U.S. FOOD & DRUG ADMINISTRATION

FDA Study Data Technical Rejection Update

PDUFA VI

Public Meeting

April 7, 2021

Agenda

- Technical Rejection Criteria for Study Data (TRC) – What's New
- FDA's Study Data Guidance and Requirements
- TRC Conformance Statistics and Trends
- Addressing the Most Common TRC Errors
- Summary

Technical Rejection Criteria for Study Data (TRC) – What's New

Technical Rejection Criteria for Study Data – What's New

- TRC effective date published on FDA's *Electronic Common Technical Document (eCTD)* web page and within TRC document
- Warning notice if submission contained study information and failed eCTD validations in TRC
  - CDER sending notice in ESG 3rd acknowledgement
  - CBER sending notice from CBER-edata account
- Starting Sept 15th, 2021, if submission contains study information and fails eCTD validations in TRC, CDER and CBER will reject

FDA's Electronic Common Technical Document (eCTD) web page was updated on March 5th 2021

Study Data Standards Resources

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Study data standards describe a standard way to exchange clinical and nonclinical study data. These standards provide a consistent general framework for organizing study data, including templates for datasets, standard names for variables, identify appropriate controlled terminology and standard ways of doing calculations with common variables. Data standards also help FDA receive, process, review, and archive submissions more efficiently and effectively.

Quick Links

- Data Standards Catalog v7.0 (March 15, 2021)
- Study Data Technical Conformance Guide v4.6 (November 2020)

This Study Data Resources page includes required items and helpful tools for submission of study data to FDA's Center for Biologics Evaluation and Research (CBER), Center for Drug Evaluation and Research (CDER), and Center for Devices and Radiological Health (CDRH).

1. FDA Data Standards Catalog

FDA accepts electronic submissions that provide study data using the standards, formats, and terminologies described in the FDA Data Standards Catalog.

- FDA Data Standards Catalog v7.0 (XLS -71KB) (March 15, 2021)

Electronic Common Technical Document (eCTD)

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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

Reminder: Per Providing Regulatory Submissions In Electronic Format — Standardized Study Data, Guidance for Industry, electronic submission of standardized study data is required for NDA, BLA, ANDA, and Commercial IND. FDA plans to implement eCTD validation checks when submissions contain content under modules 4 and 5 beginning **September 15, 2021**. Submissions which fail this validation will be subject to rejection. Please see the Technical Rejection Criteria for Study Data and the eCTD Validation Criteria (error code 1734, 1735, 1736, 1789) for details.

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

Quick Links

- NDA to BLA eCTD Transition Instruction to Industry (PDF - 90 KB)
- eCTD Guidance (Final, Rev 7) (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 Information
- eCTD Submission Types and Sub-Types (PDF - 630 KB)

Notices

- FDA announces effective date for study data information NEW

www.fda.gov

Technical Rejection Criteria updated on March 15th, 2021

The Technical Rejection Criteria (Revised 03/15/21) was updated to reflect the effective dates for implementation of the criteria and published to FDA's website on the *Study Data for Submission to CDER and CBER* web page.

Technical Rejection Criteria for Study Data

Study data standards are required in clinical and nonclinical studies that start after December 17, 2016.[1] Technical rejection criteria have been added to the existing electronic common technical document (eCTD) validation criteria to enforce the deadlines below[2] and will become effective on September 15, 2021.

Study Data for Submission to CDER and CBER

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Data standards enable FDA to modernize and streamline the review process. They also enable more consistent use of analysis tools to better view drug data and highlight areas of concern.

Study data standards describe a standard way to exchange clinical and nonclinical research data between computer systems. These standards provide a consistent general framework for organizing study data, including templates for datasets, standard names for variables, and standard ways of doing calculations with common variables.

FDA is instituting new requirements for data standards that will apply to most study data submitted to FDA's Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER).

Beginning after the dates specified below, FDA may refuse to file for New Drug Applications (NDAs) and Biologics License Applications (BLAs) or refuse to receive for Abbreviated NDAs (ANDAs) any electronic submission whose study data do not conform to the required standards specified in the FDA Data Standards Catalog. See the Technical Rejection Criteria for Study Data (PDF) for more information. FDA conducted an analysis of study data conformance on submissions received during a

Stay Connected

If you have study data questions for CDER, please contact the CDER eDATA Team at cder-edata@fda.hhs.gov.

For electronic submissions, contact the CDER Electronic Submission (ESUB) Support Team at esub@fda.hhs.gov.

If you have study data questions for CBER, please contact CBER-edata@fda.hhs.gov.

For electronic submissions, contact CBER ESUB at esubprep@fda.hhs.gov.

Where to Find the TRC Effective Date

The Effective Dates for validation criteria 1734, 1735, 1736, and 1789 have been added to the "Technical Rejection Criteria for Study Data" and the "Specifications for eCTD Validation Criteria" documents.

Number:	1734
Group:	General
Description:	A dataset named ts.xpt with information on study start date must be present for each study in Module 4, sections 4.2.3.1, 4.2.3.2, 4.2.3.4, and in Module 5, sections 5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2
Severity Description:	High
US DTD Version	2.01 and 3.3
Effective Date:	9/15/2021

Number:	1735
Group:	STF
Description:	The correct STF file-tags must be used for all standardized datasets and corresponding define.xml files in Module 4, sections 4.2.3.1, 4.2.3.2, 4.2.3.4, and in Module 5, sections 5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2
Severity Description:	High
US DTD Version	2.01 and 3.3
Effective Date:	9/15/2021

Number:	1736
Group:	General
Description:	For Standard for Exchange of Nonclinical Data (SEND) data, a Demographic (DM) dataset and define.xml must be submitted in Module 4, sections 4.2.3.1, 4.2.3.2, 4.2.3.4 For Study Data Tabulation Model (SDTM) data, a DM dataset and define.xml must be submitted in Module 5, sections 5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2 For Analysis Data Model (ADaM) data, an ADaM Subject level analysis dataset (ADSL) dataset and define.xml must be submitted in Module 5, sections 5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2
Severity Description:	High
US DTD Version	2.01 and 3.3
Effective Date:	9/15/2021

Number:	1789
Group:	STF
Description:	A file has been submitted in a study section without providing an STF file. STFs are not required for 4.3 Literature references, 5.2 Tabular listings, 5.4 Literature references and 5.3.6 Postmarketing reports
Severity Description:	High
US DTD Version	2.01 and 3.3
Effective Date:	9/15/2021

TRC Warnings

Sponsors will receive warnings from FDA when a TRC error is identified in submissions received between March 15 and September 15, 2021. Warning notices will specify each error and provide: Error Code; Error Reason; STF Study ID; eCTD Section (if applicable)

CDER Notice included in the ESG 3rd Acknowledgement

ASR Successful and 3rd Acknowledgement PDF notification with
▼SPECIAL WARNING▼

Your submission has been successfully processed, however, during eCTD validation it was noted that this submission contains the following error information listed in the table below:

▼Warning: Per the 'Specifications for eCTD Validation Criteria', the severity level of the following error codes will be effective as a High error as of 09/15/2021

Error Code	STF Study ID	eCTD section	Error Reason
1734	uat	m4-2-3-1-single-dose-toxicity	No ts.xpt found for this study

Note: If a study for this submission received validation error code 1734, the given study was not validated for other error codes 1735 and 1736

Warning: Per the 'Specifications for eCTD Validation Criteria', the severity level of the following error codes will be effective as a High error as of 09/15/2021

Error Code	Reason	Findings
1789	Files in study sections without STF reference	m5/53-clin-stud-rep/535-rep-effic-safety-stud/confusion/5351-stud-rep-contr/uat-1/rptamnd-1.pdf [a5]

This is an informational notice that after 09/15/2021 submissions with an error code, where the error code corresponds to a particular study data format requirement, will be rejected per the published Technical Rejection Criteria for Study Data/Specifications for eCTD Validation Criteria (https://www.fda.gov/drugs/electronic-regulatory-submission-and-review/electronic-common-technical-document-ectd), as discussed in the eCTD guidance, Providing Regulatory Submissions in Electronic Format – Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications.

Application Type/Number: NDA444493
eCTD Sequence Number: 0006
CoreID: ci1613111075001.2641324_Test@fdsuv08654_te1

CBER Warnings sent from the CBER-edata account

Dear XXXXX,

Your submission below was successfully processed on MM/DD/YYYY.

Application Type/Number: BLA XXXXXX
eCTD Sequence Number: XXXX

However, during eCTD validation it was noted that this submission contains the following error information listed in the table below:

▼Warning: future High error for study data as specified in the Study Data Technical Rejection Criteria

1734, 1735, 1736 Template Table

Error Code	STF Study ID	eCTD section	Error Reason
1734	YHTEST1	5.3.5.2	Invalid Start Date format in ts.xpt

Note: If a study for this submission received validation error code 1734, the given study was not validated for other error codes such as 1735 and 1736

1789 Template Table

Error Code	Reason	eCTD section	Findings
1789	A file has been submitted in a study section without providing an STF file.	5.3.5.1	m5/53-clin-stud-rep/531-rep-biopharm-stud/5312-compar-ba-be-stud-rep/ome-rm02-001/stf-ome-rm02-001.xml [N4765450c17914e3fa2e5314c71db1459STF]
1789	A file has been submitted in a study section without providing an STF file.	5.3.5.1	m5/53-clin-stud-rep/531-rep-biopharm-stud/5312-compar-ba-be-stud-rep/ome-rm02-001/stf-ome-rm22222-001.xml [N4765450c17914e3fdfdfg45dfgdgd5314c71db1459STF]

This is an informational notice that after September 15, 2021 submissions with an error code, where the error code corresponds to a particular study data format requirement, will be rejected per the published Technical Rejection Criteria for Study Data/Specifications for eCTD Validation Criteria (https://www.fda.gov/drugs/electronic-regulatory-submission-and-review/electronic-common-technical-document-ectd), as discussed in the eCTD guidance, Providing Regulatory Submissions in Electronic Format – Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications.

FDA's Study Data Guidance and Requirements

Purpose of eCTD and Study Data Requirements

- Reviewing study data in a timely manner is critical for FDA's review process (e.g. Reviewers have 30 days to review an IND application)
- When sponsors submit data to the FDA in a reliable and accessible format, it improves efficiency and consistency of review decisions
- CDISC Standards enable FDA to streamline the review process:
  - Reduce time for reviewers to locate and identify study data
  - Reduce the burden on sponsors and reviewers from IRs (Information Requests)
  - Reduce review time by enabling the use of COTS reviewer's tools such as JReview, JMP Clinical, etc. to automate review analyses
  - Support data driven decisions by applying data mining and data analytic techniques

"The agreement to assemble all the Quality, Safety and Efficacy information in a common format (called CTD - Common Technical Document) has revolutionized the regulatory review processes, led to harmonized electronic submission that, in turn, enabled implementation of good review practices. For industries, it has eliminated the need to reformat the information for submission to the different ICH regulatory authorities."

Source: https://www.ich.org/products/ctd.html

FDA Guidance and Data Standards Catalog

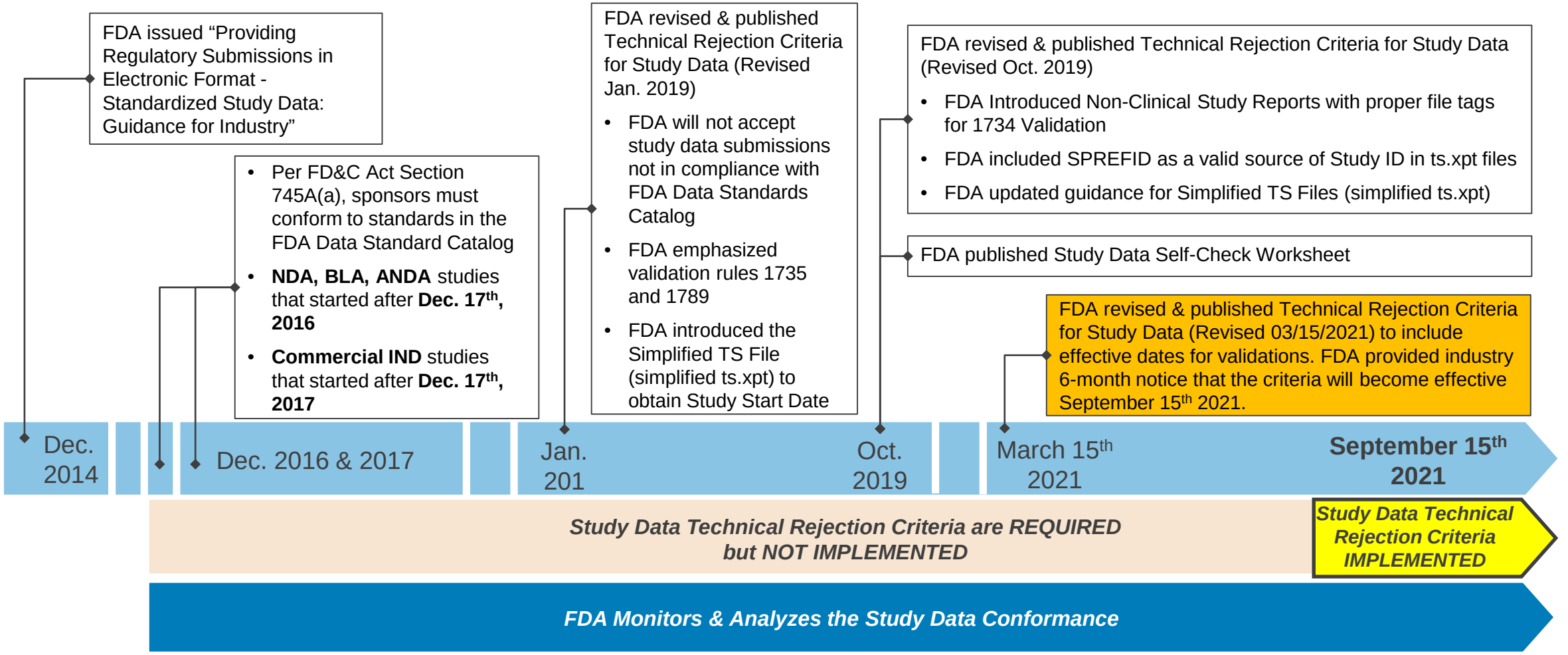
- Per FD&C Act Section 745A(a), drug application sponsors must use the standards defined in the FDA Data Standards Catalog starting 24 months after final guidance for a specific submission type
- FDA issued “Providing Regulatory Submissions in Electronic Format - Standardized Study Data: Guidance for Industry” in December 2014 (updated in October 2020)
- Sponsors must conform to standards in the FDA Data Standards Catalog:
  - NDA, BLA, ANDA studies that started after December 17th, 2016
  - Commercial IND studies started after December 17th, 2017
- Sponsors are obligated to meet Technical Rejection Criteria for Study Data which determine whether a submission complies with FDA’s standards for study data

Warning

Even if your study started prior to the dates above, it will need to include a trial summary file (contains the study start date and/or reason code for standardized data not applicable) if files are submitted under sections listed in the Technical Rejection Criteria for Study Data

Technical Rejection Criteria Revisions Timeline

September 15th 2021: The eCTD validations listed in the Technical Rejection Criteria become effective. FDA will reject submissions that fail these validations.



FDA Technical Rejection Criteria for Study Data (SDTRC)

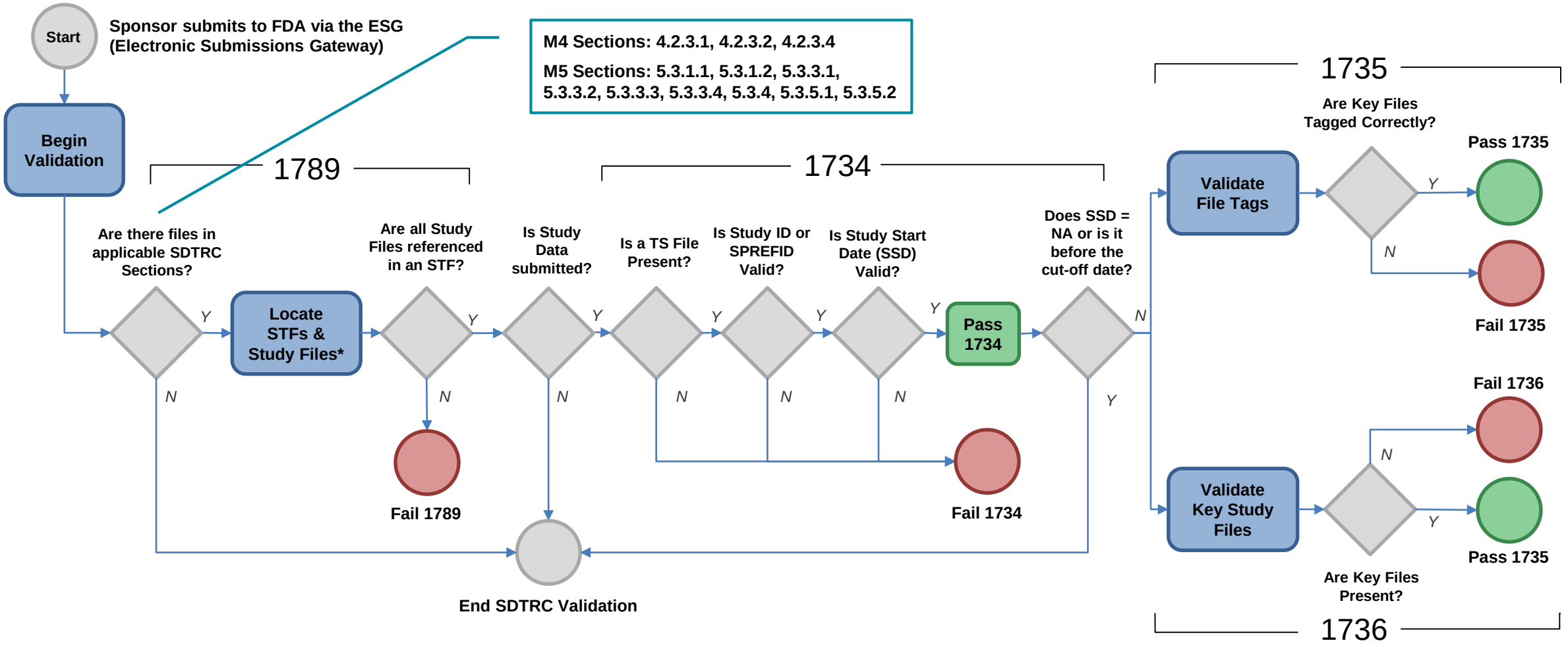
- Study Data Technical Conformance Guide provides technical recommendations for submitting study data according to CDISC standards

- Technical Rejection Criteria for Study Data provides the conditions under which FDA will not accept submissions with study data

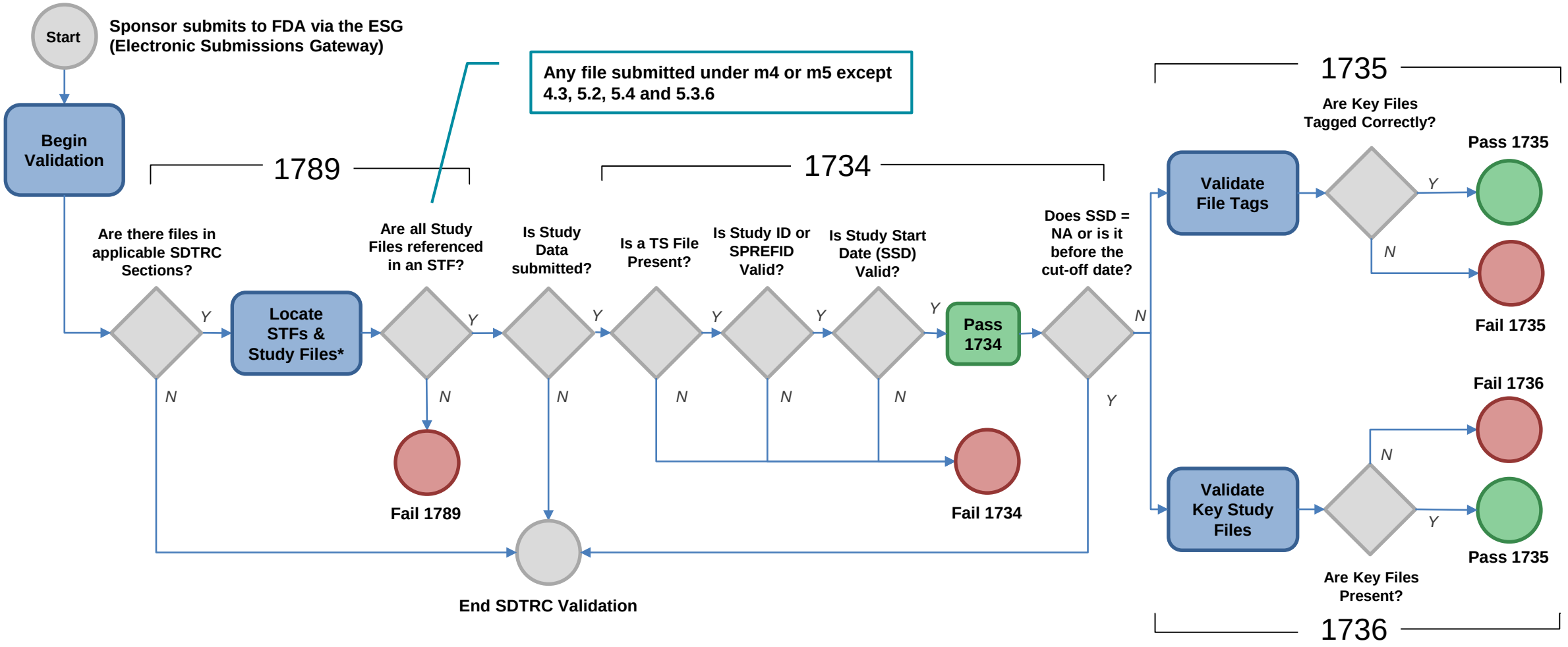
Error	Description (Reference to FDA Study Data Technical Rejection Criteria March 2021 version)	Severity Level
1734	A dataset named ts.xpt with information on study start date must be present for each study in required sections*	High
1735	The correct STF file-tags must be used for all standardized datasets and corresponding define.xml files in required sections*	High
1736	For Standard for Exchange of Nonclinical Data (SEND) data, a Demographic (DM) dataset and define.xml must be submitted in Module 4 required sections* For Study Data Tabulation Model (SDTM) data, a DM dataset and define.xml must be submitted in Module 5 required sections* For Analysis Data Model (ADaM) data, an ADaM Subject level analysis dataset (ADSL) dataset and define.xml must be submitted in Module 5 required sections*	High
1789	A file has been submitted in a study section without providing an STF file. STFs are not required for 4.3 Literature references, 5.2 Tabular listings, 5.4 Literature references and 5.3.6 Postmarketing reports	High

** Module 4 sections: 4.2.3.1, 4.2.3.2, 4.2.3.4*
Module 5 sections: 5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2

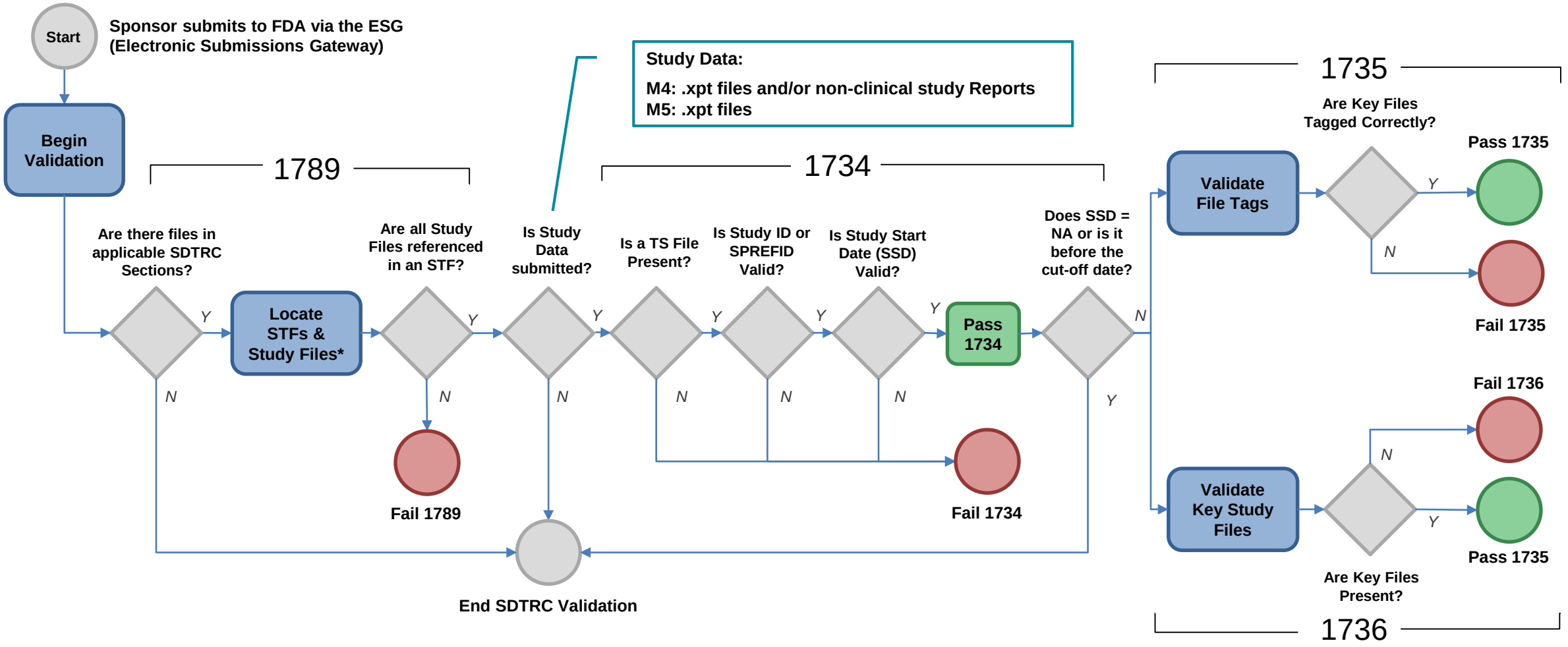
TRC Validation Rule Testing



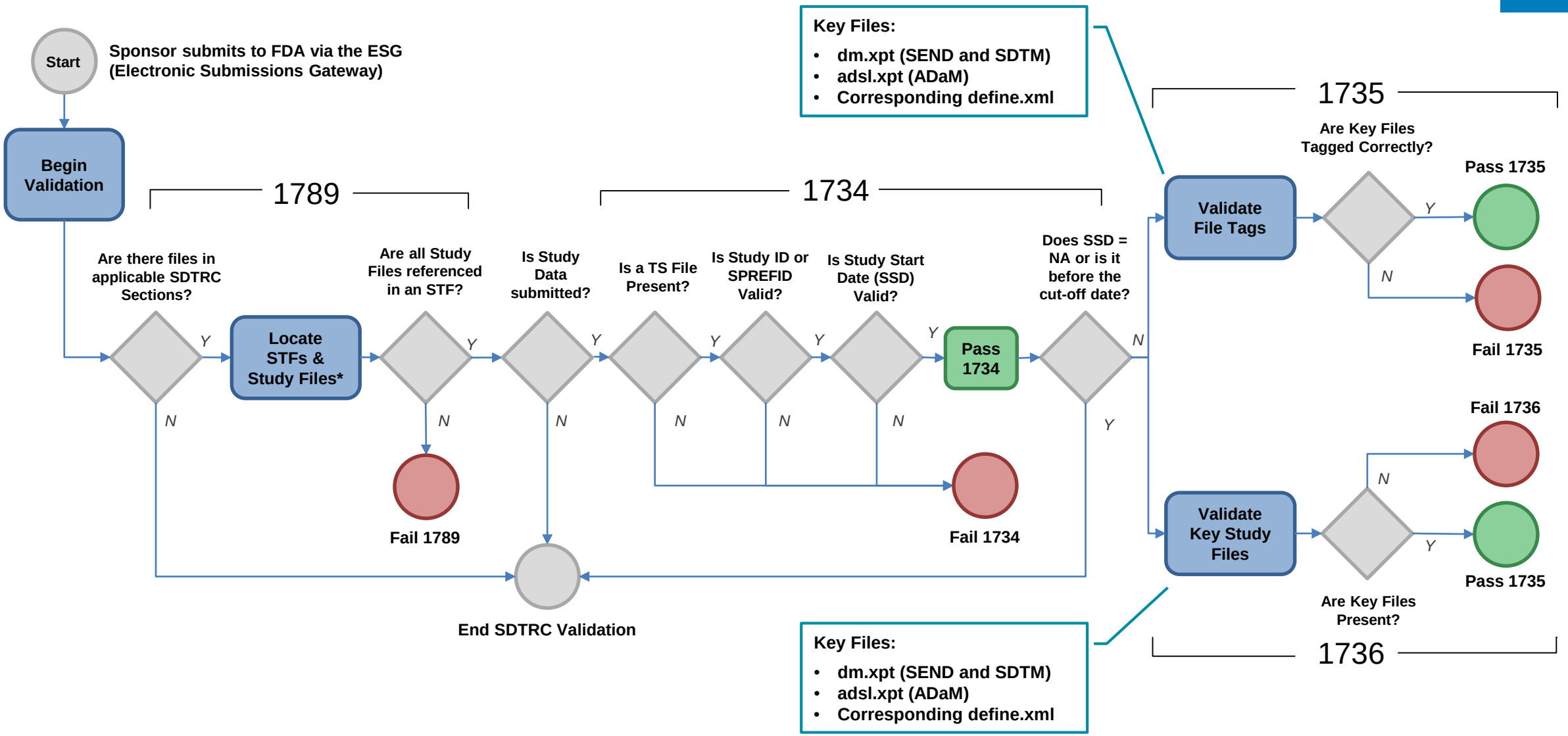
TRC Validation Rule Testing



TRC Validation Rule Testing

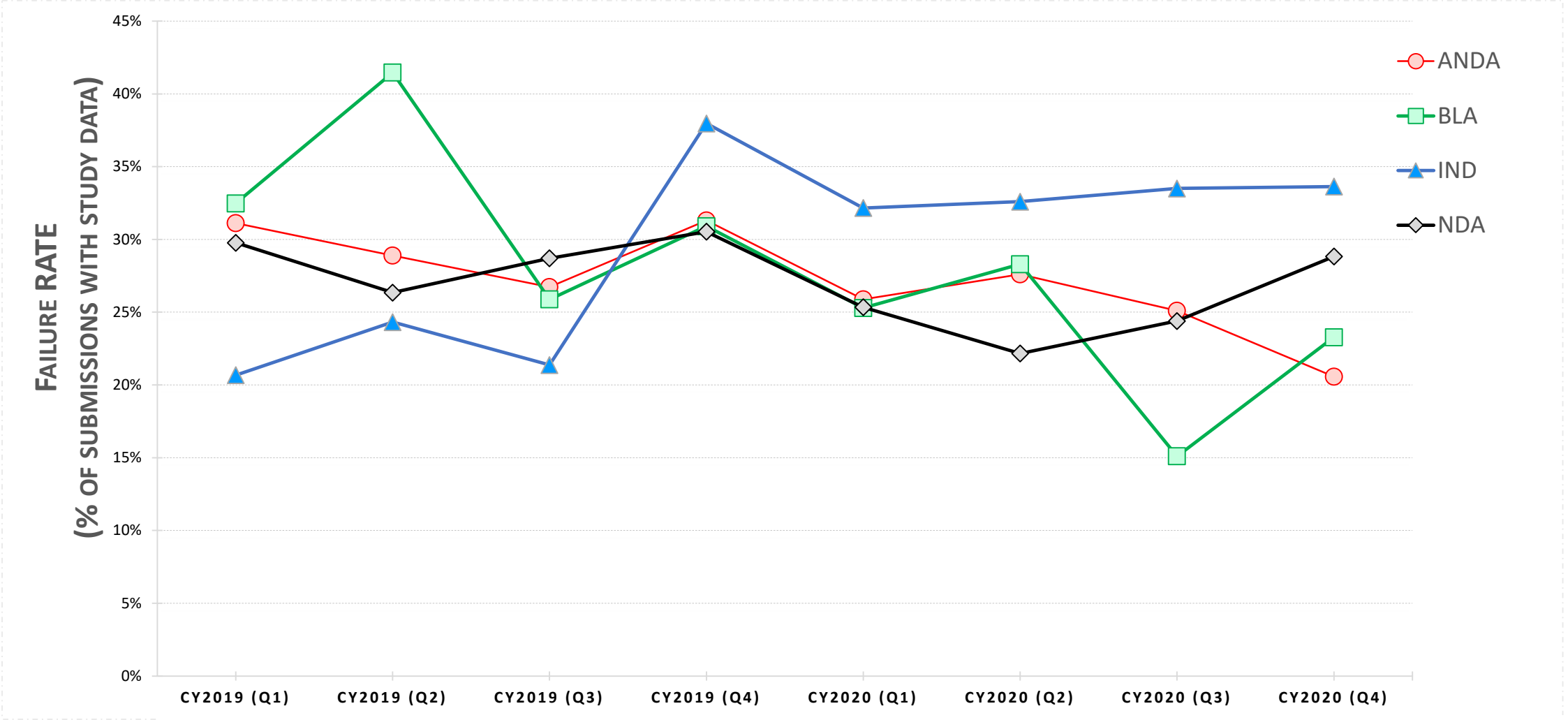


TRC Validation Rule Testing



TRC Conformance Statistics and Trends

CDER CY2019 & CY2020 Conformance Trend:
TRC Validation Errors 1734 & 1736



Notes:

1) CY2019 and CY2020 analysis was conducted according to the TRC (Revised Oct. 2019)
2) Analysis includes NDA, BLA, ANDA and Commercial IND Sequence received by CDER between 1/1/2019 and 12/31/2020
3) Validation of error 1736 is not performed if a study has error 1734
4) M4 Definition of Study Data - .xpt files and/or a Study Report tagged as pre-clinical-study-report, legacy-clinical-study-report, or study-report-body present in eCTD module 4
5) M5 Definition of Study Data - .xpt files present in eCTD module 5

CDER CY2020 Submission Level Conformance:
Validation Errors 1734 & 1736

ANDA, NDA, BLA, and Commercial IND Submissions received by CDER between 1/1/2020 and 12/31/2020, were assessed for conformance to the two high-level errors as revised in the Technical Rejection Criteria for Study Data (Revised March 2021)

		ANDA	BLA	NDA	Comm. IND**	All
a	**Total Number of Submissions**	61,525	19,808	55,817	95,222	232,372
b	**Total Number of Submissions with Study Data***	704	388	1073	3291	5456
c	**Total Number of Submissions with Study Data* in TRC Applicable Sections**	635	268	693	1907	3503
d	**Total Number Submissions with Critical Errors (e or f)**	**175**	**90**	**271**	**1086**	**1622**
e	**Error 1734**	164	87	263	1045	1559
f	**Error 1736**	28	7	21	62	118
g	**Failure Rate (% among submissions with Study Data* in TRC Applicable Sections) [d/c]**	27.56%	33.58%	39.11%	56.95%	46.30%
h	**Failure Rate (% among submissions with Study Data*) [d/b]**	**24.86%**	**23.20%**	**25.26%**	**33.00%**	**29.73%**
I	**Failure Rate (% among all submissions) [d/a]**	0.28%	0.45%	0.49%	1.14%	0.70%

Notes:

1) CY2020 analysis was conducted according to the TRC (Revised Oct. 2019)
2) Analysis includes NDA, BLA, ANDA and Commercial IND Sequence received by CDER between 1/1/2020 and 12/31/2020
3) Validation of error 1736 is not performed if a study has Error 1734
4) * M4 Definition of Study Data - .xpt files and/or a Study Report tagged as pre-clinical-study-report, legacy-clinical-study-report, or study-report-body present in eCTD module 4
5) * M5 Definition of Study Data - .xpt files present in eCTD module 5
6) **Comm. IND Clinical studies are included in this analysis which constitutes a very small fraction of the total submissions with critical errors. Comm. IND clinical studies are not subject to errors 1734, 1735, 1736, or 1737

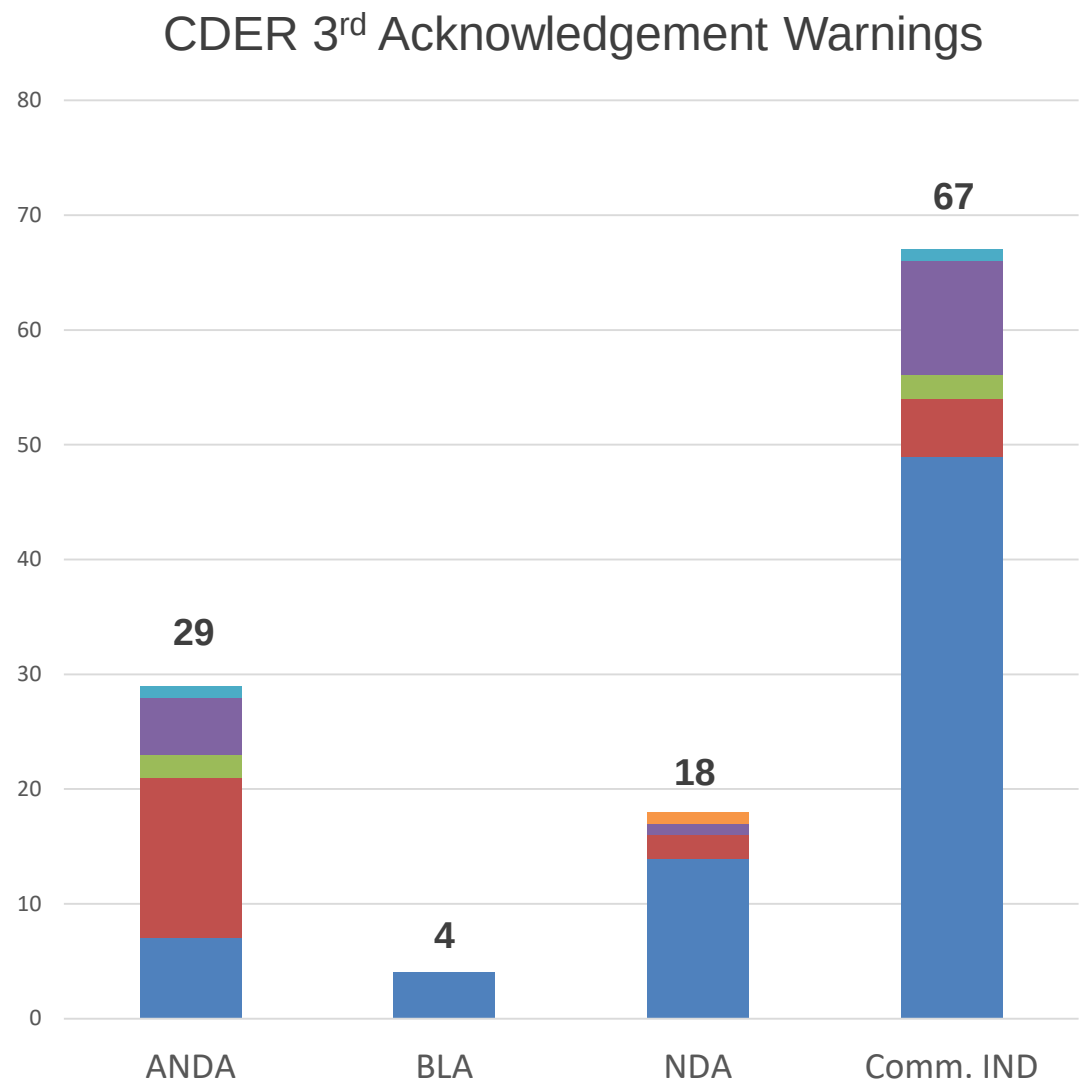
CDER CY2020 Study Level Conformance for Validation Errors 1734 & 1736

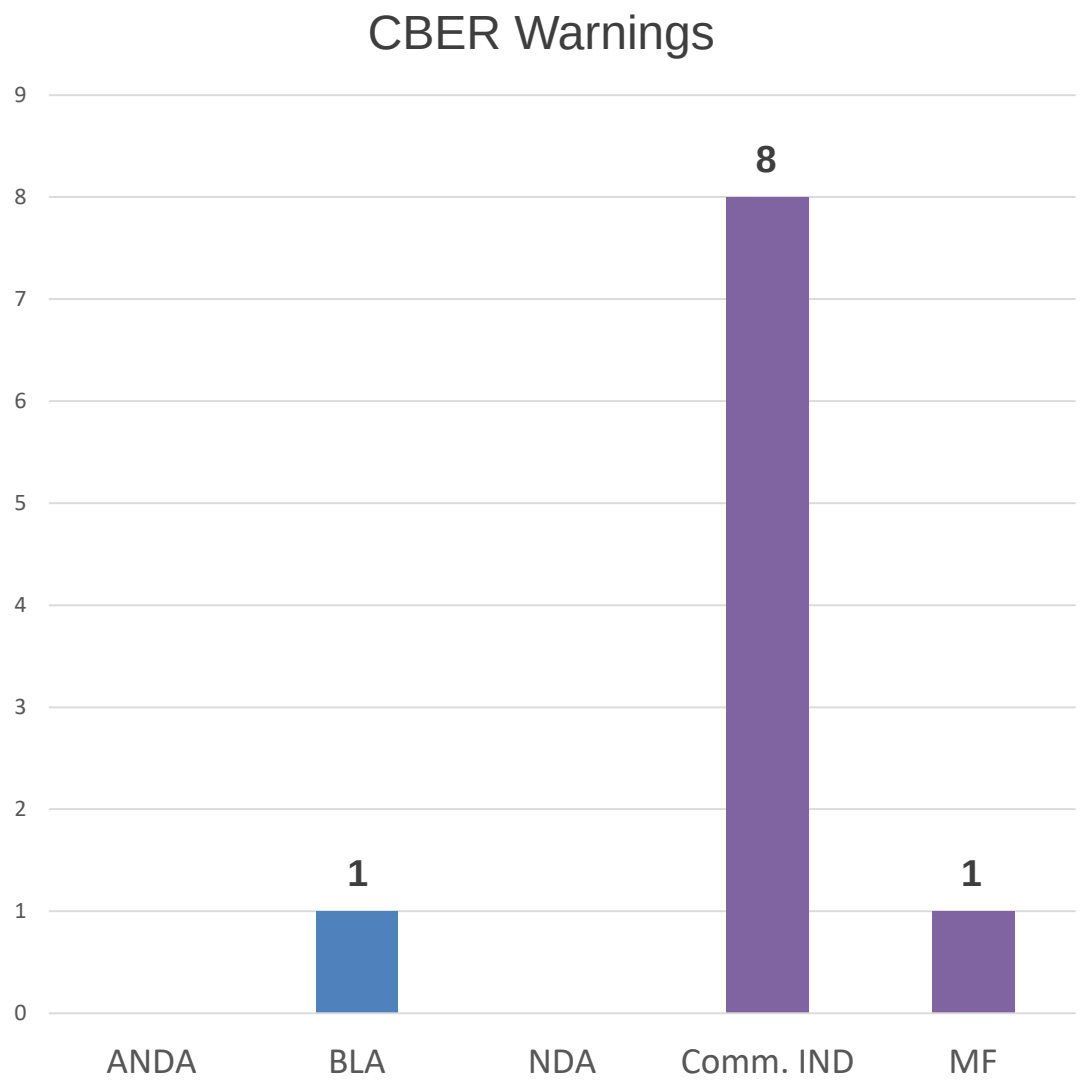
- A high number of non-clinical (m4) studies fail Validation Rule 1734 because of a missing trial summary dataset
- A trial summary dataset (ts.xpt) is required when a non-clinical study report is submitted (TRC Revised March 2021)

		ANDA		BLA		NDA		Comm. IND	Total	Total
		m4	m5	m4	m5	m4	m5	m4	m4	m5
a	Total Number of Studies*	45	1398	1041	796	5477	2556	33534	40097	4750
b	Total Number of Studies* in TRC Applicable Sections	15	1222	136	453	868	1645	5619	6638	3320
c	Total Number Studies with Critical Errors (d or f)	**12**	**342**	**82**	**109**	**349**	**334**	**3272**	3715	785
d	Error 1734	12	277	82	104	348	333	3173	3615	714
f	Error 1736	0	65	0	5	1	24	99	100	94
g	Error Rate (% among failed studies with Study Data* Data in TRC Applicable Sections**) [c/b]	80.0%	28.0%	60.3%	24.1%	40.2%	20.3%	58.2%	55.97%	23.64%
h	Error Rate (% among Total Number of Studies) [c/a]	**26.7%**	**24.5%**	**7.9%**	**13.7%**	**6.4%**	**13.1%**	**9.8%**	9.27%	16.53%

Notes:
(1) CY2020 analysis was conducted according to the TRC (Revised Oct. 2019)
(2) Validation of errors 1736 is not performed if a study has Error 1734
(3) *M4 Definition of Study - .xpt files and/or a Study Report tagged as pre-clinical-study-report, legacy-clinical-study-report, or study-report-body present in TRC applicable sections
(4) *M5 Definition of Study - .xpt files present in TRC applicable sections

Warnings from CDER & CBER





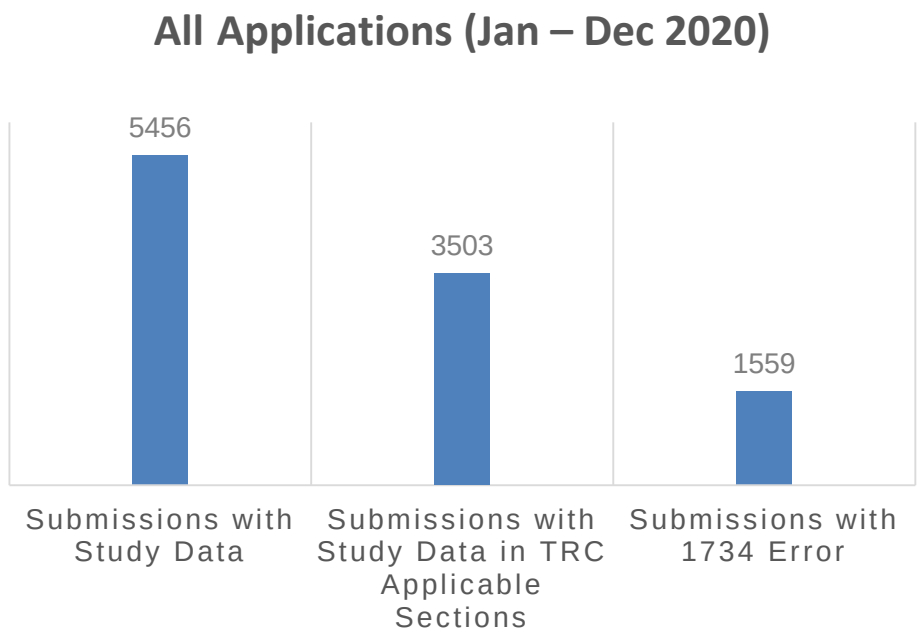
Notes: *Metrics generated from data between March 15, 2021 and March 30, 2021*
CBER SEND mandatory requirement starts March 15, 2023
Error 1789 applies to all application types

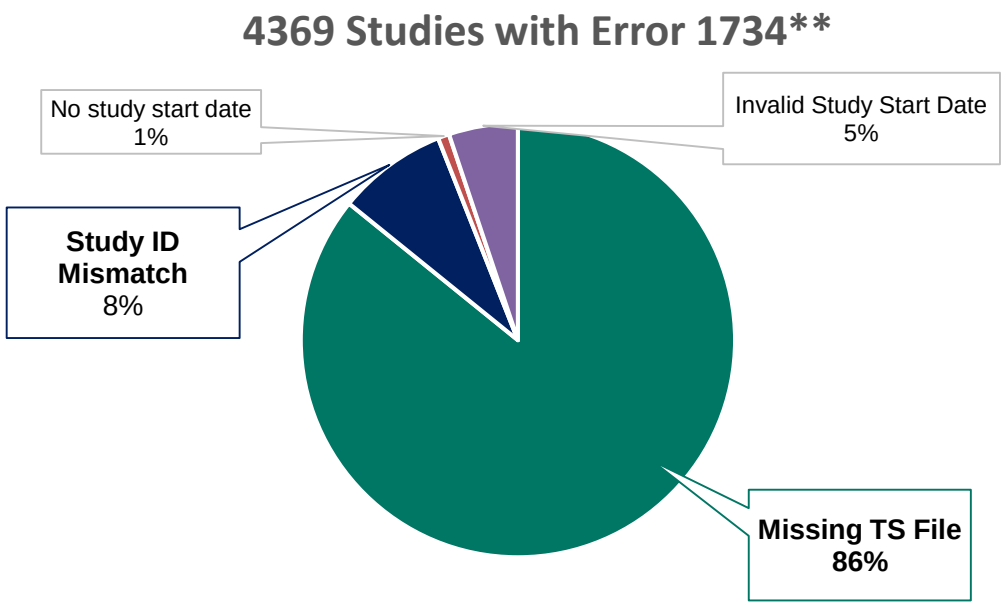
Addressing the Most Common TRC Errors

Most Common Error Reasons for Validation Rule 1734

Error	Description
1734	Trial Summary (TS) dataset (ts.xpt) with information on study start date must be present for required sections*

- Common error reasons for all application types:
  - A missing ts.xpt file
  - Study ID Mismatch between TS and STF





** Module 4 sections: 4.2.3.1, 4.2.3.2, 4.2.3.4*
Module 5 sections: 5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2

*** 4369 studies within 1559 different submissions*

Missing TS Files for Non-Clinical Studies

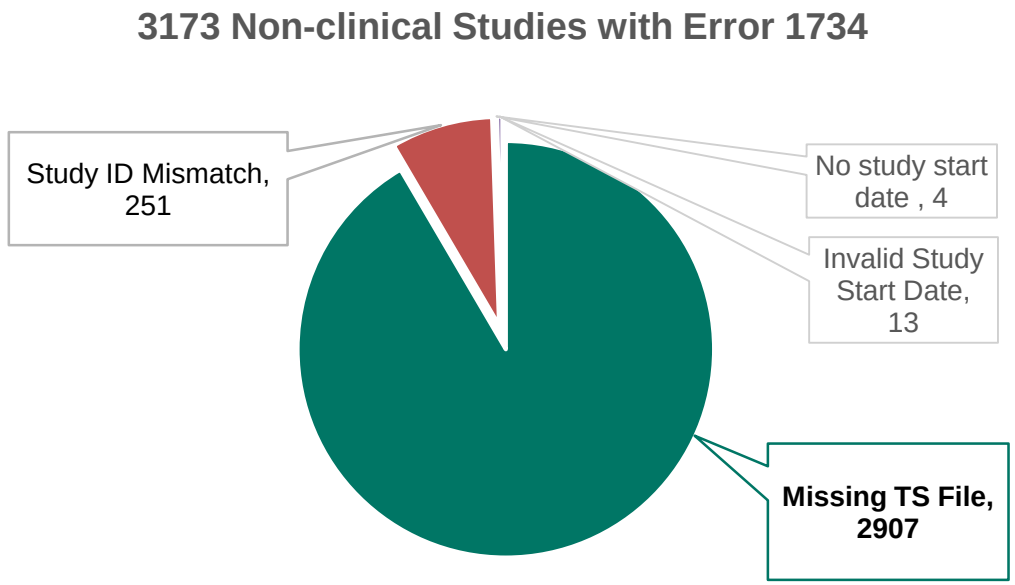
- 3,173 IND non-clinical studies fail for TRC rule 1734
- 2,907 of those studies fail due to a missing ts.xpt

	Count
Studies with study data or reports	2,907
Studies with only study reports	2,807

2,907 IND non-clinical studies were missing the ts.xpt

Toxicology Sections	Count
Repeat dose toxicology (m4.2.3.2)	2,115
Single dose toxicology (m4.2.3.1)	621
Carcinogenicity (m4.2.3.4)	171

72.8% of the 2907 non-clinical studies with missing ts.xpt are in the repeat dose toxicology eCTD section



- Submitting a simplified ts.xpt for all these non-clinical studies will greatly reduce the 1734 error rate
- SEND datasets require a full ts.xpt files

Missing TS File

Study Report File Tag Criteria					
Study Start Date	Application Type	Data Type	Study Sections	Expectation by Center	
				CDER	CBER
Prior to or on 17-Dec-2017	Commercial INDs	Nonclinical	4.2.3.1, 4.2.3.2, 4.2.3.4	Rejection criteria will be applied if a study report with the proper file tags and/or an xpt file is submitted. Submit a simplified TS whether or not the study contains an xpt dataset (other than the ts.xpt)	Rejection criteria will not be applied
		Clinical	5.3.1.1, 5.3.1.2, 5.3.3.1z, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2	Rejection criteria will not be applied	
After 17-Dec-2017	Commercial INDs	Nonclinical	4.2.3.1, 4.2.3.2, 4.2.3.4	Rejection criteria will be applied; submit a full TS	Rejection criteria will not be applied
		Clinical	5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2	Rejection criteria will not be applied	
Prior to or on 17-Dec-2016	NDA, BLA, ANDA	Nonclinical	4.2.3.1, 4.2.3.2, 4.2.3.4	Rejection criteria will be applied if a study report with the proper file tags and/or an xpt file is submitted. Submit a simplified TS whether or not the study contains an xpt dataset (other than the ts.xpt)	Rejection criteria will not be applied
		Clinical	5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2	Rejection criteria will be applied; submit a simplified TS if the study contains an xpt dataset (other than the ts.xpt)	

Missing TS File

- A Simplified ts.xpt file would be expected when a non-clinical study report is submitted but SEND datasets are not required
- Simplified ts.xpt:
  - Sponsors should submit a dataset named ‘ts.xpt’ with four variables: STUDYID, TSPARMCD, TSVAL, and TSVALNF
- Example of Simplified ts.xpt Dataset:

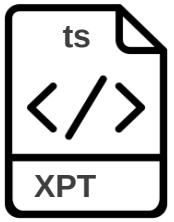
STUDYID	TSPARMCD	TSVAL	TSVALNF
• Study ID in STF File	• SSTDTC for a clinical study • STSTDTC for a nonclinical study	• Format: yyyy-mm-dd • Left blank when study start date is not available or relevant	• Left blank when study start date is provided in TSVAL • “NA”

References:
FDA Study Data Technical Conformance Guide (Version 4.6, November 2020)
FDA Technical Rejection Criteria for Study Data (Revised March 2021)

Example: Simplified TS Files

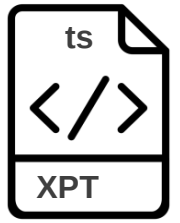
Example of a Simplified TS file submitted for a non-clinical study with study-id “S107” in the STF file:

	STUDYID	TSPARMCD	TSVAL	TSVALNF
1	S107	STSTDTC	2014-10-26	



Example of a Simplified TS file submitted for a non-clinical study with study-id “S107” in the STF file without a study start date:

	STUDYID	TSPARMCD	TSVAL	TSVALNF
1	S107	STSTDTC		NA



Tools for Industry

FDA has provided tools to help sponsors meet study data standard requirements and provide more transparency on the validation process.

www.fda.gov

Sponsor reviews Study Data Standards & Resources:

1. **Study Data Technical Rejection Criteria**
2. **Simplified TS File Generator Utility (PHUSE) & Simplified TS File Creation Guide**
3. **Study Data Self-Check Worksheet**

Prepare Submission

4. **Sponsor submits an eCTD and/or Standardized Data Sample to the FDA to receive feedback, highlighting errors found during processing of the sample**

Gateway

Sponsor submits an application with study data

1. **Technical Rejection Criteria for Study Data (Revised March 2021)**
   - Clarifies the requirements for eCTD Validation of submissions with study data
   - Provides a validation table and examples in Appendix 1 and Appendix 2 to illustrate the requirements
2. **Simplified TS File Generator Utility (PHUSE) & Simplified TS File Creation Guide**
   - Helps sponsors easily generate a Simplified TS file to provide a Study Start Date for a study

3. Study Data Self-Check Worksheet

- Helps sponsors understand criteria for submissions with study data to pass TRC validations
- Dynamically guides sponsors to prepare study data files according to TRC requirements

4. eCTD and/or Standardized Data Sample Validation

- Allows sponsors to validate sample submissions and receive feedback prior to submission

Summary

- Overall Error rate of TRC rule 1734 and 1736 has not significantly reduced from CY2019 to CY2020
- FR Notice was published (March 3rd, 2021) and announced an update to FDA Data Standards Catalog. Catalog contains a footnote stating TS.XPT file is required for studies
- TRC effective date published on FDA's *Electronic Common Technical Document (eCTD)* web page and in the TRC document
- ESG 3rd Acknowledgement from CDER now includes warning if submission contained study information and failed eCTD validations in TRC
- Starting Sept 15th, 2021, if submission contains study information and fails eCTD validations in TRC, CDER and CBER will reject

References

❖ Study Data Standards Resources

- Providing Regulatory Submissions In Electronic Format - Standardized Study Data: Guidance For Industry [Oct 2020]
- Study Data Technical Conformance Guide [Nov 2020]
- FDA Data Standards Catalog [March 2021]
- Link: https://www.fda.gov/industry/fda-resources-data-standards/study-data-standards-resources

❖ Study Data for Submission to CDER and CBER

- Technical Rejection Criteria For Study Data [March 2021]
- Technical Rejection Criteria Self-Check Worksheet
- Technical Rejection Criteria Self-Check Worksheet Instructions
- Link: https://www.fda.gov/industry/study-data-standards-resources/study-data-submission-cder-and-cber

❖ Providing Regulatory Submissions In Electronic Format - Submissions Under Section 745a(a) Of The FD&C Act: Guidance For Industry

- Link: https://www.fda.gov/regulatory-information/search-fda-guidance-documents

Acknowledgments

The author would like to thank Nitin Guptan, Ryan Olivett, Anthony Fata, Heather Crandall, Jonathan Resnick, Lina Cong, Jiang Xu, Gang Wang, and other FDA staff for their time and effort in helping collect and analyze data and information as presented.