CDISC 360:
Evolving our standards towards end to end automation

Peter van Reusel
Sam Hume
Barry Cohen
Agenda

1. Where are we today
2. What is CDISC 360
3. Project Approach
4. Relationship to Other Initiatives
5. Expected outcomes
1. Where are we today
Today we are here

CDISC Standards in the Clinical Research Process

PRE-CLINICAL
- ORGANIZE
  - ORGANIZE
  - SEND

CLINICAL
- PLAN
- COLLECT
- ORGANIZE
- ANALYZE
- SUBMIT PUBLISH REPORT

DATA EXCHANGE
- ODM-XML
- SDM-XML
- CDASH
- SDTM
- ADaM

TAUGS

BRIDG, CONTROLLED TERMINOLOGY AND GLOSSARY
Defined structures

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

The information itself is not defined

- We do not need new structures
- We need to define
  - Entities
  - Semantics (meaning)
  - Relationships between information
  - Rules in the data lifecycle
Why Change?
Industry needs are maturing

- Machine-readable standards
- Move beyond normative structural description of data
- Provide semantic relations between data – add meaning
- Add process metadata to enable end-to-end automation
- We want non-standard experts to use our standards
2. What is CDISC 360
What is the CDISC 360 Project?
Adding a conceptual layer to standards

- Create and store standards as concepts which create meaning between data
- A serious attempt to store and use data standards as linked metadata
- Add computer readable process metadata which enables end to end automation
- Evolve from normative to informative standards
- CDISC 360 will develop concept-based standard definitions, and test and demonstrate end-to-end automation of study specification and data processing

➤ Test and demonstrate, but not building software

CDISC
Biomedical Concept

→ Data is expressed through the CDISC Foundational Models
→ Can be mapped to BRIDG Reference Model
Biomedical Concept

Attributes are linked to the element

<table>
<thead>
<tr>
<th>Variable Name</th>
<th>Variable Label</th>
<th>Type</th>
<th>Controlled Terms, Codelist or Format</th>
<th>Role</th>
<th>CDISC Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>LBDTC</td>
<td>Date/Time of Specimen Collection</td>
<td>Char</td>
<td>ISO 8601</td>
<td>Timing</td>
<td>Date/time of specimen collection represented in ISO 8601 character format.</td>
</tr>
</tbody>
</table>

Legend:
- LBDTC
- Date/Time of Specimen Collection
- Char
- ISO 8601
- Timing
- Date/time of specimen collection represented in ISO 8601 character format.
Biomedical Concept

Linking controlled terminology to the variable
Biomedical Concept

Standardize value level metadata

Key
- Specimen
- Assessor
- Observation
- Observation Result
- Time Point
- Terminology
- SDTH Variable
- Validation Rule
Machine readable definition of validation rules
Analysis Concept

Refer to Section X-X of the SAP for windowing algorithm based on ADHBA1C_ADY. Baseline visit is defined as the last available value prior to randomization.
The Biomedical Concept and Analysis Concept are ONE MODEL
The Power of a Conceptual Model for Data Standards

- Linking controlled terminology to the variable – standardize value level metadata
- Machine readable definition of validation rules
- Linking derivations and algorithms to variable(s)
  - Include process metadata (ETL instructions)
- Possibility to standardize Analysis outputs and Collection instruments
  - Combining layout, variables, process information together
- Link Analysis Concepts to Biomedical Concepts
  - Choose an analysis and automatically obtain all related end-to-end metadata

→ All of the above: enables automation, increase confidence in results, true analysis traceability
Use Case 1: End to Start Specification
Selecting standards concepts and linked metadata needed for a study
CDISC Library API extension

Knowledge graph

LOAD

Biomedical Concepts
Analysis Concepts
Foundational Standards

Call

API

Extend Current
Set of APIs

API metadata Return

| PAA | BBB | X-3 | Y+H | DEF | 1+2 | ...
|-----|-----|-----|-----|-----|-----|-----
| • Dataset metadata  | • Process metadata  
| • Concept metadata  | • Configuration  
| • Concept relations  | Defaults and options  
| • Controlled terminology  |   |

Return

Dataset metadata
Concept metadata
Concept relations
Controlled terminology
DISCLAIMER NOTE

The following is not a software demonstration. Sole purpose is to illustrate how data standards can enable tools.
Welcome

Login: CDarwin
Password: ************

SIGN IN >>
**SDTM**

**DOMAIN**
SDTM Variable
Value Level Metadata
Controlled Terminology

**ADaM**

**DOMAIN**
ADaM Variable
ADaM Parameters
Controlled Terminology
Computational algorithm

---

**CDASH**

**DOMAIN**
CDASH Variable
Value Level Metadata
Controlled Terminology

---

**Figures**

- Graphical Approaches to the Analysis of Safety Data from Clinical Trials”. Amit, et. al.
- From “Graphical Approaches to the Analysis of Safety Data from Clinical Trials”. Amit, et. al.
- Mean Change from Baseline in QTc by time and treatment.
- Distribution of ASAT by time and treatment
- Distribution of maximum LFT values by treatment.
- Panel of LFT shift from baseline to maximum by treatment
- LFT Patient profiles
- Most Frequent On Therapy Adverse Events
- Cumulative distribution (with SEs) of time to first AE of special interest
Listings

Listing 2.4 Current Cancer History – All Treated Patients Experiencing Critical Events
Listing 2.5 Prior and Concomitant Medication – All Treated Patients Experiencing Critical Events
Listing 2.6 Physical Examination at Screening – All Treated Patients Experiencing Critical Events
Listing 3.1 Reference Chemotherapy and Concomitant Chemotherapies – All Treated Patients Experiencing Critical Events
Listing 4.1 Adverse Event Listing. All Pre-Treatment Adverse Events – All Treated Patients Experiencing Critical Events
Listing 4.2 Adverse Event Listing. Treatment Emergent Adverse Events – All Treated Patients Experiencing Critical Events
Listing 4.3 Adverse Event Listing. Serious Treatment Emergent Adverse Events – All Treated Patients Experiencing Critical Events
Listing 4.4 Adverse Event Listing. Serious Treatment Emergent Adverse Events Related To Study Drug – All Treated Patients Experiencing Critical Events
Listing 4.5 Adverse Event Listing. Serious Treatment Emergent Adverse Events Related To Treatment
### Listing 4.5 Adverse Event Listing. Serious Treatment Emergent Adverse Events Related To “Treatment” – All Treated Patients Experiencing Critical Events

<table>
<thead>
<tr>
<th>Site/ Country</th>
<th>Start Date/Time</th>
<th>Stop Date/Time</th>
<th>Day Duration</th>
<th>Intensity of Occurrence</th>
<th>Action Taken</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient/ ID</td>
<td>XX/MM DD/MM/YYYY/MM:HH</td>
<td>XX/MM DD/MM/YYYY/MM:HH</td>
<td>XX</td>
<td>Intermittent</td>
<td>Grade X</td>
<td>Possibly</td>
</tr>
</tbody>
</table>

**Analysis dataset:** <DATA> SAS REPT ddmmmyyyy hh:mm

**Note:**
- Critical events are defined as: Serious Adverse Events (extracted from the clinical database reconciled with the safety database), Suspected Unexpected Serious Adverse Reactions (extracted from the safety database), wrong study medication used (patients who received a wrong medication due to mistake in one cycle, resulting in the administration of drug from both treatment groups during the study).
- "Treatment" related adverse events are adverse events with a missing relationship to “Treatment” or assessed by the investigator as definite, probable, possible or unassessable.
- Program: <DIRECTORY PATH>/ddmmmyyyy.sas; Date & Time program was run: ddmmmyyyy hh:mm; Date & Time analysis dataset was run: ddmmmyyyy hh:mm
<table>
<thead>
<tr>
<th>Dataset</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADAE</td>
<td>One record per subject per adverse event, per date</td>
</tr>
<tr>
<td>Domain</td>
<td>Name</td>
</tr>
<tr>
<td>--------</td>
<td>-------------</td>
</tr>
<tr>
<td>ADAE</td>
<td>USUBJID</td>
</tr>
<tr>
<td>ADAE</td>
<td>SUBJID</td>
</tr>
<tr>
<td>ADAE</td>
<td>SITEID</td>
</tr>
<tr>
<td>ADAE</td>
<td>DOSEAONU</td>
</tr>
<tr>
<td>ADAE</td>
<td>DOSEAEON</td>
</tr>
<tr>
<td>ADAE</td>
<td>COUNTRY</td>
</tr>
<tr>
<td>ADAE</td>
<td>ASTTM</td>
</tr>
<tr>
<td>ADAE</td>
<td>ASTDT</td>
</tr>
<tr>
<td>ADAE</td>
<td>AETERM</td>
</tr>
<tr>
<td>ADaM Variable</td>
<td>Reference</td>
</tr>
<tr>
<td>---------------</td>
<td>-----------</td>
</tr>
<tr>
<td>ADE.AENDT</td>
<td></td>
</tr>
<tr>
<td>ADE.ADURN</td>
<td></td>
</tr>
<tr>
<td>ADE.DOSEAEON</td>
<td></td>
</tr>
<tr>
<td>ADE.DOSEAEONU</td>
<td></td>
</tr>
<tr>
<td>ADE.DOSEAEON</td>
<td></td>
</tr>
</tbody>
</table>

**Related metadata:**

- **SDTM**: Domain, Variables, Computational Algorithm
- **CDASH**: Domain, Variables
**ADaM Domain Computational Algorithm**

**Reference**

ADAE.DOSEAEON Equals to EX.EXDOSE where the numeric version of EX.EXSTDTC <= ASTDT <= the Numeric version of EX.EXENDTC.

**Name** | **Label** | **Origin** | **Role** | **Core**  
--- | --- | --- | --- | ---  
AESTDTC | Start date/Time of Adverse Event | CRF | Timing | Exp  
EXDOSE | Dose per administration | Derived | Record Qualifier | Exp  
EXTDTC | Start date/Time of treatment | CRF | Timing | Exp  
EXENDTC | End date/Time of treatment | CRF | Timing | Perm

**ADaM Variable**

**Domain** | **Name** | **Question**  
--- | --- | ---  
AE | AESTDAT | Start Date  
AE | AESTIM | Start Time  
EX | EXAMONT | Dose  
EX | EXAMONTU | Units  
EX | EXENDAT | End Date  
EX | EXENTIM | End Time  
EX | EXSTDAT | Start Date

Related metadata: SDTM, CDASH
Use Case 1: End to Start specification
Selecting standards concepts and linked metadata needed for a study
Use Case 2: Start to End Study Metadata

Adding study design, concept configuration & generate artifacts
Study Build

- Configured study metadata
  - SDM / XML
  - Study builder tool

Create artifacts (use case 2)

Study Configuration

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

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

Study workflow

Schedule of Activities (SoA)

Study Design

Study Parameters (TS)
<table>
<thead>
<tr>
<th>STUDYID</th>
<th>DOMAIN</th>
<th>TSSEQ</th>
<th>TSGRPID</th>
<th>TSPARMCD</th>
<th>TSPARM</th>
<th>TSVAL</th>
<th>TSVALNF</th>
<th>TSVALCD</th>
<th>TSVCDREF</th>
<th>TSVCDVER</th>
</tr>
</thead>
<tbody>
<tr>
<td>XYZ</td>
<td>TS</td>
<td>1</td>
<td>ADDON</td>
<td>TSPARM</td>
<td>Added on to Existing Treatments</td>
<td>Y</td>
<td>C49488</td>
<td>CDISC</td>
<td>2011-06-10</td>
<td></td>
</tr>
<tr>
<td>XYZ</td>
<td>TS</td>
<td>1</td>
<td>AGEMAX</td>
<td>TSPARM</td>
<td>Planned Maximum Age of Subjects</td>
<td>P70Y</td>
<td>ISO 8601</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>XYZ</td>
<td>TS</td>
<td>1</td>
<td>AGEMIN</td>
<td>TSPARM</td>
<td>Planned Minimum Age of Subjects</td>
<td>P18M</td>
<td>ISO 8601</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>XYZ</td>
<td>TS</td>
<td>1</td>
<td>LENGTH</td>
<td>TSPARM</td>
<td>Planned Trial Length</td>
<td>P3M</td>
<td>ISO 8601</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>XYZ</td>
<td>TS</td>
<td>1</td>
<td>PLANSUB</td>
<td>TSPARM</td>
<td>Planned Number of Subjects</td>
<td>300</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>XYZ</td>
<td>TS</td>
<td>1</td>
<td>RANDOM</td>
<td>TSPARM</td>
<td>Trial is Randomized</td>
<td>Y</td>
<td>C49488</td>
<td>CDISC</td>
<td>2011-06-10</td>
<td></td>
</tr>
<tr>
<td>XYZ</td>
<td>TS</td>
<td>1</td>
<td>SEXPOP</td>
<td>TSPARM</td>
<td>Sex of Participants</td>
<td>BOTH</td>
<td>C49636</td>
<td>CDISC</td>
<td>2011-06-10</td>
<td></td>
</tr>
<tr>
<td>XYZ</td>
<td>TS</td>
<td>1</td>
<td>STOPRULE</td>
<td>TSPARM</td>
<td>Study Stop Rules</td>
<td>INTERIM ANALYSIS FOR FUTILITY</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>XYZ</td>
<td>TS</td>
<td>1</td>
<td>TBLIND</td>
<td>TSPARM</td>
<td>Trial Blinding Schema</td>
<td>DOUBLE BLIND</td>
<td>C15228</td>
<td>CDISC</td>
<td>2011-06-10</td>
<td></td>
</tr>
<tr>
<td>XYZ</td>
<td>TS</td>
<td>1</td>
<td>TCNTRL</td>
<td>TSPARM</td>
<td>Control Type</td>
<td>PLACEBO</td>
<td>C49648</td>
<td>CDISC</td>
<td>2011-06-10</td>
<td></td>
</tr>
<tr>
<td>XYZ</td>
<td>TS</td>
<td>1</td>
<td>TDIGRP</td>
<td>TSPARM</td>
<td>Diagnosis Group</td>
<td>Neurofibromatosis Syndrome (Disorder)</td>
<td>19133005</td>
<td>SNomed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>XYZ</td>
<td>TS</td>
<td>1</td>
<td>TNTPREP</td>
<td>TSPARM</td>
<td>Trial Indication Type</td>
<td>TREATMENT</td>
<td>C49656</td>
<td>CDISC</td>
<td>2011-06-10</td>
<td></td>
</tr>
</tbody>
</table>
Study Design

<table>
<thead>
<tr>
<th>Run-in Epoch</th>
<th>First Treatment Epoch</th>
<th>Second Treatment Epoch</th>
<th>Follow Up Epoch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm AB</td>
<td>A 5 mg</td>
<td>A 10 mg</td>
<td>B 5 mg</td>
</tr>
<tr>
<td>Arm BA</td>
<td>B 5 mg</td>
<td>B 10 mg</td>
<td>A 5 mg</td>
</tr>
</tbody>
</table>

Note: Arm AB and Arm BA refer to different study arms.
# Schedule of Activities (SoA)

<table>
<thead>
<tr>
<th>Procedures</th>
<th>Screening</th>
<th>Enrollment/Baseline (Visit 1)</th>
<th>Follow-Up (Visit 2)</th>
<th>Follow-Up (Visit 3)</th>
<th>Follow-Up (Visit 4)</th>
<th>Follow-Up (Visit 5)</th>
<th>Follow-Up (Visit 6)</th>
<th>Follow-Up (Visit 7)</th>
<th>Follow-Up (Visit 8)</th>
<th>Follow-Up (Visit 9)</th>
<th>Follow-Up (Visit 10)</th>
<th>Follow-Up (Visit 11)</th>
<th>Follow-Up (Visit 12)</th>
<th>Final Study Visit (Visit 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Informed consent</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demographics</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical history</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Randomization</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Administer Investigational Product</td>
<td>x</td>
<td>x</td>
<td></td>
<td>x</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concurrent meds</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical exam</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vital signs</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Performance status</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CBC w/diff, pltS</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum chemistry a</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum Pregnancy test b</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EKG (as indicated)</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adverse event evaluation</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiologic evaluation/imaging</td>
<td>X</td>
<td></td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Use Case 3: Start to End Data Processing

Automatic population of data into artifacts
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.
Biomedical Concept Map
### Table 3.2.1: Summary of Post-Meal Hypoglycemic Episodes by Severity – Table Shell

Hypoglycemic episodes within 2 hours since last meal by severity

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Drug A (%)</th>
<th>E</th>
<th>N</th>
<th>Drug B (%)</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>xxx</td>
<td></td>
<td>xx</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diurnal</td>
<td>xxx</td>
<td>(xx.x)</td>
<td>xxx</td>
<td>xx</td>
<td>(xx.x)</td>
<td>xxx</td>
</tr>
<tr>
<td>Documented Symptomatic</td>
<td>xx</td>
<td>(xx.x)</td>
<td>xx</td>
<td>xx</td>
<td>(xx.x)</td>
<td>xx</td>
</tr>
<tr>
<td>Pseudo Symptomatic</td>
<td>xx</td>
<td>(xx.x)</td>
<td>xx</td>
<td>xx</td>
<td>(xx.x)</td>
<td>xx</td>
</tr>
<tr>
<td>Probable Symptomatic</td>
<td>x</td>
<td>(xx.x)</td>
<td>xx</td>
<td>x</td>
<td>(x.x)</td>
<td>x</td>
</tr>
<tr>
<td>Nocturnal</td>
<td>x</td>
<td>(x.x)</td>
<td>x</td>
<td>x</td>
<td>(x.x)</td>
<td>x</td>
</tr>
<tr>
<td>Documented Symptomatic</td>
<td>x</td>
<td>(x.x)</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probable Symptomatic</td>
<td>x</td>
<td></td>
<td></td>
<td>xx</td>
<td>(x.x)</td>
<td>x</td>
</tr>
</tbody>
</table>

N: Number of subjects; %: Percentage of subjects; E: Number of events
### Table 3.3.1: ADHYSUM Analysis Dataset

<table>
<thead>
<tr>
<th>ID</th>
<th>STUDYID</th>
<th>USUBJID</th>
<th>PARAMCD</th>
<th>STUDYID</th>
<th>USUBJID</th>
<th>AVISIT</th>
<th>VISIT</th>
<th>TRIDURD</th>
<th>SEX</th>
<th>AGE</th>
<th>COUNTRY</th>
<th>TRTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>XYZ00008</td>
<td>000008</td>
<td>A5116P</td>
<td>Week 1</td>
<td>3</td>
<td>72</td>
<td>F</td>
<td>25</td>
<td>DZA</td>
<td>Drug B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>XYZ00008</td>
<td>000008</td>
<td>A5116P</td>
<td>Week 1</td>
<td>3</td>
<td>72</td>
<td>F</td>
<td>25</td>
<td>DZA</td>
<td>Drug B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>XYZ00008</td>
<td>000008</td>
<td>A5116P</td>
<td>Week 1</td>
<td>3</td>
<td>72</td>
<td>F</td>
<td>25</td>
<td>DZA</td>
<td>Drug B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>XYZ00008</td>
<td>000008</td>
<td>A5116P</td>
<td>Week 1</td>
<td>3</td>
<td>72</td>
<td>F</td>
<td>25</td>
<td>DZA</td>
<td>Drug B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>XYZ00008</td>
<td>000008</td>
<td>A5116P</td>
<td>Week 1</td>
<td>3</td>
<td>72</td>
<td>F</td>
<td>25</td>
<td>DZA</td>
<td>Drug B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>XYZ00008</td>
<td>000008</td>
<td>A5116P</td>
<td>Week 1</td>
<td>3</td>
<td>72</td>
<td>F</td>
<td>25</td>
<td>DZA</td>
<td>Drug B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>XYZ00008</td>
<td>000008</td>
<td>A5116P</td>
<td>Week 1</td>
<td>3</td>
<td>72</td>
<td>F</td>
<td>25</td>
<td>DZA</td>
<td>Drug B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>XYZ00008</td>
<td>000008</td>
<td>A5116P</td>
<td>Week 1</td>
<td>3</td>
<td>72</td>
<td>F</td>
<td>25</td>
<td>DZA</td>
<td>Drug B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>XYZ00008</td>
<td>000008</td>
<td>A5116P</td>
<td>Week 1</td>
<td>3</td>
<td>72</td>
<td>F</td>
<td>25</td>
<td>DZA</td>
<td>Drug B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>XYZ00008</td>
<td>000008</td>
<td>A5116P</td>
<td>Week 1</td>
<td>3</td>
<td>72</td>
<td>F</td>
<td>25</td>
<td>DZA</td>
<td>Drug B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>XYZ00008</td>
<td>000008</td>
<td>A5116P</td>
<td>Week 1</td>
<td>3</td>
<td>72</td>
<td>F</td>
<td>25</td>
<td>DZA</td>
<td>Drug B</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 3.3.2: ADHYSUM Dataset Metadata

<table>
<thead>
<tr>
<th>Dataset Name</th>
<th>Dataset Description</th>
<th>Dataset Location</th>
<th>Dataset Structure</th>
<th>Keys</th>
<th>Class</th>
<th>Documentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHYSUM</td>
<td>Hypoglycemic Episodes Summary Data</td>
<td>ADHYSUM.spt</td>
<td>One record per subject per analysis visit per parameter</td>
<td>STUDYID, USUBJID, AVISIT, TRIDURD, PARAMCD</td>
<td>BDS</td>
<td>ADHYSUM SAS/SAP</td>
</tr>
</tbody>
</table>

### Table 3.3.3: ADHYSUM Variable Metadata

<table>
<thead>
<tr>
<th>Variable Name</th>
<th>Variable Label</th>
<th>Type</th>
<th>Length/Display Format</th>
<th>Codes/Controlled Terms</th>
<th>Source/Derivation/Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>STUDYID</td>
<td>Study Identifier</td>
<td>text</td>
<td>$12</td>
<td>ADSL.STUDYID</td>
<td></td>
</tr>
<tr>
<td>USUBJID</td>
<td>Unique Subject Identifier</td>
<td>text</td>
<td>$50</td>
<td>ADSL.USUBJID</td>
<td></td>
</tr>
<tr>
<td>PARAMCD</td>
<td>Parameter Code</td>
<td>text</td>
<td>$8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PARAM</td>
<td>Parameter</td>
<td>text</td>
<td>$80</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AVISIT</td>
<td>Analysis Visit</td>
<td>text</td>
<td>$13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAL</td>
<td>Analysis Value</td>
<td>integer</td>
<td>$8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRIDURD</td>
<td>Total Treatment Duration (Days)</td>
<td>integer</td>
<td>$8</td>
<td>ADSL.TRIDURD</td>
<td></td>
</tr>
<tr>
<td>SEX</td>
<td>Sex</td>
<td>text</td>
<td>$1</td>
<td>ADSL.SEX</td>
<td></td>
</tr>
<tr>
<td>AGE</td>
<td>Age</td>
<td>integer</td>
<td>$8</td>
<td>ADSL.AGE</td>
<td></td>
</tr>
<tr>
<td>COUNTRY</td>
<td>Country</td>
<td>text</td>
<td>$3</td>
<td>ADSL.COUNTRY</td>
<td></td>
</tr>
<tr>
<td>TRTA</td>
<td>Actual Treatment</td>
<td>text</td>
<td>$32</td>
<td>ADSL.TRTA01A</td>
<td></td>
</tr>
</tbody>
</table>
### Tabulation Metadata

<table>
<thead>
<tr>
<th>Row</th>
<th>STUDVID</th>
<th>DOMAIN</th>
<th>USUBJID</th>
<th>CSEQ</th>
<th>CEGAT</th>
<th>CETERM</th>
<th>CEDECOD</th>
<th>CERESP</th>
<th>CEORCUX</th>
<th>CESTDTC</th>
<th>CESTDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>XYZ</td>
<td>CE</td>
<td>XYZ-001-001</td>
<td>2</td>
<td>HYPO SYMPTOMS</td>
<td>SWEATING</td>
<td>Hypothermia</td>
<td>Y</td>
<td>N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>XYZ</td>
<td>CE</td>
<td>XYZ-001-001</td>
<td>3</td>
<td>HYPO SYMPTOMS</td>
<td>TREMORS/TREMBLING</td>
<td>Tremor</td>
<td>Y</td>
<td>N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>XYZ</td>
<td>CE</td>
<td>XYZ-001-001</td>
<td>4</td>
<td>HYPO SYMPTOMS</td>
<td>DIZZINESS</td>
<td>Dizziness</td>
<td>Y</td>
<td>N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>XYZ</td>
<td>CE</td>
<td>XYZ-001-001</td>
<td>5</td>
<td>HYPO SYMPTOMS</td>
<td>COGNITIVE IMPAIRMENT</td>
<td>Cognitive Disorder</td>
<td>Y</td>
<td>Y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>XYZ</td>
<td>CE</td>
<td>XYZ-001-001</td>
<td>6</td>
<td>HYPO SYMPTOMS</td>
<td>LOSS OF CONSCIOUSNESS</td>
<td>Loss of Consciousness</td>
<td>Y</td>
<td>Y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>XYZ</td>
<td>CE</td>
<td>XYZ-001-001</td>
<td>7</td>
<td>HYPO SYMPTOMS</td>
<td>CONVULSIONS/SEIZURES</td>
<td>Convulsions</td>
<td>Y</td>
<td>N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>XYZ</td>
<td>CE</td>
<td>XYZ-001-001</td>
<td>8</td>
<td>HYPO SYMPTOMS</td>
<td>COMA</td>
<td>Coma</td>
<td>Y</td>
<td>N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>XYZ</td>
<td>CE</td>
<td>XYZ-001-001</td>
<td>9</td>
<td>HYPO SYMPTOMS</td>
<td>HYPOGLYCEMIA EVENT</td>
<td>Hypoglycemia</td>
<td>2011-09-24T08:48</td>
<td>30</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Row</th>
<th>RELMIDS</th>
<th>MID</th>
<th>MIDSTDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (cont)</td>
<td>DURING</td>
<td>HYPO1</td>
<td>2011-09-01T11:00</td>
</tr>
<tr>
<td>2 (cont)</td>
<td>DURING</td>
<td>HYPO1</td>
<td>2011-09-01T11:00</td>
</tr>
<tr>
<td>3 (cont)</td>
<td>DURING</td>
<td>HYPO1</td>
<td>2011-09-01T11:00</td>
</tr>
<tr>
<td>4 (cont)</td>
<td>DURING</td>
<td>HYPO1</td>
<td>2011-09-01T11:00</td>
</tr>
<tr>
<td>5 (cont)</td>
<td>DURING</td>
<td>HYPO1</td>
<td>2011-09-01T11:00</td>
</tr>
<tr>
<td>6 (cont)</td>
<td>DURING</td>
<td>HYPO1</td>
<td>2011-09-01T11:00</td>
</tr>
<tr>
<td>7 (cont)</td>
<td>DURING</td>
<td>HYPO1</td>
<td>2011-09-01T11:00</td>
</tr>
<tr>
<td>8 (cont)</td>
<td>DURING</td>
<td>HYPO1</td>
<td>2011-09-01T11:00</td>
</tr>
<tr>
<td>9 (cont)</td>
<td>DURING</td>
<td>HYPO1</td>
<td>2011-09-01T11:00</td>
</tr>
</tbody>
</table>

**supp.cpt**

<table>
<thead>
<tr>
<th>Row</th>
<th>STUDVID</th>
<th>DOMAIN</th>
<th>USUBJID</th>
<th>DVAR</th>
<th>IDVARVAL</th>
<th>QNAM</th>
<th>QLABEL</th>
<th>QVAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>XYZ</td>
<td>CE</td>
<td>XYZ-001-001</td>
<td>CSEQ</td>
<td>1</td>
<td>WHEDCC</td>
<td>When did the hypoglycemic event occur?</td>
<td>BETWEEN BEDTIME AND WAKING</td>
</tr>
<tr>
<td>2</td>
<td>XYZ</td>
<td>CE</td>
<td>XYZ-001-001</td>
<td>CSEQ</td>
<td>8</td>
<td>WHENCC</td>
<td>When did the hypoglycemic event occur?</td>
<td>BETWEEN BEDTIME AND WAKING</td>
</tr>
</tbody>
</table>

**is.cpt**

<table>
<thead>
<tr>
<th>Row</th>
<th>STUDVID</th>
<th>DOMAIN</th>
<th>USUBJID</th>
<th>SPDEVID</th>
<th>LSEQ</th>
<th>LBTESTCD</th>
<th>LBTEST</th>
<th>LBRES</th>
<th>LBRESU</th>
<th>LBSTRES</th>
<th>LBSTRESU</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>XYZ</td>
<td>LS</td>
<td>XYZ-001-001</td>
<td>GLUCOSE METER</td>
<td>1</td>
<td>GLUC</td>
<td>GLUCOSE</td>
<td>60</td>
<td>mg/dL</td>
<td>3.5</td>
<td>mmol/L</td>
</tr>
<tr>
<td>2</td>
<td>XYZ</td>
<td>LS</td>
<td>XYZ-001-001</td>
<td>GLUCOSE METER</td>
<td>2</td>
<td>GLUC</td>
<td>GLUCOSE</td>
<td>65</td>
<td>mg/dL</td>
<td>3.4</td>
<td>mmol/L</td>
</tr>
</tbody>
</table>

**mst.cpt**

<table>
<thead>
<tr>
<th>Row</th>
<th>STUDVID</th>
<th>DOMAIN</th>
<th>USUBJID</th>
<th>LSEQ</th>
<th>MLTSEQ</th>
<th>MLTTRT</th>
<th>MLSTDTC</th>
<th>RELMIDS</th>
<th>MIDS</th>
<th>MIDSTDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>XYZ</td>
<td>ML</td>
<td>XYZ-001-001</td>
<td>1</td>
<td>MEAL</td>
<td>2013-09-31T20:00</td>
<td>LAST MEAL PRIOR TO</td>
<td>HYPO1</td>
<td>2011-09-01T11:00</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>XYZ</td>
<td>ML</td>
<td>XYZ-001-001</td>
<td>2</td>
<td>MEAL</td>
<td>2013-09-31T23:30</td>
<td>LAST MEAL PRIOR TO</td>
<td>HYPO1</td>
<td>2011-09-01T11:00</td>
<td></td>
</tr>
</tbody>
</table>
### Collection Metadata

#### Example CRF 5: Hypoglycemia

<table>
<thead>
<tr>
<th>Event Type</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycemic Events</td>
<td>Yes</td>
</tr>
<tr>
<td>Event Definition</td>
<td>Yes</td>
</tr>
<tr>
<td>Date of Event</td>
<td>Yes</td>
</tr>
<tr>
<td>Date Time of Event</td>
<td>Yes</td>
</tr>
<tr>
<td>Duration of Event</td>
<td>Yes</td>
</tr>
<tr>
<td>Duration of Hypoglycemia</td>
<td>Yes</td>
</tr>
<tr>
<td>Blood Glucose at Onset of Event</td>
<td>Yes</td>
</tr>
<tr>
<td>Blood Glucose at End of Event</td>
<td>Yes</td>
</tr>
</tbody>
</table>

#### Related Events

- Other related events
- Other information

---

**Notes:**
- This CRF is designed to capture any hypoglycemic events that occur in patients with diabetes.
- Data collection includes the date, time, and duration of the event, as well as blood glucose levels at the onset and end of the event.
- Additional related events and information are also captured to provide a comprehensive view of the patient's condition.

---

**Data Quality:**
- Data submitted must be accurate and complete.
- Regular audits are conducted to ensure data quality.

---

**Disclosures:**
- All data is anonymized and protected according to local regulations.
- Participants have the right to withdraw from the study at any time.
3. Project Approach
WS 3
Add transformation semantics

WS 1
Create concepts in knowledge graphs

WS 2
Transform concepts in machine readable form

Biomedical Concepts
Analysis Concepts
Foundational Standards

Load into library

API
Extend API’s

WS 4
Identify and select standards specification (Use Case 1)

WS 5
Configure study specification and create artifacts (Use Case 2)

WS 6
Automatically process and transform data (Use Case 3)
Workstream 1 & 2

- **Workstream 1 - End-to-end concept development**
  - Design concept maps
  - Semantic end-to-end expression of concepts
  - Final analysis output to data collection instruments
  - Includes transformation information
  - Combine Biomedical Concepts (BC) with Analysis Concepts (AC)

- **Workstream 2 - Machine-readable End-to-end concept development**
  - Transform concepts in machine readable form
  - Load in to CDISC Library
  - Extend API’s to extract multifunctional metadata
Workstream 3 & 4

- Workstream 3 - Standard dataset definition extension to include transformation information
  - Add semantics in the form of transformation information (ETL)

- Workstream 4 - End-to-start standards specification development (Use Case 1)
  - Demonstrate identify and select capability
  - Ensure API output is complete
  - Combine all metadata in specification pool
Workstream 5

- Workstream 5 - Start-to-end study metadata development (Use Case 2)
  - Study specific configuration of standards metadata
  - Instantiate metadata on a study level
  - Demonstrate study build process (includes trial design information)
  - Create study artifacts
    - Datasets
    - Define xml
    - Analysis shells
Workstream 6

- Workstream 6 - Start-to-end auto process and transform (Use Case 3)
  - Process data from collection to analysis
    - Extract data from collection instruments
    - Create operational database (ODM v2)
    - Map and transform SDTM and ADaM data
    - Auto generate analysis outputs
  
- Currently out of scope
  - Creation of study Protocol, SAP, CSR
  - Automated business rules (validation)
Agile Scrum Methodology and Timeframe

- **What is agile scrum methodology**
  - Continuous flexible development process: workstreams to be nimble, iterative, innovative, incremental, evolutionary, quality driven, adaptive, organized, and collaborative.

- **Why use agile scrum methodology**
  - Flexible mechanism to handle moments of change; e.g., technical limitations, requirements, or communication.

- **Project timeframe: 18 months**

  [Diagram showing Scrum Sprint Snapshot]

  - Sprint Planning
    - Kickoff or Team Brainstorming
    - Prioritize Work
    - Define Current Sprint

  - Sprint Prep
    - Agile-Based Readiness

  - Next Sprint Starts

  - Current Sprint Ends

  - Sprint Development
    - 1-2 Days
    - 6-10 weeks

  - Sprint Review
    - Achievements, Reflections, Lessons Learned
    - Focus towards the end of the Sprint

  - Sprint Increment
    - Incremental release of sprint functionality

  - Sprint Retrospective
    - 1 Day

  - www.agilemanifesto.org
Project Status

Done
• Project scope
• Buy in
• Identify CDISC member participants
• Advisory Committee setup
• Onboard participants
• Kickoff

Ahead
• Workstreams Briefing
• Sprints execution
4. Relationship to other Initiatives
Relationship to other initiatives

- Helmsley Transformational Grant
- Blue Ribbon Commission
- TransCelerate Digital Data Flow
- CDISC Data Exchange Standards
  - ODM v2
  - SDM-XML

→ **CDISC 360**: a blueprint for the next generation data standards, aligned with key initiatives
Digital Data Flow Initiative

CDISC / TransCelerate
Digital Data Flow
Move from current state to a future state

Manual Process
• Implementation variances
• Data quality issues
• Untimely
• Cost prohibitive
• Inefficient

Automated Process
• Implementation consistencies
• Data quality improvements
• Timely
• Cost effective
• Efficient
Collaboration Scope
High-Level Overview

360 Project

- Develop concept based data standards model to enable:
  - Auto-prepare study specification
  - Auto-create study metadata and data artifacts
  - Auto-process study data

Collaboration Activities

- Digitize study design, leveraging existing CDISC standards
- Share learnings & identify enhancements in the use of data standards to enable automation

DDF

- Develop blueprint for tech vendors to build “study builder”; will include:
  - Data Standards Requirements, if/as identified
  - Design Patterns
  - Design Principles
  - Reference architecture
  - User requirements
5. Expected outcome
Expected Outcome

• Learn
  • What works and what doesn’t

• Assessment
  • Technology Gap Analysis
  • Standards Gap Analysis

• Building a base for the future
  • Effort calculation
  • Cost / Benefit Analysis
  • Scale up to deliver the standards metadata needed
  • Partnerships with vendors to ensure tools are made available
Thank You!

Peter Van Reusel
Sam Hume
Barry Cohen