Regulatory Submissions, Information, and Document Management Forum

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Technical Rejection Criteria for Study Data and Self-Check Worksheet

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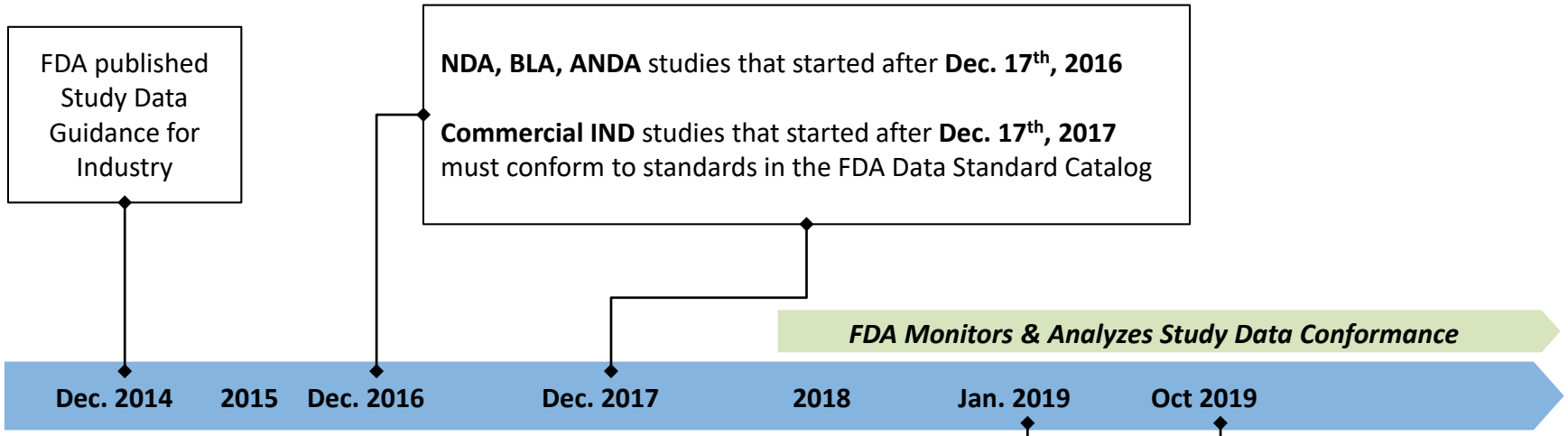
Agenda

- Revised Technical Rejection Criteria for Study Data
- Technical Rejection Criteria Validation Process
- Implementation Timeline
- Demo of the Self-Check Worksheet

Study Data Technical Rejection Criteria (SDTRC) Revisions



Significant Technical Rejection Criteria Revisions:

- FDA **will not accept** study data submissions not in compliance with FDA Data Standards Catalog
- FDA emphasized validation rules 1735 and 1789
- FDA introduced the Simplified TS File (simplified ts.xpt) to obtain Study Start Date

Technical Rejection Criteria for Study Data (Revised Jan. 2019)

Significant Technical Rejection Criteria Revisions:

- FDA included SPREFID as a valid source of Study ID in ts.xpt files
- FDA updated guidance for Simplified TS Files (simplified ts.xpt)

Technical Rejection Criteria for Study Data (Revised Oct. 2019)

Study Data Technical Rejection Criteria (SDTRC) Revisions (Jan. 2019)

Refuse to file → Will not accept	
The FDA may refuse to file (RTF) for NDAs and BLAs, or refuse to receive (RTR) for ANDAs, an electronic submission that does not have study data in conformance to the required standards specified in the FDA Data Standards Catalog	**FDA will not accept** an electronic submission that does not have study data in compliance with the required standards specified in the FDA Data Standards Catalog

Revised TRC rules and elevated 1735 and 1789 to high severity errors

Error	Description	Severity
1734	Trial Summary (TS) dataset (ts.xpt) with information on study start date must be present for required sections*	High
1735	Correct STF file-tags must be used for all standardized datasets and corresponding define.xml files in required sections*	High
1736	For SEND data, a DM dataset and define xml must be submitted in required sections* For SDTM data, a DM dataset and define.xml must be submitted in required sections* For ADaM data, an ADSL dataset and define.xml must be submitted in required sections*	High
1789**	Study files must be referenced in a Study Tagging File (STF)	High

References:
FDA Study Data Technical Rejection Criteria (Revised Jan. 2019); FDA Study Data Technical Rejection Criteria (Revised Oct. 2019)

Qualification and Exemption for Non-Clinical Studies (Oct. 2019)

- Nonclinical study that are required to qualify for TRC including any study in module 4 ECTD modules 4.2.3.1, 4.2.3.2, or 4.2.3.4 that includes one of the one of the following three file tags

‘pre-clinical-study-report’ | ‘legacy-clinical-study-report’ | ‘study-report-body’

- The qualifying non-clinical study must be submitted according to SEND specification.
- Certain Non-Clinical studies are exempted for TRC (See Study Data Technical Conformance Guide Section 8.2.2 for details https://www.fda.gov/media/131872/download):
  - Non-Clinical Studies does not require SEND Data
  - Non-Clinical Study Initiation Dates not relevant
- A simplified ts.xpt must submitted for exempted Non-Clinical Studies as below:

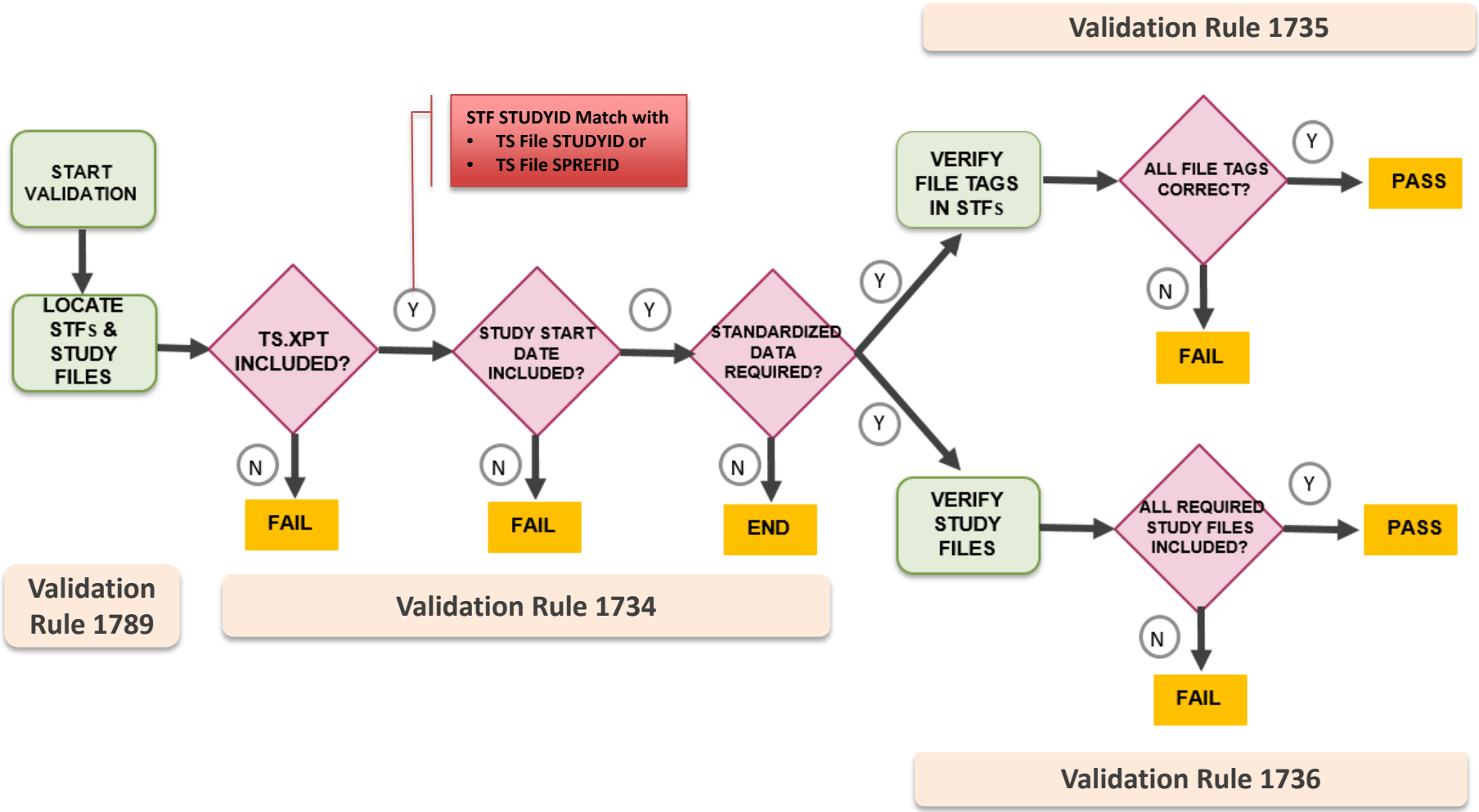
STUDYID	TSPARMCD	TSVAL	TSVALNF
study ID in STF	STSTDTC		Use the value ‘NA’

Included Additional Reference for Study ID Match (Oct. 2019)

- Feedback from industry pointed scenarios where ts.xpt study-id may not be able to matched (Ex. when a study is bought by another company and the study id is already established)
- Proposed solution with feedback was inclusion of Sponsor Reference ID (SPREFID) parameter to match the STF study-id
- After analysis, SPREFID parameter matching with STF study-id added to October 2019 SDTRC revision

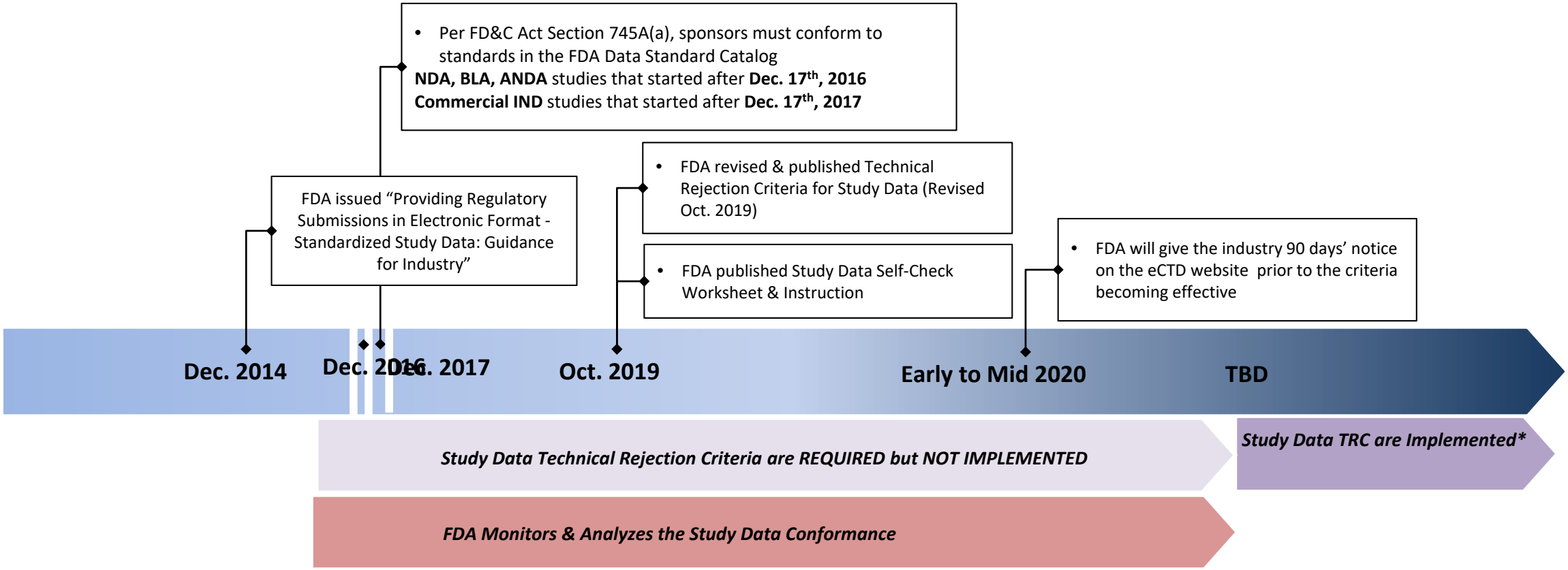
Included SPREFID for Study ID matching	
TRC January 2019	**TRC October 2019**
If a file is referenced within a study section in Module 4 or 5, a STF and ts.xpt must be present to identify the study ID and SSD to which the file belongs. The ts.xpt and STF need to contain matching study ID values.	If a file is referenced within a study section in Module 4 or 5, a STF and ts.xpt must be present to identify the study ID and SSD to which the file belongs. The ts.xpt needs to contain either a study ID (STUDYID) or Sponsor Reference ID (SPREFID) value that matches with the STF study ID.

SDTRC High Level Validation Process (Revised Oct. 2019)



Implementation Timeline

FDA published Revised Study Data Technical Rejection Criteria (Revised Jan. 2019) and Study Data Self-Check Worksheet to assist sponsors with the TRC Conformance



** Note: When a submission is technically-rejected, the submission sequence is not transferred into the FDA electronic document rooms*

Tools for Industry

FDA is developing tools and resources to help sponsors meet study data standard requirements and provide more transparency on the validation process

Online Resources

Sponsor reviews Study Data Standard Resources and Tools for Industry:

- **Study Data Technical Rejection Criteria with *eCTD Validation Table and Example Submission Scenarios***
- **Simplified TS File Generator Utility (PhUSE)**
  OR
  Simplified TS File Creation Guide
- **Study Data Self-Check Worksheet & Instructions**

Sponsor submits a eCTD and/or Standardized Data Sample to the FDA for validation

After review, FDA will provide with feedback, highlighting the errors found during the processing of the sample submission

Gateway

Sponsor submits an application with study data

Common TRC Errors Based on CY2019 conformance analysis

- **1734** - Trial Summary (TS) dataset (ts.xpt) with information on study start date must be present for required sections
  - Missing ts.xpt when the CDER or CBER when expect to find one
    - Simplified ts.xpt
    - Full ts.xpt
  - Non-matching study-id or SPREFID
  - Missing or incorrectly formatted study start date
- **1735 & 1736** – For SEND, SDTM, & ADaM datasets a define.xml and dm.xpt and/or adsl.xpt must present and file-tagged correctly
  - Missing and/or improperly tagged
    - Define.xml
    - dm.xpt
    - adsl.xpt

Self-Check Worksheet: https://www.fda.gov/media/123098/download

Questions

- For questions about submitting study data please contact: edata@fda.hhs.gov

- For questions about eCTD, including stf.xml and file-tags, please contact: esub@fda.hhs.gov