



DS06

Standards Subject to Change: Data Standards Flexibility in an Evolving Landscape

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Data Standards

Standards should be built to support flexibility and growth with relatively little disruption.

Two main reasons

- Data standards will and do evolve within the industry and as we learn and move into different disease areas.
- The FDA (and other agencies) expects sponsors to use the most current version of standards.

With this potential changing landscape and expectations, how can sponsors and CROs upgrade their data standards in a timely and efficient manner, while involving all relevant stakeholders in the upgrade assessment?

Agencies

- FDA issued the final binding guidance “Providing Regulatory Submissions In Electronic Format — Standardized Study Data” on Dec. 17, 2014
- PMDA set Oct. 2016 as the starting date to begin receiving data in CDISC format
- This includes standards, formats, and terminologies specified in the FDA Standards Catalog (CDISC SDTM, Analysis Data Model (ADaM), Controlled Terminology as well as other standards (e.g., SNOMED, MedDRA, etc.))

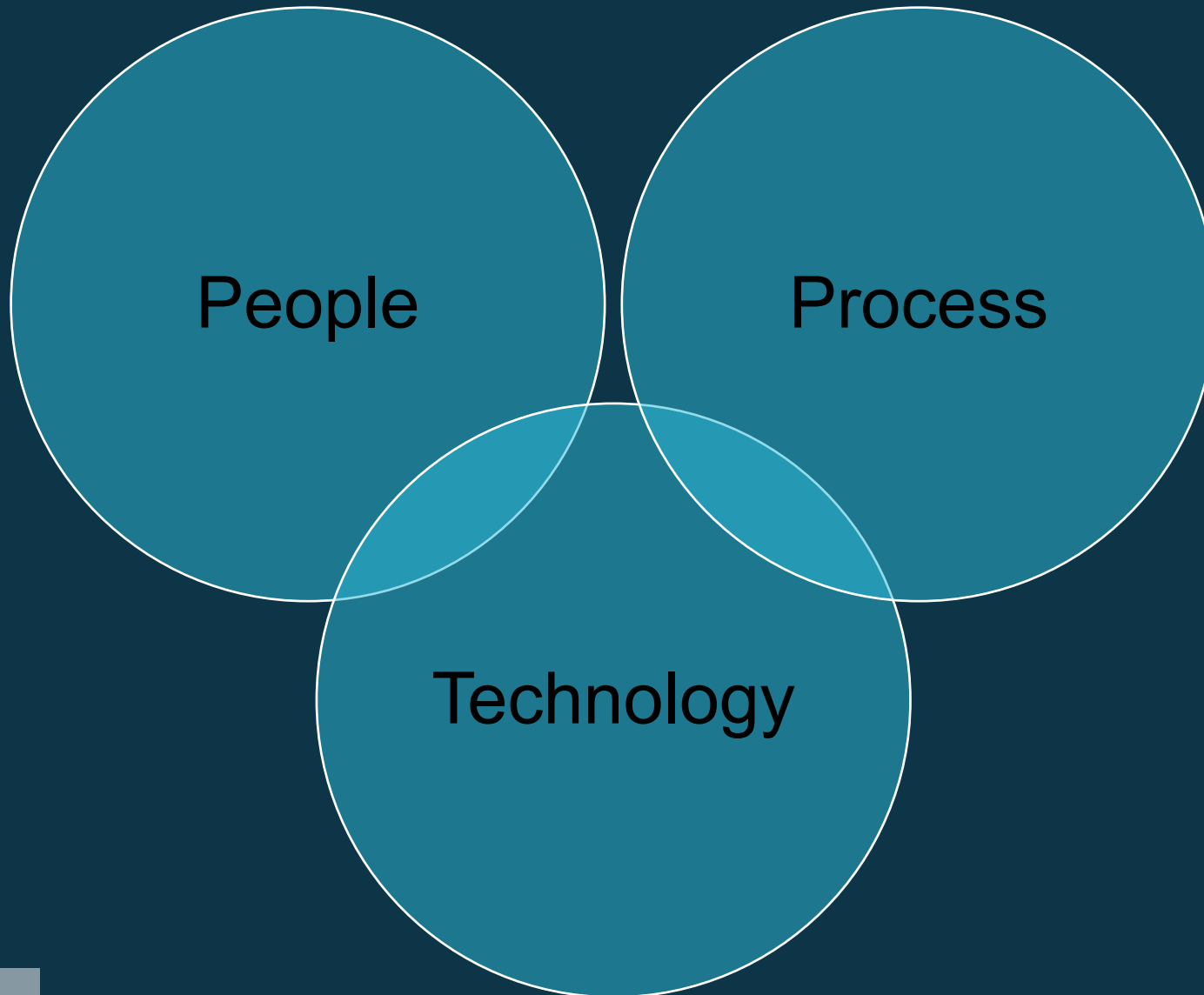
BUT we must remember these standards are all about the submission and not the collection or storage of the data

Why do we need Standards?

Regardless of the regulations one of the major motivations for imposing company standards on the definition, management, analysis and reporting of clinical trial data, is to ensure that the data from all studies conducted on a drug product or even across drug products within a TA can be combined to support aggregated reporting for regulatory submission, commercialization, product defense, data mining and modeling & simulation.

Remember we don't submit studies, we submit submissions

Data Standards



Scope

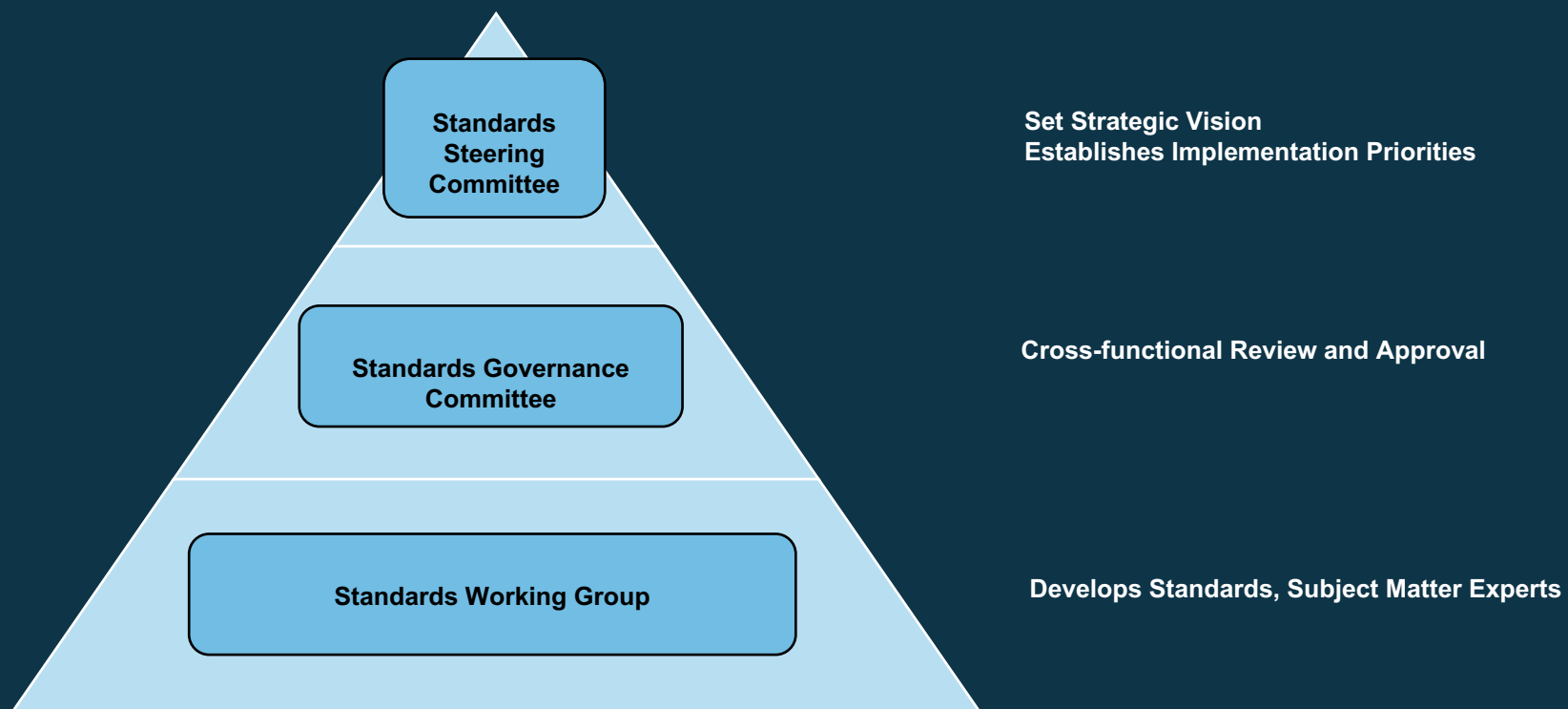
Before we can design how we update our standards we need to have our standards in place

Firstly, what is the scope of your standards you want to maintain & govern?

Data Collection (EDC, Labs, CTMS, etc.), Data Storage (CDR, Data Marts, etc.), Data Reporting (SDTM, AdAM, etc.)

What is the Data Standards Scope in your organization?

People & Process



Process

One basic philosophy for data standards is to collect data as close to how we will submit it (e.g., use standard variable names such as CDASH and SDTM, and controlled terminology) as much as possible

BUT this philosophy does not work for everyone

Who does not follow this philosophy?

Process

Advantage's of this type this Philosophy

- Follow's the “**traceability**” requirements outlined in the **FDA Technical Conformance Guide**
- Allows all internal and external stakeholders to have a **common understanding** throughout the lifecycle of what the definition of a piece of data is
- Aim is to **eliminate or minimize the transformation of data** and thus the level of validation needed

Process

Benefits of this Philosophy

- When defining standard's we think beyond the individual study's immediate needs. All studies use Global Standards.
- Requests submitted/processed for updates to global metadata based on study protocol requirements before a study DB can go into production
- Standard metadata is available for future studies that may need to collect the same information
- Studies are collecting data in a standard format from the beginning

Process

Disadvantages / Challenges

- Puts standards on the critical path in terms of study timelines
- Decisions need to be made quickly
- SME's need to have dedicated time

Who Should be Involved in Standards Definition and Change

- Clinical Data Standards & Integration (CDSI) - Global & Proj. Standards
- Global Trial Management and Monitoring
- Clinical Pharmacology
- Clinical Quality Assurance
- Clinical Research Science
- Data Management
- Drug Safety & Risk Management
- Medical Affairs
- Programming
- Statistics

Members need to ensure that at least one representative from their functional area attends each meeting.

Technology

- MDR (MetaData Repository)
 - Many companies on the market
- Excel
 - Many companies are still using Excel

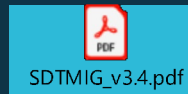
Are you using an MDR and if so which one?

Updating Standards

- Now we have
 - Scope
 - Process
 - People to be involved
 - Governance model
 - And where applicable technology

Updating Standards

- For the purposes of this presentation we will look at a CDISC change
- Scope of change :
 - Changes can be found at this location <https://www.cdisc.org/members-only/cdisc-library-archives>
 - Excel version of changes (see attached)
 - Appendix E: Revision History



SDTMIG_v3.4.pdf

Microsoft Excel
Worksheet

Updating Standards

According to the website the following changes have been made throughout:

- Text and examples have been clarified as needed.
- Text was updated to reflect new table names in SDTM v2.0.
- Values were updated to current CDISC Controlled Terminology.
- ISO formats were made more granular.
- New variables from SDTM v2.0 have been added.
- Tables with domain codes and descriptions at the start of a section have been replaced with a sectional table of contents since each domain section already contains all of the information previously in the tables
- With few exceptions (e.g., the DM domain), the names of supplemental qualifier variables have been updated to include 2-character domain abbreviations at the start of the variable name.
- Assumptions which provided domain definitions were removed as these are provided under the Description/Overview for each domain.
- Where numbered lists occurred in CDISC Notes, these have been converted to text for consistency with the rest of the document.
- Links were updated as needed.
- Typographical errors were corrected.

Updating Standards

According to the website the following changes have been made throughout:

- Updated the Tumor/Lesion (TU and TR) domain assumptions to describe use of indicator questions, disease recurrence conventions, and modeling of location of interest.
- Expanded the scope of the SC domain to support collection over time.
- Updated guidance and examples for the FA domain.
- Corrected Core values for the following variables: DSDY, DSSTDY, LBSTREFC, MILOBXFL, and MIBLFL.
- Updated Controlled Terminology for applicable variables across all domains, if available.
- Removed Appendix C1, Trial Summary Codes

Assessing Changes

There is no right or wrong way to assess these differences

If we look at the excel sheet in the BASIC tab is where we will find the details

Column Name	Description
Updated Version	Newer version of the standards being compared.
Previous Version	Older version of the standards being compared.
Action	Change to the standard; possible values are "Add", "Drop", "Type Update", and "Value Update".
Impact	Metadata changed in the newer standard; possible values are "CDISC Notes", "Core", "Dataset Label", "Dataset", "Role", "Structure", "Variable Label", "Variable", "describedValueDomain", "description", "label"
Change Level	Only applies to "Value Update" Category. Possible values are "Minor" (Non-alphanumeric changes or case changes only) and "Major" (Alphanumeric changes other than case)
Class	Class in which the variable is defined in the implementation guide. The column includes the Events, Findings, and Interventions Observation Classes as well as classes for Relationship and Special-Purpose datasets.
Dataset Name	Name of the SDTMIG or SENDIG dataset.
Variable Name	Name of the SDTMIG or SENDIG variable.
Attribute (updated)	Value of the metadata in the newer version of the standards being compared.
	When text is in this format, the text has not changed. When text is in this format, the text has been updated/added.
	When text is in this format, the text has been removed between the two consecutive highlighted characters.
Attribute (previous)	Value of the metadata in the older version of the standards being compared.
	When text is in this format, the text has not changed. When text is in this format, the text has been updated/removed.
	When text is in this format, the text has been added between the two consecutive highlighted characters.

Assessing Changes

All of the changes are also documented in Appendix E of the SDTM 3.4 version

My personal preference is

- to review the high level description from the website (which we already did)
- then read through Appendix E
- then if necessary further drill down with the spreadsheet details

Assessing Changes

Morphology (MO) domain was removed

- When the Morphology domain was introduced in SDTMIG v3.2, the SDS Team planned to represent morphology and physiology findings in separate domains: morphology findings in the MO domain and physiology findings in separate domains by body systems.
- Since then, the team found that separating morphology and physiology findings was more difficult than anticipated and provided little added value.
- This led to the decision to expand the body system-based domains to cover both morphology and physiology findings and to deprecate MO in SDTMIG v3.4.
- Submissions using that later SDTMIG version would represent morphology results in the appropriate body system-based physiology/morphology domain.
- For data prepared using a version of the SDTMIG that includes both the MO domain and body system-based physiology/morphology domains, morphology findings may be represented in either the MO domain or in a body-system based physiology/morphology domain.
- Custom body system-based domains may be used if the appropriate body system-based domain is not included in the SDTMIG version being used.

Assessing Changes

Morphology (MO)

- **Do we use this domain currently?**
- **What are the implications for submission?**
 - **Do we have to map to another domain to submit?**
 - **Or can we still submit in the retired domain?**

These steps will be appropriate for any retired domains / variables

Appendix E Review

New domains

- Biospecimen Events BE
- Biospecimen Findings BS
- Cell Phenotyping Findings CP
- Genomics Findings GF
- Related Specimens RELSPEC

BE, BS, and RELSPEC domain specifications, assumptions, and examples were copied and minimally updated from the provisional SDTMIG-PGx, published 2015-05-26. This was done in preparation for the retirement of the SDTMIG-PGx upon publication of SDTMIG v3.4. These domains are currently under extensive revision for inclusion in a future SDTMIG publication, after v3.4.

Appendix E Review

Check New Domains

- Do we use this domain currently?
- Do we collect this data in a custom domain?
- What are the implications for submission?
 - Do we have to map to another domain to submit?
 - Or can we still submit in the current domain?

These steps will be appropriate for any retired domains / variables

Appendix E – Overview of Changes by Section

Review each of the changes asking the following questions

Do we use this part of SDTM?

- NO, do not review this change further

Does the change drop anything?

Does the change add anything?

Does the change the meaning of anything?

Does the change add clarity to anything?

Appendix E – Section 2.1 - Example

V3.3 Rule variables, which express an algorithm or executable method to define start, end, and branching or looping conditions in the Trial Design model

V3.4 Rule variables, which describe the condition to start, end, branch, or loop in the Trial Design Model

Do we use this part of SDTM? yes

Does the change drop anything? no

Does the change add anything? no

Does the change the meaning of anything? no

Does the change add clarity to anything? yes

Assess impact - NONE

Standards Changes

Review each change and make a determination on impact for your organization
This is really the same process whether internal change or external change

The next step is the challenging step

You know the change but now when and how do I implement it???

Retired studies??

Ongoing studies??

New studies??

What is your methodology??

In Conclusion

- Internal standards strategy and governance should be in place
- Dependent on that company strategy
 - Do not make changes
 - Map at submission time
 - Make changes to new studies only
 - Ongoing studies to be map at submission
 - Make changes to new and ongoing
 - Migration of existing ongoing studies

NO Simple Answer

Thank You!

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