Regulatory Submissions, Information, and Document Management Forum

February 6-8, 2017

Bethesda North Marriott Hotel and Conference Center

North Bethesda, MD

DIA

Disclaimer

The views and opinions expressed in the following PowerPoint slides are those of the individual presenter and should not be attributed to DIA, its directors, officers, employees, volunteers, members, chapters, councils, Communities or affiliates, or any organization with which the presenter is employed or affiliated.

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.

U.S. FOOD & DRUG ADMINISTRATION

General Updates

Jonathan Resnick
Electronic Submission Support Team
Office of Business Informatics, CDER

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

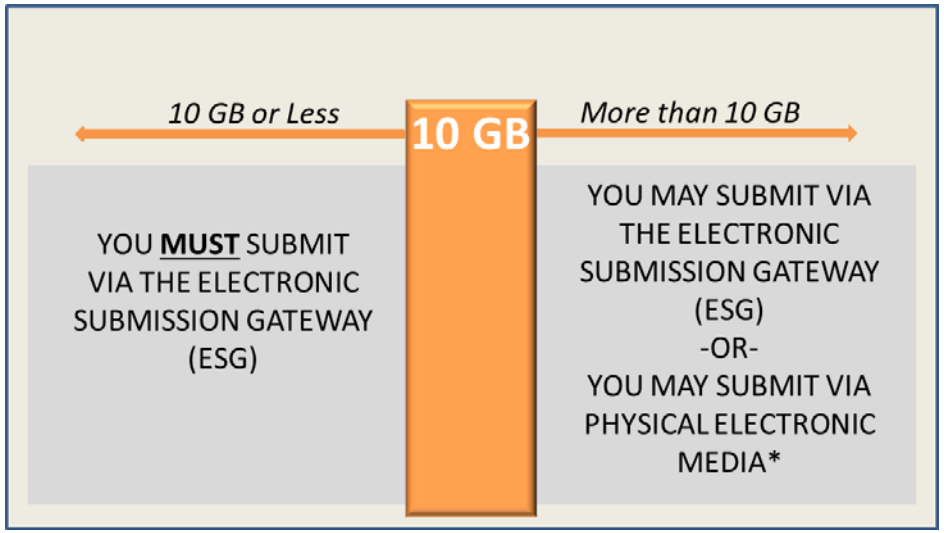
- Exemptions are outlined in the guidance
- Submissions that do not adhere to the requirements stated in the eCTD Guidance will be **not be filed or received**
- Please see the eCTD web page www.fda.gov/ectd for further information

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



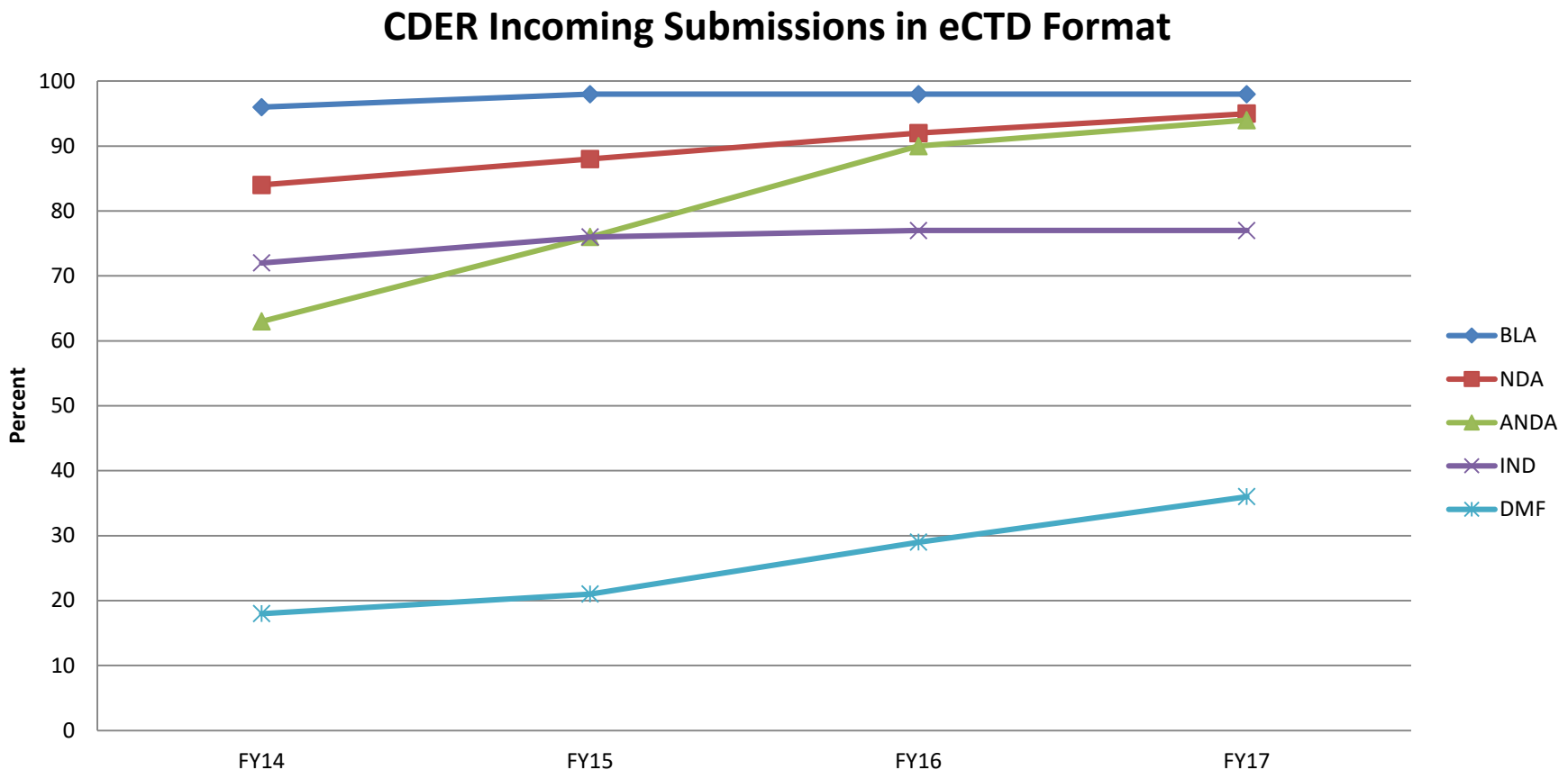
*See Transmission Specification for additional details

Deadlines for standardized study data

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

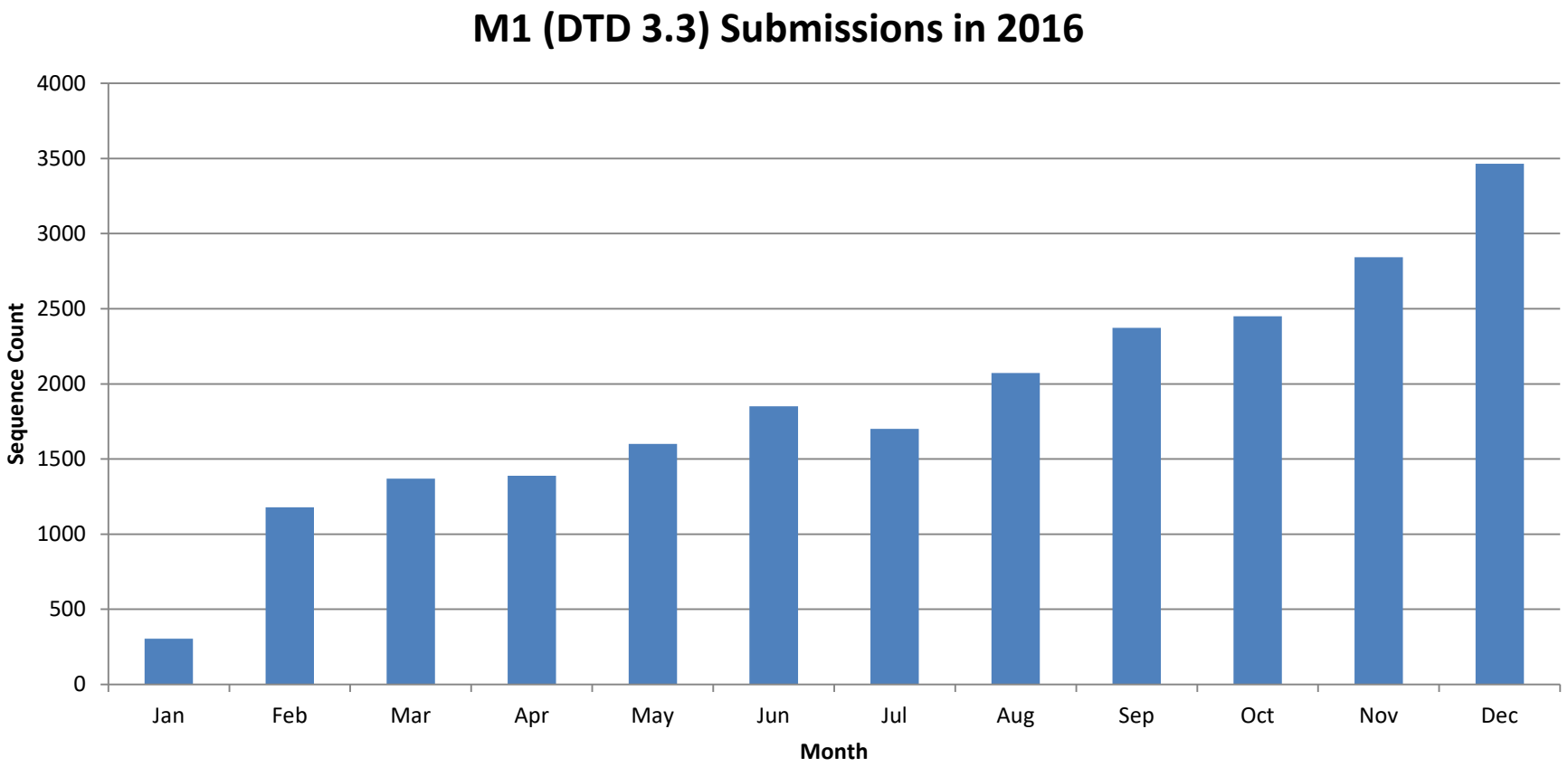
- For IND submissions, the date is December 17, 2017

Submission Metrics & Milestones



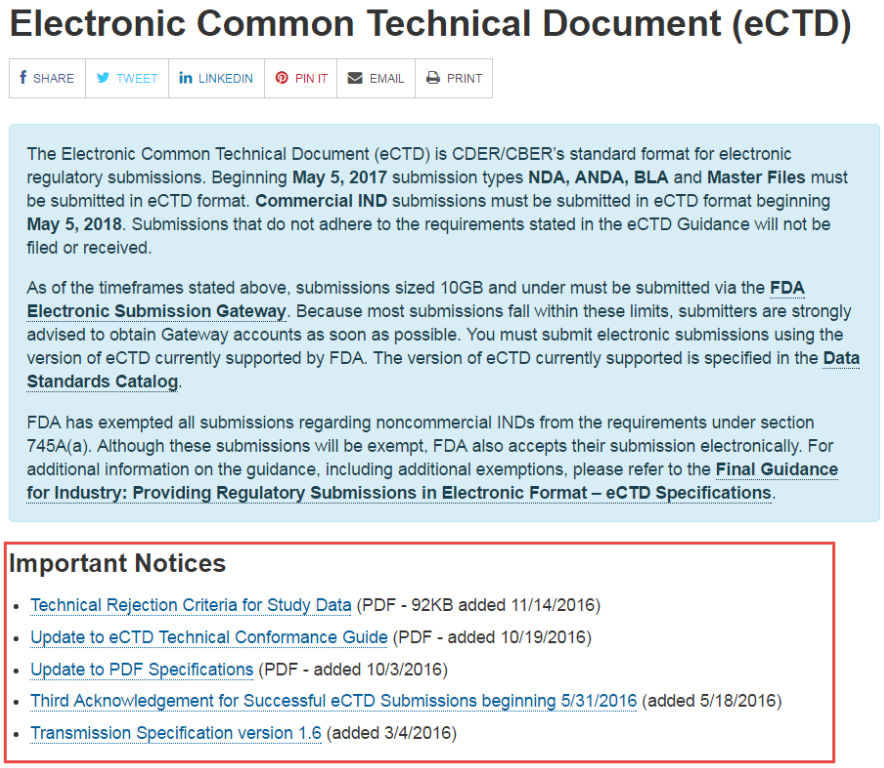
EXCLUDES PROMOTIONAL ADVERTISING & LABELING SUBMISSIONS

Submission Metrics & Milestones



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..



Electronic Common Technical Document (eCTD)

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

The Electronic Common Technical Document (eCTD) is CDER/CBER's standard format for electronic regulatory submissions. Beginning **May 5, 2017** submission types **NDA, ANDA, BLA** and **Master Files** must be submitted in eCTD format. **Commercial IND** submissions must be submitted in eCTD format beginning **May 5, 2018**. Submissions that do not adhere to the requirements stated in the eCTD Guidance will not be filed or received.

As of the timeframes stated above, submissions sized 10GB and under must be submitted via the **FDA Electronic Submission Gateway**. Because most submissions fall within these limits, submitters are strongly advised to obtain Gateway accounts as soon as possible. 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**.

FDA has exempted all submissions regarding noncommercial INDs from the requirements under section 745A(a). Although these submissions will be exempt, FDA also accepts their submission electronically. For additional information on the guidance, including additional exemptions, please refer to the **Final Guidance for Industry: Providing Regulatory Submissions in Electronic Format – eCTD Specifications**.

Important Notices

- Technical Rejection Criteria for Study Data (PDF - 92KB added 11/14/2016)
- Update to eCTD Technical Conformance Guide (PDF - added 10/19/2016)
- Update to PDF Specifications (PDF - added 10/3/2016)
- Third Acknowledgement for Successful eCTD Submissions beginning 5/31/2016 (added 5/18/2016)
- Transmission Specification version 1.6 (added 3/4/2016)

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

TEST PURPOSE ONLY

Your submission was successfully processed into the CDER Electronic Document Room, and is available to the assigned review division.

Application Type/Number: IND123456
eCTD Sequence Number: 0001
CoreID: ci1441927177074.54973@fdsul08620_te2

Your official receipt date is calculated in accordance with the following final Guidance for Industry:
http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072385.pdf

Contact Information:

For technical assistance only: eSUB@fda.hhs.gov

For all other questions regarding your submission, contact your review division.

Thank you,

Electronic Document Room
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

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

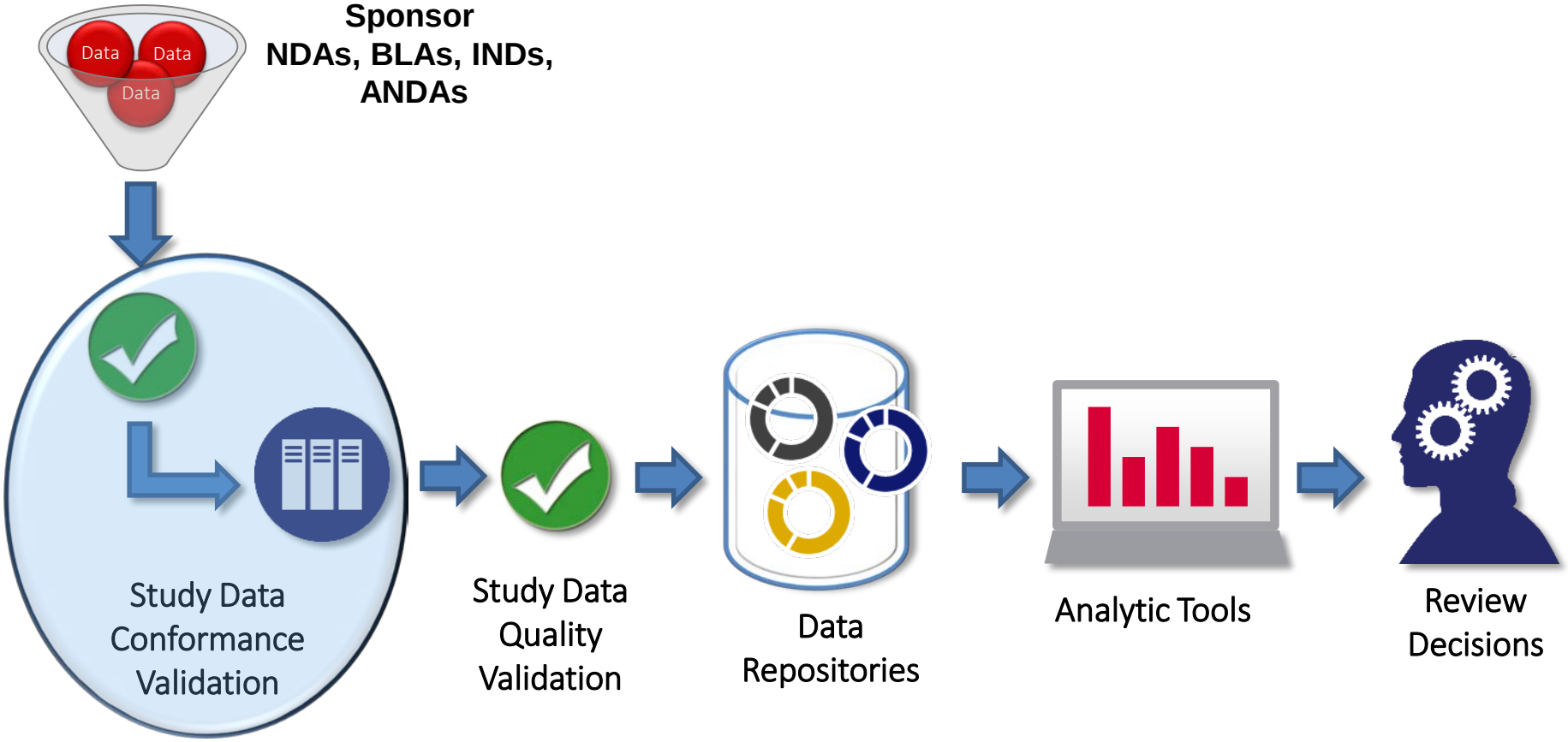
- Validation Codes
  - Technical Rejection Criteria for Study Data
  - Specifications for eCTD Validation Criteria

  http://www.fda.gov/ectd

- When

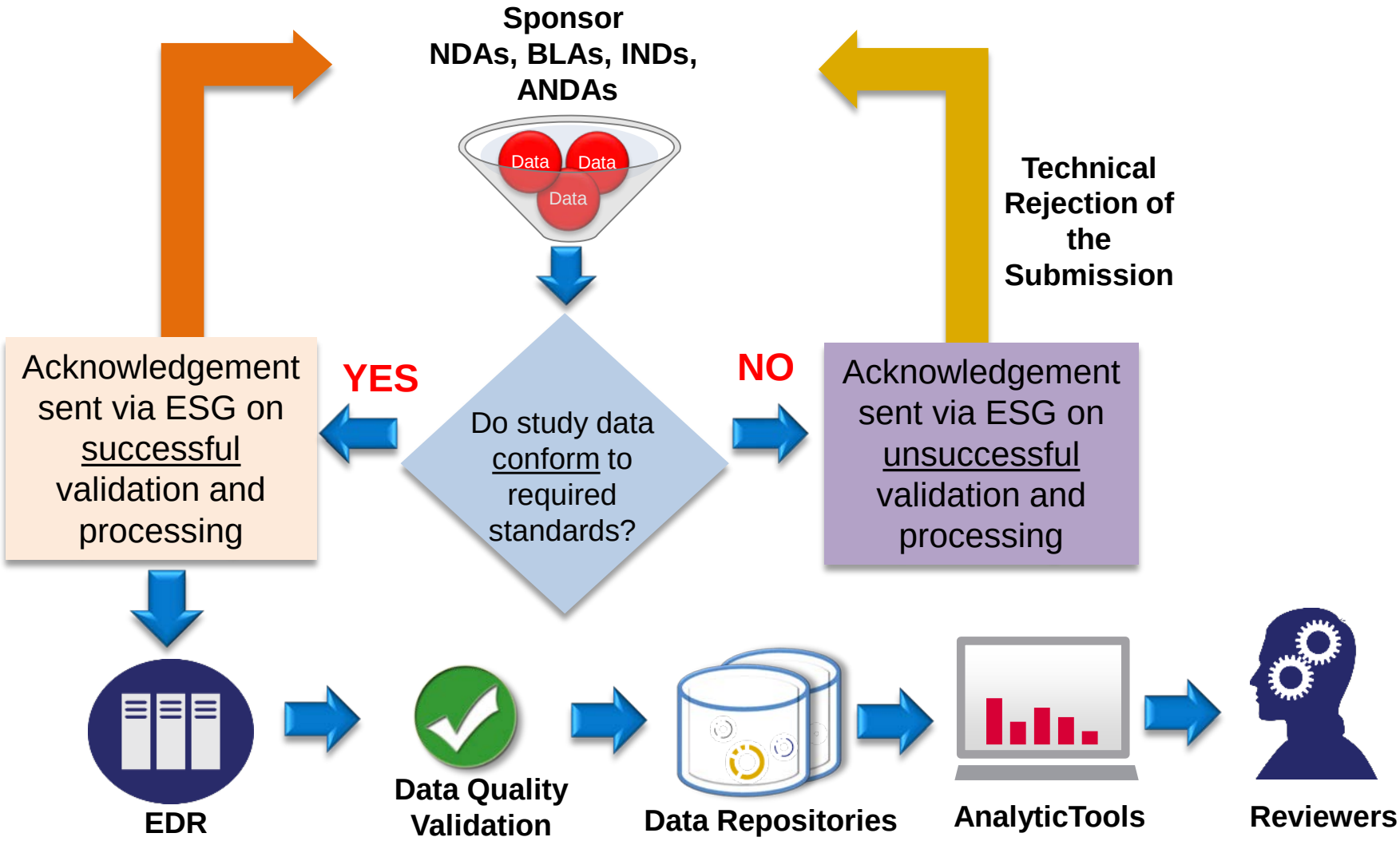
  CDER will start using the new validation criteria - TBD

Study Data Standards Validation Using the eCTD Validation Criteria



Conformance Validation…

How will it work?



eCTD Study Data Validation Criteria and Severity Levels

High	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
High	Trial Summary (TS) dataset must be present for each study in eCTD section 4.2 and 5.3
Medium	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
Medium	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:
  http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm229642.htm
- Questions about submitting electronically to CDER:
  ESUB@fda.hhs.gov

Thank You

Jonathan Resnick
Jonathan.resnick@fda.hhs.gov
ESUB@fda.hhs.gov
www.fda.gov/ectd

Ask