

# How to submit study data to comply with Technical Rejection Criteria for Study Data PP15

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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 for Study Data are being included to the existing electronic common technical document (eCTD) validation criteria and will become effective on September 15, 2021. Warning notice will be sent between March 15th and Sept. 15th, 2021 for submissions failing eCTD validations in Technical Rejection Criteria for Study Data (TRC). From analyzing Warning Notice that we sent out the most of Warning Notice error code related the study data are validation criteria 1734. The validation criteria 1734 is related to Trial Summary dataset (ts.xpt) and study start date, therefore, properly submitting ts.xpt is the key to pass the validation for technical rejection criteria.

The paper dissects Warning Notice that sent out by CDER and common reasons result in validation failures for different application types, use questions and answers tell sponsors or applicants how to submit study data in different application types to comply with Technical Rejection Criteria, for Study Data.

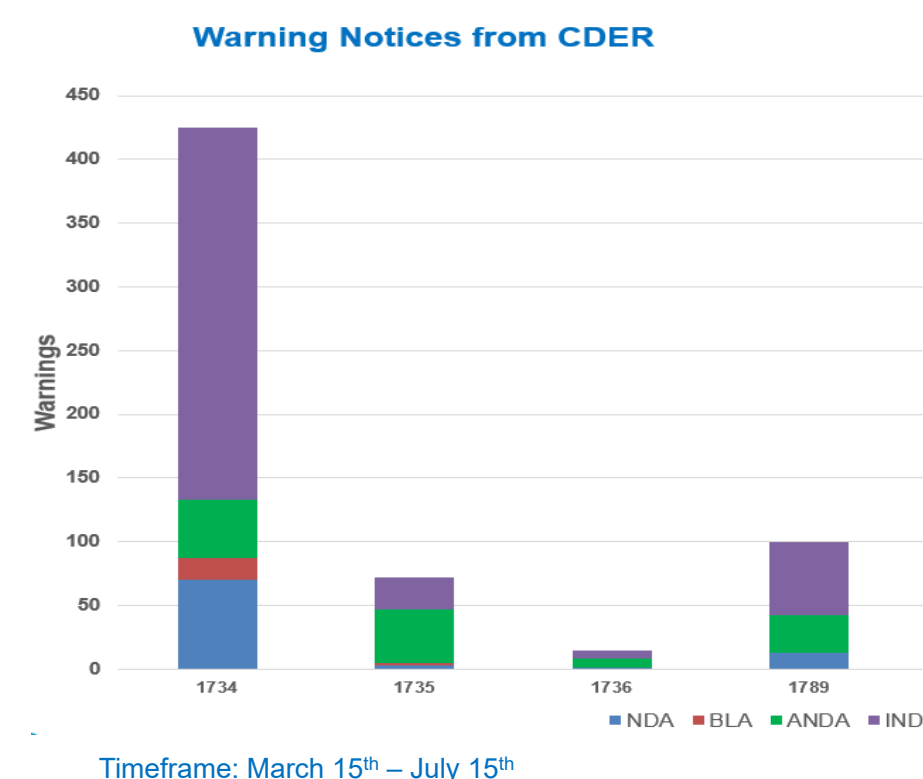
## Introduction

As we know CDISC standards are required if a study starts on/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 valid study tagging files (stf) have been included in the study data submission if a study starts on/ after FDA data standards required dates. A simplified TS.xpt is required if a study starts before FDA data standards required dates or is a type of study not applicable to the FDA data standards.

The poster will discuss 1734 validation error code - ts.xpt, cover different types of validation failures that may be occurred on the validation for TRC. and Questions and Answers for TRC validation. 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 July 15, 2021 for ANDA, BLA, Commercial IND and NDA.



### Summary of TRC Warning Notices

- TRC warning notices reveal that 1734 error code is common failure reason that affect TRC conformance rate.
- The most of 1734 errors occurred to Commercial IND.

#### Error reasons of 1734 for non- Clinical Studies of Commercial IND

| Error Reason             | # of 1734 Errors | % of all 1734 Errors |
|--------------------------|------------------|----------------------|
| Missing TS File          | 545              | 92%                  |
| Study ID Mismatch        | 40               | 7%                   |
| Invalid Study Start Date | 4                | 1%                   |
| Missing Study Start Date | 4                | 1%                   |
| Total                    | 593              |                      |

- The most of 1735 errors occurred to ANDA.

#### Error reasons of 1735 for ANDA Clinical Studies

| Error Reason                            | # of 1735 Errors | % of all 1735 Errors |
|-----------------------------------------|------------------|----------------------|
| Invalid File Tag for DM                 | 0                | -                    |
| Invalid File Tag for ADSL               | 0                | -                    |
| Invalid File Tag for Define             | 53               | 98%                  |
| Invalid File Tag for DM & Define        | 1                | 2%                   |
| Invalid File Tag for ADSL & Define      | 0                | -                    |
| Invalid File Tag for DM, ADSL, & Define | 0                | -                    |
| Total                                   | 54               |                      |

## Questions and Answers for TRC validation

- Question 1:** We received a warning notice with the validation code of 1734 – no ts.xpt found in this study from IND non-clinical submission. Is the ts.xpt required to be included even when only single PDF file for the nonclinical report is submitted?
- Answer1:** Yes, a simplified ts.xpt is required if a study started prior to Dec 17, 2017 or SEND datasets are required if a study starts on/after Dec 17, 2017 for non-clinical study of commercial IND with non-clinical study if a study report with the file tag ‘pre-clinical-study-report’, ‘legacy-clinical-study-report’, or ‘study-report-body’ in the study tagging file (STF), and/or an xpt file is submitted.
- Question 2:** We got the error message 1735 error about Incorrect File Tag for define.xml files in the recently submitted ANDA as original application. We use tag file ‘analysis-dataset-adam’ for ADaM define file and ‘data-tabulation-dataset-sdtm’ for SDTM define file. Could you advise which file tag we should use for the define files?
- Answer 2:** The file tag ‘analysis-data-definition’ should be used for ADaM define files and ‘data-tabulation-data-definition’ for SDTM define files.
- Question 3:** We received a 1789 error for our submission. How can we fix this in the future?
- Answer 3:** Validation rule 1789 checks that all files submitted in a study section are included in a Study Tagging File (STF). In future submissions, ensure that all study files have an associated STF file.
- Question 4:** We submitted SDTM and ADaM datasets in the initial filing for a study. If we submit the safety update datasets for this study, do we need to resubmit ts.xpt, DM.xpt, ADSL.xpt and define files for the study?
- Answer 4:** The validation checks past sequences so there is no need to resubmit those datasets if there are no updates to the files.

## Conclusions

From conformance analysis of warning notice 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 includes the Questions and Answers for TRC validation to tell sponsors and applicants how to submit study data to comply with Technical Rejection Criteria. These may help sponsors to understand why error occurred and how to resolve the issues during the preparation their submissions.

## References

- “Providing Regulatory Submissions in Electronic Format -Standardized Study Data: Guidance for Industry”  
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- “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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