CDISC 360
The Journey so Far and the Road Ahead

Peter Van Reusel
28 April 2020
Agenda

1. What is CDISC 360?
2. The Art of the Possible
3. Project Approach
4. The Journey So Far
5. What Follows 360?
What is CDISC 360?
Today we are here

CDISC Standards in the Clinical Research Process

PRE-CLINICAL
ORGANIZE
SEND

PLAN
COLLECT
ORGANIZE
ANALYZE
SUBMIT PUBLISH REPORT

DATA EXCHANGE
ODM-XML
SDM-XML

DATA EXCHANGE
ODM-XML

DATA EXCHANGE
Define - XML
Dataset - XML

TAUGS

BRIDG, CONTROLLED TERMINOLOGY AND GLOSSARY
Benefits Today

- CDISC Foundational models provide much needed structure
  - Normative Content
  - 2 dimensional (tables, columns)
  - Standard to represent data

- Standards must now evolve to address further challenges to take standards benefits to next level
How do we evolve?
The CDISC 360 Project: Adding a conceptual layer to standards

- Create and store standards as concepts which create meaning between data
- Electronically publish data standards as linked metadata
- Add computer executable process metadata which enables end to end automation
- CDISC 360 will develop concept-based standard definitions, and test and demonstrate end-to-end automation of study specification, data processing, and analysis

➤ Test and demonstrate, but **not building software**
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Biomedical Concept

Attributes are linked to the element

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<th>Findings</th>
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<td>Variable Label</td>
<td>Result or Finding in Original Units</td>
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<td>Type</td>
<td>Char</td>
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<tr>
<td>Core</td>
<td>Exp</td>
</tr>
<tr>
<td>Role</td>
<td>Result Qualifier</td>
</tr>
<tr>
<td>CDISC Notes</td>
<td>Result of the measurement or finding as originally received or collected.</td>
</tr>
<tr>
<td>Core</td>
<td>Exp</td>
</tr>
</tbody>
</table>

Sourced from SDTM 1.4 SDTMIG 3.2

CDASH.LB–Local Processing.LBORRES
CDASH.LB–Local Processing.LBORRESU
SDTM.LB.LBORRES
SDTM.LB.LBST
SDTM.LB.LBSTRESN
BRIDG.PerformedObservationResult.value
Analysis Result Concept
One Model

The Biomedical Concept and Analysis Concept are **ONE MODEL**
The Art of the Possible
CDISC 360 – Art of the Possible

• What will follow is a User Experience presentation

• Purpose:
  • Illustrate how the CDISC 360 concept model will enable automation
  • For illustration only: CDISC 360 will not deliver software to the industry

• UX presentation link:
  • https://xd.adobe.com/view/93e3e8f6-5b33-405f-4e76-e17af5f29990-e5d2/
Project Approach
Use Case 1: Define
Selecting standards concepts and linked metadata needed for a study
Use Case 2: **Build**
Adding study design, concept configuration & generate artifacts
Study Build

Configured study metadata

SDM / XML

Digital Data Flow Project

Study Designer tool

Standards Selection

Study design
- Visits
- Arm’s
- Epochs.....

Study parameters (TS)
- Eligibility criteria
- Schedule of activities (SOA)
- Study workflow

Create artifacts (use case 2)

Study Configuration

Study workflow

Schedule of Activities (SoA)

Study Design

Run-in Epoch
- Arm AB
  - Run-in
- Arm BA
  - Run-in

First Treatment Epoch
- Run-in
- A 5 mg
- A 10 mg

Second Treatment Epoch
- B 5 mg
- B 10 mg

Follow Up Epoch
- A 5 mg
- A 10 mg
- Follow Up

Study Parameters (TS)
Use Case 3: **Execute**

Automatic population of data into artifacts

- **Operational Database**
- **EDC Extract Database**
- **Tabulation Datasets**
- **ADaM Creation**
- **Analysis Datasets**
- **Analysis Results Creation**
- **Endpoints**
- **Clinical Study Reports**

**Operational Database**
- **CDASH**
- **EDC**
- **eDT**
- **eHR**
- **ePRO**

**Configured study metadata**

**Process Study Data**

**PDF**
Expected Outcome

• **Learn**
  - What works and what doesn’t

• **Assessment**
  - Technology Gap Analysis
  - Standards Gap Analysis

• **Building a base for the future**
  - Inform and involve stakeholders
  - Cost / Benefit Analysis
  - Scale up to deliver the standards metadata needed
  - Partnerships with vendors to ensure tools are made available
Reason for this scope: the Diabetes TAUG provides standardized artifacts from analysis outputs to data collection. This allows the project team to focus on innovation and not on establishing a new data standard.
Reason for this scope: Document FDA standard safety analysis requirements that may be expressed in the analysis concept maps; ensure the enhanced standards meet reviewers’ needs.
CDISC 360 Workstreams

**Workstream 1 - ENHANCE STANDARDS**
Create concepts in knowledge graphs

**Workstream 2 - PUBLISH STANDARDS**
Load into library

Biomedical Concepts
Analysis Concepts
Foundational Standards

Extend API’s

Transform concepts in machine readable form

**Workstream 3**

**Workstream 4 - DEFINE**
Identify and select standards specification (Use Case 1)

**Workstream 5 - BUILD**
Configure study specification and create artifacts (Use Case 2)

**Workstream 6 - EXECUTE**
Automatically process and transform data (Use Case 3)
360 Participation Summary

Project Kickoff:

36 Resources specified
20 Organizations

Today:

107 Resources specified
38 Organizations

- Pharma-Biotech Sponsor: 20
- CRO: 6
- Technology Provider: 11
- Regulatory: 1

→ Still onboarding new participants

→ Contributions vary due to project complexity and time available
The Journey So Far
## Project Timeline

<table>
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<tr>
<th>#</th>
<th>Stage</th>
<th>Start</th>
<th>End</th>
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<tr>
<td>1</td>
<td>Initiation, scoping, and internal staffing</td>
<td>Oct 2018</td>
<td>Nov 2019</td>
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<td>2</td>
<td>Planning, recruiting CDISC member participants</td>
<td>Dec 2019</td>
<td>Feb 2019</td>
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<td>3</td>
<td>Align with Transcelerate Digital Data Flow Initiative</td>
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<td>Onboarding CDISC member participants</td>
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<td>5</td>
<td>Kickoff, workstreams briefing</td>
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<td>Execution of agile sprints</td>
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<td>Project evaluation – Stage 2 (CDISC EU Interchange)</td>
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<td>Execution of agile sprints</td>
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CDISC 360 To Date – March 2020

2020 - MAR
EU Interchange
- Create study designs using standards and study metadata library
- Automated, metadata-driven creation of SDTM and ADaM datasets, and TFLs

2020 - JAN
Building Momentum
- ISO11179 concept based templates, metamodels, bindings
- Include data & TFL transformation engines
- Expand cloud infrastructure

2019 – April 8th
Kick-off
- Kick-off meeting
- Workstreams Briefing
- Over 45 participants

2019 - JUL
Gaining Traction
- More volunteers, tools, access, training
- User story development
- Initial concept-based standards
- Test study definitions and data

2019 - OCT
US Interchange
- Convert concepts to machine-readable form
- Study Metadata Library prototype
- “360 Test Study” components and metadata
- Identify two safety endpoint analyses with FDA

15 sprints across 12 months
Increasing our concept-based standards knowledge in iterative fashion
Workstream Highlights
Concept Development Highlights

• Adapting biomedical concepts to ISO11179
  • ISO 11179 is an international standard for representation of metadata

• Linking biomedical concept templates to binding files

• Defined approach to add transformations and derivations to concept maps
CDISC 360 ISO 11179 Model

Biomedical Concept Layer

Standards Metadata Representation Layer

- Observation Concept
- Role
- Property
- Object Class
- Data Element Concept
- Enumerated Conceptual Domain
- Described Conceptual Domain
- Conceptual Domain
- Data Element
- Value Domain
- Enumerated Value Domain
- Described Value Domain
- Context
Concept Development based on ISO 11179: Systolic Blood Pressure
## Binding Files

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Using BC Maps and Binding Files Together
Concept Development: Next Steps

• Biomedical and Analysis concepts model and templates:
  • Test BCs (Lab, Exposure, Demographics, Trial Design, Vital Signs)
  • Test ACs (ADSL)
  • CRFs

• Data flow metadata:
  • System-agnostic transformations and derivations
  • Link data flow metadata to concepts
  • Test use of data flow metadata

• End-to-End from CDASH to ADSL:
  • For metadata (data state and data flow) and data
Use Case 2: Build

Adding study design, concept configuration & generate artifacts
### Objectives and Endpoints

#### Objectives for the study

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Use Case 3: **Execute**

Automatic population of data into artifacts

**Data Collection Scope**
Use Case 3: Execute
Automatic population of data into artifacts
CDISC360 – WS6 TFL Automation

Customize Template

Generate SAS Program and XML

[Diagram of TFL Automation process with steps numbered 1, 2, and 3]

1. Choose Folder
3. Download or SAS Code button

Study - CDISC
Table 14.1.1.1
Demographic characteristics (Safety Population)

Population Dataset: add
Population Variable: SAFPL
Population Comparator: EQ
Population Value: Y

Across Variable: TREAT
Row Label Header: Characteristics
Across Label Header 1: METFORMIN
Across Label Header 2: HUMAN INSULIN

Analysis Dataset: add
Analysis Variable: AGE

n
Mean
SD
Min
Q25
Median
Q75

XX
XXX
XXX
XX
XX
XXX
XX
XX
XX
XX

Analysis Dataset: add
Analysis Variable: AGE
What Follows 360?
WS 1: Enhance Standards
WS 2: CDISC Library
WS 4: Define (Use Case 1)
WS 5: Build (Use Case 2)
WS 6: Execute (Use Case 3)

Proof Of Concept
Implement

CDISC
Enhance Standards

Industry Implementation

Provide requirements
Submission data following regulatory requirements

Regulatory
What Follows 360 - Inventory of Work (1)

- **Missing** standards
  - Data Collection instruments
  - Analysis Results
  - Endpoint definitions
  - Safety User Guide
    - Collection ➔ Tabulation ➔ Analysis

- **Enrich** existing standards
  - What
    - Clinical assessments
    - Interventions
    - Events
    - Therapeutic Areas
  - How
    - Stabilize Biomedical and Analysis concept templates
    - Add transformations and derivations content
What Follows 360 - Inventory of Work (2)

- **Evolve library technology and schema**
  - Refine and test the CDISC 360 models
  - Refine and deploy CDISC 360 software tools
  - Integrate the CDISC 360 models into the CDISC Library model
  - Update the API to add new CDISC 360 model endpoints
  - Update the CDISC Library Data Standards Browser to include CDISC 360 content
  - Update the CDISC Library standards load software

- **Evolve toward collaborative curation**
  - Develop and rollout governance process
  - Create CDISC Library standards development and curation tools
  - Develop standards curation training
  - Enhance CDISC Library to load community standards implementations
Thank you