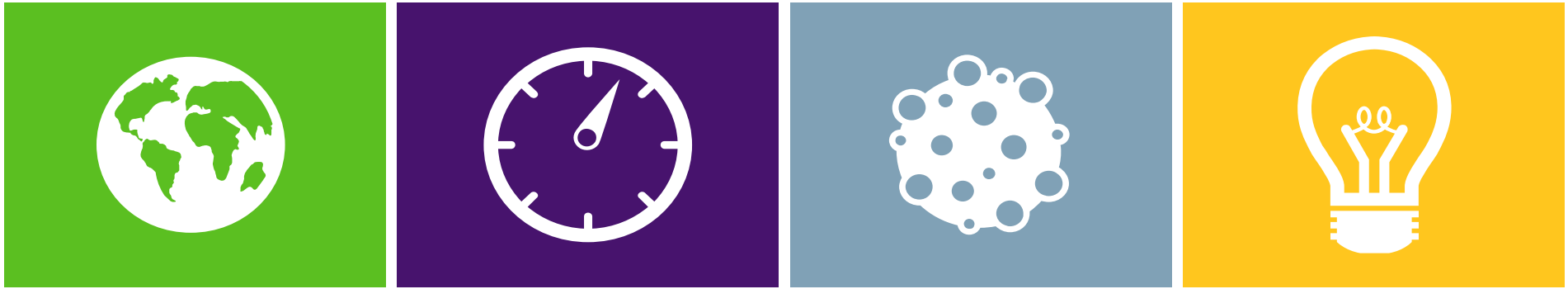

CDISC SDTM Standards Implementation – Common Challenges and Best Practices

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Agenda

- Introduction
- SDTM Implementation Challenges and Best Practices
- Summary
- Q&A

Introduction

- One criticism of the SDTM standards is that they are continually changing, with new versions released frequently.
- CDISC claims that SDTM standards are backward compatible. According to the CDISC SDS Team, CDISC standards evolve, as any standard does. This brings up lot of implementation challenges to Industry.

Introduction (contd.)

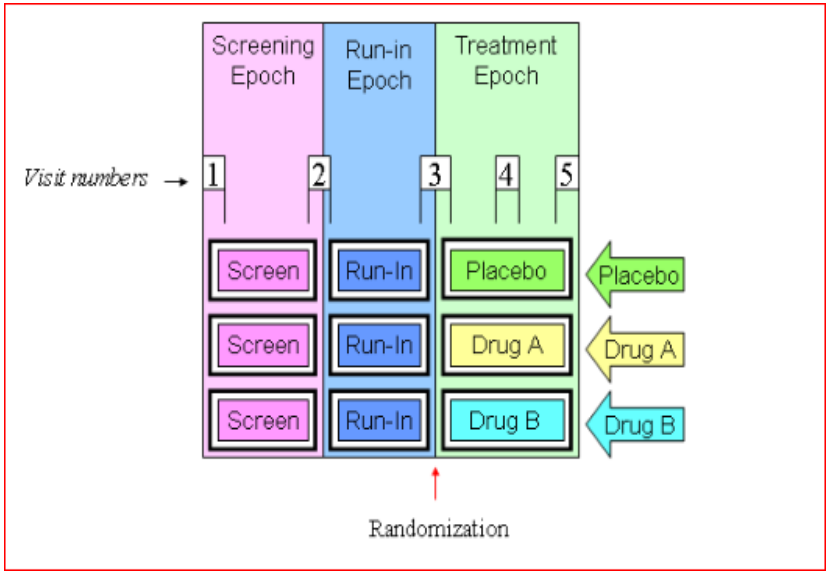
+ A small change in SDTM could have a huge impact on the ADaM (Analysis Database), Tables, Listings and Figures and the Define package.
+ This presentation focusses on best practices for SDTM Implementation to gain efficiency & avoid rework in downstream steps.

SDTM Implementation Challenges and Best Practices

- Key to success is proactive management of **Client expectations**.
- During Beginning of Project, ensure to follow-up on
  - Correct **SDTM IG version** per Client expectation
  - **Client Specific mapping guidelines**, Sponsor specific controlled terminology, unit conversion guidelines if any.
  - **Sister studies** to have project level consistency as required
  - Whether requirement is for "**Legacy** Data conversion" or "**Ongoing Study**".
  - Key Milestones & High level Timeline. Ex: DMC
  - Number of Vendor Data Types & complexities

SDTM Implementation Challenges and Best Practices

- **Trial Design Model (TA, TE, TS, TD, TV, TI)**
  - Ensure to get all versions of protocol (including latest) & SAP if available
  - Ensure to get latest CRF, Study Data Specification(DB Design)
  - Check availability of Study Data.
  - Please note when DM is also contracted within same company, it is better to check internally on EDC Go-live, FPFV details.



SDTM Implementation Challenges and Best Practices

- **SDTM Mapping Specification**
  - **Understanding Data** and ensuring mapping to correct SDTM Domain
  - It is **<u>extremely</u>** beneficial at the mapping stage, to have a senior SDTM experienced programming member **review** the team's **mapping specification**. Their review would be focused on **ensuring mapping accuracy**, providing guidance on **what source data is best suited for which SDTM domains** and providing mentorship through the test transfer setup.
  - It is a good idea to **collaborate with your statistician** (if available) when drafting SDTM specifications **to ensure all data points required for analysis are included** within CDISC SDTM. Also, it is good to refer **Mock shell & SAP.**

SDTM Implementation Challenges and Best Practices

SDTM Mapping Specification

+ Ensuring correct metadata (Dataset/variable/Value level/CT) defined to aid in **Define.xml** at later stages
+ **Duplicate mapping** should be avoided
+ Ensure to consistently follow SDTM IG/client specific guidelines & clearly document mapping logic, derivation.

SDTM Implementation Challenges and Best Practices

- **Datasets Programming**
  - Ensure no data is inadvertently **missed out/dropped** during mapping to **avoid rework**. i.e., **map all necessary records collected** in clinical database & data coming from **Vendor/third party data**. Keep an eye on **DB modifications** on ongoing studies, **Data cuts** to be used for each delivery.
  - For study teams new to SDTM tasks, it is **strongly** advised to have **experienced SDTM programming support** available to mentor the team.
  - **Data quality issues** should be addressed through Good Clinical Data Management Practices and are **not specifically SDTM** conformance

SDTM Implementation Challenges and Best Practices

Datasets Programming (contd)

+ Ensure Date variables are mapped correctly in **ISO8601** format
+ Check with Client on Blank dataset
+ Ensure to populate dependent variable. Ex: Dose, Dose Unit
+ Similar **variables** across domains must be **consistent** in their data stored values and SAS attributes (labels, lengths, etc), example TI vs IE, DM vs TA

SDTM Implementation Challenges and Best Practices

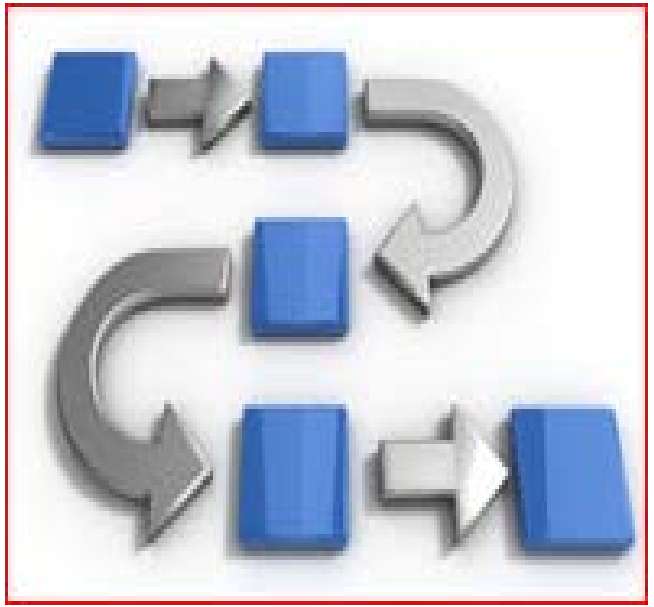
- **Define.xml.**
  - Good to do at the end of study when SDTM, ADaM quite stable
  - Ensure to have SDRG up-to-date with all comments
  - Ensure to have SDTM annotated CRF, Specification, Datasets are in place
  - Good to have a macro developed to save time
  - An SDTM annotated CRF should reflect the data that are expected to be submitted within the SDTM.

SDTM Implementation Challenges and Best Practices

- **Other Considerations:**
  - Often useful to follow **logical** order. i.e., starting with Trial Design Model, SDTM Annotation(using latest CRF), Mapping Specification creation, Datasets & Define.xml.
  - **Controlled terminology standards** are an important component of study data standardization. The **analysis of study data** is greatly facilitated by the use of controlled terms. It's also useful when **consistently applied across studies to facilitate integrated analyses**.
  - Usage of Validation Tool (Ex. **OpenCDISC/** now **Pinnacle 21**) & manual review to ensure Submission compliance

SDTM Implementation Challenges and Best Practices

- Important component of a regulatory review is the **traceability** of the sponsor's results back to the CRF data. It's an understanding of the **relationships between the analysis results, analysis datasets, tabulation datasets, and source data**. Ex: **XX**SPID can be used.



SDTM Implementation Challenges and Best Practices

Unique Subject Identifier (USUBJID)

+ Each individual subject should be assigned a single unique identifier **across the entire application**.
+ **Improper** implementation of the USUBJID variable is a common error with applications and often requires sponsors to re-submit their data.

SUPPQUAL (Supplemental Qualifier)

+ In general, variables used **to support key analyses** should not be represented in SUPPQUAL.
+ Discussion with the review division should occur if the sponsor intends to include important variables (e.g., that support **key** analyses) in SUPPQUAL datasets, and reflected in the Study Data Reviewer's Guide (SDRG).

SDTM Implementation Challenges and Best Practices

Rescreened Subjects:

+ If the same subject is **screened more than once** in a trial, then the subject's SUBJID should be different.

Adjudication Data

+ There are **no existing standards**. Until standards for adjudication data are developed, it is advised that sponsors discuss their proposed approach with the **FDA** review division and also include details about the presence, implementation approach, and **location of adjudication data in the SDRG**.
+ Whenever adjudication data is provided it **should be clearly identified** so that the reviewer can distinguish the results of adjudication from data as originally collected.

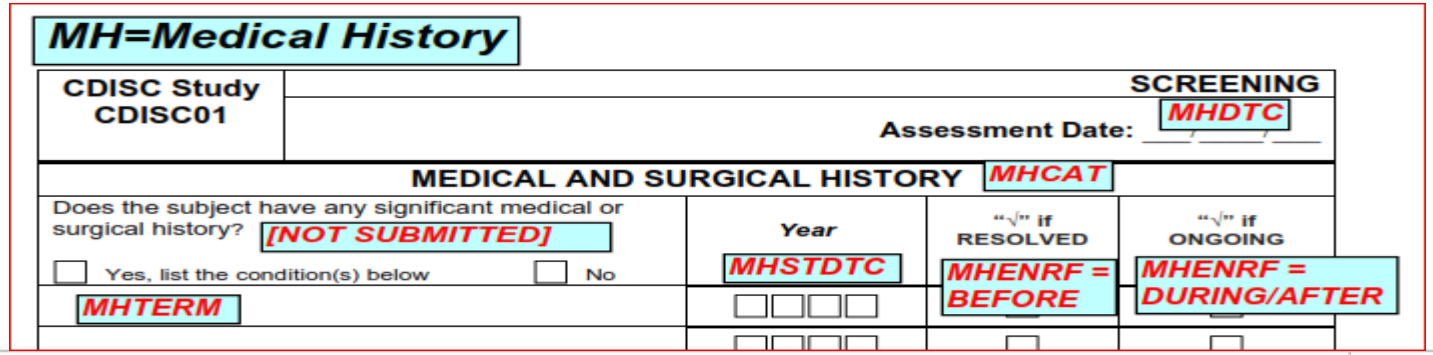
SDTM Implementation Challenges and Best Practices

- **Custom Domains**
  - The SDTMIG permits the creation of custom domains if the data do not fit into an existing domain.
  - Prior to creating a custom domain, sponsors should **confirm that the data do not fit** into an existing domain.
  - If it is necessary to create custom domains, sponsors should follow the recommendations in the SDTMIG.
  - In addition, sponsors should present their implementation approach in the **SDRG**.

SDTM Implementation Challenges and Best Practices

+ Annotated Case Report Form (aCRF) for SDTM

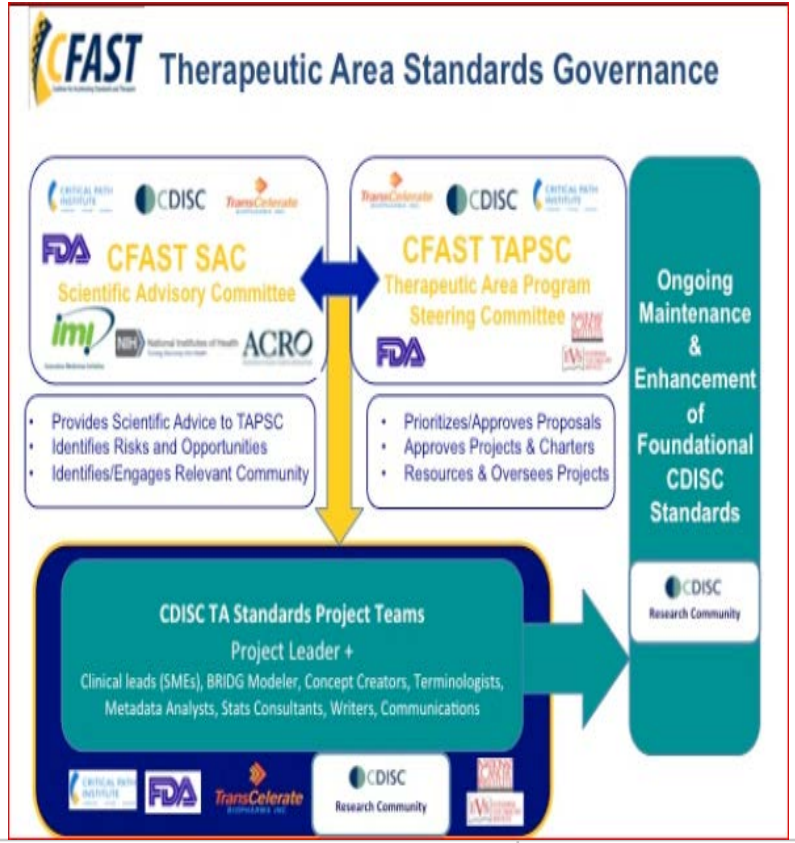
- + Regardless of whether the clinical database is legacy or SDTM compliant, an aCRF should be submitted. The aCRF should be provided as a PDF with the file name "**acrf.pdf.**"
- + When data are recorded on the CRF but are not submitted, the CRF should be annotated with the text "NOT SUBMITTED." There should be an explanation in the SDRG stating why data have not been submitted.



SDTM Implementation Challenges and Best Practices

Therapeutic Area Standards

+ It is **not** supported by FDA **until FDA performs acceptance testing** to determine its ability to support new TA data elements. When using new data elements that are not in a SDTMIG currently supported by FDA, sponsors should describe the rationale for their use in the **SDRG**.
+ Following **therapeutic areas** are **currently supported by FDA**: *Chronic Hepatitis C, Dyslipidemia, Diabetes, QT Studies and Tuberculosis*



SDTM Implementation Challenges and Best Practices

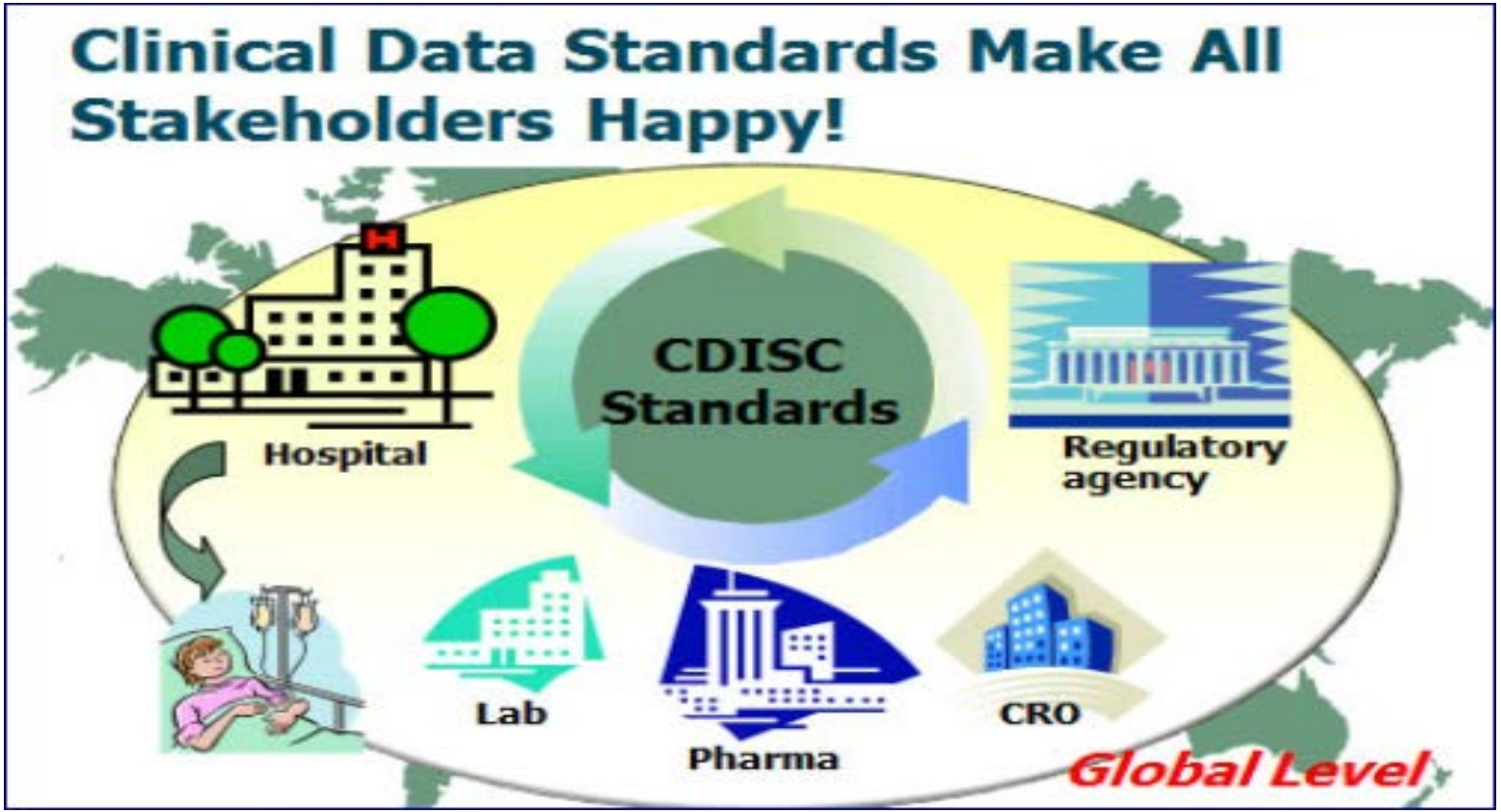
Legacy Data Conversion: To mitigate **traceability issues** when converting legacy data, FDA recommends the following:

+ Prepare and Submit a **Legacy Data Conversion Plan and Report**. Record significant data issues, clarifications, explanations of traceability, and adjudications in the SDRG.
+ Legacy data (i.e., legacy aCRF, legacy tabulation data, and legacy analysis data) may be needed in addition to the converted data.

Summary

+ Standardization is **KEY** in each step of process **to realize Benefits** (both cost & process benefits)
+ CDISC estimates a 60% savings in costs and increase in efficiency by using standards from the start of a study.
+ Standards makes data more **powerful**, **meaningful** and **reduce rework**
+ **Early start helps**: Planning for SDTM before start building the eCRF using SDTM-friendly protocols and CDASH eCRFs standards will reduce the challenges of data standardization
+ As standards are continuously evolving, following best practices & proactively managing client expectations will help **to achieve overall efficiency(TIME, COST, BUDGET)**

Summary


Clinical Data Standards Make All Stakeholders Happy!
CDISC Standards
Hospital
Regulatory agency
Lab
Pharma
CRO
Global Level

Q&A

THANK YOU

For further questions, please reach at
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