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

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Office of Business Informatics
FDA Center for Drug Evaluation and Research

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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.


- 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)

<table>
<thead>
<tr>
<th></th>
<th>NDA</th>
<th>ANDA</th>
<th>BLA</th>
<th>Comm. IND</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CY2018</td>
<td>CY2019 (Q1)</td>
<td>CY2018</td>
<td>CY2019 (Q1)</td>
<td>CY2018</td>
</tr>
<tr>
<td>Total Number of</td>
<td>41,077</td>
<td>11,011</td>
<td>62,695</td>
<td>14,776</td>
<td>11,042</td>
</tr>
<tr>
<td>Submissions</td>
<td></td>
<td></td>
<td>14,776</td>
<td>2997</td>
<td></td>
</tr>
<tr>
<td>Error 1789</td>
<td>43</td>
<td>11</td>
<td>225</td>
<td>53</td>
<td>1</td>
</tr>
<tr>
<td>Failure Rate (%)</td>
<td>0.10%</td>
<td>0.10%</td>
<td>0.36%</td>
<td>0.36%</td>
<td>&lt;0.01%</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th></th>
<th>NDA</th>
<th>ANDA</th>
<th>BLA</th>
<th>Comm. IND</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>CY2018</td>
<td>CY2019 (Q1)</td>
<td>CY2018</td>
<td>CY2019 (Q1)</td>
<td>CY2018</td>
<td>CY2019 (Q1)</td>
</tr>
<tr>
<td>Total Number of Submissions with Study Data</td>
<td>877</td>
<td>270</td>
<td>1078</td>
<td>243</td>
<td>291</td>
</tr>
<tr>
<td>Total Number of Submissions with Study Data in TRC Applicable Sections</td>
<td>204</td>
<td>689</td>
<td>181</td>
<td>54</td>
<td>15</td>
</tr>
<tr>
<td>Total Number Submissions with Critical Errors</td>
<td>215</td>
<td>71</td>
<td>689</td>
<td>181</td>
<td>54</td>
</tr>
<tr>
<td>Error 1734</td>
<td>185</td>
<td>52</td>
<td>186</td>
<td>53</td>
<td>48</td>
</tr>
<tr>
<td>Error 1735</td>
<td>34</td>
<td>23</td>
<td>497</td>
<td>130</td>
<td>5</td>
</tr>
<tr>
<td>Error 1736</td>
<td>16</td>
<td>3</td>
<td>88</td>
<td>21</td>
<td>2</td>
</tr>
<tr>
<td>Failure Rate (% among submissions with Study Data)</td>
<td>24.50%</td>
<td>26.30%</td>
<td>63.90%</td>
<td>73.70%</td>
<td>18.60%</td>
</tr>
<tr>
<td>Failure Rate (% among submissions with Study Data in TRC Applicable Sections)</td>
<td>34.80%</td>
<td>80.10%</td>
<td>26.30%</td>
<td>24.40%</td>
<td>46.90%</td>
</tr>
</tbody>
</table>

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)

<table>
<thead>
<tr>
<th></th>
<th>CY2018</th>
<th>CY2019 (Q1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Number of studies with Study Data</td>
<td>6062</td>
<td>1644</td>
</tr>
<tr>
<td>Error 1789</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Failure Rate (% among studies with Study Data)</td>
<td>0.1%</td>
<td>0%</td>
</tr>
<tr>
<td>Total Number of Submissions with Study Data in TRC Applicable Sections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Number studies with Critical Errors</td>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>Error 1734</td>
<td>14</td>
<td>5</td>
</tr>
<tr>
<td>Error 1735</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Error 1736</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Failure Rate (% among studies with Study Data)</td>
<td>30.6%</td>
<td>50.0%</td>
</tr>
<tr>
<td>Failure Rate (% among submissions with Study Data in TRC Applicable Sections)</td>
<td>50.0%</td>
<td></td>
</tr>
</tbody>
</table>

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

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)
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.


- FDA published Study Data Guidance for Industry

NDA, BLA, ANDA studies that started after Dec. 17th, 2016
Commercial IND studies that started after Dec. 17th, 2017 must conform to standards in the FDA Data Standard Catalog

FDA Monitors & Analyzes the Study Data Conformance

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

www.fda.gov
## Update to SDTRC List of High Errors (Revised Jan. 2019)

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

<table>
<thead>
<tr>
<th>Error</th>
<th>Description (Reference to FDA Study Data Technical Rejection Criteria Jan. 2019 version)</th>
<th>Severity Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>1734</td>
<td>Trial Summary (TS) dataset (ts.xpt) with information on study start date must be present for required sections*</td>
<td>High</td>
</tr>
<tr>
<td>1735</td>
<td>Correct STF file-tags must be used for all standardized datasets and corresponding define.xml files in required sections*</td>
<td>High</td>
</tr>
<tr>
<td>1736</td>
<td>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*</td>
<td>High</td>
</tr>
<tr>
<td>1789**</td>
<td>Study files must be referenced in a Study Tagging File (STF)</td>
<td>High</td>
</tr>
</tbody>
</table>

* 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

<table>
<thead>
<tr>
<th>Study Start Date</th>
<th>Application Type</th>
<th>Data Type</th>
<th>Study Sections</th>
<th>Expectation by Center</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior to or on 17-Dec-2017</td>
<td>Commercial INDs</td>
<td>Nonclinical</td>
<td>4.2.3.1, 4.2.3.2, 4.2.3.4</td>
<td>Rejection criteria will be applied; submit a simplified TS whether or not the study contains an xpt dataset (other than the ts.xpt)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clinical</td>
<td>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</td>
<td>Rejection criteria will not be applied</td>
</tr>
<tr>
<td>After 17-Dec-2017</td>
<td>Commercial INDs</td>
<td>Nonclinical</td>
<td>4.2.3.1, 4.2.3.2, 4.2.3.4</td>
<td>Rejection criteria will not be applied</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clinical</td>
<td>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</td>
<td>Rejection criteria will not be applied</td>
</tr>
<tr>
<td>Prior to or on 17-Dec-2016</td>
<td>NDA, BLA, ANDA</td>
<td>Nonclinical</td>
<td>4.2.3.1, 4.2.3.2, 4.2.3.4</td>
<td>Rejection criteria will be applied; submit a simplified TS whether or not the study contains an xpt dataset (other than the ts.xpt)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clinical</td>
<td>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</td>
<td>Rejection criteria will not be applied</td>
</tr>
<tr>
<td>After 17-Dec-2016</td>
<td>NDA, BLA, ANDA</td>
<td>Nonclinical</td>
<td>4.2.3.1, 4.2.3.2, 4.2.3.4</td>
<td>Rejection criteria will be applied; submit a full TS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clinical</td>
<td>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</td>
<td>Rejection criteria will not be applied</td>
</tr>
</tbody>
</table>
Published SDTRC and Self-Check Worksheet

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 Biological License Applications (BLAs) or refuse to receive for Abbreviated New Drug Applications (ANDAs) any electronic submission whose study data do not conform to the required standards specified in the FDA Data Standard Catalog. See the Technical Rejection Criteria for Study Data (PDF) for more information.

Stay Connected
If you have study data questions for CDER, please contact the CDER eDATA Team at eder-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 CBERR-edata@fda.hhs.gov.
For electronic submissions, contact CBER ESUB at esubrop@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

- FDA published Study Data Guidance for Industry
- NDA, BLA, ANDA studies that started after Dec. 17th, 2016
- Commercial IND studies that started after Dec. 17th, 2017 must conform to standards in the FDA Data Standard Catalog
SDTRC High Level Validation Process (Revised Jan. 2019)

Validation Rule 1734

Validation Rule 1735

Validation Rule 1736

Validation Rule 1789
## Self-Check Worksheet

**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

### Section Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Contents</th>
</tr>
</thead>
</table>
| 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 |

### Section 1: Application & Submission Information

1a. FDA Center  
1b. Application Type  
1c. Application Number  
1d. eCTD Sequence Number  
1e. eCTD Submission Type  
1f. eCTD Submission Sub Type

**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.

**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

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**Fillable Self-Check Worksheet - Coming Soon!**
### Section 4: TS File Information

<table>
<thead>
<tr>
<th>Study Start Date</th>
<th>Application Type</th>
<th>Data Type</th>
<th>Study Section</th>
<th>Required TS File Type (by Center)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior to on 17-Dec-10</td>
<td>NDA, BLA, or ANDA</td>
<td>Nonclinical</td>
<td>4.2.3.1, 4.2.3.2, 4.2.3.4</td>
<td>Simplified TS</td>
</tr>
<tr>
<td>Prior to on 17-Dec-10</td>
<td>NDA, BLA, or ANDA</td>
<td>Clinical</td>
<td>5.3.1.1, 5.3.1.2, 5.3.4.1, 5.3.6.1, 5.3.6.2</td>
<td>Simplified TS</td>
</tr>
<tr>
<td>Prior to on 17-Dec-17</td>
<td>Commercial IND</td>
<td>Nonclinical</td>
<td>4.2.3.1, 4.2.3.2, 4.2.3.4</td>
<td>Simplified TS</td>
</tr>
<tr>
<td>Prior to or on 17-Dec-17</td>
<td>Commercial IND</td>
<td>Clinical</td>
<td>5.3.1.1, 5.3.1.2, 5.3.4.1, 5.3.6.1, 5.3.6.2</td>
<td>Not Required</td>
</tr>
<tr>
<td>After 17-Dec-10</td>
<td>NDA, BLA, or ANDA</td>
<td>Nonclinical</td>
<td>4.2.3.1, 4.2.3.2, 4.2.3.4</td>
<td>Full TS</td>
</tr>
<tr>
<td>After 17-Dec-10</td>
<td>NDA, BLA, or ANDA</td>
<td>Clinical</td>
<td>5.3.1.1, 5.3.1.2, 5.3.4.1, 5.3.6.1, 5.3.6.2</td>
<td>Full TS</td>
</tr>
<tr>
<td>After 17-Dec-17</td>
<td>Commercial IND</td>
<td>Nonclinical</td>
<td>4.2.3.1, 4.2.3.2, 4.2.3.4</td>
<td>Full TS</td>
</tr>
<tr>
<td>After 17-Dec-17</td>
<td>Commercial IND</td>
<td>Clinical</td>
<td>5.3.1.1, 5.3.1.2, 5.3.4.1, 5.3.6.1, 5.3.6.2</td>
<td>Not Required</td>
</tr>
</tbody>
</table>

If you answered “Not Required” in Field 4a, then Validation Rules 1724, 1725, and 1736 do not apply. Do not proceed.

4b. Is TS File Included?*
- Yes
- No

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

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

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

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

<table>
<thead>
<tr>
<th>STUDYID</th>
<th>TSPARMCD</th>
<th>TSVAL</th>
<th>TSVALNF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study ID in STF</td>
<td>STSTDTC (Nonclinical) or SSTDTC (Clinical)</td>
<td>yyyy-mm-dd</td>
<td><em>Can be left blank when valid study start date is provided in TSVAL</em></td>
</tr>
</tbody>
</table>

### Study without a valid Study Start Date

<table>
<thead>
<tr>
<th>STUDYID</th>
<th>TSPARMCD</th>
<th>TSVAL</th>
<th>TSVALNF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study ID in STF</td>
<td>STSTDTC (Nonclinical) or SSTDTC (Clinical)</td>
<td><em>Can be left blank when a study start date is not available</em></td>
<td><em>Exception code as specified in the ISO 21090</em></td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Example</th>
<th>Self-Check Worksheet</th>
</tr>
</thead>
</table>
| 1. Study Files and/or datasets submitted in m5-3-5-3 (TRC not applicable study section) | 4a. What Type of TS File is Required? (Refer to guidelines in chart below.)
| TRC Requirement: No ts.xpt is needed | □ Full TS  □ Simplified TS  □ Not Required |
| | Study Start Date | Application Type | Data Type | Study Section | Required TS File Type (by Class) | Required TS File Type (by Class) |
| | 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, 5.3.12, 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, 5.3.12, 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, 5.3.12, 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, 5.3.12, 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 |

Pass
No Further Validation Needed
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**

<table>
<thead>
<tr>
<th>Study Start Date</th>
<th>Application Type</th>
<th>Data Type</th>
<th>Study Section</th>
<th>Required TS File Type (by Center)</th>
<th>Required TS File Type (by Center)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior to or on 17-Dec-16</td>
<td>NDA, BLA, or ANDA</td>
<td>Nondiagnostic</td>
<td>4.2.3.1, 4.2.3.2, 4.2.3.4</td>
<td>Simplified TS</td>
<td>Not Required</td>
</tr>
<tr>
<td>Prior to or on 17-Dec-16</td>
<td>NDA, BLA, or ANDA</td>
<td>Clinical</td>
<td>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</td>
<td>Simplified TS</td>
<td>Simplified TS</td>
</tr>
<tr>
<td>Prior to or on 17-Dec-17</td>
<td>Commercial IND</td>
<td>Nondiagnostic</td>
<td>4.2.3.1, 4.2.3.2, 4.2.3.4</td>
<td>Simplified TS</td>
<td>Not Required</td>
</tr>
<tr>
<td>Prior to or on 17-Dec-17</td>
<td>Commercial IND</td>
<td>Clinical</td>
<td>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</td>
<td>Not Required</td>
<td>Not Required</td>
</tr>
<tr>
<td>After 17-Dec-16</td>
<td>NDA, BLA, or ANDA</td>
<td>Nondiagnostic</td>
<td>4.2.3.1, 4.2.3.2, 4.2.3.4</td>
<td>Full TS</td>
<td>Not Required</td>
</tr>
<tr>
<td>After 17-Dec-16</td>
<td>NDA, BLA, or ANDA</td>
<td>Clinical</td>
<td>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</td>
<td>Full TS</td>
<td>Full TS</td>
</tr>
<tr>
<td>After 17-Dec-17</td>
<td>Commercial IND</td>
<td>Nondiagnostic</td>
<td>4.2.3.1, 4.2.3.2, 4.2.3.4</td>
<td>Full TS</td>
<td>Not Required</td>
</tr>
<tr>
<td>After 17-Dec-17</td>
<td>Commercial IND</td>
<td>Clinical</td>
<td>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</td>
<td>Not Required</td>
<td>Not Required</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Example</th>
<th>Self-Check Worksheet</th>
</tr>
</thead>
</table>
| 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 | **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  

<table>
<thead>
<tr>
<th>Study Start Date</th>
<th>Application Type</th>
<th>Data Type</th>
<th>Study Section</th>
<th>Required TS File Type (by Center)</th>
<th>Required TS File Type (by Center)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior to or on 17-Dec-16</td>
<td>NDA, BLA, or ANDA</td>
<td>Nonclinical</td>
<td>4.1.3.1, 4.2.3.2, 4.2.3.4</td>
<td>Simplified TS</td>
<td>Not Required</td>
</tr>
<tr>
<td>Prior to or on 17-Dec-16</td>
<td>NDA, BLA, or ANDA</td>
<td>Clinical</td>
<td>5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2</td>
<td>Simplified TS</td>
<td>Simplified TS</td>
</tr>
<tr>
<td>Prior to or on 17-Dec-17</td>
<td>Commercial IND</td>
<td>Nonclinical</td>
<td>4.2.3.1, 4.2.3.2, 4.2.3.4</td>
<td>Simplified TS</td>
<td>Not Required</td>
</tr>
<tr>
<td>Prior to or on 17-Dec-17</td>
<td>Commercial IND</td>
<td>Clinical</td>
<td>5.3.1.1, 5.3.1.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2</td>
<td>Not Required</td>
<td>Not Required</td>
</tr>
<tr>
<td>After 17-Dec-16</td>
<td>NDA, BLA, or ANDA</td>
<td>Nonclinical</td>
<td>4.2.3.1, 4.2.3.2, 4.2.3.4</td>
<td>Full TS</td>
<td>Not Required</td>
</tr>
<tr>
<td>After 17-Dec-16</td>
<td>NDA, BLA, or ANDA</td>
<td>Clinical</td>
<td>5.3.1.1, 5.3.1.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2</td>
<td>Full TS</td>
<td>Full TS</td>
</tr>
<tr>
<td>After 17-Dec-17</td>
<td>Commercial IND</td>
<td>Nonclinical</td>
<td>4.2.3.1, 4.2.3.2, 4.2.3.4</td>
<td>Full TS</td>
<td>Not Required</td>
</tr>
<tr>
<td>After 17-Dec-17</td>
<td>Commercial IND</td>
<td>Clinical</td>
<td>5.3.1.1, 5.3.1.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2</td>
<td>Not Required</td>
<td>Not Required</td>
</tr>
</tbody>
</table>
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)

### ALL APPLICATION TYPES

- 66%: Missing ts.xpt
- 25%: Missing Study Start Date in ts.xpt
- 6%: Invalid Study Start Date in ts.xpt
- 2%: Multiple Study Start Dates in ts.xpt
- <1%: Study IDs Mismatch

[Pie chart showing error distribution]
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

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

### 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

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

4b. Is TS File Included?*

- [ ] Yes
- [ ] No

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

4d. Does Study ID in STF (Field 3d) & TS Files Match?

- [ ] Yes
- [ ] No

If you answered “No” in Field 4e, Validation Rule 1734 FAILS. Do not proceed.

4e. Study Start Date in TS File

- [ ] Yes
- [ ] No

If Study Start Date exists, Is it Valid?

- [ ] Yes
- [ ] No

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

---

**www.fda.gov**
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

**References:**
**TRC Validation Rule 1734 (Section 4c)**

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

<table>
<thead>
<tr>
<th>Example</th>
<th>Self-Check Worksheet</th>
</tr>
</thead>
</table>
| 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]**

- **3d. Study ID in STF File**
  - **Study ABC**

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

**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
<table>
<thead>
<tr>
<th>Format</th>
<th>SAS Date Format</th>
<th>mm/dd/yyyy</th>
<th>dd-mm-mmm-yyyy</th>
<th>yyyy-mm-dd</th>
<th>dd-mmm-yyyy</th>
</tr>
</thead>
<tbody>
<tr>
<td>mm/dd/yyyy</td>
<td>dd-mm-mmm-yyyy</td>
<td>dd-mm-yyyy</td>
<td>dd-mmm-yyyy</td>
<td>yyyy-mm-dd</td>
<td>dd-mmm-yyyy</td>
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<tr>
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<tr>
<td>yyyy</td>
<td>month-yyyy</td>
<td>yyyy-mm-dd</td>
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<td></td>
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<td>yyyy-mm-dd</td>
</tr>
</tbody>
</table>

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## 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

<table>
<thead>
<tr>
<th>Example</th>
<th>Self-Check Worksheet</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Study Files and/or datasets submitted in m5-3-5-1 (TRC applicable study section)</td>
<td></td>
</tr>
<tr>
<td>Study Start Date: 2018-01-01</td>
<td></td>
</tr>
<tr>
<td>TRC Requirement: Full TS is needed</td>
<td></td>
</tr>
</tbody>
</table>

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

### Study Date Format Requirement

- **TS.XPT**
  - Study Start Date: 42622
  - Study Start Date in SAS Date Format: **Fail Rule 1734**
## Self-Check Worksheet (1735 & 1736 Validation Error)

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

<table>
<thead>
<tr>
<th>Study Start Date</th>
<th>Application Type</th>
<th>Standardized Datasets Required?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior to or on 17-Dec-18</td>
<td>NOA, IUA, or IHEOA</td>
<td>Not Required</td>
</tr>
<tr>
<td>After 17-Dec-18</td>
<td>NOA, IUA, or IHEOA</td>
<td>Required</td>
</tr>
<tr>
<td>Prior to or on 17-Dec-17</td>
<td>Commercial IND</td>
<td>Not Required</td>
</tr>
<tr>
<td>After 17-Dec-17</td>
<td>Commercial IND</td>
<td>Required</td>
</tr>
</tbody>
</table>

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 date is after the date stated, however, clinical data technical rejection criteria will not be applicable until further notice.

### Clinical (inSDTM datasets)

**5g. Is DM File Included?**
- **Yes**
- **No**

**5h. Is Define File Included?**
- **Yes**
- **No**

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

### Analysis (inADaM datasets)

**5j. Is ADSL File Included?**
- **Yes**
- **No**

**5k. Is Define File Included?**
- **Yes**
- **No**

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

### Reference:

“Technical Rejection Criteria Self-Check Worksheet”
[https://www.fda.gov/media/123098/download](https://www.fda.gov/media/123098/download)

“Technical Rejection Criteria Self-Check Worksheet Instructions”
[https://www.fda.gov/media/123099/download](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)
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)

---

**Self-Check Worksheet**

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

<table>
<thead>
<tr>
<th>Study Start Date</th>
<th>Application Type</th>
<th>Standardized Datasets Required?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior to or on 17-Dec-16</td>
<td>NDA, BLA, or ANDA</td>
<td>Not Required</td>
</tr>
<tr>
<td>After 17-Dec-16</td>
<td>NDA, BLA, or ANDA</td>
<td>Required</td>
</tr>
<tr>
<td>Prior to or on 17-Dec-17</td>
<td>Commercial IND</td>
<td>Not Required</td>
</tr>
<tr>
<td>After 17-Dec-17</td>
<td>Commercial IND</td>
<td>Required</td>
</tr>
</tbody>
</table>

---

**Files Referenced in stf.xml**

- acrf.pdf
- ds.xpt
- mah.xpt
- suppda.xpt
- suppdm.xpt
- suppdx.xpt
- ts.xpt
- tv.xpt
- aex.xpt
- dvl.xpt
- pex.xpt
- suppda.xpt
- suppdm.xpt
- svx.xpt
- vs.xpt
- cm.xpt
- eg.xpt
- sdx.xpt
- suppd.xpt
- tx.xpt
- co.xpt
- ex.xpt
- sdx.xpt
- suppeg.xpt
- te.xpt
- cдрq.pdf
- iex.xpt
- suppae.xpt
- suppex.xpt
- ti.xpt

---

**Fail Rule 1736**

- dm.xpt and define.xml are missing

---
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)

ALL APPLICATION TYPES

- Incorrect define.xml file tag (42%)
- Incorrect define.xml & XPT dataset file tags (17%)
- Incorrect XPT dataset file tag (14%)
- Legacy Datasets Submitted When Standardized Required (27%)
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)

Files Referenced in stf.xml
- define.xml
- dm.xpt

Define.xml is tagged as “data-tabulation-dataset-sdtm”

**Fail Rule 1735**
FDA published Revised Study Data Technical Rejection Criteria (Revised Jan. 2019) and Study Data Self-Check Worksheet to assist sponsors with the TRC Conformance

- Per FD&C Act Section 745A(a), sponsors must conform to standards in the FDA Data Standard Catalog
- NDA, BLA, ANDA studies that started after Dec. 17th, 2016
- Commercial IND studies that started after Dec. 17th, 2017
- FDA issued “Providing Regulatory Submissions in Electronic Format - Standardized Study Data: Guidance for Industry”
- FDA published Study Data Self-Check Worksheet & Instruction
- FDA will give the industry 90 days’ notice on the eCTD website prior to the criteria becoming effective

**Implementation Timeline**

- Study Data Technical Rejection Criteria are **REQUIRED** but **NOT IMPLEMENTED**
- FDA Monitors & Analyzes the Study Data Conformance

* Note: When a submission is technically-rejected, the submission sequence is not transferred into the FDA electronic document rooms
The author would like to thank In Young Choi, Lina Cong, Jiang Xu, Jonathan Resnick, Heather Crandall, Jeffery Florian, Lisa Lin, Gang Wang, and other FDA staff for their time and effort in helping collect and analyze data and information as presented in this presentation.