful validation and processing

NO

Acknowledgement sent via ESG on unsuccessful validation and processing

Acknowledgement sent via ESG on unsuccessful validation and processing

EDR

Data Quality Validation

Data Repositories

AnalyticTools

Reviewers

Technical Rejection of the Submission
Demographic dataset (DM) and the define.xml must be submitted in Module 4 for nonclinical data; DM dataset, the subject-level analysis dataset (ADSL) and define.xml must be submitted in Module 5 for clinical data.

Trial Summary (TS) dataset must be present for each study in eCTD section 4.2 and 5.3.

Correct STF file-tags must be used for all standardized datasets in section 4.2 and 5.3:
- Data-tabulations-dataset-sdtm
- Data-tabulations-dataset-send
- Analysis-dataset-adam

For each study in eCTD section 4.2 and section 5.3, no more than one dataset of the same name should be submitted as new.
Study Data Standards Validation

For more information

CDER submissions, contact: 
EDATA@fda.hhs.gov

CBER submissions, contact: 
CBER.CDISC@fda.hhs.gov
Lessons Learned When Implementing eCTD

• Rejections
• Common Submission Errors (new M1)
Rejections

Most common reasons for rejections

• Duplicate Submissions
  – You send the same submission sequence more than once

• Submitted to Wrong Center
  – Selecting wrong center when using gateway (e.g., CDER instead of CBER)

• Mismatched Application/Sequence Type
  – Specifying NDA in us-regional.xml while indicating BLA in 356h Form

• Invalid File Type
  – Submitting file types such as zip and exe

• Not in Standard eCTD Format
  – Missing key files such as us-regional.xml and index.xml
Common Submission Errors with M1 (DTD 3.3)

Errors Specific to M1 (DTD v3.3)

1. Choosing a Submission Type and Submission Subtype that starts a new Regulatory Activity but providing a Submission-ID different to the Sequence Number

2. Choosing a Submission Subtype of Amendment and specifying an incorrect Submission-ID

3. Transitioning from paper to eCTD and choosing a submission type of original application and submission subtype of amendment.
References

- eCTD Web Page:
  http://www.fda.gov/ectd

- Electronic Submissions Gateway:
  http://www.fda.gov/esg

- Electronic Submissions Presentations:

- Questions about submitting electronically to CDER:
  ESUB@fda.hhs.gov
Thank You

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www.fda.gov/ectd
Ask