SDTM/ADaM Compliant or Sufficient Submission for Legacy Studies

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Objectives

Clinical trials conducted after December 2016 are required to have data submitted in SDTM/ADaM format by the US Food & Drug Administration (FDA). When submitting data for legacy studies that did not implement SDTM/ADaM specifications, it is important to submit data that are in a user friendly format for FDA reviewers. Several options are proposed to show content of the data submission package from different approaches for preparing SDTM/ADaM compliant or sufficient data submission for legacy studies.

Methods

Based on the stage of the legacy study and how Tables/Figures/Listings (TFL) are programmed, several approaches with varying cost and time required are available for consideration when preparing for data submission. The content for the data submission package will be either compliant or sufficient as a SDTM/ADaM submission. The goal is to provide data and supporting documents that are compatible with SDTM/ADaM requirements.

A SDTM/ADaM compliant data submission starts with a locked collection database.

Components of a CDISC (Clinical Data Interchange Standards Consortium) compliant data collection and submission process flow from:

CDASH (Clinical Data Acquisition Standards Harmonization) collection database with:

- Data domains and specifications
- Variable names and formats
- Code lists

→ SDTM (Standard Data Tabulation Module) Packet

- SDTM datasets in xpt format - derived from CDASH data according to SDTM specifications
- Annotated Case Report Form (aCRF)
- Define.xml - a data definition file describing structure and content of the dataset
- Study Data Reviewer's Guide (SDRG) - data description and conformance

→ ADaM (Analysis Data Module) Packet

- ADaM datasets in xpt format - derived from SDTM according to Statistical Analysis Plan and ADaM specifications
- Define.xml - describes format and derivation of analysis variables
- Analysis Data Reviewer's Guide (ADRG) - links between SDTM datasets, ADaM datasets and TFL in the clinical study report (CSR)
- Program codes used to generate TFL from ADaM datasets

*Open CDISC (now Pinnacle 21 Community) conformance check should be run for both SDTM and ADaM datasets and define.xml with flagged issues addressed or explained

Results

Different approaches are appropriate based on status of the study and cost ($) and time (🕘) considerations.

SDTM/ADaM compliant submission (SDTM/ADaM prepared following requirements):

- CSR not finalized – implement the full SDTM and ADaM standards; $ and 🕘
- CSR finalized but recreated – implement the full SDTM/ADaM standards then recreated the TFL and CSR using SDTM/ADaM; $$$ and 🕘🕘🕘
- No change to final CSR – prepared SDTM/ADaM datasets and program TFL accordingly. Confirm new TFL are the same as the ones in the final CSR with a compare and provide proof, final CSR remains as is; $$ and 🕘🕘

SDTM/ADaM sufficient submission (no change to datasets and finalized CSR):

- If TFL programmed off collection datasets – provide datasets, aCRF, data definition, reviewer's guide, and SAS/program codes; $ and 🕘
- If analysis datasets used for TFL – provide collection datasets, aCRF, collection data definition, collection data reviewer's guide plus analysis datasets, analysis data definition with analysis data derivation details, and analysis data reviewer's guide linking analysis datasets to collection datasets and TFL; $ and 🕘

*Any issues that will not pass an OPEN CDISC equivalent check should be mentioned in the reviewer's guide for proper clarification to reduce potential reviewer questions.

Conclusions

To fully convert a finalized legacy study to follow SDTM/ADaM specifications for data submission is time consuming and costly while retrospectively created SDTM data do not provide adequate links to the TFL in the final CSR for reviewer verification. It is possible to prepare a successful data submission for legacy studies if complete data and necessary information are provided to regulatory reviewers. An appropriate approach to successful data submission to the FDA can be determined for legacy studies based on the status of the study, structure of the data, how TFL are programmed and time/cost factor. The basic concepts and specifications of FDA required SDTM/ADaM submission packets provide valuable guidance on what information a reviewer would need to effectively perform regulatory responsibility in a timely fashion. The key is to ensure that transparency and traceability are achieved in any data submission for a smooth regulatory review.