

FDA Study Data Technical Conformance Guide v4.2

November 2018

Helena Sviglin, MPH

Regulatory Information Specialist

Computational Science Center | CDER

Topics Covered in this Webinar



- New content for v4.2
 - Appendices
 - New parameter codes
 - New TAUG
 - Protocol Deviations
- Updates
 - SEND

Revision History

| | | |
|--------------|-----|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| October 2018 | 4.2 | <p>Section 6.6.1.1 (General Considerations) – Updated text</p> <p>Section 3.3.5 (Special Characters: Variables and Datasets) – Added clarification text</p> <p>Section 4.1.1.3 (SDTM Domain Specifications) – Additional text and table under DM and Trial Design Model sections, added DV Domain section</p> <p>Section 4.1.2.10 (Software Programs) – Clarified text</p> <p>Section 4.1.3.2 (General Considerations) – Updated text</p> <p>Section 4.1.3.3 (SEND Domain Specification) – Added Lab Test Results, Body Weight, and Comments domains, updated Pharmacokinetics Concentrations Domain and Trial Design Model sections</p> <p>Section 4.1.4.1 (Variables in SDTM and SEND: Required, Expected, and Permissible) – Updated text</p> <p>Section 5.2 (Supported Therapeutic Areas) – Added TA sections</p> <p>Section 6.6.1.1 (General Considerations) – Updated text</p> <p>Section 7.1 (eCTD Specifications) – Updated text</p> <p>Section 8.2.2 (Support on Data Validation Rules) – Updated text</p> <p>Appendix B, C, D, E, F, G - Added</p> |
|--------------|-----|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

October Study Data Technical Conformance Guide v4.2

NEW CONTENT



Appendix B: Trial Summary (TS) Parameters for Submission – Clinical

- 60 parameters, using CDISC controlled terminology
- These parameters are desired if it makes sense for the trial
- Otherwise, follow the appropriate implementation guide

Appendix C: Trial Summary (TS) Parameters for Submission – Nonclinical



- 41 parameters, using CDISC controlled terminology
- These parameters are desired if it makes sense for the trial
- Otherwise, follow the appropriate implementation guide

Appendix D: Additional Documents Evaluated By FDA



Agency encourages use of the documents listed in this appendix.

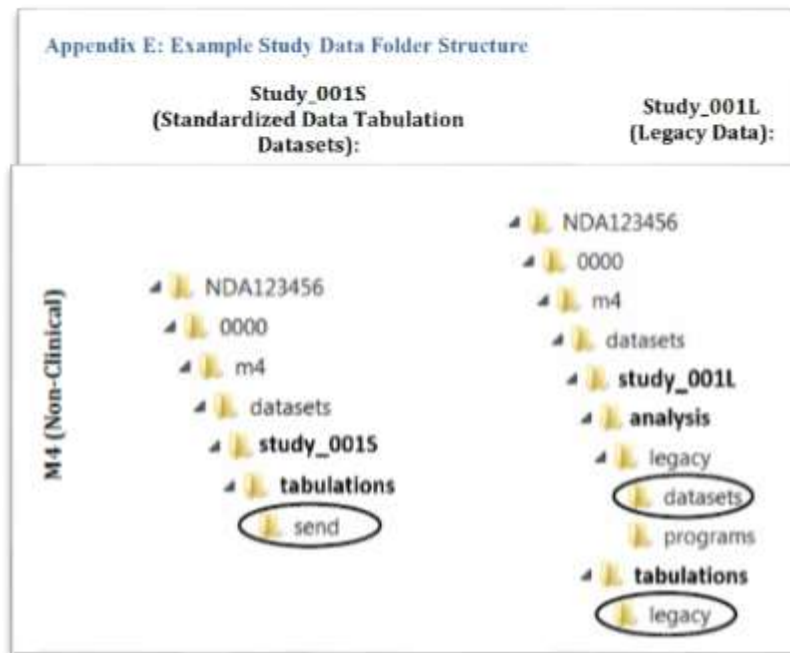
EX. Confirmed Data Endpoints for Exchange (CoDEx) for SENDIG v3.0 Data

Appendix E: Example Study Data Folder Structure

Structure



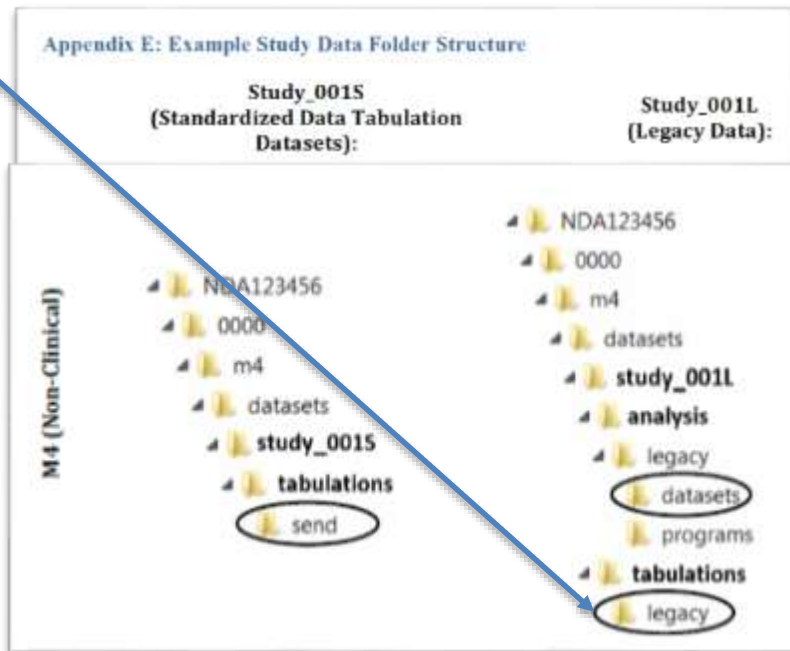
Detailed example of file folder structures for non-clinical datasets in both standardized and legacy formats



Appendix E: Example Study Data Folder Structure



Even when SEND is required and submitted, tumor.xpt should be placed in analysis/dataset/legacy (see 4.1.3.3)



Appendix F: Example Of Simplified TS Dataset For Clinical Data



Used to establish study start date during eCTD validation

Appendix F: Example Of Simplified TS Dataset For Clinical Data

| STUDYID | TSPARMCD | TSVAL |
|----------------------------------|-----------------|--------------|
| 'study ID in study tagging file' | SSTDTC | yyyy-mm-dd |

Appendix G: Example Of Simplified TS Dataset For Nonclinical Data



Used to establish study start date during eCTD validation

Appendix G: Example Of Simplified TS Dataset For Nonclinical Data

| STUDYID | TSPARMCD | TSVAL |
|----------------------------------|-----------------|--------------|
| 'study ID in study tagging file' | STSTDTC | yyyy-mm-dd |

Section 4.1.1.3 New Parameter Codes



- Allows Agency to understand which Therapeutic Area User Guides (TAUGs), Technical Specifications, Implementation Guides, and Models were utilized for a particular study
- Agency worked with EVS for these terminology extensions for the variables TSPARM and TSPARMCD

Section 5.2 Therapeutic Area User Guides (TAUGs), 1 of 2



- Added version numbers to TAUGs
- Added trial summary parameters capture use

Section 5.2 Therapeutic Area User Guides (TAUGs), 2 of 2



- New TAUGs for October TCG:
 - *Major Depressive Disorder Therapeutic Area User Guide v1.0*
 - *Duchenne Muscular Dystrophy Therapeutic Area User Guide v1.0*
 - *Traumatic Brain Injury Therapeutic Area User Guide v1.0*
 - *Vaccines Therapeutic Area User Guide v1.1*

Section 4.1.1.3



DV Domain (Protocol Deviations), 1 of 2

“The DV domain should be included in your submission. It will be used by reviewers to examine protocol deviation trends of various study sites in order to facilitate the Bioresearch Monitoring Program (BIMO) clinical investigator site selection process, and once FDA tools are developed to extract and format needed data from SDTM, to populate line listings used by the Office of Regulatory Affairs (ORA) investigators during inspections...”

Section 4.1.1.3



DV Domain (Protocol Deviations), 2 of 2

...The following variables besides CDISC required variables should be included in the DV domain when submitting DV data: DVSPID, DVTERM, DVDECOD, DVCAT, DVSCAT, DVSTDTC, DVENDTC and EPOCH.”

October Study Data Technical Conformance Guide v4.2

SEND UPDATES

Elaine E. Thompson, PhD

Senior Staff Fellow

High-performance Integrated Virtual Environment (HIVE)

Office of Biostatistics and Epidemiology

CBER | FDA

Summary of major SEND updates

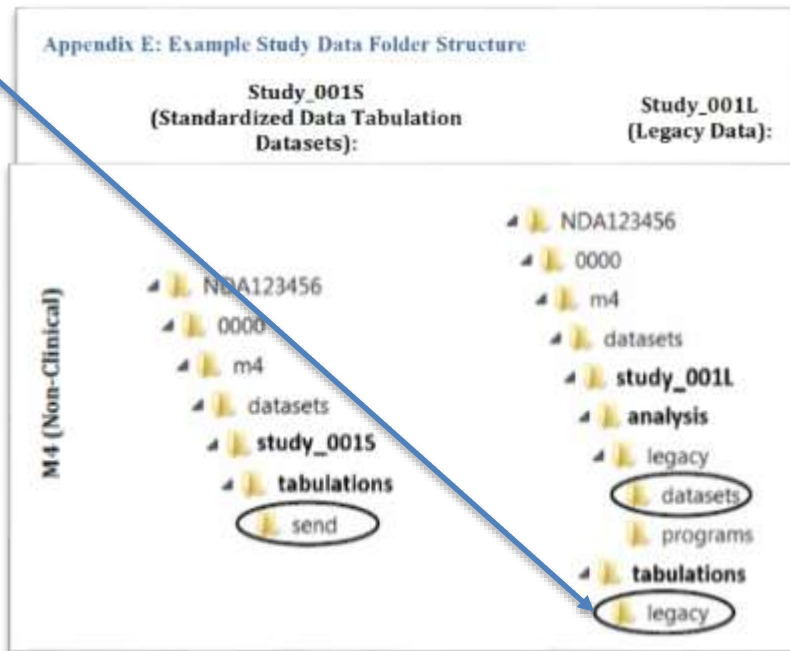


- Place tumor.xpt in analysis/dataset/legacy
- Include a simplified ts.xpt with tumor.xpt
- Categorical data in LB should be placed in LBSTRESC
- Detailed instructions for LOQ and --CALCN have been provided
- BG is not required for CDER submissions
- CO should be limited to relevant content
- Use of the CoDEX is encouraged

Appendix E: Example Study Data Folder Structure



Even when SEND is required and submitted, tumor.xpt should be placed in analysis/dataset/legacy (see 4.1.3.3)



Section 4.1.3.3 – LB Domain



“Categorical, noncontinuous results reported as incidence counts rather than summary statistics (i.e. mean and standard deviation) should be placed in LBSTRESC even if the categories are numbers. LBSTRESN should be null. Specifically, this includes urinalysis tests where the results are values on a scale. For example, if the allowable values for a urine glucose dipstick test are: ‘NEGATIVE’, ‘100’, ‘250’, ‘500’, ‘1000’, ‘>2000’, results should only be placed in LBSTRESC. Placing categorical results in –STRESC allows straightforward creation of incidence tables on –STRESC.”

- Some tests like dipsticks give categorical results
 - Ex. A scale of negative, 100, 250, 500, >1000
- Place all results in LBSTRESC
- Leave LBSTRESN null

Section 4.1.3.3 – LB Domain



“When a laboratory test result is either above or below the limit of quantification (LOQ) for the measurement method and this result was used in calculation of group means in the study report, the value used for calculation should be submitted using the supplemental qualifier variable --CALCN.”

- It may not be clear what number was used in the Study Report group means for tests outside the limit of quantification (LOQ)
- Place numbers necessary to reproduce the group means in SUPPLB in LBCALCN

Section 4.1.3.3 – PC Domain



When a test result is below a LOQ, it should be submitted using the following instructions:

- PCORRES should contain the actual/verbatim test result.
- The value of 'BLQ' should be in PCSTRESC to signify that the result is below the LOQ.
- PCSTRESN should be blank.
- Standardized units for LOQ should be in PCSTRESU.
- PCLLOQ should be populated.
- “When a numeric value has been assigned to a result that is below the LOQ for the purpose of group summary statistics, that value should be submitted in SUPPPC as QNAM= 'PCCALCN' to allow the group statistics presented in the study report to be reproduced. When a value that is below the lower LOQ is excluded from group statistics, no PCCALCN entry is needed.”

- Different implementations of results below the limit of quantitation are complicated to use
- More detail about how to handle <LOQ results has been added

Section 4.1.3.3 - BG Domain

“It is not necessary to include a BG domain in CDER submissions.”

- CDER is currently only using the BW domain to review changes in body weight
- Other centers are still evaluating BG

Section 4.1.3.3 - CO Domain

“Comments submitted in the CO domain should be relevant to study interpretation.”

- Review software displays all comments submitted, sometimes making it difficult to locate those that are relevant
- Limit comments to those relevant to the study



Q&A and Resources

Click for:

- [Study Data Resources Website](#)
- [Study Data Technical Conformance Guide v4.2](#)
- [PDF of today's slides](#)
- Additional questions to CDER?
Email: cder-edata@fda.hhs.gov
- Additional questions to CBER?
Email: cber.cdisc@fda.hhs.gov

Open Q&A begins shortly – type in your questions now.

[*Click Here for Evaluation and Certificate*](#)

*Learn about other resources from CDER Small Business & Industry Assistance:
[Visit Our Website!](#)*