

How to Submit Trial Summary dataset in different situations of study data submissions to improve the conformance rate

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Abstract

As part of the human drug application submission process clean, complete and validated study data is critical to accelerate human drug application review and approval process.

Technical Rejection Criteria for Study Data are being included to the existing electronic common technical document (eCTD) validation criteria and will take effect soon. From current study data conformance analysis approximately 90% high-level eCTD validation errors related the study data are validation error 1734 (which fails the validation for 1734 validation criteria). The validation criteria 1734 are related to Trial Summary dataset (ts.xpt) and study start date, therefore, properly submitting ts.xpt is the key to improve the conformance rate for technical rejection criteria.

The poster will describe common reasons result in 1734 validation failures and how to properly submit ts.xpt in different scenarios that will cover submitting ts.xpt at multiple eCTD sections for a study, avoiding submitting more than one ts.xpt under a study tagging file or an eCTD section, and so on.

Introduction

To enforce and monitor submitting CDISC standards data to FDA the validation of Technical Rejection Criteria for Study Data will take effective in the near future. The study data for the submission to FDA should conform to the required standards described in the FDA Data Standards Catalog.

As we know CDISC standards are required if a study starts after Dec 17, 2016 for NDA, BLA, and ANDA and Dec 17, 2017 for Commercial IND. Therefore, the study data in CDISC format should be submitted after cut-off date and the validation will be performed to verify if full ts.xpt with DM, Define and ADSL have been included in the study data submission. Simplified ts.xpt is also required if a study starts before or on Dec 17, 2016 for NDA, BLA, and A NDA and Dec 17, 2017 for Commercial IND.

The poster discusses the conformance rate, Validation Criteria 1734 – ts.xpt, and Tips for Submitting ts.xpt in Special Scenarios. It will give the sponsor’s an idea to handle the upcoming validation for technical rejection criteria.

Conformance Analysis

- Data for conformance analysis are received by CDER from Jan 1, 2019 to Jun 30, 2020 for ANDA, BLA, IND and NDA.
- Conformance analysis reveals 1734 validation failure is key factor affected the conformance rate.

Conformance Analysis
From Jan 1, 2019 to June 30 2020

Application Type	Number of Submissions with Datasets and Reports*	Number and % of Submissions with Validation Errors 1734	Number and % of Submissions with validation Errors 1736	Number and % of Submissions with High level Errors 1734 and 1736	Number and % of 1734 errors in all High level Errors
ANDA	1131	287 (25.4%)	87 (7.7%)	366 (32.4%)	287 (78.4%)
BLA	374	144 (38.5%)	17 (4.5%)	158 (42.2%)	144 (91.1%)
IND	2724	1655 (60.8%)	80 (2.9%)	1712 (62.8%)	1655 (96.7%)
NDA	1116	430 (38.5%)	39 (3.5%)	459 (41.1%)	430 (93.7%)
All Applications	5345	2516 (47.1%)	223 (4.2%)	2695 (50.4%)	2516 (93.4%)

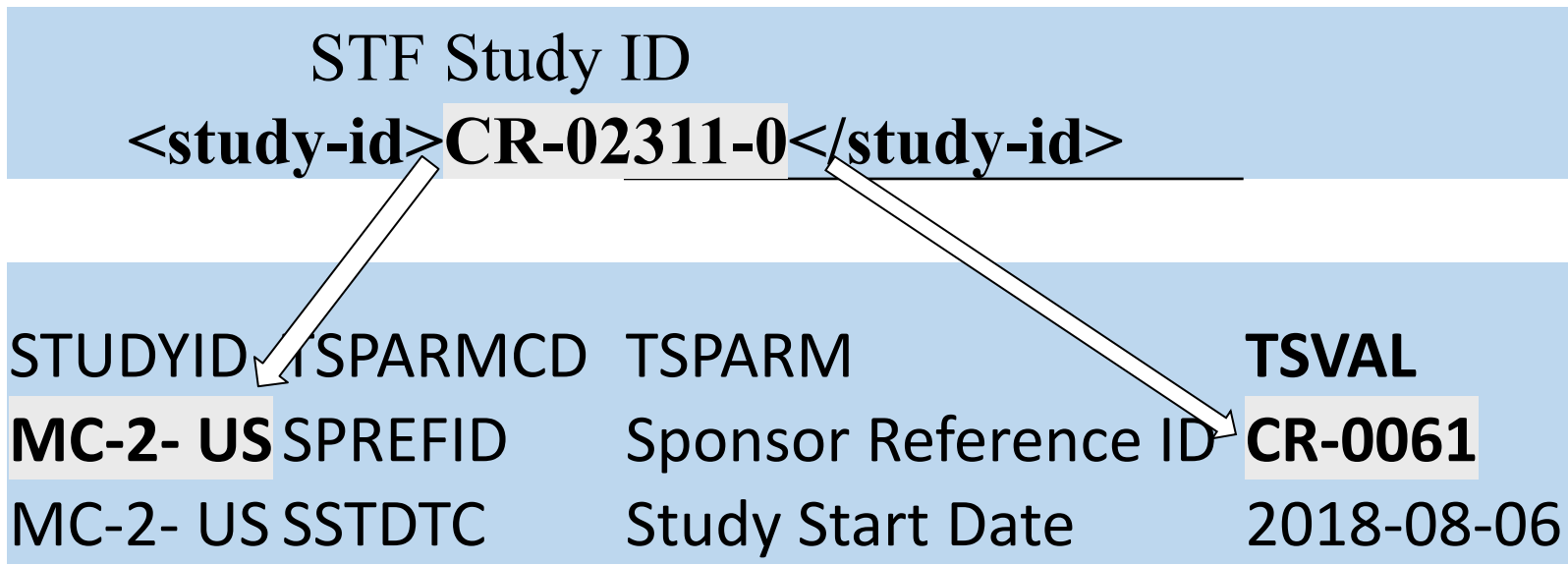
*Submissions with study data and/or reports in eCTD sections that apply to Technical Rejection Criteria.

Validation Criteria 1734 – ts.xpt

1734 validation criteria: ts.xpt must be present and have information on study start date for each study in eCTD section 4.2 and 5.3.

➤ Common reasons result in 1734 validation failures

- Missing ts.xpt
- STUDYID mismatch



- ts.xpt doesn’t contain study start date
 - Invalid value for study start date
- How to submit ts.xpt to pass 1734 validation
- Submitting a ts.xpt in required eCTD section
 - ts.xpt should contain either a study ID (STUDYID) or Sponsor Reference ID (SPREFID) value that matches with the STF study ID.
 - ts.xpt should have valid study start date

Tips for Submitting ts.xpt in Special Scenarios

➤ Legacy study data converting to standardized study data

When submitting SDTM and ADaM datasets from legacy data conversion the legacy datasets are also included in the submission. In this case ts.xpt is not required for the legacy data submission if legacy data and standardized data are on the same submission or legacy data are submitted after standardized data.

- study-a
 - analysis
 - adam
 - legacy
 - tabulations
 - legacy
 - ts.xp is not required
 - sdm
 - ts.xpt

➤ Datasets for safety update

When submitting the datasets for safety update a ts.xpt is not required if there is a ts.xpt submitted in previous submission.

➤ Information Request (IR) for study data

It is not necessary to submit a ts.xpt dataset for IR dataset submission If CDISC standardized datasets or legacy datasets with ts.xpt had been submitted before information request,

➤ Study data are submitted to multiple eCTD sections

- When study data are submitted to two different eCTD sections and these two eCTD sections are applied for Technical Rejection Criteria, ts.xpt should be submitted for both eCTD sections even if a study started before the cut-off date.
- When study data will be submitted to two different eCTD sections that one eCTD section is applied for Technical Rejection Criteria and the other one doesn’t. A ts.xpt should be only submitted for the eCTD section is applied for Technical Rejection Criteria .

Conclusions

From conformance analysis we can see that validation error 1734 totally affect the conformance rate. Properly submitting the ts.xpt is the most important for improving the quality of study data and technical rejection criteria conformance rate. The poster demonstrates the common reasons caused validation error 1734 and solution for how to submit ts.xpt in common cases and special scenarios. These may help sponsors to understand why validation error 1734 occurred and how to resolve the issues during the preparing the submission.

References

- “Providing Regulatory Submissions in Electronic Format -Standardized Study Data: Guidance for Industry”
<https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM292334.pdf>
- “Technical Rejection Criteria For Study Data”
<https://www.fda.gov/media/100743/download.pdf>
- “Study Data Technical Conformance Guide”
<https://www.fda.gov/media/136460/download.pdf>
- “FDA Data Standards Catalog”
<https://www.fda.gov/industry/fda-resources-data-standards/study-data-standards-resources>
- “Providing Regulatory Submissions In Electronic Format - Submissions Under Section 745a(a) Of The FD&C Act: Guidance For Industry”
<https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-regulatory-submissions-electronic-format-submissions-under-section-745aa-federal-food-drug.pdf>