How to submit datasets in study data submissions to comply with Technical Rejection Criteria PP07

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Abstract

As part of the human drug application submission process clean, complete and validated study data are critical to accelerate human drug application review and approval process. Technical Rejection Criteria (TRC) for Study Data were added to the existing electronic common technical document (eCTD) validation criteria and will take effect on Sep 15, 2021. Current conformance monitoring reveals the most common TRC failure to be eCTD validation 1734. eCTD validation study data for Technical Rejection Criteria the most of high-level eCTD validation failures related the study data are validation criteria 1734. The validation criteria 1734 is related to the Trial Summary dataset (ts.xpt) which contains the study start date and field to indicate if the study is not applicable to study data standards. Therefore, properly submitting a ts.xpt is the key to pass the validation for technical rejection criteria.
This paper will describe common reasons for1734 validation failures, how to properly submit ts.xpt in different scenarios, and cover other types of validation failures that may occurred on the validation for Technical Rejection Criteria.

Introduction

To enforce and monitor submitting CDISC data standards data to FDA the Technical Rejection Criteria for Study Data will take effect on Sept 15, 2021. As of March 15th, 2021 FDA has been sending a warning notice to sponsors if a submission contains study information and fails eCTD validations in TRC.

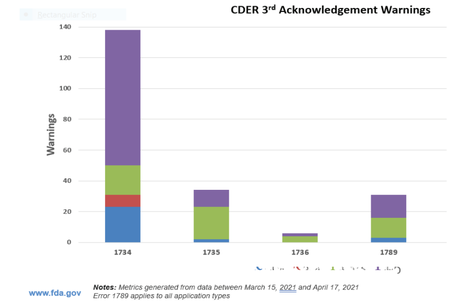
As we know CDISC standards are required if a study starts after Dec 17, 2016 for NDA, BLA, and ANDA and Dec 17, 2017 for Commercial IND. Therefore, the study data should be submitted in CDISC standards formats listed in the FDA Data Standards Catalog. The TRC validation will verify if full TS.xpt with DM, Define, ADSL and invalid study tagging files (stf) have been included in the study data submission if a study starts after FDA data standards required dates. A simplified TS.xpt is required if a study starts before FDA data standards required dates or or is a type of study not applicable to the FDA data standards.

The poster will discuss1734 validation error code - ts.xpt, and Tips for Submitting ts.xpt in Special Scenarios. These will give the sponsor an idea how to handle the upcoming validation in TRC.

TRC Warning Notices

- TRC Warning Notices are sent by CDER from March 15, 2021 to April 17, 2021 for ANDA, BLA, IND and NDA.
- TRC warning notices reveal that 1734 error is common failure reason that affect TRC conformance rate.

WARNINGS FROM CDER



1734 Validation error – ts.xpt

1734 validation error: ts.xpt must be present and have information on study start date for each study in TRC applied eCTD sections.

➢ Common reasons result in 1734 validation failures

- Missing ts.xpt
- STUDYID mismatch: A study ID (STUDYID) or Sponsor Reference ID (SPREFID) value doesn't match with the STF study ID
- ts.xpt doesn't contain study start date or TSVALNF=NA
- Invalid value for study start date

➢ How to submit ts.xpt to pass1734 validation

- Submitting a ts.xpt in TRC applied eCTD sections
- ts.xpt should contains 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 or or TSVALNF=NA

Tips for Submitting ts.xpt in Special Scenarios

➢ Legacy Study Data Conversion to Standardized Study Data

When submitting SDTM and ADaM data from legacy data conversion "The legacy data (i.e., aCRF, legacy tabulation data, and legacy analysis data) may be needed in addition to the submission of converted data." In this case it is not necessary to submit a ts.xpt with the legacy data if legacy data and CDISC standards data are on same submission or legacy data submission is after CDISC standards data submission.

➢ Safety update (datasets) with study data submission

When submitting the safety update datasets, 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 needed to submit ts.xpt dataset for IR datasets submission if CDISC standards datasets or legacy datasets with ts.xpt had submitted before information request.

➢ Study data submitted to multiple eCTD sections

- When a study has study data that will be submitted to two different TRC applied eCTD sections, a ts.xpt should be submitted for both eCTD sections even if a study started before the cut-off date.
- When a study has study data that will subm it to two different eCTD sections where one eCTD section is required to submit data in CDISC format but the other one doesn't. ts.xpt should be only submitted for the eCTD section to which TRC applies.

Conclusions

From conformance analysis we can see that 1734 errors (ts.xpt) totally affect TRC 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 1734 errors and solution for how to submit ts.xpt in common cases and special scenarios. These may help sponsors to understand why 1734 error occurred how to resolve the issues during the preparation these 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

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