CDISC Standards Development Project for Type 1 Diabetes

Public Webinar
Tuesday 17th April 2018
11:00-12:30 (ET)
Topics Covered

• Introduction to the CDISC T1D project funded by The Leona M. and Harry B. Helmsley Charitable Trust
• How and Why CDISC Develops Standards
• The CDISC Standards Development Process
• Current CDISC Diabetes Standards
• Planning for the T1D Project
• How you can get involved
Type 1 Diabetes (T1D)

- T1D is an autoimmune condition
- The body’s immune system attacks insulin producing cells in the pancreas and destroys them
- Leading to the body’s inability to regulate glucose levels in the blood
- This can lead to damage to other organs of the body
- Precise cause of T1D is unknown

https://jdrf.org.uk/information-support/about-type-1-diabetes/
Helmsley Grant for T1D Standards Development

2018  2019  2020

Type 1 Diabetes

Pediatrics & Devices
Prevention & Exercise
- Observational Study
- Recruitment of 1400 babies (pregnancy>6 months old)
- Where T1D is present in an immediate family member (Mother, Father, Brother, Sister)
- Study will look at
  - Genetics of child and family member with T1D
  - Mother’s biome
  - Weight gain during pregnancy and early life
  - Method of birth delivery
  - Mother’s nutrition during pregnancy and breastfeeding
  - Duration of Breast Feeding
  - Child’s immune system and timing of vaccinations
  - Exposure to viruses
- Aims to identify factors that may initiate islet autoimmunity in early life, could lead to providing a means of preventing T1D before the autoimmune process begins

About CDISC

- **Global Standards Development Organization (SDO)**
  - Founded in 1997 (all volunteers)
  - Incorporated in 2000 as a non-profit organization
  - Acts as a trusted neutral, third party
  - Engaged in pre-competitive standards development
  - Convenes industry, academia, and government for standards development
About CDISC

• CDISC has established **worldwide industry standards** to support the electronic acquisition, exchange, submission and archiving of clinical research data and metadata to improve data quality and streamline medical and biopharmaceutical product development and research processes

• **Consensus-based** development

• Standards are **freely available** at [www.cdisc.org](http://www.cdisc.org)

• IP Policy ensures **open standards**
Why are standards needed?

Data Sharing

You *can’t share data* in a meaningful and efficient way without addressing each of the above aspects.
CDISC Standards Development

Drivers

- Regulation
- New scientific discovery
- FHIR, claims and other data sources
- Consumer-driven healthcare

CDISC Team & Volunteers

- >440 organizational members
- Community consensus standards development for clinical & translational research

SHARE Ecosystem

- Ongoing global research support in the Americas, Europe, Japan, China, India, Korea and other regions
- Standards downloaded in 90+ countries

www.cdisc.org
CDISC Standards do NOT Dictate Scientific Questions or Conduct

CDISC Standards in the Clinical Research Process

CDISC Standards improve and maintain consistent DATA QUALITY and improve TRACEABILITY across the research value chain
Support Common Functions for All Research

Providing Common Structure & Terminology for:

- Data Collection
- Data Aggregation (Tabulation)
- Data Analysis
- Data Transfer
Factors for Adoption of CDISC Standards

• Regulatory drivers (US FDA and Japanese PMDA require CDISC standards)
• Increasing pressure to share data (e.g., FAIR data sharing policy)
• Academic journals
  • Requesting use of standards in their publication acceptance requirements
  • Requiring authors to include a data sharing plan and statements addressing how the data will be shared and when the data will become available
• International tasks forces are recommending principles for sharing and reuse of participant data from clinical trials
• Data sharing initiatives (e.g., Project DataSphere)
• Involvement of CDISC member companies in the development projects to raise awareness of the standards developed
• Involvement of academic/research organisations to raise awareness of the standards
What CDISC Does

• Collaborates with industry, regulators, NPOs and academia to develop and maintain data standards for research

• Supports and facilitates standards development teams to create open, free standards (models, implementation guides, supplements, user guides and other documentation)

• Facilitates educational meetings and provides authoritative training on the standards

www.cdisc.org/foundation-standards
Published Standards

• B2E Foundational Standards
  • Protocol - Data Collection - Aggregation - Analysis - Reporting
  • Operational Data Model
  • Controlled Terminology

• Therapeutic Area Standards
  • Examples of how to implement the foundational standards for particular disease or therapeutic area research
Concepts already covered in SDTMIG may only require discussion or development of examples (e.g., vital signs, conmeds, adverse events).

Concepts not covered in the IGs require development of new domains, variables, controlled terminology and examples.
Diabetes Standards Already Developed

- Diabetes V1
  - Released Aug 2014
- Diabetes ADaM Supplement V1
  - Released Dec 2015
- Diabetic Kidney Disease V1
  - Released Dec 2016
T1D Standards Development

SCOPE = New T1D Concepts for Pediatrics & Devices and Exercise & Prevention (not already covered in previous guides)
Diabetes Concepts Already Developed

Diabetes Version 1.0
Released Aug 2014

Subject and Disease Characteristics
- Diagnosis
- Complication History
- Treatment Nalve

Disease Assessments
- Laboratory Tests
  - Glucose Homeostasis and Diabetes Related Markers
  - Lipid Panel
  - Kidney Function
  - Liver Function
  - Other Risk Factor Tests

- Hypoglycemic Events
  - Classification of Hypoglycemic events
  - Event and Symptom Data
  - Blood Glucose Concentration Data
  - Last Meal and Last Diabetic Study Treatment
  - Precipitating Factors, Third Party Assistance, Adverse Event
  - Treatment for the Hypoglycemic Event

- Glucose Measurements
  - Self-Monitoring of Blood Glucose
  - Meal Data in a Meal Tolerance Test

Routine Data
- Concomitant Medications
- Vital Signs
  - Waist & Hip Circumference, Waist/Hip Ratio

Cardiovascular Events/Outcomes
Diabetes Concepts Already Developed

Diabetes ADaM Supplement
Released Dec 2015

Subject-Level Analysis Data
- ADSL
- Stratification Variables
- ADSL Example

Analysis of Glucose Levels
- Self-Monitored Glucose Profile Analysis Dataset
- Mixed-Meal Tolerance Test Dataset
- Self-Monitored Glucose Analysis Results
- Mixed Meal Tolerance Test Analysis Results

Analysis of Glycated Hemoglobin
- HbA1c Analysis Dataset
- HbA1c Analysis Results

Analysis of Hypoglycemic Episodes
- Hypoglycemic Episodes Analysis Dataset
- Hypoglycemic Episodes Analysis Results
- Hypoglycemic Episodes Summary Dataset
- Hypoglycemic Episodes Summary Analysis Results
Diabetic Kidney Disease
Released Dec 2016

Renal Endpoints
- End-Stage Renal Disease (ESRD)
- CDASH SDTM
- Renal Death SDTM

Disease Assessments
- Measures of Renal Function
  - Measured GFR
  - Estimated GFR
  - Proteinuria
  - Common Laboratory Tests
- Chronic Kidney Disease Staging

Analysis Data
- Intermediate Analysis Datasets
  - ADGFR
  - ADrenal
  - AdoM
- Time-To-Event Analysis Datasets
  - ADTIE

Subject and Disease Characteristics
- Diabetes History

Routine Data
- Adverse Events
  - Hypoglycemic Events
- Concomitant Medications
- Vital Signs
• Deliverables for Scoping package for T1D
  • Draft Project Charter
  • Draft Project Plan
  • Scoping Checklist
  • Concept Listing Spreadsheet
  • Initial Gap Analysis
  • Regulatory Input (if applicable)
  • List of Key Medical/Regulatory References
  • Development Team Member list
  • Review Team Member list
Scoping Aims

Type 1 Diabetes

- Pediatrics & Devices
  - 10 Clinical Concepts
  - 10 QRS Instruments

- Prevention & Exercise
  - 10 Clinical Concepts
  - 10 QRS Instruments
Content of TA User Guide (TAUG)

- Explanatory Text
- Concept Maps
- Examples
- Metadata Tables
- References
Concept Map Example - Diabetes Diagnosis

Concept Map 1: Diagnosis of Diabetes

Subject

participates in

Diagnostic Process

has date

results in

Diagnosis

has category=Diabetes

has value

is one of

Type 1 Diabetes

Type 2 Diabetes
CDASH Example – Diabetes Diagnosis History

Annotated CRF: Diabetes History

- **Diagnosis Date**: Enter the date of diagnosis of diabetes.
  - **Prompt**: date
  - **Type**: MHDAT
  - **CDASH Variable Name**: MHDAT
  - **SDTM Variable Name**: MHDAT
  - **Case Report Form completion instructions**: Map directly to SDTM
  - **Implementation Instructions**: Full Date Optional, Year expected.

- **Type of Diabetes**: Select the specific type of diabetes.
  - **Prompt**: text
  - **Type**: MHDTERM
  - **CDASH Variable Name**: MHDTERM
  - **SDTM Variable Name**: MHDTERM
  - **Case Report Form completion instructions**: Map directly to SDTM
  - **Implementation Instructions**: Examples of codestlist could be “Type 1 Diabetes” and “Type 2 Diabetes”, which types to collect is a judgment to be made by the sponsor.

View CRF Metadata

<table>
<thead>
<tr>
<th>Question Text</th>
<th>Prompt</th>
<th>Type</th>
<th>CDASH Variable Name</th>
<th>CDASH Core</th>
<th>SOTM Variable Name</th>
<th>SDTM Core</th>
<th>Case Report Form completion instructions</th>
<th>Mapping Instructions</th>
<th>Implementation Instructions</th>
<th>Permissible Values</th>
<th>Pre-specified Value</th>
<th>Hide?</th>
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<td>date</td>
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<td>MHDAT</td>
<td>HR</td>
<td>MHDAT</td>
<td>Perm</td>
<td>Enter the date of diagnosis of diabetes.</td>
<td>Map directly to SDTM</td>
<td>Also maps to QA in SUPP NH with QNAM= MHDXDT and QLABEL= Date of Diagnosis</td>
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<td>N/A</td>
<td>text</td>
<td>MHEVDTYP</td>
<td>O</td>
<td>MHEVDTYP</td>
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<td>RC</td>
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<td>When MHTERM is pre-specified, this value is &quot;Y&quot;.</td>
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<td>RC</td>
<td>MHOCUR</td>
<td>Perm</td>
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<td>R/C</td>
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SDTM Example – Diabetes Diagnosis History

### mh.xpt

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<th>USUBJID</th>
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### MH NSV Metadata

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### Table 3.11: ADHYPO Analytic Dataset

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</table>
Current Development Plan

2018

Project 1: T1D pediatrics and device concepts
- Stage 0: Planning
- Stage 1: Identification/Modeling of Concepts
- Stage 2: Standards Development
- Stage 3a: Internal Review
- Stage 3b: Public Review
- Stage 3c: Publication
- Stage 4: Education Course Development

Project 2: T1D Prevention and Exercise concepts
- Stage 0: Planning

2019

Project 1: T1D pediatrics and device concepts
- Stage 2: Planning
- Stage 3a: Identification/Modeling of Concepts
- Stage 3b: Standards Development
- Stage 3c: Internal Review
- Stage 3d: Public Review
- Stage 3e: Publication
- Stage 4: Education Course Development

Project 2: T1D Prevention and Exercise concepts
- Stage 0: Planning

2020

Project 1: T1D pediatrics and device concepts
- Stage 3c: Planning

Project 2: T1D Prevention and Exercise concepts
- Stage 3a: Planning
- Stage 3b: Identification/Modeling of Concepts
- Stage 3c: Standards Development
- Stage 3d: Internal Review
- Stage 3e: Public Review
- Stage 4: Education Course Development
The Global Team

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**Doers**
- Forms the core standards development team
- CDISC standards development experts
- Diabetes SMEs from external organizations

**Reviewers**
- Provide concepts from Real World Data
- Forms the global standards review community
- Leads to consensus based standards
Reviewers – what we need from you

- Provide feedback on existing diabetes standards
  - Are they working for you or do we need to adapt them?
- Do the current standards allow you to model data in the T1D focus areas?
  - Pediatrics
  - Devices
  - Prevention
  - Exercise
- What gaps do you see in the current standards in relation to diabetes concepts?
- Can you provide examples of data collection (CDASH), data tabulation (SDTM), and data analysis (ADaM) diabetes concepts that prove difficult to model?
Reviewers – what we need from you

• Add your contact details to the T1D targeted reviewers list

• Email information to: jowen.external@cdisc.org and astclair@cdisc.org
  • Provide input for scoping team evaluation into the project
  • Receive targeted status and update information
  • Plan for review cycles within your organization
  • Targeted invitation to future T1D public webinars
Scoping Process for T1D – Next steps

• Finalize Scoping team members – in progress
• Arrange kick-off meeting with Pediatrics and Devices scoping team – anticipated early May 2018
• Arrange initial concept brainstorm meetings to discuss concepts relevant to pediatrics and devices with scoping team
Scoping Process for T1D – P&D/E&P

- Diagnosis
- History
- Lab tests
- Glucose measurements
- Height/Weight (BMI) growth curve (abnormal growth patterns)
- Self/assisted management
- Motivational studies (educational)
- Remote monitoring

- Routine device data (total daily dose, total daily basal dose, Insulin/Carb. Ratio, time spent in target range. Time above/below target range)
- Device characteristics (type, version, software)
- Device Peripherals (dosing cartridges, needle/canula (infusion set)
- Continuous Glucose Monitors
- Censor augmented pumps
- Closed loop devices (hybrid versus fully automated)
- Bionic Pancreas/Implanted artificial pancreas
- User questionnaires on device usage
- Encapsulated islet cells

- Exercise diaries
- Types of exercise and data collected
- Duration of exercise
- Intensity of exercise
- Automatic data capture devices for exercise
- Managing glucose levels pre/post exercise – smart calculators
- Data integration to manage exercise related hypoglycaemia
- Dual hormone delivery (insulin/glucagon)
- Pattern recognition/learning

- Currently no way to prevent T1D
- Screening programs for early stage T1D
- Prevention or delay of complications (e.g., maintaining target in-range blood glucose levels, medical check-ups)
- Managing high blood pressure/cholesterol
- Flu prevention
- Beta-cell preservation (primary, secondary, tertiary)