Implementing SDTM More Easily and More Broadly

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Agenda

1. Broader Scope of SDTM Implementation Advice
2. Deeper Implementation Support
3. Upcoming Changes to SDTMIG

Broader Scope of SDTM Implementation Advice

Tobacco Implementation Guide

Observational Studies

Rare Diseases TAUG

Tobacco Implementation Guide

- Developed with support from the U.S. Food & Drug Administration (FDA) Center for Tobacco Products (CTP)
- Covers new types of data
  - Product description
  - In vitro genetic toxicology
  - Population modeling (Product Impact on Population Health)
- Addresses all foundational standards

<table>
<tr><th>Use Case</th><th>Data Collection</th><th>Data Tabulation</th><th>Data Analysis</th><th>Data Exchange</th></tr>
<tr><td>Product Description</td><td rowspan="2"></td><td rowspan="3">Section x.x, Standards for Tabulation</td><td>Section x.x, Standards for Analysis</td><td rowspan="4">Section x.x, Standards for Data Exchange</td></tr>
<tr><td>Nonclinical</td><td></td></tr>
<tr><td>Product Impact on Individual Health</td><td>Section x.x, Standards for Collection</td><td rowspan="2">Section x.x, Standards for Analysis</td></tr>
<tr><td>Product Impact on Population Health</td><td colspan="2"></td></tr>
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Tobacco Implementation Guide Timeline

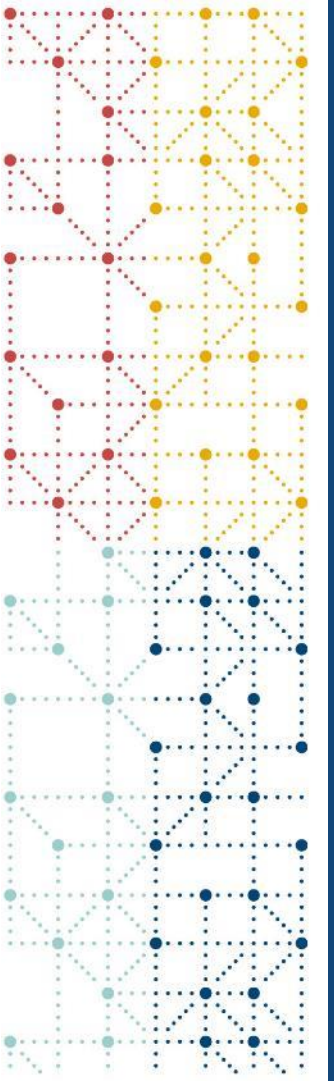
- Currently resolving issues from Internal Review
- Public Review Q4 2023
- Release Q2 2024

SDTM for Observational Studies v1.0

- Public Review through September 28 (today!)
- Use cases include case control, cohort, and external control arm studies
- Types of commonly encountered issues
  - Using AE and CE domains
  - Using Exposure and CM domains
  - Representing cohorts with planned and actual arm variables
  - Handling study days and reference dates
- Advice on conformance rules and validation checks
- Examples for DM, TS, and TA
  - For DM, includes domain specification with added columns for challenges and “Proposed Core for Observational Studies”
  - Dataset examples for use cases

Rare Diseases TAUG

- Publication Imminent (Q3 2023)
- Study conduct issues common to many rare diseases
  - Trial inclusion/exclusion
  - Withdrawals/discontinuations
  - Use of external control arm (see SDTM for Observational Studies)
- CDASH and SDTM examples for multiple domains and a variety of rare diseases
  - Concepts not addressed or not completely addressed by existing implementation guides
- ADaM examples
  - Composite Endpoint
  - Response Rate Endpoint
  - Survival Endpoint
  - Seizure Frequency Endpoint



Deeper Implementation Support

Non-standard variable (NSV) Registry

Conformance Rules (CORE)

Biomedical Concepts

NSV Registry

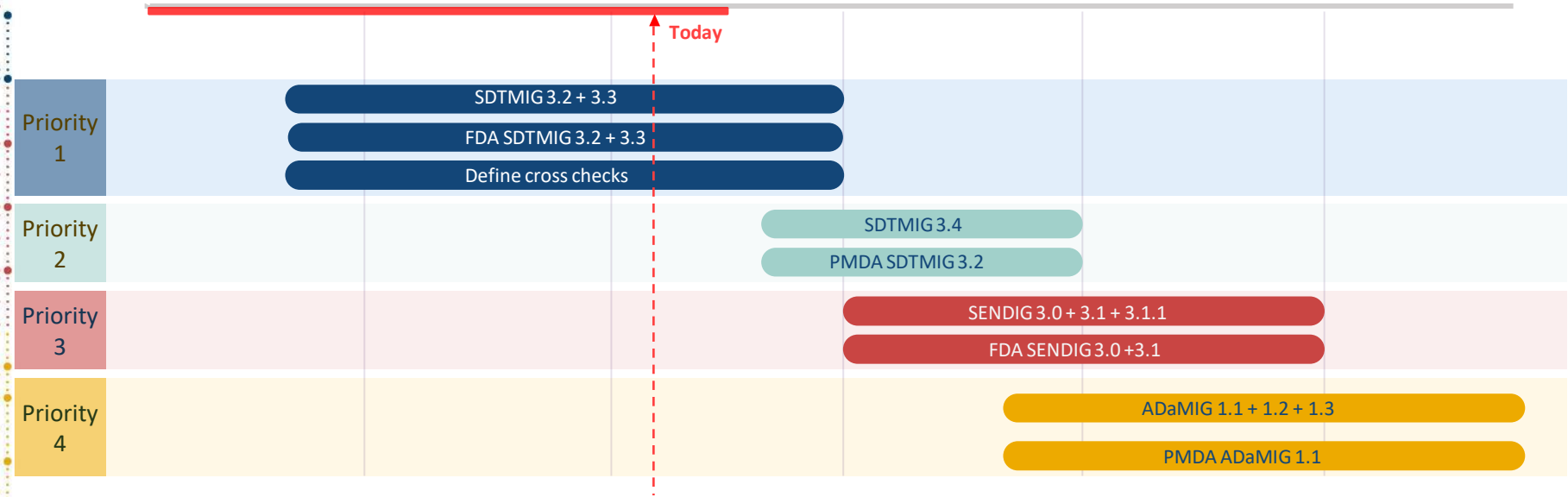
- The TAUGs and implementation guides have introduced non-standard variables in their examples.
- Later developments have affected some of those older NSVs, and they are scattered across multiple documents
- NSVs were consolidated, reviewed and curated.
  - Approved NSVs on CDISC website https://www.cdisc.org/standards/terminology/non-standard-variables
  - Spreadsheets of NSVs and fragments can be downloaded.

CORE for Conformance Rules

- CORE stands for CDISC Open-source Rules Engine
- Aim is to develope unambiguous, executable conformance rules
- Can be retrieved from the CDISC Library
- Tutorial and technical information on the CDISC website

- CDISC US Interchange Core sessions
  - CDISC Strategic Updates – Biomedical Concepts and Core
  - CORE Workshop

Rules Development Priority



➡ *Timelines depend on community engagement*

Biomedical Concepts

- A biomedical concept can be thought of as a set of variables plus controlled terminology supporting a particular test or observation, like value level metadata.
- Project is at an early stage, but an initial set of biomedical concepts are already available from the CDISC Library.
- Concepts are being developed at both a conceptual level, and at an SDTM implementation level
  - Additional implementations (e.g., CDASH, HL7 FIHR) expected in future
- Current development driven by needs of other CDISC projects (e.g., Digital Data Flow).
- Plan to collaborate with early adopters to migrate BCs from external sources.

Upcoming Changes to SDTMIG

New format for Non-Standard Variables

Support for Multiple Subject Participation

Event Adjudication

Metadata Restructuring

Standards Roadmap on CDISC Website

- https://www.cdisc.org/standards/roadmap
- Timelines diagram
  - SDTMIG v4.0, SENDIG v4.0 and associated version of SDTM will be released together
  - Planned Public Review Q3 2024, Release Q1 or Q2 2025
- Scoping table has tabs for each foundational standard, for example:

SEND | CDASH | SDTMIG | Medical Devices IG | ADaM | QRS

Document	Proposed Scope/Change	Proposed Scope/Change Description	Impacts	Benefits
SDTMIG v4.0	SUPP to NSV	Prior to SDTMIG v4.0, SUPP datasets need to be transposed before appending to the parent dataset. The proposed structure of the new NSV datasets is already horizontal which will make it much easier for reviewers to join the data back to the parent. NSVs can have defined variable level metadata in addition to value level metadata.	Sponsors and the industry at large will need to update their tools and conformance rules to handle the creation of NSV datasets rather than SUPPQUAL. Review and validation tools will need to be updated as well. The post-processing steps would be simplified, and it would make the merge easier.	Easier for reviewers to join the data back to the parent NSV variable-level metadata - For example, data type or length vs only having 'text' for SUPP.QVAL, you can have numeric values and additional qualifiers. It aligns visually with the TAUG representations. Many sponsors already store their SDTM datasets in a structure that appends the NSVs to the parent domains.

New format for Non-Standard Variables

- “Horizontal” NSV datasets for each domain can be easily merged with parent domains
- IDVAR specified for each kind of domain
  - For NSDM IDVAR and IDVARVAL are null. Merge is on STUDYID, USUBJID
  - For NSSV, IDVAR is VISITNUM
  - For all other domains, IDVAR is --SEQ
- Eliminating other IDVARs may increase dataset size compared to old supplemental qualifier dataset but simplifies merging.

Support for Multiple Subject Participation

- Introduces DC domain, with one record per participation
  - E.g., each screening or enrollment
- Catches SDTMIG up with FDA TCG, but with more complete assumptions

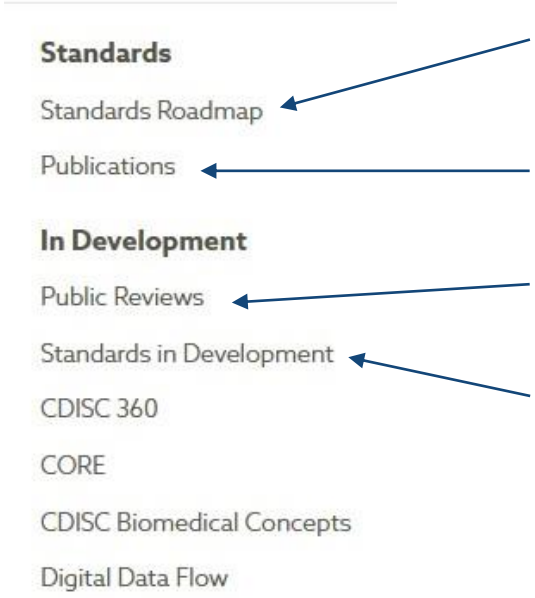
Event Adjudication

- Incorporates approach from PHUSE white paper into SDTMIG
  - https://phuse.s3.eu-central-1.amazonaws.com/Deliverables/Optimizing+the+Use+of+Data+Standards/Best+Practices+for+Submission+of+Event+Adjudication+Data.pdf
- Builds on approach to findings adjudication originally developed for oncology
  - --ACPTFL variable used to mark which of multiple findings records for the same test but by different evaluators is accepted
- Event Adjudication uses Findings About structure, with --OBJ the event being adjudicated, and --TEST the aspect of the event being adjudicated
  - E.g., whether event satisfies protocol-defined endpoint criteria, when it occurred, type according to some classification system

Metadata Restructuring

- Builds on metadata restructuring in SDTM v2.0.
- “Controlled Terms, Codelist, or Format” separated into three items
- Modifiers of “Qualifier” role removed
  - Result, Grouping, Synonym, Variable, or Record Qualifier
- New informative Variable Groups added
- New linking phrases between variables replace old vague “variables qualified”
  - For example, “--ORRESU” qualifies “--ORRES” replaced by “--ORRESU is the unit for the value in --ORRES”
- Variable C-Codes and Definitions Added.
- CDISC notes replaced by “Notes” referring to general or domain-specific assumptions
  - Involved moving some text into new assumptions
- Examples in a separate column.

More on the CDISC Website (hover over “Standards” on home page)



Timeline and scope for updates to foundational standards

Published standards, newest to oldest

Currently under public review

Stage of development, and projected release date

Thank You!