CDISC News

- **Possible hurdles and timelines for FDA adding SDTM 3.3 and Define.xml 2.1 to the Standards Catalog**
- **Upcoming ADaM updates**
- **SHARE moving to a new platform and being rebranded as CDISC Library**
- **New and upcoming Therapeutic Area User Guides**
- **Recent and ongoing organizational changes at CDISC**

ADaM Updates

- ADaM documents in the CDISC development cycle
  - 1 doc recently published

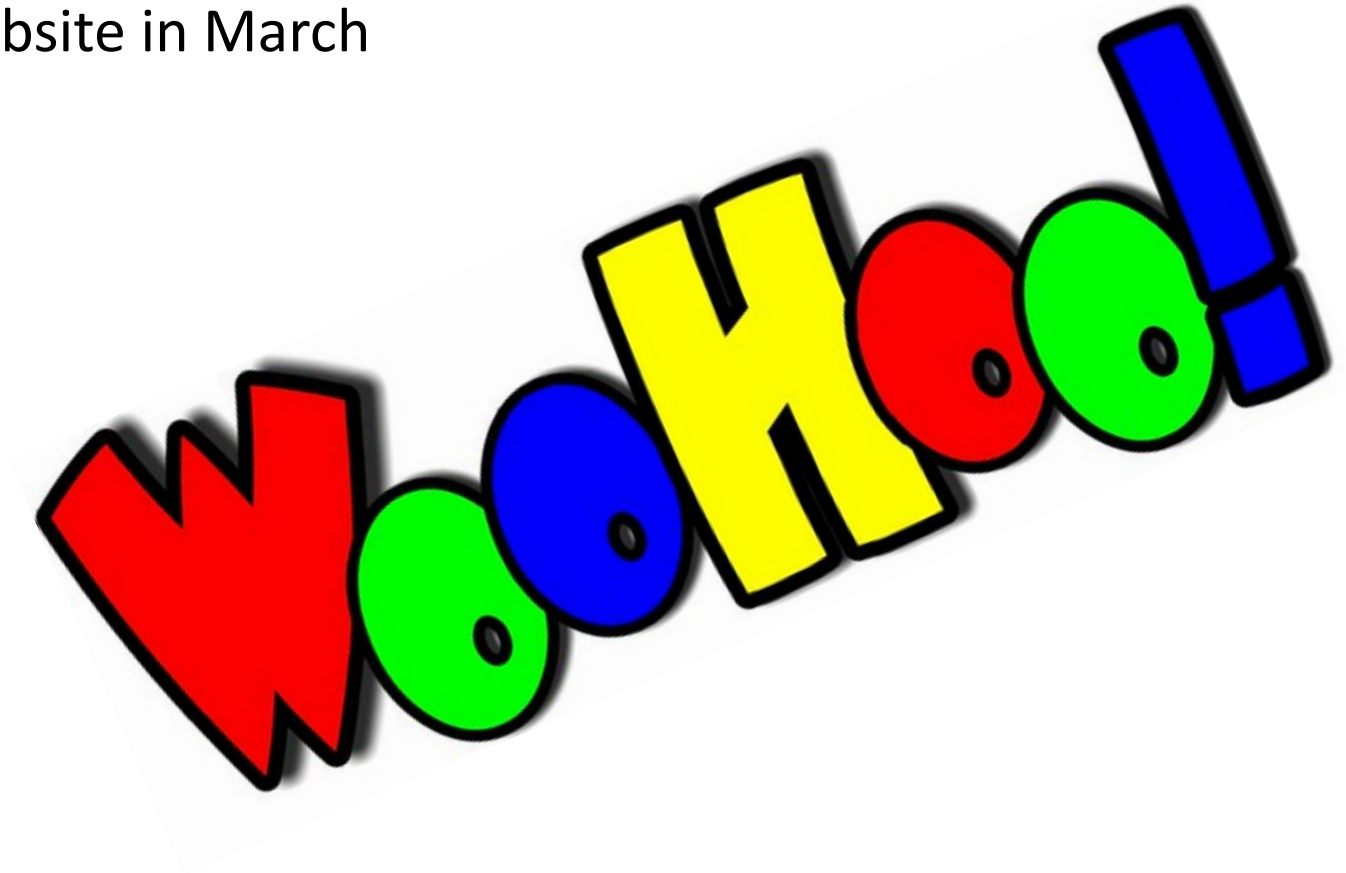
  - 3 docs soon to be finalized
  - 1 doc in public review
  - 2 docs preparing for public review
  - 6+ docs in development

  ———

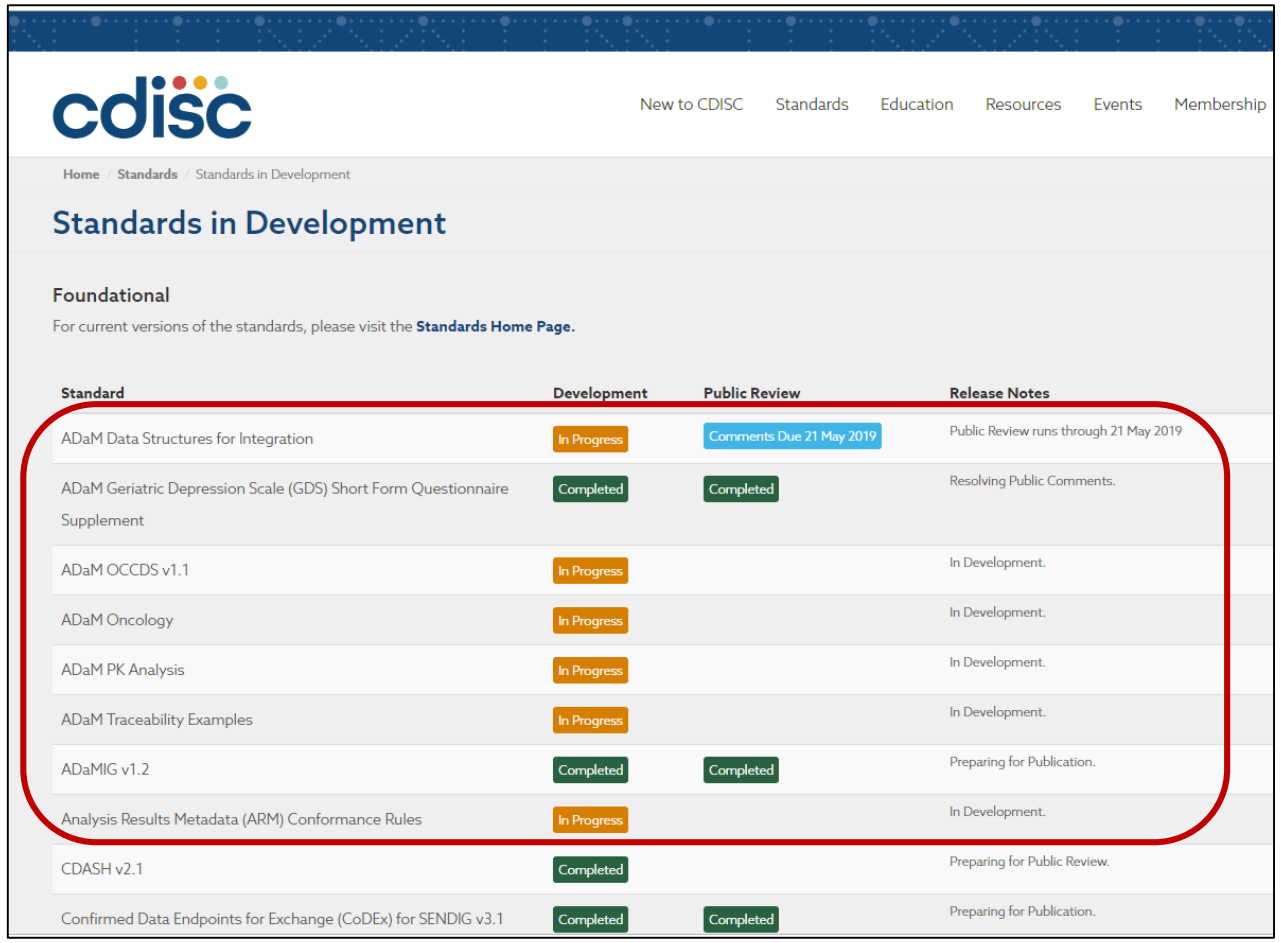
  12+ ADaM docs in various stages of development

Recently Finalized ADaM doc

- ADaM Conformance Rules v2.0
  - Published to CDISC website in March
  - Includes rules for
    - ADaMIG v1.0 and 1.1
    - OCCDS v1.0



https://www.cdisc.org/standards/in-development



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New to CDISC | Standards | Education | Resources | Events | Membership

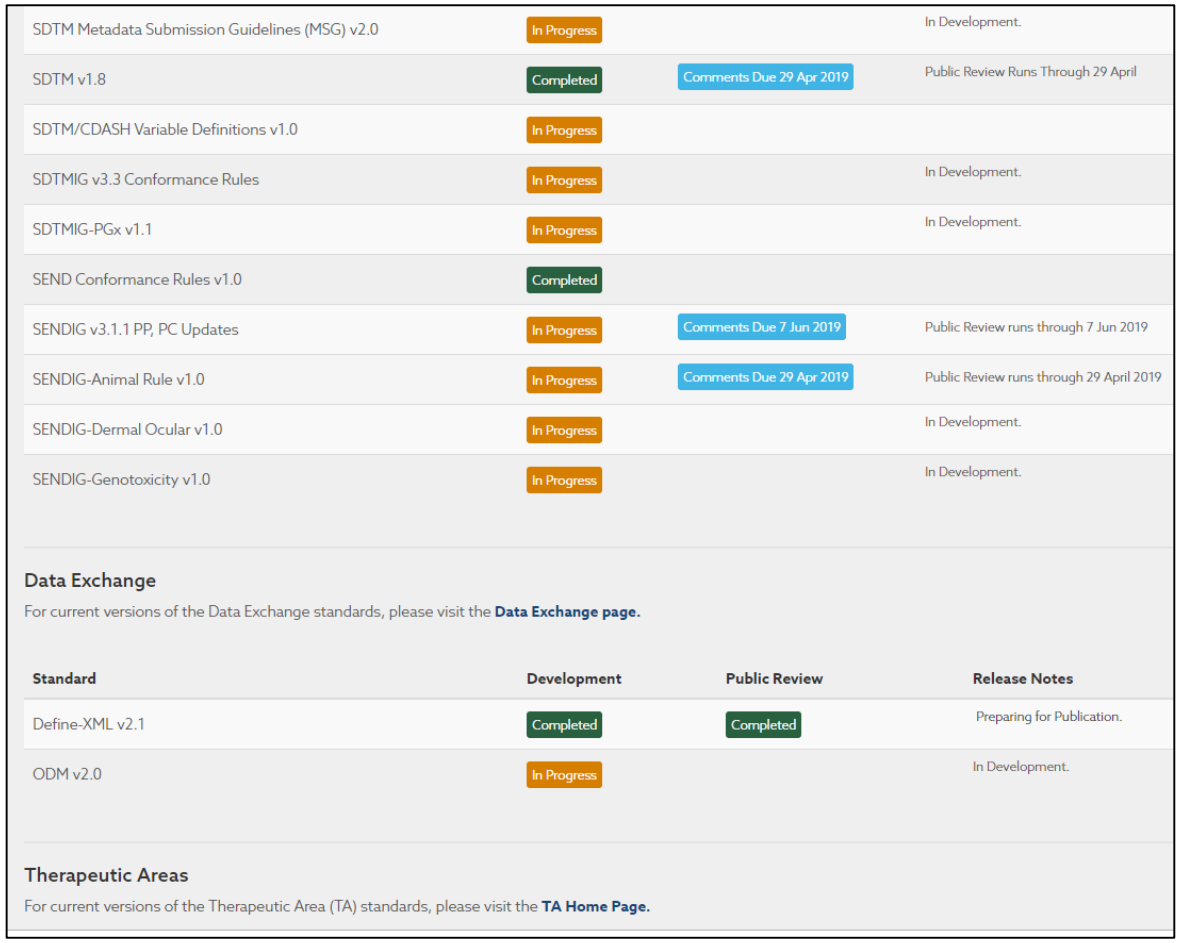
Home / Standards / Standards in Development

Standards in Development

Foundational

For current versions of the standards, please visit the **Standards Home Page.**

Standard	Development	Public Review	Release Notes
ADaM Data Structures for Integration	In Progress	Comments Due 21 May 2019	Public Review runs through 21 May 2019
ADaM Geriatric Depression Scale (GDS) Short Form Questionnaire Supplement	Completed	Completed	Resolving Public Comments.
ADaM OCCDS v1.1	In Progress		In Development.
ADaM Oncology	In Progress		In Development.
ADaM PK Analysis	In Progress		In Development.
ADaM Traceability Examples	In Progress		In Development.
ADaMIG v1.2	Completed	Completed	Preparing for Publication.
Analysis Results Metadata (ARM) Conformance Rules	In Progress		In Development.
CDASH v2.1	Completed		Preparing for Public Review.
Confirmed Data Endpoints for Exchange (CoDEx) for SENDIG v3.1	Completed	Completed	Preparing for Publication.



SDTM Metadata Submission Guidelines (MSG) v2.0	In Progress		In Development.
SDTM v1.8	Completed	Comments Due 29 Apr 2019	Public Review Runs Through 29 April
SDTM/CDASH Variable Definitions v1.0	In Progress		
SDTMIG v3.3 Conformance Rules	In Progress		In Development.
SDTMIG-PGx v1.1	In Progress		In Development.
SEND Conformance Rules v1.0	Completed		
SENDIG v3.1.1 PP, PC Updates	In Progress	Comments Due 7 Jun 2019	Public Review runs through 7 Jun 2019
SENDIG-Animal Rule v1.0	In Progress	Comments Due 29 Apr 2019	Public Review runs through 29 April 2019
SENDIG-Dermal Ocular v1.0	In Progress		In Development.
SENDIG-Genotoxicity v1.0	In Progress		In Development.

Data Exchange

For current versions of the Data Exchange standards, please visit the **Data Exchange page.**

Standard	Development	Public Review	Release Notes
Define-XML v2.1	Completed	Completed	Preparing for Publication.
ODM v2.0	In Progress		In Development.

Therapeutic Areas

For current versions of the Therapeutic Area (TA) standards, please visit the **TA Home Page.**

Soon to be Finalized ADaM docs

- ADaM v2.1 Considerations *(imminent)*
  - 1-page doc to be attached to ADaM v2.1
  - Describes things to be aware of when using the doc created in 2009:
    - Points to OCCDS (structure not mentioned in ADaM v2.1)
    - Points to Define-XML (more metadata than in Define-XML v1.0)
    - Points to table titled "Other CDISC Documents and their Applicability to ADaMIG Versions”
- ADaMIG v1.2 *(summer?)*
  - Adds stratification variables, bi-directional tox variables
  - Clarifies pre-ADSL, relationships between primary and secondary variables
  - Does not include PARQUAL
- ADaM Geriatric Depression Scale (GDS) Short Form Questionnaire Supplement *(summer?)*

ADaM docs in Public Review

- ADaM Structures for Integration – public comment closes May 21
  - See other presentation for details

ADaM docs Preparing for Public Review

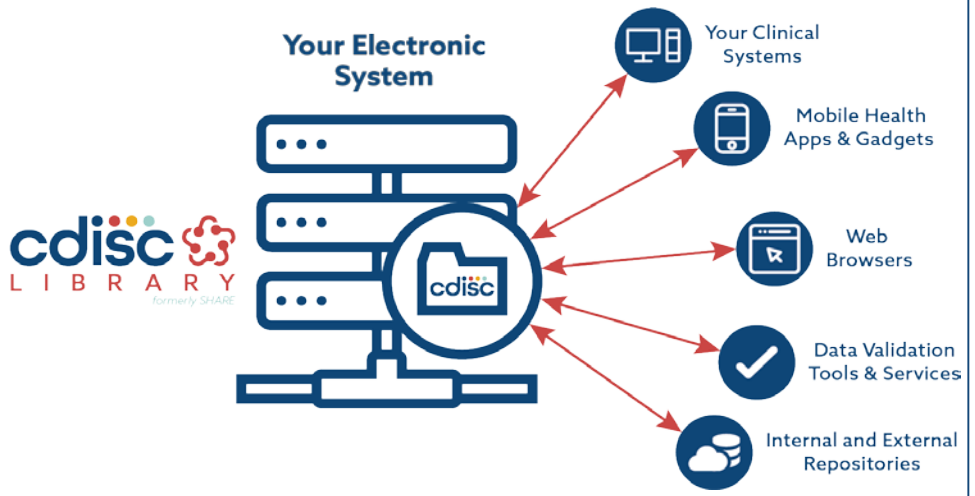
- ADaMIG-MD (Medical Devices) is with CDISC Copy Editing
  - Applies ADSL, BDS, and OCCDS to medical devices
  - Adds SPDEVID
  - Adds structure ADDL (Device-Level Analysis Dataset)
- OCCDS v1.1 is wrapping up CDISC Internal Review
  - Adds more complex examples
    - Multiple input datasets
    - Multiple coding paths
  - Adds SRCDOM and SRCVAR variables (same as in BDS)

ADaM docs in Development

- ADNCA (Non-Compartmental Analysis) doc for PK data
- ADaM Traceability Examples doc
- ADaM Oncology doc
- Additional ADaM Questionnaire Supplements
- More ADaM Conformance Rules for

  Analysis Results Metadata, ADaMIG v1.2, …
- ADaM v3.0
  - Project to combine all (or most?) ADaM documents together

cdisc LIBRARY
formerly SHARE



- New platform based on semantic technol
- Linked metadata model better suited for development of CDISC standards conten
- Expanded Restful API

- General release April 10 2019.

Form

Content:

DataCollection:
CDASH 1-0
CDASHIG 1-1-1
CDASHIG 2-0

DataTabulation:
SDTM 1-2
SDTM 1-3
SDTM 1-4
SDTM 1-5
SDTM 1-6
SDTM 1.7

DataAnalysis:
ADaM-ADAE-1-0
ADaM-TTE-1-0
ADaM –OCCDS-1-0
ADaMIG-1-0
ADaMIG-1-1

SDTMIG 3-1-2
SDTMIG 3-1-3
SDTMIG 3-2
SDTMIG 3-3
SDTMIG AP 1-0
SDTMIG MD 1-1
SDTMIG PGx 1-0

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Recent and Upcoming TAUGS

Therapeutic Area	Development	Public Review	Release Notes
Acute Kidney Injury Therapeutic Area User Guide v1.0	In Progress		In Development.
CDAD Therapeutic Area User Guide v1.0	Completed	Completed	Preparing for Publication.
Congestive Heart Failure Therapeutic Area User Guide v1.0	In Progress		In Development.
Crohn's Disease Therapeutic Area User Guide v1.0	In Progress		**In Development.**
Diabetes - Type 1 Therapeutic Area User Guide v1.0	In Progress		In Development.
Lung Cancer Therapeutic Area User Guide v1.0	Completed	Completed	Resolving Public Comments.
Nutrition Therapeutic Area User Guide v1.0	Completed	Completed	Resolving Public Comments.
Psoriasis Therapeutic Area User Guide v1.0	In Progress		In Development.
Traditional Chinese Medicine - Acupuncture	In Progress		In Development.
Traditional Chinese Medicine - Coronary Artery Disease/Angina Therapeutic Area User Guide v1.0	Completed	Completed	Preparing for Publication.

Other topics

1. **Implications of the FDA's 2017 Technical Rejection Criteria**
   - **Issues surrounding last month's ADaM 1.0 end-of-service and which ADaM version is referenced in define.xml, with Pinnacle 21 Community's current inability to evaluate later versions**
   - **The requirement for the value of STUDYID in TS to match the study tag in the eCTD**

2. **A conversation with Ram and DJ:**
   - **Practical problems of doing enterprise-level implementations**
   - **Methods for effective governance**
   - **Trying to achieve efficiencies that aren't overwhelmed by the requirement for governance and the complexities of the implementation**
   - **…**

U.S. FOOD & DRUG ADMINISTRATION

FDA View:
Technical Rejection Criteria for Study Data

Presented to: PhUSE US Connect 2018

Ethan Chen, Office of Business Informatics, CDER
Lilliam Rosario, Office of Computational Science, CDER
Ron Fitzmartin, Data Standards Team, CDER
Virginia Hussong, Data Standards Program, CBER

https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM610548.pdf

June 6, 2018

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

eCTD Study Data Validation Criteria and Severity Levels

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

1734: Trial Summary (TS) dataset must be present for each study in eCTD section 4.2 and 5.3

Medium

1735: Correct STF file-tags must be used for all standardized datasets in section 4.2 and 5.3

- Data-tabulations-dataset-sdtm
- Data-tabulations-dataset-send
- Analysis-dataset-adam

Medium

1737: For each study in eCTD section 4.2 and section 5.3, no more than one dataset of the same name should be submitted as new.

Common Technical Rejection Criteria Validation Errors

❖Top Errors for Error 1734 (968):

- ❑ Missing ts.xpt file for a study (753)
- ❑ No Study Start Date (231)
- ❑ Invalid Study Start Date. Study Start Date must be in the format of (yyyy-mm-dd) (75)
- ❑ Study files in index.xml are not correctly linked to contents in study tag files (4)

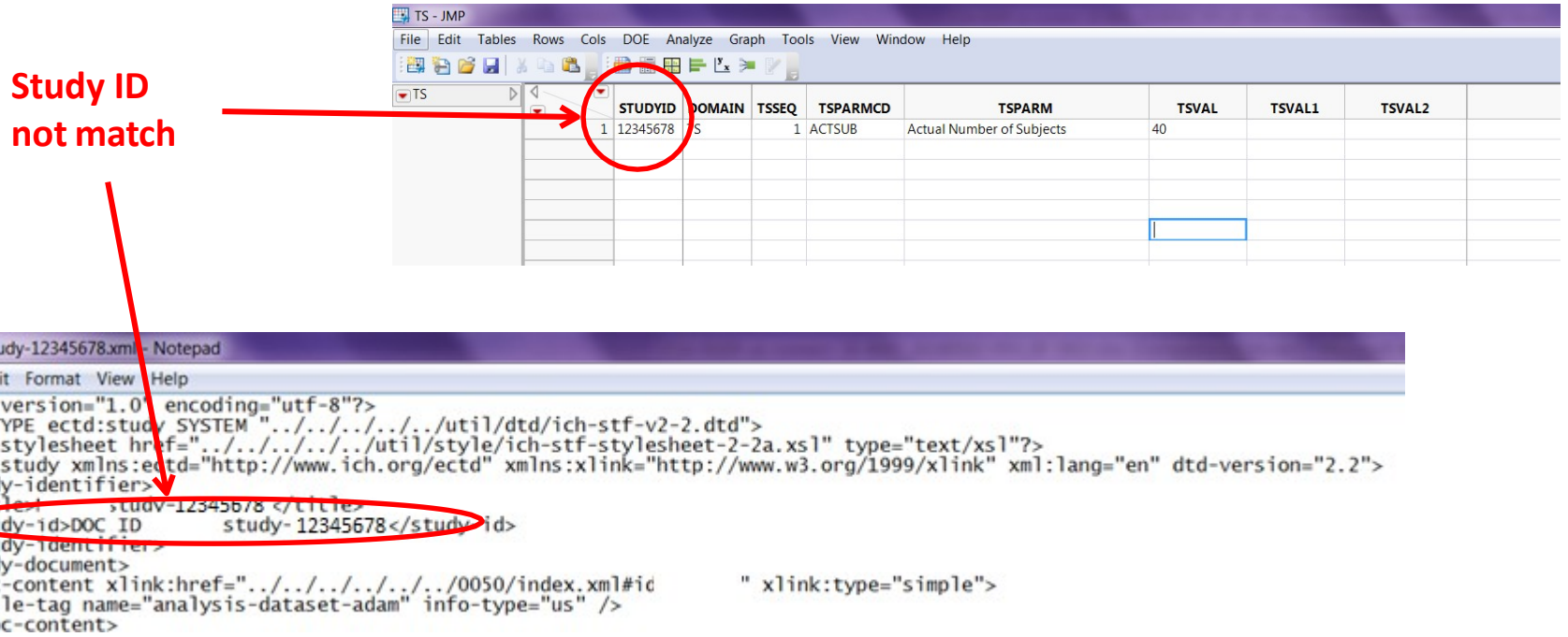
❖ Top Errors for Error 1736 (84):

- ❑ Missing adsl.xpt or corresponding define.xml for a study (52)
- ❑ Study Definition File define.xml with file tag name related to analysis does not exist for a study (38)
- ❑ Missing define.xml for a study (36)
- ❑ Missing dm.xpt or corresponding define.xml for a study (23)

Note: Number in parentheses indicates the occurrence of the error type.

Rule 1734 Top Error Examples

- **Missing ts.xpt file for a study (753): The validation tool cannot find the study start date to determine if the Technical Rejection Criteria is met or not.**
  - ❑ The Study ID tag in the STF file does not match the study id in ts.xpt file



Summary

- Based on the analysis, less than 70% all submissions were received with non-critical errors. However, identified errors are not difficult to correct.
- FDA requires the submission of standardized Study Data as defined in the FDA Data Standard Catalog.
- FDA has not rejected any submission that contains errors as reflected in this analysis.
- FDA plans to use technical rejection criteria to identify applications that are not fulfilling this requirement.

TIP

To avoid validation errors, it is important for sponsors and applicants to understand the requirements specified in guidance and recommendations for submitting study data in the Study Data Technical Conformance Guide.

References

- **“Providing Regulatory Submissions In Electronic Format - Standardized Study Data: Guidance For Industry”**
  HTTPS://WWW.FDA.GOV/DOWNLOADS/DRUGS/GUIDANCECOMPLIANCEREGULATORYINFORMATION/GUIDANCES/UCM292334.PDF

- **“Providing Regulatory Submissions In Electronic Format - Submissions Under Section 745a(a) Of The FD&C Act: Guidance For Industry”**
  HTTPS://WWW.FDA.GOV/DOWNLOADS/DRUGS/GUIDANCECOMPLIANCEREGULATORYINFORMATION/GUIDANCES/UCM384686.PDF

- **“Technical Rejection Criteria For Study Data”**
  HTTPS://WWW.FDA.GOV/DOWNLOADS/DRUGS/DEVELOPMENTAPPROVALPROCESS/FORMSSUBMISSIONREQUIREMENTS/ELECTRONICSUBMISSIONS/UCM523539.PDF

- **“Study Data Technical Conformance Guide”**
  HTTPS://WWW.FDA.GOV/DOWNLOADS/FORINDUSTRY/DATASTANDARDS/STUDYDATASTANDARDS/UCM384744.PDF

- **“FDA Data Standards Catalog”**
  HTTPS://WWW.FDA.GOV/FORINDUSTRY/DATASTANDARDS/STUDYDATASTANDARDS/DEFAULT.HTM

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    - **Trying to achieve efficiencies that aren't overwhelmed by the requirement for governance and the complexities of the implementation**
    - **...**

Issues, Governance & Efficiencies

Enterprise-level Implementations

IT, Security, $$

Change Management

Effective Governance

Usable

Real-Time

What differences actually matter?

Automation Key

Achieving Efficiencies

Baseline

Business-Critical Metrics