Study Data Technical Rejection Criteria, Validation, and Self-Check Worksheet

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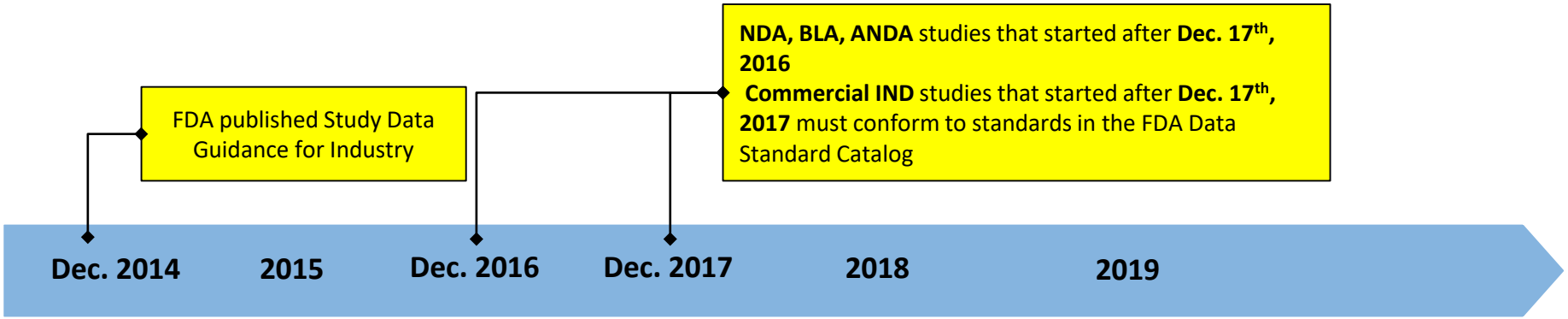
Agenda

- FDA Guidance and Data Standards Catalog
- Study Data Technical Rejection Criteria Conformance Trend
- Revised Technical Rejection Criteria for Study Data
- Technical Rejection Criteria Validation Process
- Typical Error Examples and Demo of the Self-Check Worksheet
- Implementation Timeline

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.
- 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



CDER Conformance: Validation Error 1789

- ANDA, NDA, BLA, and Commercial IND Submissions were assessed for conformance to high-level error, 1789, as defined in the Technical Rejection Criteria for Study Data (Revised Jan. 2019)

	NDA		ANDA		BLA		Comm. IND		All	
	CY2018	CY2019 (Q1)	CY2018	CY2019 (Q1)	CY2018	CY2019 (Q1)	CY2018	CY2019 (Q1)	CY2018	CY2019 (Q1)
Total Number of Submissions	41,077	11,011	62,695	14,776	11,042	2997	79,473	22,226	194,287	51,010
Error 1789	43	11	225	53	1	0	193	62	462	126
Failure Rate (% among submissions with Study Data)	0.10%	0.10%	0.36%	0.36%	<0.01%	0.00%	0.24%	0.28%	0.24%	0.20%

Notes:

1) One drug application could contain multiple submissions throughout its review life-cycle, such as original, supplements, and amendments
2) Each submission may contain more than one study
3) Analysis includes NDA, BLA, ANDA and Commercial IND submissions received by CDER between 1/1/2018 to 3/31/2019
4) Analysis is conducted according to the revised TRC

Reference: FDA Study Data Technical Rejection Criteria (Revised Jan. 2019)

CDER Conformance: Validation Errors 1734, 1735 & 1736

- ANDA, NDA, BLA, and Commercial IND Submissions were assessed for conformance to three high-level error, 1734, 1735, & 1736, as defined in the Technical Rejection Criteria for Study Data (Revised Jan. 2019)
- Failure Rate for all applications increased 2.3% (average) between 2018 and 2019

	NDA		ANDA		BLA		Comm. IND		All	
	CY2018	CY2019 (Q1)	CY2018	CY2019 (Q1)	CY2018	CY2019 (Q1)	CY2018	CY2019 (Q1)	CY2018	CY2019 (Q1)
Total Number of Submissions with Study Data	877	270	1078	243	291	77	649	183	2895	773
Total Number of Submissions with Study Data in TRC Applicable Sections		204		226		57		172		659
Total Number Submissions with Critical Errors	215	71	689	181	54	15	134	42	1092	309
Error 1734	185	52	186	53	48	15	96	24	515	144
Error 1735	34	23	497	130	5	0	26	15	562	168
Error 1736	16	3	88	21	2	0	18	5	124	29
Failure Rate (% among submissions with Study Data)	**24.50%**	**26.30%**	**63.90%**	**73.70%**	**18.60%**	**19.50%**	**20.60%**	**23.00%**	**37.70%**	**40.00%**
Failure Rate (% among submissions with Study Data in TRC Applicable Sections)		**34.80%**		**80.10%**		**26.30%**		**24.40%**		**46.90%**

Notes:

1) One drug application could contain multiple submissions throughout its review life-cycle, such as original, supplements, and amendments
2) Analysis includes NDA, BLA, ANDA and Commercial IND submissions received by CDER between 1/1/2018 to 3/31/2019
3) Submission with multiple studies can report both Errors 1734, 1735 and 1736
4) Validation of errors 1735 and 1736 are not performed if a study has Error 1734
5) Analysis is conducted according to the revised TRC

CBER Conformance: Validation Errors 1734, 1735, 1736 & 1789

- CBER BLA Submissions were assessed for conformance to four high-level errors, 1734, 1735, 1736 and 1789 as defined in the Technical Rejection Criteria for Study Data (Revised Jan. 2019)

	BLA	
	CY2018	CY2019 (Q1)
Total Number of studies with Study Data	6062	1644
Error 1789	6	0
Failure Rate (% among studies with Study Data)	**0.1%**	**0%**

	BLA	
	CY2018	CY2019 (Q1)
Total Number of studies with Study Data	49	12
Total Number of Submissions with Study Data in TRC Applicable Sections		12
Total Number studies with Critical Errors	15	6
Error 1734	14	5
Error 1735	3	1
Error 1736	1	1
Failure Rate (% among studies with Study Data)	**30.6%**	**50.0%**
Failure Rate (% among submissions with Study Data in TRC Applicable Sections)		**50.0%**

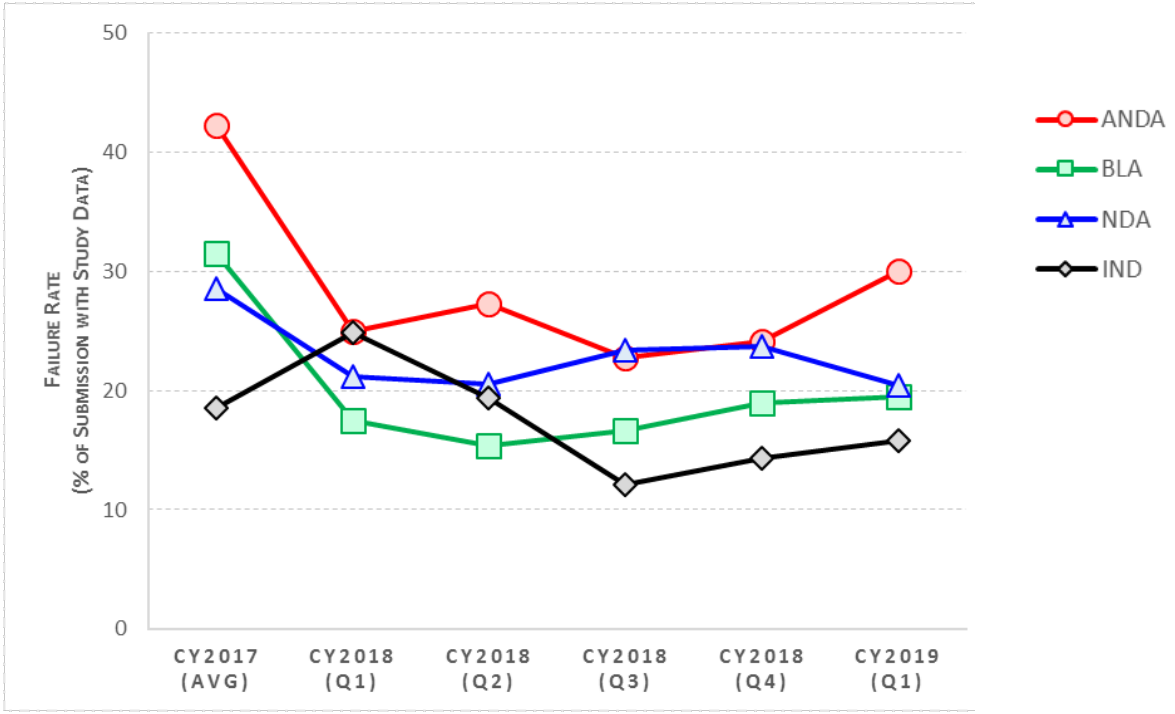
Notes:

1) One drug application could contain multiple submissions throughout its review life-cycle, such as original, supplements, and amendments
2) Analysis includes BLA submissions received by CBER between 1/1/2018 to 3/31/2019
3) Analysis is conducted according to the revised TRC
4) Submission with multiple studies can report both Errors 1734, 1735 and 1736
5) Validation of errors 1735 and 1736 are not performed if a study has Error 1734

Reference: FDA Study Data Technical Rejection Criteria (Revised Jan. 2019)

Overall Conformance Trend for Validation Errors 1734 & 1736

- Submissions with study data shows overall decreases in Validation Error 1734 and 1736 in all application types
- NDAs and INDs are showing the greatest improvements in conformance



Notes:

1) CY2017 analysis is conducted according to TRC (Revised May 2018)
2) CY2018 & CY2019 (Q1) analysis are conducted according to the TRC (Revised Jan. 2019)

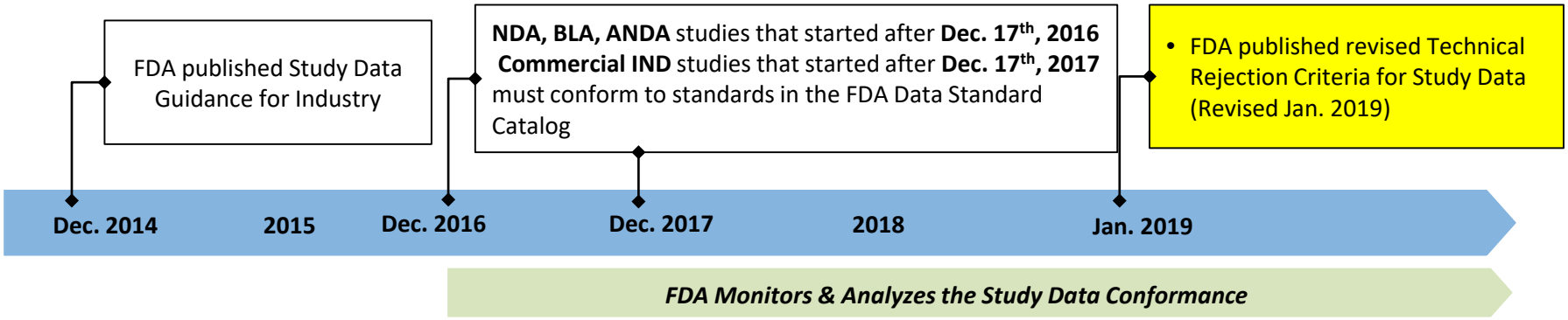
Study Data Technical Rejection Criteria (SDTRC) Revision (Jan. 2019)

Technical Rejection Criteria for Study Data (Revised 05/01/2018)

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

Technical Rejection Criteria for Study Data (Revised 01/22/2019)

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



References:
FDA Study Data Technical Rejection Criteria (Revised May 2018); FDA Study Data Technical Rejection Criteria (Revised Jan. 2019)

Update to SDTRC List of High Errors (Revised Jan. 2019)

Error	Description (Reference to FDA Study Data Technical Rejection Criteria May 2018 version)	Severity Level
1734	Trial Summary (TS) dataset must be present for each study in eCTD section 4.2 and 5.3	High
1736	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

Error	Description (Reference to FDA Study Data Technical Rejection Criteria Jan. 2019 version)	Severity Level
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**

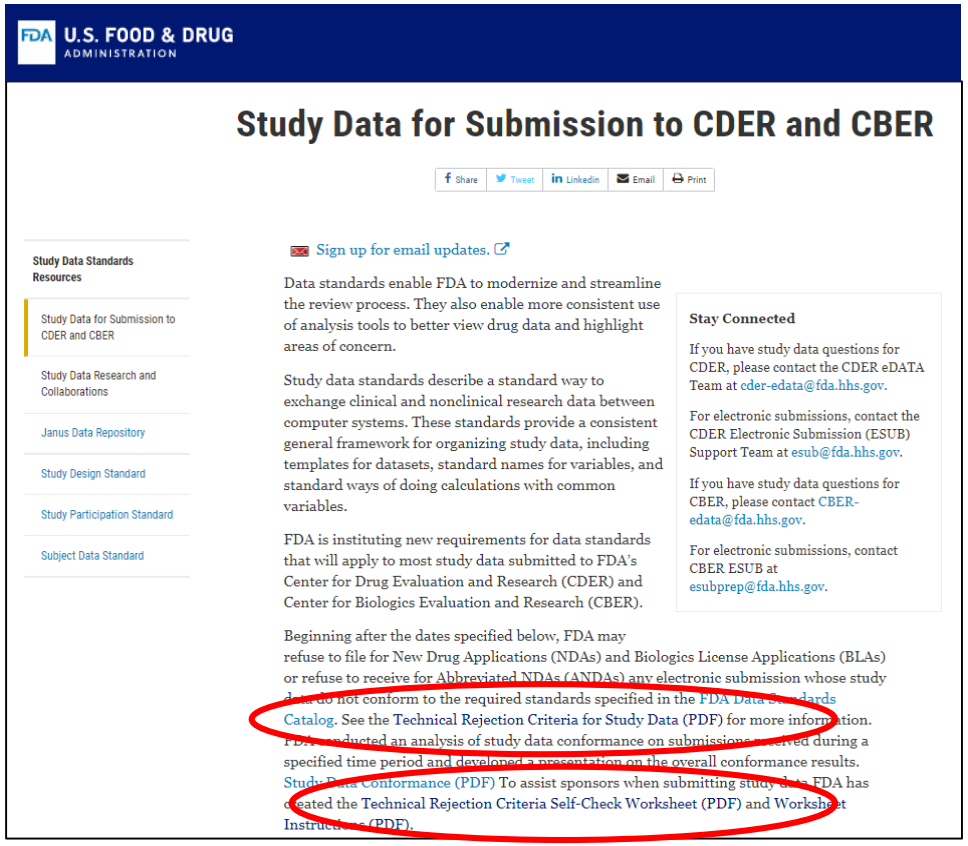
** Refer to the latest Technical Rejection Criteria for Study Data*

*** From Providing Regulatory Submissions in Electronic Format – Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specification, Section J: Datasets must only be provided in modules 3, 4, or 5 and not in modules 1 or 2*

eCTD Technical Rejection Criteria for Study Data Expectation

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; 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 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; 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)	
After 17-Dec-2016	NDA, BLA, ANDA	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 be applied; submit a full TS	

Published SDTRC and Self-Check Worksheet



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Study Data for Submission to CDER and CBER

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Study Data Standards Resources

- Study Data for Submission to CDER and CBER
- Study Data Research and Collaborations
- Janus Data Repository
- Study Design Standard
- Study Participation Standard
- Subject Data Standard

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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 specified time period and developed a presentation on the overall conformance results. Study Data Conformance (PDF) To assist sponsors when submitting study data, FDA has created the Technical Rejection Criteria Self-Check Worksheet (PDF) and Worksheet Instructions (PDF).

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.

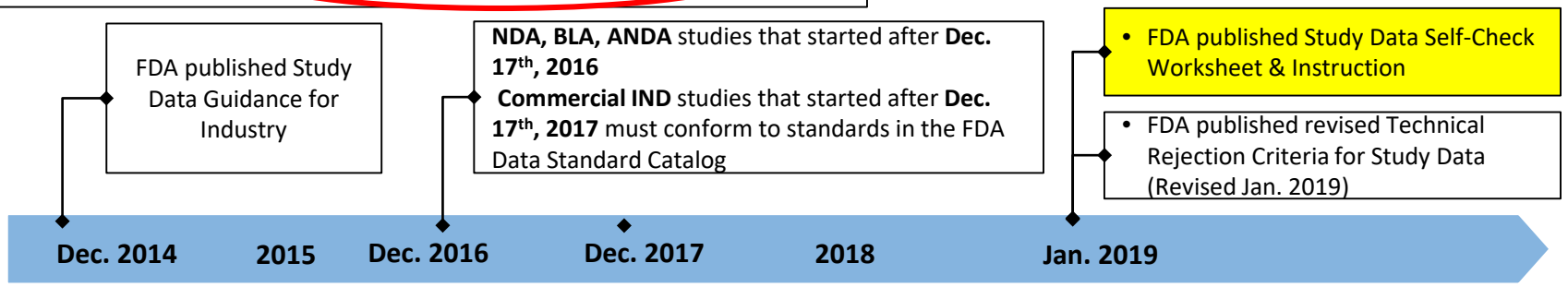
If you have study data questions for CBER, please contact CBER-edata@fda.hhs.gov.

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

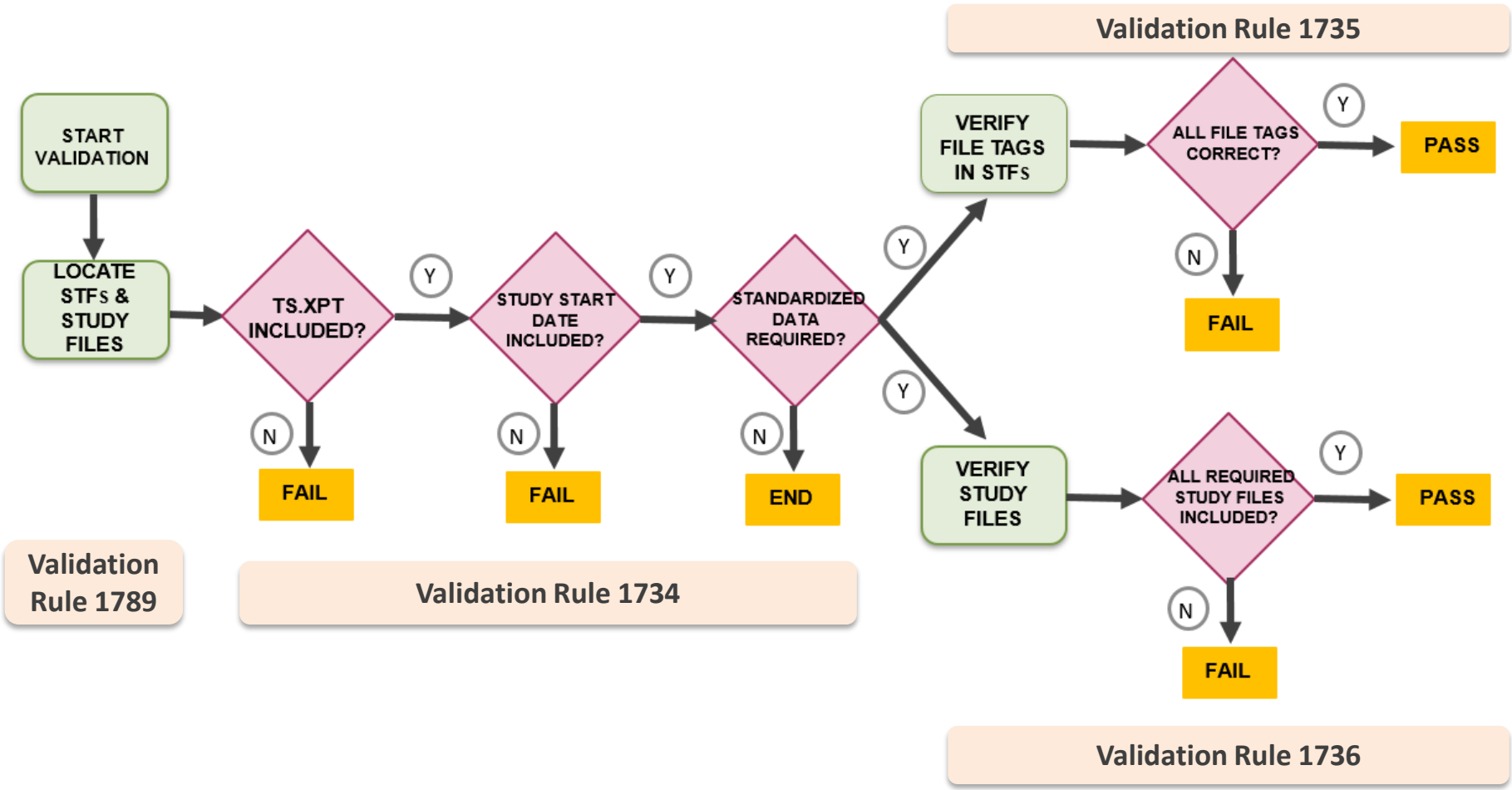
"Technical Rejection Criteria for Study Data"
https://www.fda.gov/media/100743/download

"Technical Rejection Criteria Self-Check Worksheet"
https://www.fda.gov/media/123098/download

"Technical Rejection Criteria Self-Check Worksheet Instructions"
https://www.fda.gov/media/123099/download

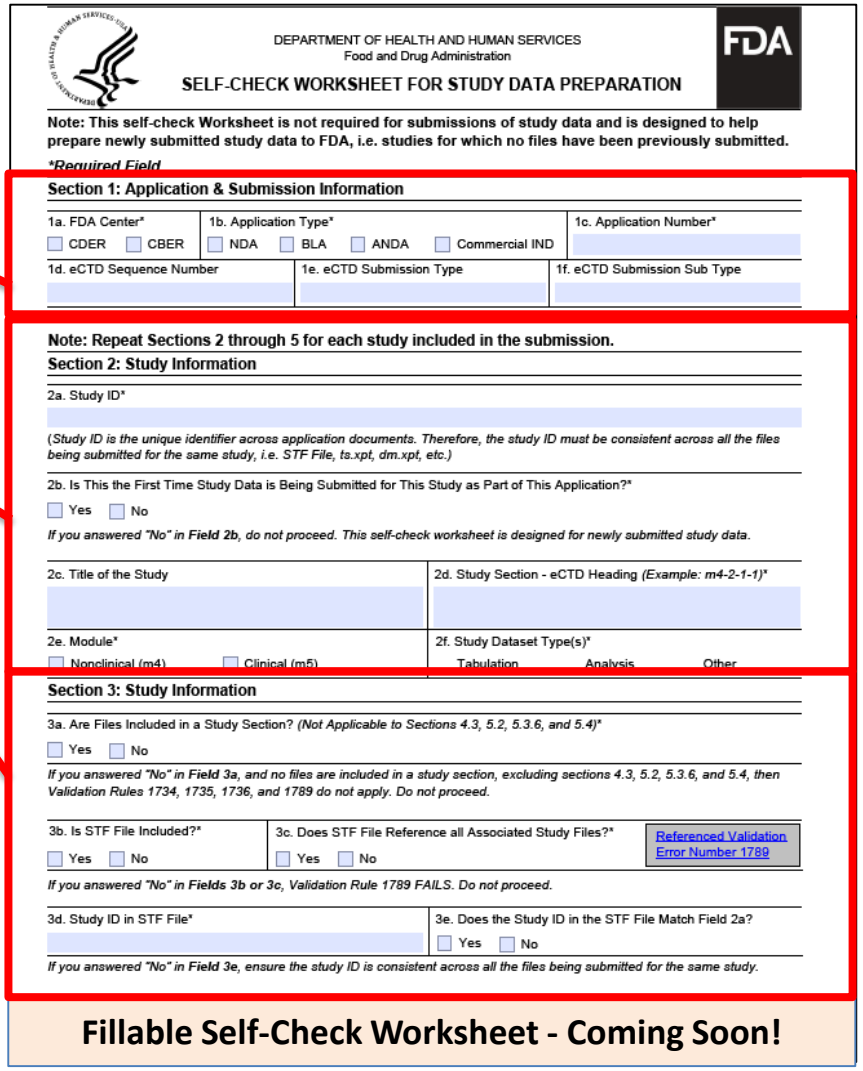


SDTRC High Level Validation Process (Revised Jan. 2019)



Self-Check Worksheet

Section	Contents
1	**Application & Submission Information** • Provides high level information about the application and submission
2	**Study Information** • Provides more detailed information about the specific study
3	**STF File Information** (1789 Validation Error) • Provide information about STF file



DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

SELF-CHECK WORKSHEET FOR STUDY DATA PREPARATION

Note: This self-check Worksheet is not required for submissions of study data and is designed to help prepare newly submitted study data to FDA, i.e. studies for which no files have been previously submitted.

**Required Field*

Section 1: Application & Submission Information

1a. FDA Center* ☐ CDER ☐ CBER | 1b. Application Type* ☐ NDA ☐ BLA ☐ ANDA ☐ Commercial IND | 1c. Application Number*

1d. eCTD Sequence Number | 1e. eCTD Submission Type | 1f. eCTD Submission Sub Type

Note: Repeat Sections 2 through 5 for each study included in the submission.

Section 2: Study Information

2a. Study ID*

(Study ID is the unique identifier across application documents. Therefore, the study ID must be consistent across all the files being submitted for the same study, i.e. STF File, ts.xpt, dm.xpt, etc.)

2b. Is This the First Time Study Data is Being Submitted for This Study as Part of This Application?* ☐ Yes ☐ No

If you answered "No" in Field 2b, do not proceed. This self-check worksheet is designed for newly submitted study data.

2c. Title of the Study | 2d. Study Section - eCTD Heading *(Example: m4-2-1-1)**

2e. Module* ☐ Nonclinical (m4) ☐ Clinical (m5) | 2f. Study Dataset Type(s)* Tabulation Analysis Other

Section 3: Study Information

3a. Are Files Included in a Study Section? *(Not Applicable to Sections 4.3, 5.2, 5.3.6, and 5.4)** ☐ Yes ☐ No

If you answered "No" in Field 3a, and no files are included in a study section, excluding sections 4.3, 5.2, 5.3.6, and 5.4, then Validation Rules 1734, 1735, 1736, and 1789 do not apply. Do not proceed.

3b. Is STF File Included?* ☐ Yes ☐ No | 3c. Does STF File Reference all Associated Study Files?* ☐ Yes ☐ No | Referenced Validation Error Number 1789

If you answered "No" in Fields 3b or 3c, Validation Rule 1789 FAILS. Do not proceed.

3d. Study ID in STF File* | 3e. Does the Study ID in the STF File Match Field 2a? ☐ Yes ☐ No

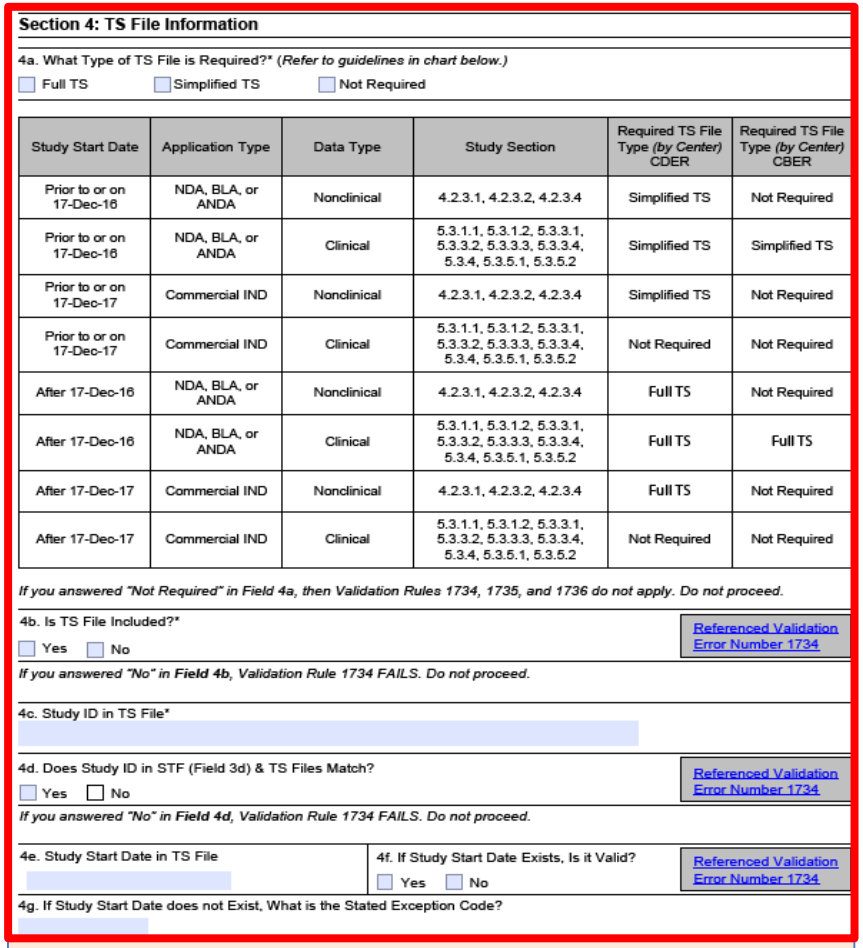
If you answered "No" in Field 3e, ensure the study ID is consistent across all the files being submitted for the same study.

Fillable Self-Check Worksheet - Coming Soon!

Reference:
"Technical Rejection Criteria Self-Check Worksheet"
https://www.fda.gov/media/123098/download
"Technical Rejection Criteria Self-Check Worksheet Instructions" https://www.fda.gov/media/123099/download

Self-Check Worksheet (1734 Validation Error)

Section	Contents
4	**TS File Information** (1734 Validation Error) • Provide information about ts.xpt file with study start date



Section 4: TS File Information

4a. What Type of TS File is Required?* (*Refer to guidelines in chart below.*)

☐ Full TS ☐ Simplified TS ☐ Not Required

Study Start Date	Application Type	Data Type	Study Section	Required TS File Type (*by Center*) CDER	Required TS File Type (*by Center*) CBER
Prior to or on 17-Dec-16	NDA, BLA, or ANDA	Nonclinical	4.2.3.1, 4.2.3.2, 4.2.3.4	Simplified TS	Not Required
Prior to or on 17-Dec-16	NDA, BLA, or ANDA	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	Simplified TS	Simplified TS
Prior to or on 17-Dec-17	Commercial IND	Nonclinical	4.2.3.1, 4.2.3.2, 4.2.3.4	Simplified TS	Not Required
Prior to or on 17-Dec-17	Commercial IND	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	Not Required	Not Required
After 17-Dec-16	NDA, BLA, or ANDA	Nonclinical	4.2.3.1, 4.2.3.2, 4.2.3.4	Full TS	Not Required
After 17-Dec-16	NDA, BLA, or ANDA	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	Full TS	Full TS
After 17-Dec-17	Commercial IND	Nonclinical	4.2.3.1, 4.2.3.2, 4.2.3.4	Full TS	Not Required
After 17-Dec-17	Commercial IND	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	Not Required	Not Required

If you answered "Not Required" in Field 4a, then Validation Rules 1734, 1735, and 1736 do not apply. Do not proceed.

4b. Is TS File Included?* ☐ Yes ☐ No — Referenced Validation Error Number 1734

If you answered "No" in Field 4b, Validation Rule 1734 FAILS. Do not proceed.

4c. Study ID in TS File*

4d. Does Study ID in STF (Field 3d) & TS Files Match? ☐ Yes ☐ No — Referenced Validation Error Number 1734

If you answered "No" in Field 4d, Validation Rule 1734 FAILS. Do not proceed.

4e. Study Start Date in TS File

4f. If Study Start Date Exists, Is it Valid? ☐ Yes ☐ No — Referenced Validation Error Number 1734

4g. If Study Start Date does not Exist, What is the Stated Exception Code?

Fillable Self-Check Worksheet - Coming Soon!

Reference:
"Technical Rejection Criteria Self-Check Worksheet"
https://www.fda.gov/media/123098/download
"Technical Rejection Criteria Self-Check Worksheet Instructions"
https://www.fda.gov/media/123099/download

Simplified vs Full ts.xpt (Section 4)

- **Full ts.xpt**
  - Sponsors should submit a dataset named 'ts.xpt' following published CDISC Standard and FDA Study Data Technical Conformance Guide
- **Simplified ts.xpt**
  - Sponsors should submit a dataset named 'ts.xpt' with four variables: STUDYID, TSPARMCD, TSVAL, AND TSVALNF)

Study with a valid Study Start Date

STUDYID	TSPARMCD	TSVAL	TSVALNF
Study ID in STF	STSTDTC (Nonclinical) or SSTDTC (Clinical)	yyyy-mm-dd	*Can be left blank when valid study start date is provided in TSVAL*

Study without a valid Study Start Date

STUDYID	TSPARMCD	TSVAL	TSVALNF
Study ID in STF	STSTDTC (Nonclinical) or SSTDTC (Clinical)	*Can be left blank when a study start date is not available*	Exception code as specified in the ISO 21090

References:
FDA Study Data Technical Conformance Guide (Appendices F & G; Version 4.2, October 2018)
FDA Study Data Technical Rejection Criteria (Revised Jan. 2019)

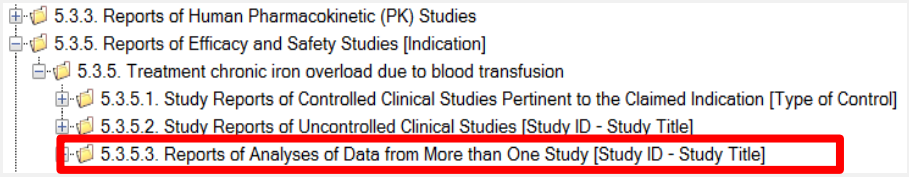
Applicable Study Sections (Section 4a)

- Technical Rejection Criteria is only applicable to Study Sections as specified in **Table 1 eCTD Technical Rejection Criteria for Study Data Expectation**

Example

1. Study Files and/or datasets submitted in **m5-3-5-3 (TRC not applicable study section)**

TRC Requirement: No ts.xpt is needed



Pass

No Further Validation Needed

Self-Check Worksheet

Section 4: TS File Information

4a. What Type of TS File is Required?* (*Refer to guidelines in chart below.*)

☐ Full TS ☐ Simplified TS ☒ Not Required

Study Start Date	Application Type	Data Type	Study Section	Required TS File Type (*by Center*) CDER	Required TS File Type (*by Center*) CBER
Prior to or on 17-Dec-16	NDA, BLA, or ANDA	Nonclinical	4.2.3.1, 4.2.3.2, 4.2.3.4	Simplified TS	Not Required
Prior to or on 17-Dec-16	NDA, BLA, or ANDA	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	Simplified TS	Simplified TS
Prior to or on 17-Dec-17	Commercial IND	Nonclinical	4.2.3.1, 4.2.3.2, 4.2.3.4	Simplified TS	Not Required
Prior to or on 17-Dec-17	Commercial IND	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	Not Required	Not Required
After 17-Dec-16	NDA, BLA, or ANDA	Nonclinical	4.2.3.1, 4.2.3.2, 4.2.3.4	Full TS	Not Required
After 17-Dec-16	NDA, BLA, or ANDA	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	Full TS	Full TS
After 17-Dec-17	Commercial IND	Nonclinical	4.2.3.1, 4.2.3.2, 4.2.3.4	Full TS	Not Required
After 17-Dec-17	Commercial IND	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	Not Required	Not Required

Simplified vs Full ts.xpt Examples (Section 4a)

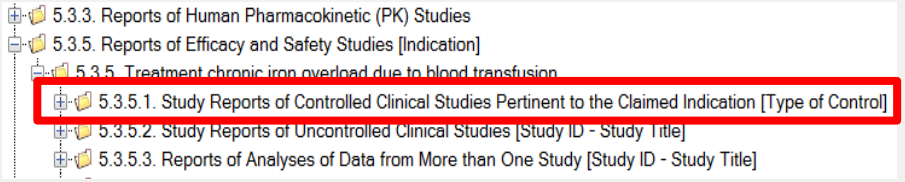
- Trial Summary (TS) dataset (ts.xpt) with information on study start date must be present for required sections

Example

2. Study Files and/or datasets submitted in **m5-3-5-1 (TRC applicable study section)**

Study Start Date: 2010-01-01

TRC Requirement: Simplified TS is needed



Self-Check Worksheet

Section 4: TS File Information

4a. What Type of TS File is Required?* *(Refer to guidelines in chart below.)*

☐ Full TS ☒ Simplified TS ☐ Not Required

Study Start Date	Application Type	Data Type	Study Section	Required TS File Type *(by Center)* CDER	Required TS File Type *(by Center)* CBER
Prior to or on 17-Dec-16	NDA, BLA, or ANDA	Nonclinical	4.2.3.1, 4.2.3.2, 4.2.3.4	Simplified TS	Not Required
Prior to or on 17-Dec-16	NDA, BLA, or ANDA	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	Simplified TS	Simplified TS
Prior to or on 17-Dec-17	Commercial IND	Nonclinical	4.2.3.1, 4.2.3.2, 4.2.3.4	Simplified TS	Not Required
Prior to or on 17-Dec-17	Commercial IND	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	Not Required	Not Required
After 17-Dec-16	NDA, BLA, or ANDA	Nonclinical	4.2.3.1, 4.2.3.2, 4.2.3.4	Full TS	Not Required
After 17-Dec-16	NDA, BLA, or ANDA	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	Full TS	Full TS
After 17-Dec-17	Commercial IND	Nonclinical	4.2.3.1, 4.2.3.2, 4.2.3.4	Full TS	Not Required
After 17-Dec-17	Commercial IND	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	Not Required	Not Required

Simplified vs Full ts.xpt Examples (Section 4a)

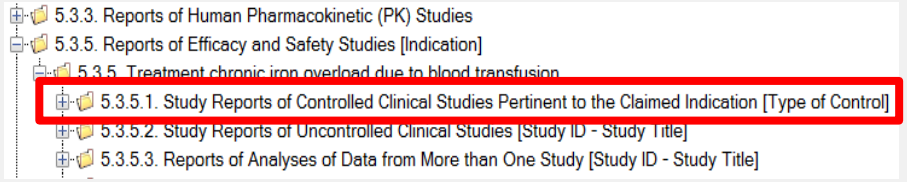
- Trial Summary (TS) dataset (ts.xpt) with information on study start date must be present for required sections

Example

3. Study Files and/or datasets submitted in **m5-3-5-1 (TRC applicable study section)**

Study Start Date: 2018-01-01

TRC Requirement: Full TS is needed



Self-Check Worksheet

Section 4: TS File Information

4a. What Type of TS File is Required?* *(Refer to guidelines in chart below.)*

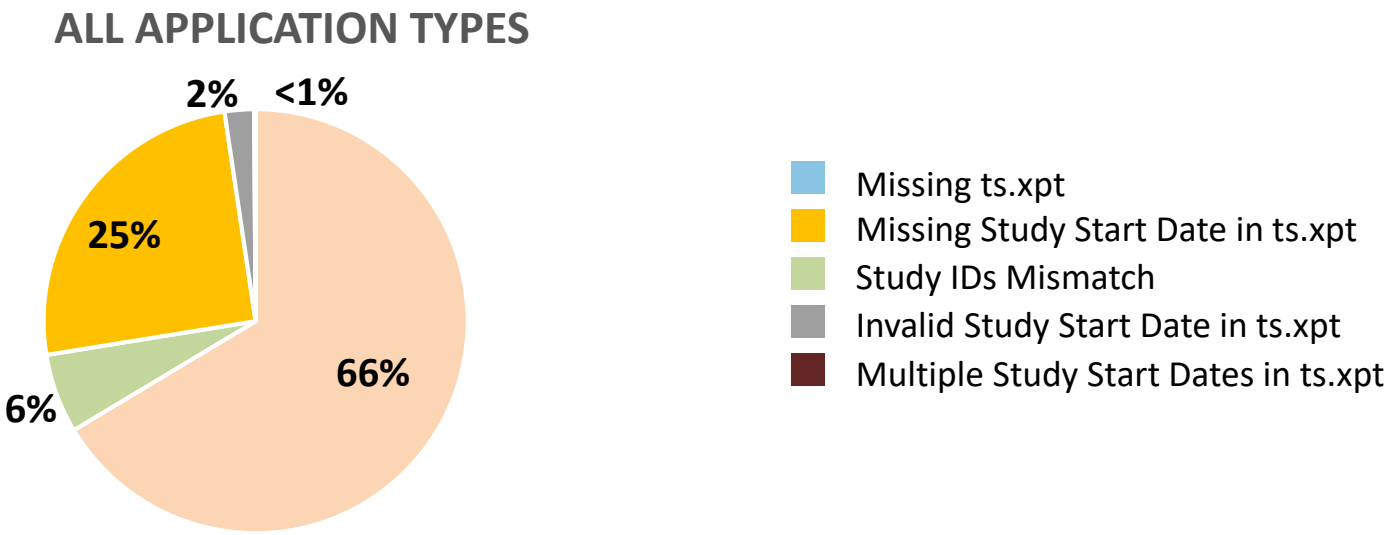
☒ Full TS ☐ Simplified TS ☐ Not Required

Study Start Date	Application Type	Data Type	Study Section	Required TS File Type *(by Center)* CDER	Required TS File Type *(by Center)* CBER
Prior to or on 17-Dec-16	NDA, BLA, or ANDA	Nonclinical	4.2.3.1, 4.2.3.2, 4.2.3.4	Simplified TS	Not Required
Prior to or on 17-Dec-16	NDA, BLA, or ANDA	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	Simplified TS	Simplified TS
Prior to or on 17-Dec-17	Commercial IND	Nonclinical	4.2.3.1, 4.2.3.2, 4.2.3.4	Simplified TS	Not Required
Prior to or on 17-Dec-17	Commercial IND	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	Not Required	Not Required
After 17-Dec-16	NDA, BLA, or ANDA	Nonclinical	4.2.3.1, 4.2.3.2, 4.2.3.4	Full TS	Not Required
After 17-Dec-16	NDA, BLA, or ANDA	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	Full TS	Full TS
After 17-Dec-17	Commercial IND	Nonclinical	4.2.3.1, 4.2.3.2, 4.2.3.4	Full TS	Not Required
After 17-Dec-17	Commercial IND	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	Not Required	Not Required

CY2018 CDER Error Reasons for Validation Rule 1734

- A dataset named ts.xpt with information on Study Start Date (SSD) must be present for each study

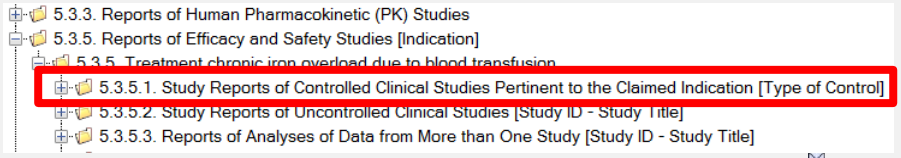
- Common error reason across all application types:
  - **missing ts.xpt file (66% of studies with error 1734)**
  - **missing study start date in the ts.xpt (25% of studies with error 1734)**



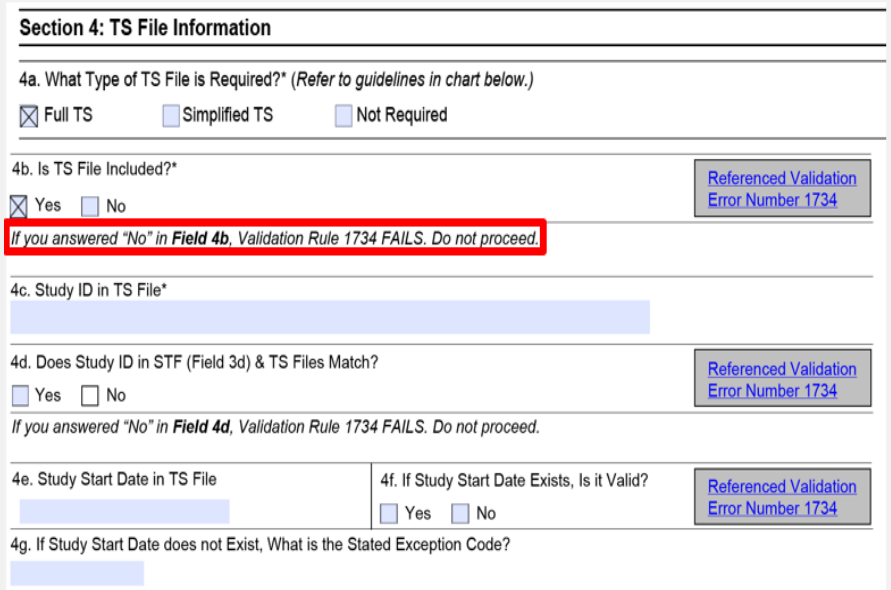
TRC Validation Rule 1734 (Section 4b)

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

Example	Self-Check Worksheet
2. Study Files and/or datasets submitted in **m5-3-5-1 (TRC applicable study section)** **Study Start Date:** 2018-01-01 **TRC Requirement**: Full TS is needed	



*If you answered "No" in **Field 4b**, Validation Rule 1734 FAILS. Do not proceed.*



Study ID Match Requirements

- STUDYID in STF.xml and ts.xpt should match
  - Based on the FDA Study Data TCG and the ICH STF Specification the Study ID **uniquely and unambiguously** identifies a particular study

ICH M2 EWG: The eCTD Backbone File Specification for Study Tagging Files (June 2008)

II. STUDY-IDENTIFIER ELEMENT

Information describing the study is contained in the *study-identifier* element of the STF. There are three elements contained in the *study-identifier* element: *title*, *study-id*, and *category*.

A. Title Element

The *title* element provides the full title of the study, not the title of each individual document.

B. study-id Element

The *study-id* is the internal alphanumeric code used by the sponsor to unambiguously identify this study.

CDISC Submission Metadata Model

The following variables are considered core selection variables for use in all CDISC domain models. These variable roles may also be defined with other roles (such as Key), and roles may differ from dataset to dataset.

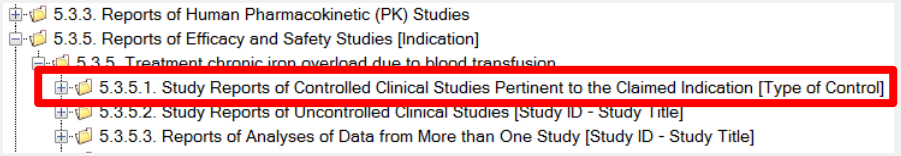
Variable Name	Variable Label	Comments	Included in:
STUDYID	Study ID	Uniquely identifies a study within a particular submission.	All files
SITEID	Site ID	Some sponsors may use INVID instead of or in addition to a SITEID.	At least one of these variables must be included in all files
INVID	Investigator ID		
USUBJID	Unique Subject ID	Must be unique subject identifier within a submission (previously defined as PID; should be consistent with PID references used elsewhere in the submission)	All files

References:
ICH M2 EWG: The eCTD Backbone File Specification for Study Tagging Files (June 2008) (http://estri.ich.org/STF/STFV2-6-1.pdf)
CDISC Submission Metadata Model
(https://www.cdisc.org/system/files/all/reference_material_category/application/pdf/submissionmetadatamodelv2.pdf)

TRC Validation Rule 1734 (Section 4c)

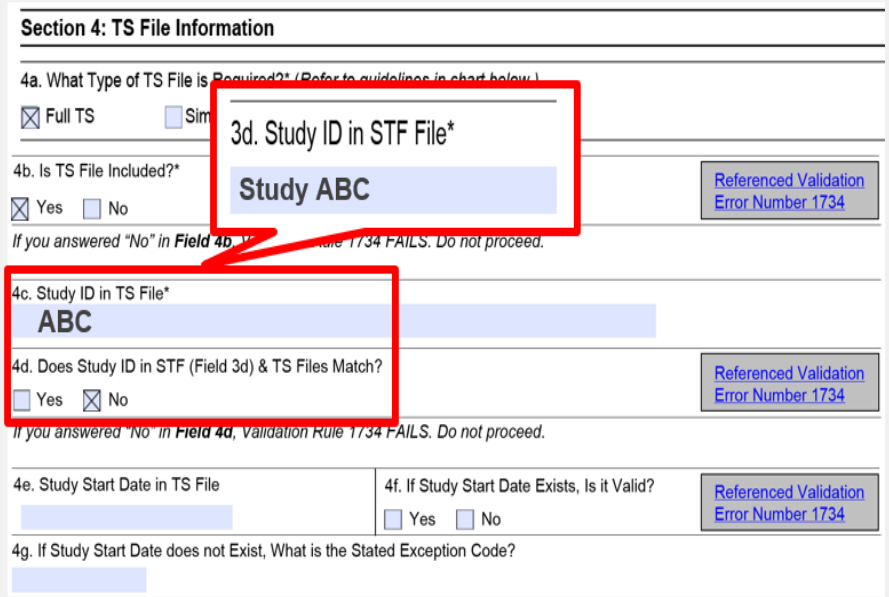
- Trial Summary (TS) dataset (ts.xpt) with information on study start date must be present for required sections

Example	Self-Check Worksheet
2. Study Files and/or datasets submitted in **m5-3-5-1 (TRC applicable study section)** **Study Start Date:** 2018-01-01 **TRC Requirement**: Full TS is needed	



[Study IDs Match Requirement]

Fail Rule 1734

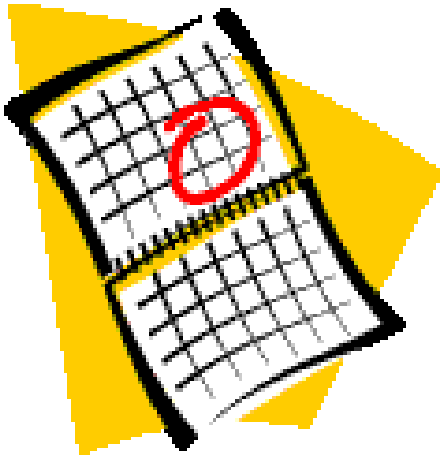


Top Error for Rule 1734: Incorrect Study Start Date Format

- A missing study start date (TSVAL) in the ts.xpt (25% of studies with error 1734)

Correct Study Start Date Format
yyyy-mm-dd

Incorrect Study Start Date Format	
yyyy-mm	dd-mmm-yyyy
SAS Date Format	dd-mm-yyyy
mm/dd/yyyy	ddmmmyyyy
dd-mmm-yy	dd.mm.yyyy
yyyy	month-yyyy
mm/dd/yy	



TRC Validation Rule 1734 (Section 4c)

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

Example	Self-Check Worksheet

2. Study Files and/or datasets submitted in **m5-3-5-1 (TRC applicable study section)**
Study Start Date: 2018-01-01
TRC Requirement: Full TS is needed

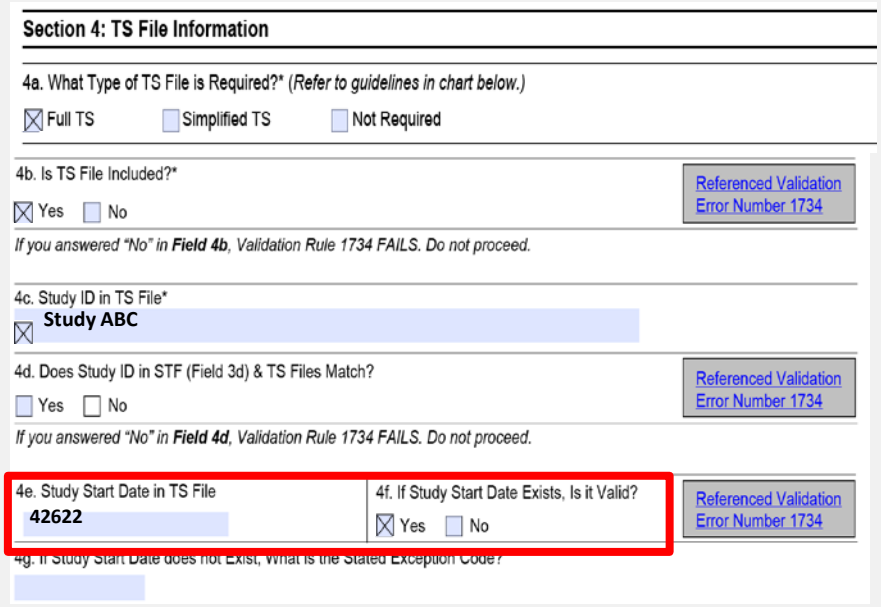
[Study Date Format Requirement]
- yyyy-mm-dd

TS.XPT

SSTDTC	Study Start Date	42622

Study Start Date in SAS Date Format

Fail Rule 1734



Section 4: TS File Information

4a. What Type of TS File is Required?* *(Refer to guidelines in chart below.)*
☒ Full TS ☐ Simplified TS ☐ Not Required

4b. Is TS File Included?*
☒ Yes ☐ No
Referenced Validation Error Number 1734

*If you answered "No" in **Field 4b**, Validation Rule 1734 FAILS. Do not proceed.*

4c. Study ID in TS File*
☒ **Study ABC**

4d. Does Study ID in STF (Field 3d) & TS Files Match?
☐ Yes ☐ No
Referenced Validation Error Number 1734

*If you answered "No" in **Field 4d**, Validation Rule 1734 FAILS. Do not proceed.*

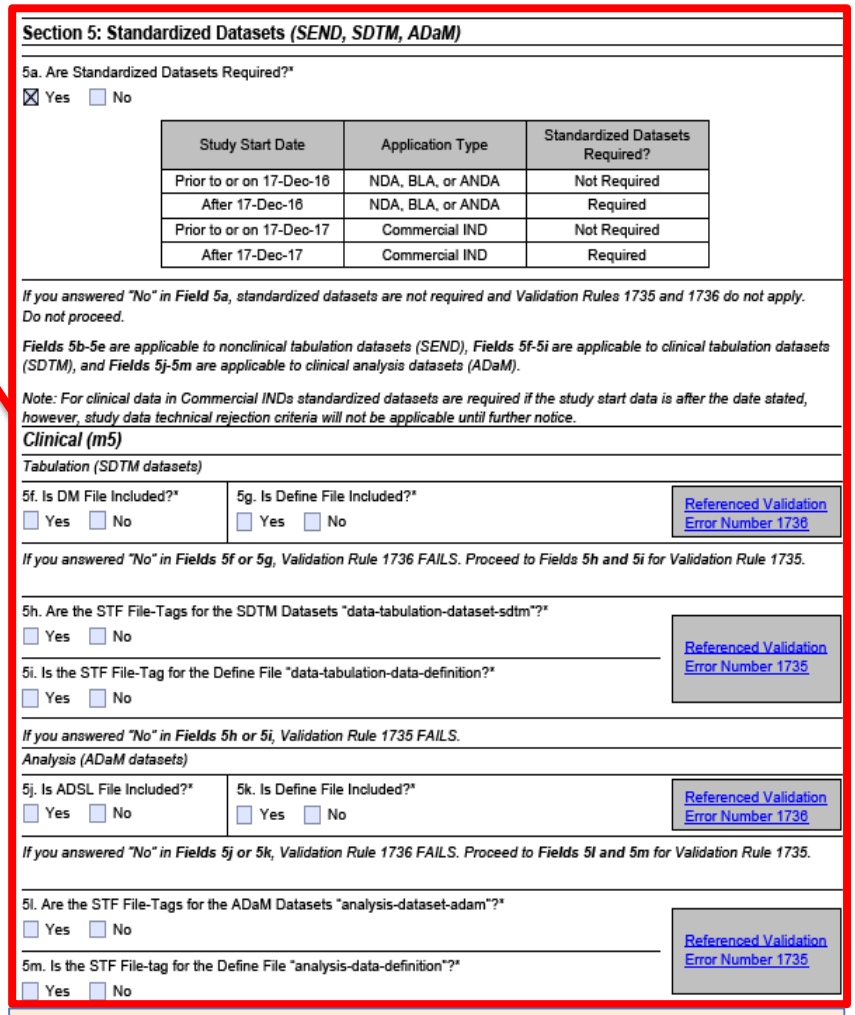
4e. Study Start Date in TS File
42622

4f. If Study Start Date Exists, Is it Valid?
☒ Yes ☐ No
Referenced Validation Error Number 1734

4g. If Study Start Date does not Exist, What is the Stated Exception Code?

Self-Check Worksheet (1735 & 1736 Validation Error)

Section	Contents
5	**Standardized Dataset Information** (1735 & 1736 Validation Error) • Provide information about SEND or STDM and/or ADaM dataset and define.xml • Provide information about STF File-tags



Section 5: Standardized Datasets *(SEND, SDTM, ADaM)*

5a. Are Standardized Datasets Required?*
☒ Yes ☐ No

Study Start Date	Application Type	Standardized Datasets Required?
Prior to or on 17-Dec-16	NDA, BLA, or ANDA	Not Required
After 17-Dec-16	NDA, BLA, or ANDA	Required
Prior to or on 17-Dec-17	Commercial IND	Not Required
After 17-Dec-17	Commercial IND	Required

*If you answered "No" in **Field 5a**, standardized datasets are not required and Validation Rules 1735 and 1736 do not apply. Do not proceed.*

***Fields 5b-5e** are applicable to nonclinical tabulation datasets (SEND), **Fields 5f-5i** are applicable to clinical tabulation datasets (SDTM), and **Fields 5j-5m** are applicable to clinical analysis datasets (ADaM).*

Note: For clinical data in Commercial INDs standardized datasets are required if the study start data is after the date stated, however, study data technical rejection criteria will not be applicable until further notice.

Clinical (m5)

Tabulation (SDTM datasets)

5f. Is DM File Included?* ☐ Yes ☐ No
5g. Is Define File Included?* ☐ Yes ☐ No
Referenced Validation Error Number 1736

*If you answered "No" in **Fields 5f or 5g**, Validation Rule 1736 FAILS. Proceed to Fields **5h and 5i** for Validation Rule 1735.*

5h. Are the STF File-Tags for the SDTM Datasets "data-tabulation-dataset-sdtm"?* ☐ Yes ☐ No
5i. Is the STF File-Tag for the Define File "data-tabulation-data-definition?* ☐ Yes ☐ No
Referenced Validation Error Number 1735

*If you answered "No" in **Fields 5h or 5i**, Validation Rule 1735 FAILS.*

Analysis (ADaM datasets)

5j. Is ADSL File Included?* ☐ Yes ☐ No
5k. Is Define File Included?* ☐ Yes ☐ No
Referenced Validation Error Number 1736

*If you answered "No" in **Fields 5j or 5k**, Validation Rule 1736 FAILS. Proceed to **Fields 5l and 5m** for Validation Rule 1735.*

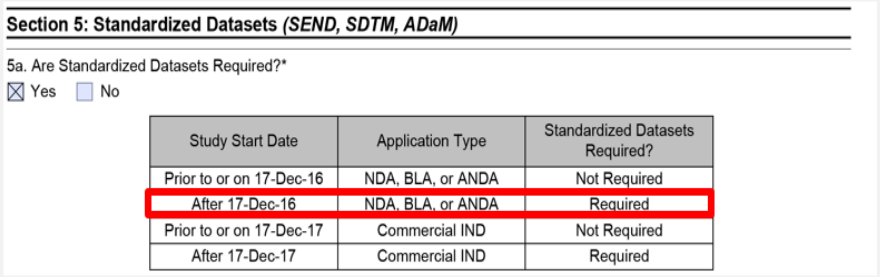
5l. Are the STF File-Tags for the ADaM Datasets "analysis-dataset-adam"?* ☐ Yes ☐ No
5m. Is the STF File-tag for the Define File "analysis-data-definition"?* ☐ Yes ☐ No
Referenced Validation Error Number 1735

Fillable Self-Check Worksheet - Coming Soon!

Reference:
"Technical Rejection Criteria Self-Check Worksheet"
https://www.fda.gov/media/123098/download
"Technical Rejection Criteria Self-Check Worksheet Instructions"
https://www.fda.gov/media/123099/download

TRC Validation Rule 1735 and 1736 (Section 5a)

- Rule 1735: Correct STF file-tags must be used for all standardized datasets and corresponding define.xml files in required sections
- Rule 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

Example	Self-Check Worksheet
Study Files and/or datasets submitted in **m5-3-5-1 (clinical)** **Study Start Date:** 2018-01-01 **Dataset Type:** Tabulation (SDTM)	

Section 5: Standardized Datasets *(SEND, SDTM, ADaM)*

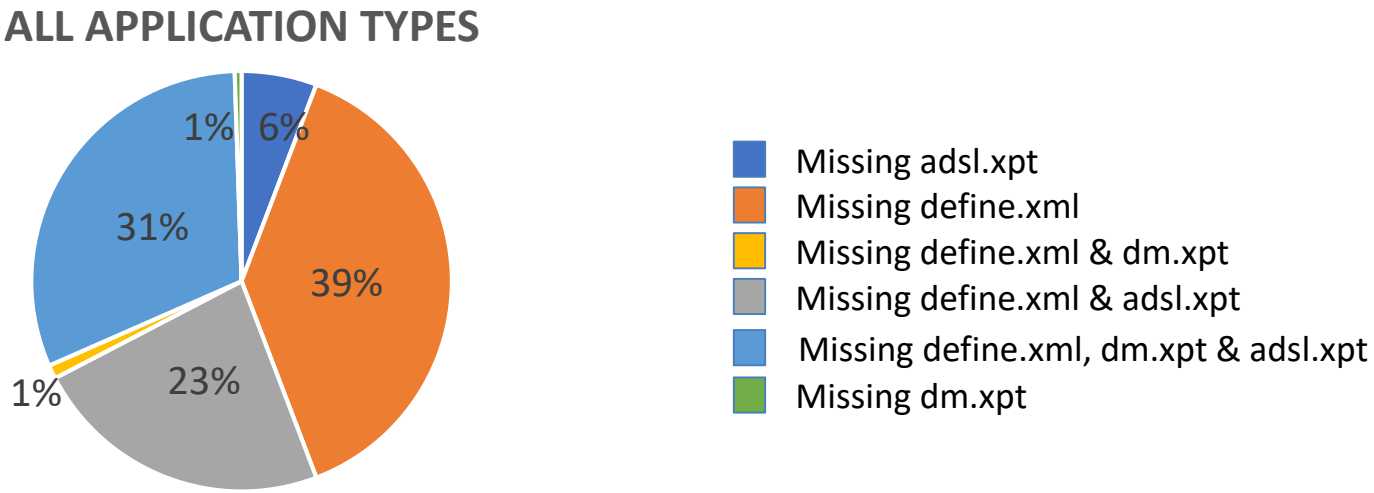
5a. Are Standardized Datasets Required?*

☒ Yes ☐ No

Study Start Date	Application Type	Standardized Datasets Required?
Prior to or on 17-Dec-16	NDA, BLA, or ANDA	Not Required
After 17-Dec-16	NDA, BLA, or ANDA	Required
Prior to or on 17-Dec-17	Commercial IND	Not Required
After 17-Dec-17	Commercial IND	Required

CY2018 CDER Error Reasons for Validation Rule 1736

- Rule 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
  - For ADaM data, an ADSL dataset and define.xml must be submitted
- Common error reason across all application types:
  - **missing define.xml file (39% of studies)**
  - **missing define.xml, dm.xpt, and adsl.xpt files (31% of studies)**
- Common error reason for NDAs:
  - **missing define.xml and adsl.xpt files**



TRC Validation Rule 1735 and 1736 (Section 5f-5g)

- Rule 1735: Correct STF file-tags must be used for all standardized datasets and corresponding define.xml files in required sections
- Rule 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

Example

Study Files and/or datasets submitted in **m5-3-5-1 (clinical)**
Study Start Date: 2018-01-01
Dataset Type: Tabulation (SDTM)

Files Referenced in stf.xml

acrf.pdf	ds.xpt	mh.xpt	suppda.xpt	suppmh.xpt	tv.xpt
ae.xpt	dv.xpt	pe.xpt	suppdm.xpt	sv.xpt	vs.xpt
cm.xpt	eg.xpt	sc.xpt	suppds.xpt	ta.xpt	
co.xpt	ex.xpt	se.xpt	suppeg.xpt	te.xpt	
csdrg.pdf	ie.xpt	suppae.xpt	suppex.xpt	ti.xpt	

dm.xpt and define.xml are missing

Fail Rule 1736

Self-Check Worksheet

Section 5: Standardized Datasets *(SEND, SDTM, ADaM)*

5a. Are Standardized Datasets Required?*
☒ Yes ☐ No

Study Start Date	Application Type	Standardized Datasets Required?
Prior to or on 17-Dec-16	NDA, BLA, or ANDA	Not Required
After 17-Dec-16	NDA, BLA, or ANDA	Required
Prior to or on 17-Dec-17	Commercial IND	Not Required
After 17-Dec-17	Commercial IND	Required

Clinical (m5)

Tabulation (SDTM datasets)

5f. Is DM File Included?*	5g. Is Define File Included?*	
☐ Yes ☒ No	☐ Yes ☒ No	Referenced Validation Error Number 1736

*If you answered "No" in **Fields 5f or 5g**, Validation Rule 1736 FAILS. Proceed to Fields **5h and 5i** for Validation Rule 1735.*

5h. Are the STF File-Tags for the SDTM Datasets "data-tabulation-dataset-sdtm"?*
☐ Yes ☐ No

5i. Is the STF File-Tag for the Define File "data-tabulation-data-definition?*
☐ Yes ☐ No

Referenced Validation Error Number 1735

*If you answered "No" in **Fields 5h or 5i**, Validation Rule 1735 FAILS.*

CY2018 CDER Error Reasons for Validation Rule 1735

- The correct STF file tags must be used for all standardized datasets and corresponding define.xml files
- Common error reason for ANDAs:
  - **incorrect file tag for a define.xml file (42% of ANDA studies with error 1735)**
- Common error reason for NDAs:
  - **dataset tagged as legacy when standardized datasets are required (80% of NDA studies with error 1735)**

TRC Validation Rule 1735 and 1736 (Section 5h-5i)

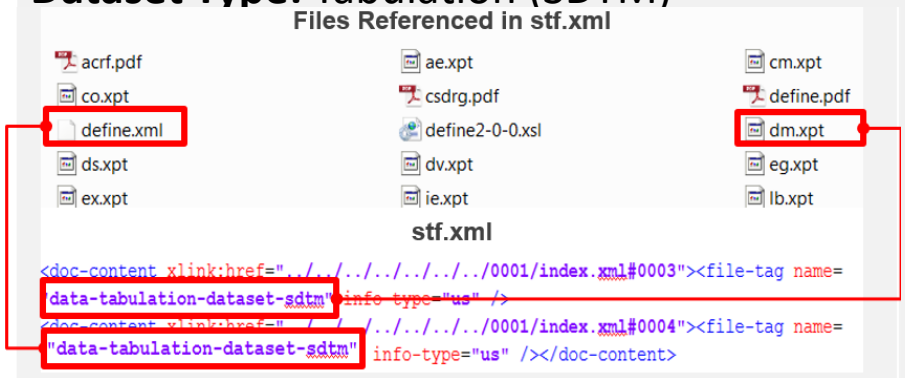
- Rule 1735: Correct STF file-tags must be used for all standardized datasets and corresponding define.xml files in required sections
- Rule 1736: For SEND data, a DM dataset and define xml must be submitted in required sections
  - For SDTM data, a DM dataset and define.xml must be submitted in required sections
  - For ADaM data, an ADSL dataset and define.xml must be submitted in required sections

Example

Study Files and/or datasets submitted in **m5-3-5-1 (clinical)**

Study Start Date: 2018-01-01

Dataset Type: Tabulation (SDTM)



define.xml is tagged as "data-tabulation-dataset-sdtm"

Fail Rule 1735

Self-Check Worksheet

Section 5: Standardized Datasets *(SEND, SDTM, ADaM)*

5a. Are Standardized Datasets Required?*

☒ Yes ☐ No

Study Start Date	Application Type	Standardized Datasets Required?
Prior to or on 17-Dec-16	NDA, BLA, or ANDA	Not Required
After 17-Dec-16	NDA, BLA, or ANDA	Required
Prior to or on 17-Dec-17	Commercial IND	Not Required
After 17-Dec-17	Commercial IND	Required

Clinical (m5)

Tabulation (SDTM datasets)

5f. Is DM File Included?* ☒ Yes ☐ No

5g. Is Define File Included?* ☒ Yes ☐ No

Referenced Validation Error Number 1736

*If you answered "No" in **Fields 5f or 5g**, Validation Rule 1736 FAILS. Proceed to Fields **5h and 5i** for Validation Rule 1735.*

5h. Are the STF File-Tags for the SDTM Datasets "data-tabulation-dataset-sdtm"?* ☒ Yes ☐ No

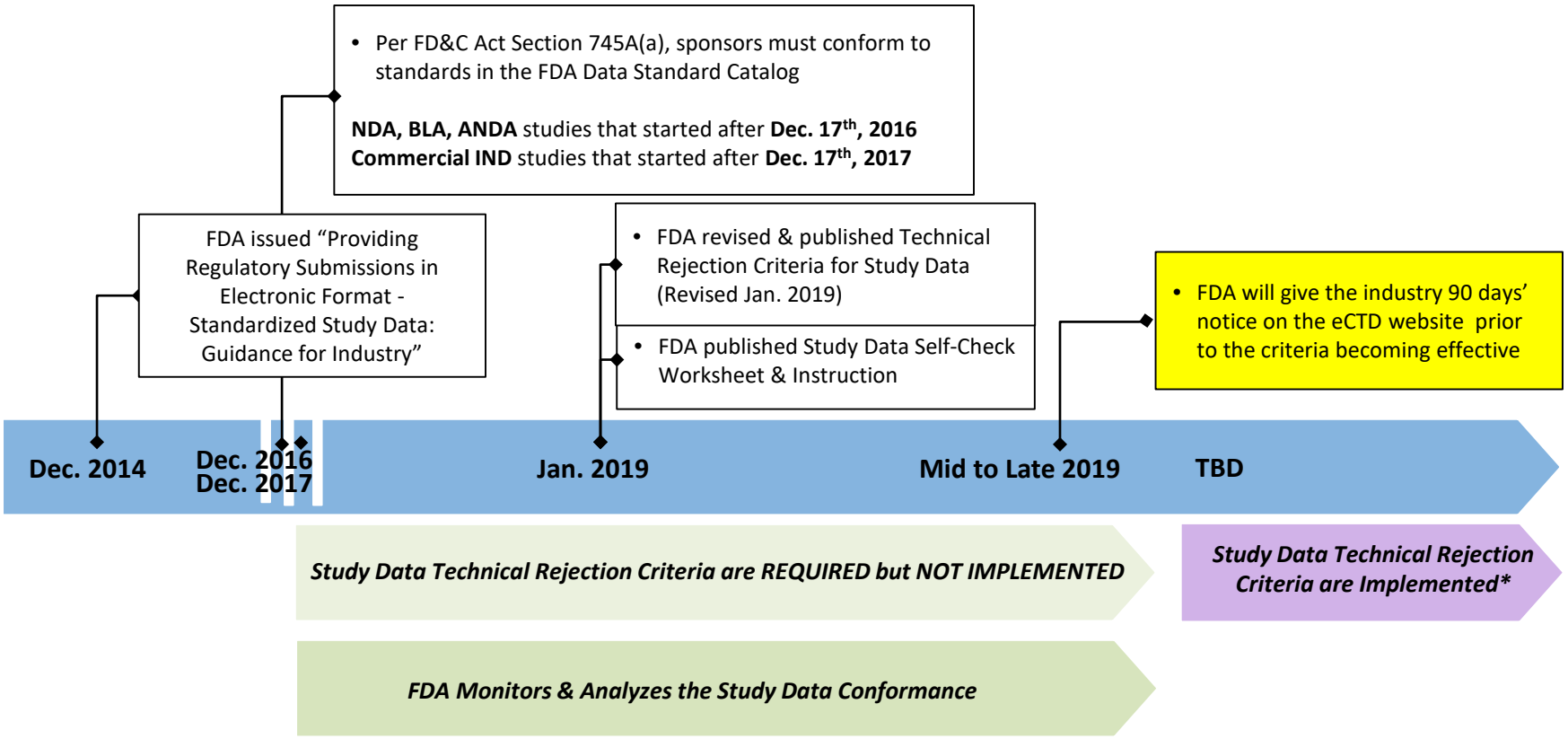
5i. Is the STF File-Tag for the Define File "data-tabulation-data-definition?* ☐ Yes ☒ No

Referenced Validation Error Number 1735

*If you answered "No" in **Fields 5h or 5i**, Validation Rule 1735 FAILS.*

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

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