CDISC Standards Development Project for Type 1 Diabetes

Public Webinar

Tuesday 17th April 2018

11:00-12:30 (ET)

Topics Covered

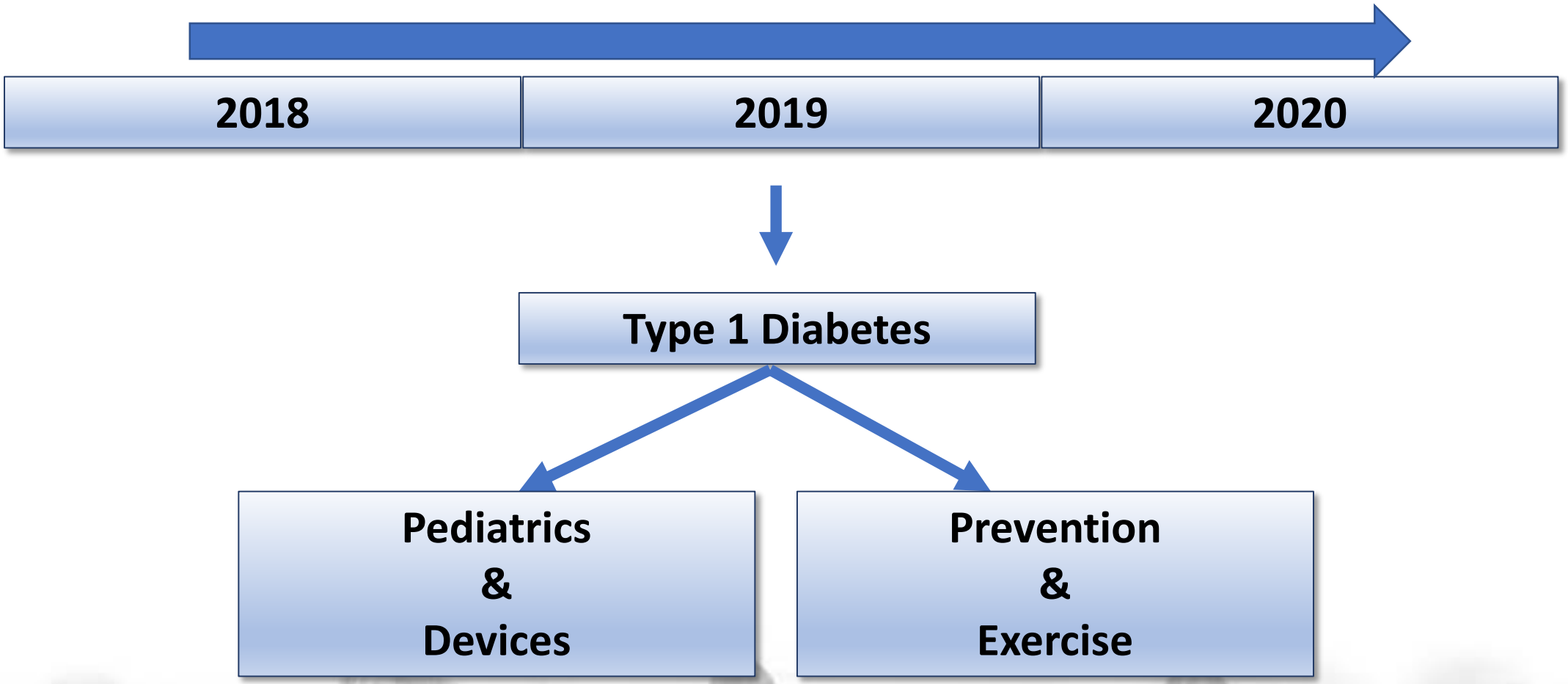
- Introduction to the CDISC T1D project funded by The Leona M. and Harry B. Helmsley Charitable Trust
- How and Why CDISC Develops Standards
- The CDISC Standards Development Process
- Current CDISC Diabetes Standards
- Planning for the T1D Project
- How you can get involved

Type 1 Diabetes (T1D)

- T1D is an autoimmune condition
- The bodies 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



Example

ENDIA environmental determinants of islet autoimmunity

THE LEONA M. AND HARRY B. HELMSLEY CHARITABLE TRUST

- Observational Study
- Recruitment if 1400 babies (pregnancy>6 months old)
- Where T1D is present in an immediate family members (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
  - Mothers nutrition during pregnancy and breastfeeding
  - Duration of Breast Feeding
  - Childs 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

http://www.endia.org.au/about-endia/

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
- IP Policy ensures **open standards**

Why are standards needed?

Homonyms

If you *misunderstand the meaning of clinical concepts* you can't merge or make any meaningful connections or conclusions.

Definitions

If you *have different definitions for clinical concepts* you can't merge or make meaningful connections or conclusions.

Tried to merge data on lesion measurements from 5 organization (Genzyme, GSK, Lilly, Mayo and MD Anderson)

Did not work due to lack of definitions and missing information.

Terminology

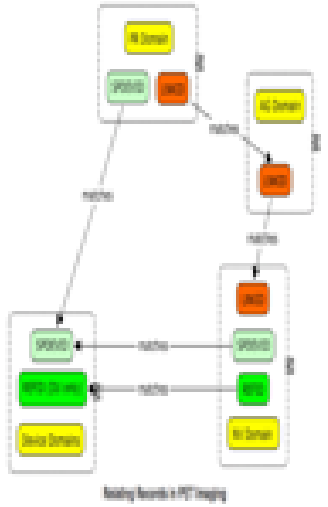
If you *can't agree on the naming conventions and where to use them*, you can't merge or make meaningful connections or conclusions.

SUBJ ID	SEX
0001	M
0002	F
0003	F
0004	M
0005	F

USUBJ ID	SEX
0001	0
0002	1
0003	1
0004	0
0005	1

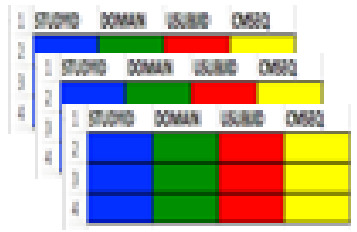
Relationships

If you *don't see the relationships* between and amongst you create variability in how standards implemented.



Organization

If you *can't find the data* you waste time and resource.



Data Sharing

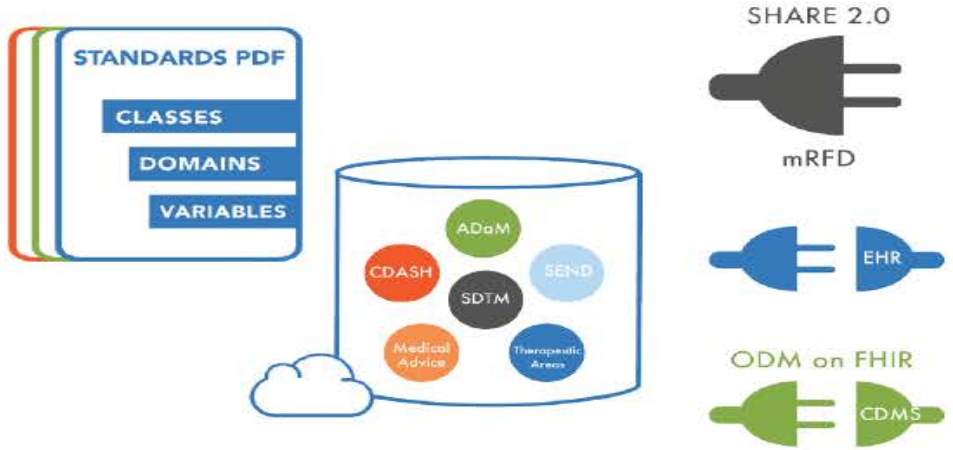
You *can't share data* in a meaningful and efficient way without addressing each of the above aspects.

CDISC Standards Development

Drivers

CDISC Team & Volunteers

SHARE Ecosystem

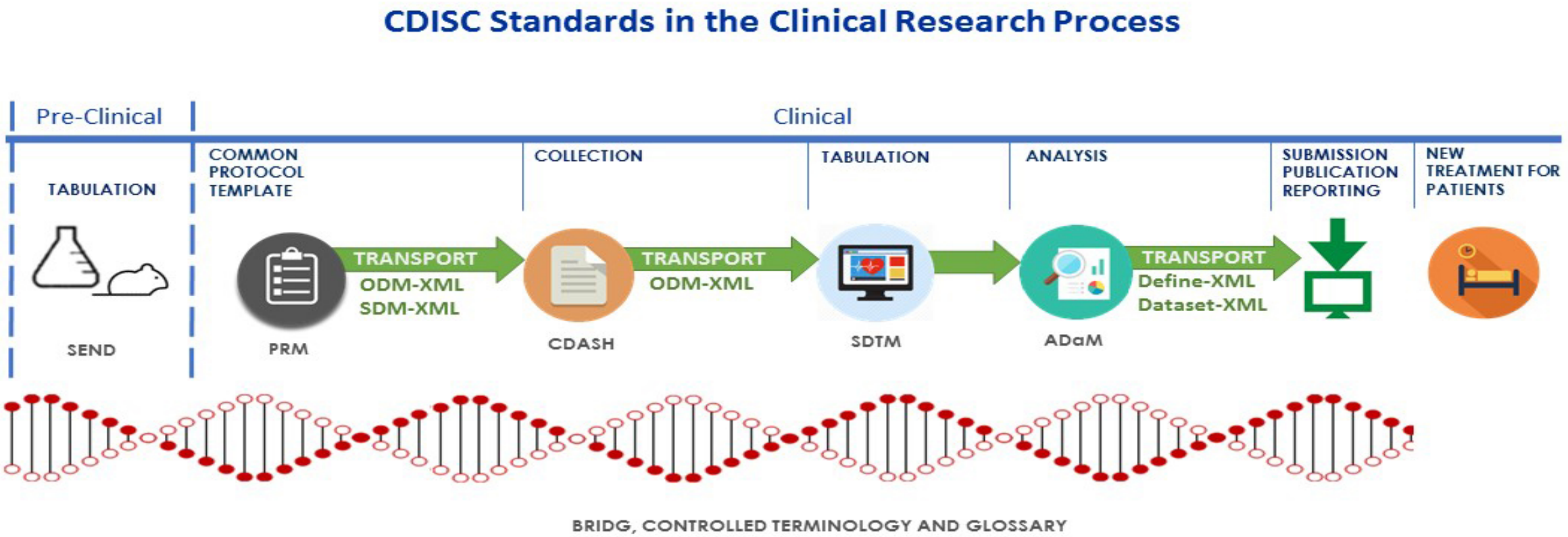


- >440 organizational members
- Community consensus standards development for clinical & translational research
- Ongoing global research support in the Americas, Europe, Japan, China, India, Korea and other regions
- Standards downloaded in 90+ countries

www.cdisc.org

CDISC Standards do NOT

Dictate Scientific Questions or Conduct



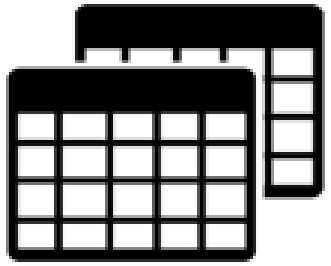
CDISC Standards improve and maintain consistent DATA QUALITY and improve TRACEABILITY across the research value chain

CDISC Standards DO

Support Common Functions for All Research

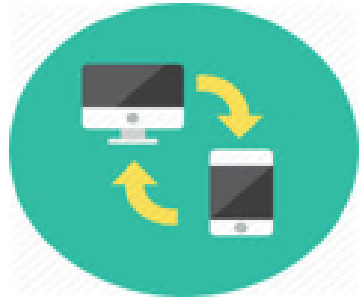
Providing Common Structure & Terminology for:

Data Collection



Data Aggregation (Tabulation)

Data Analysis



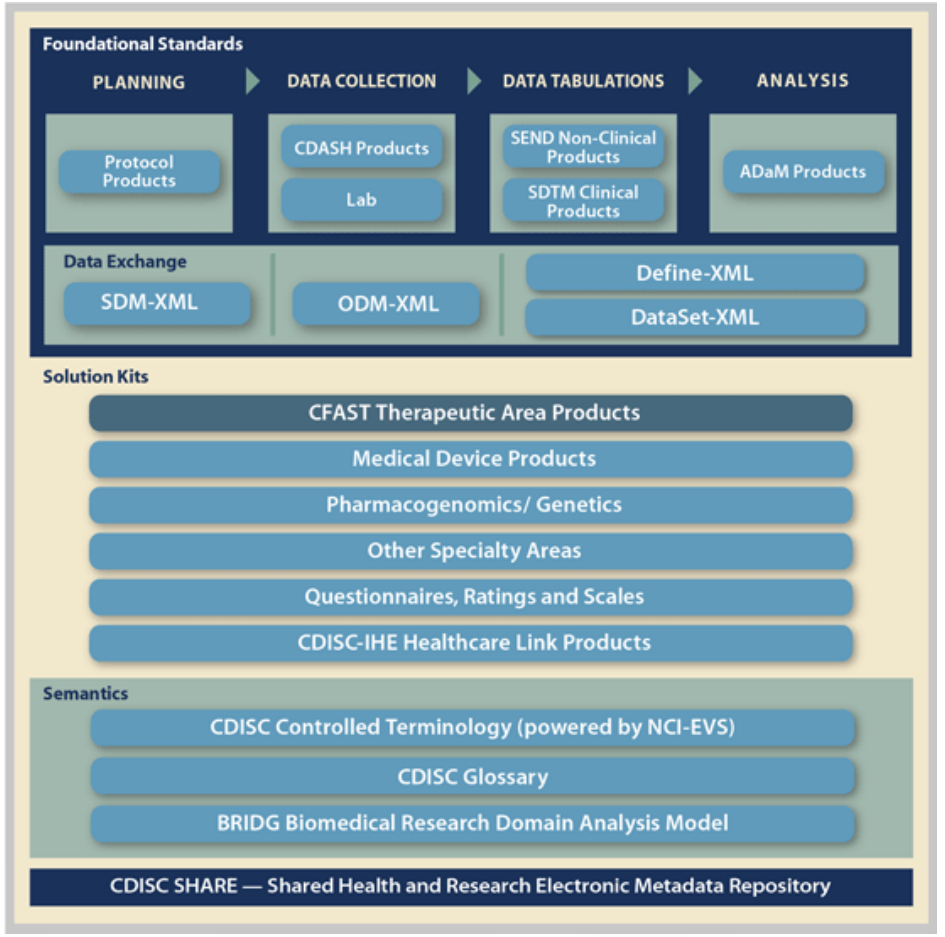
Data Transfer

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



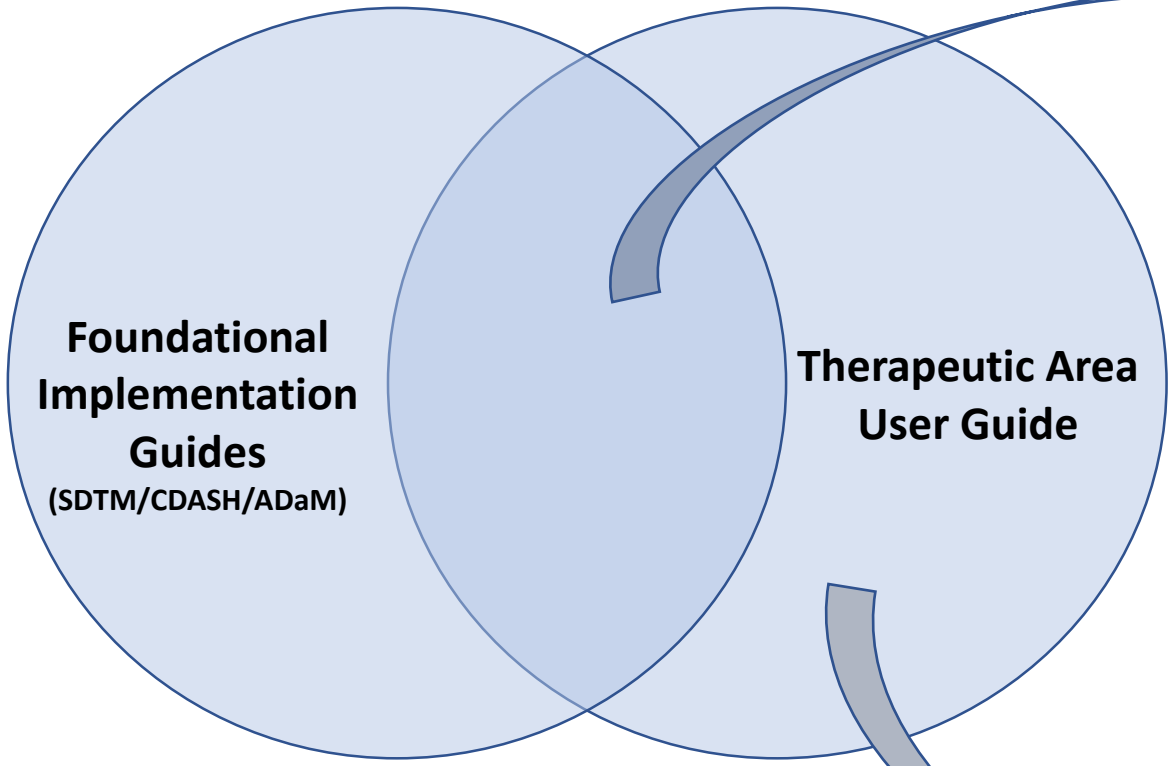
www.cdisc.org/foundation-standards

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

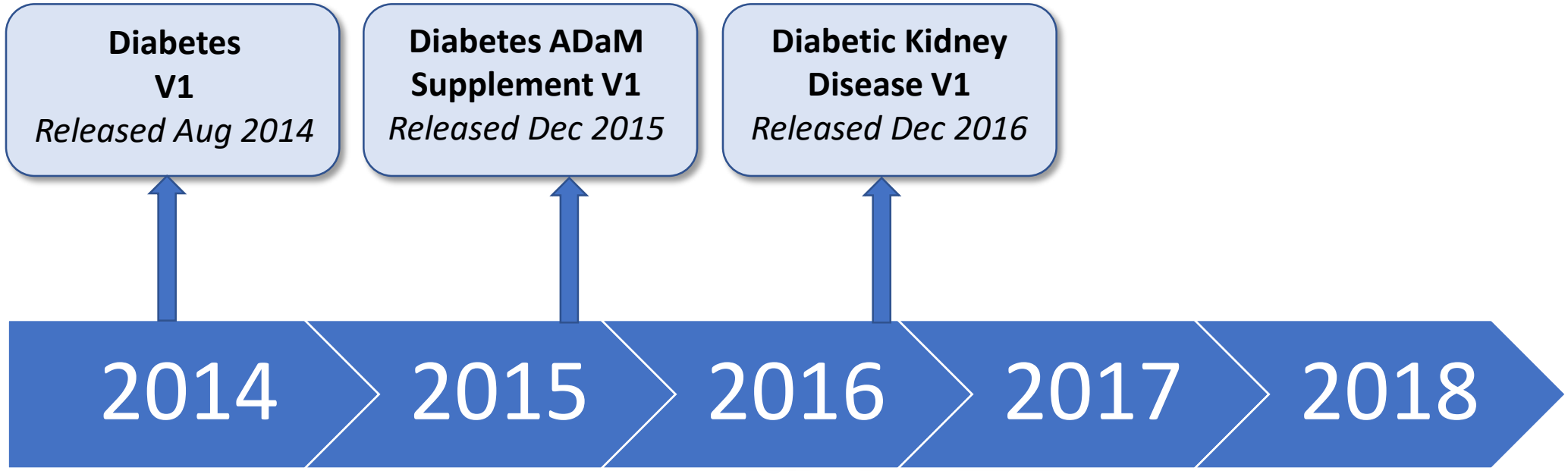
Therapeutic Area User Guide Development



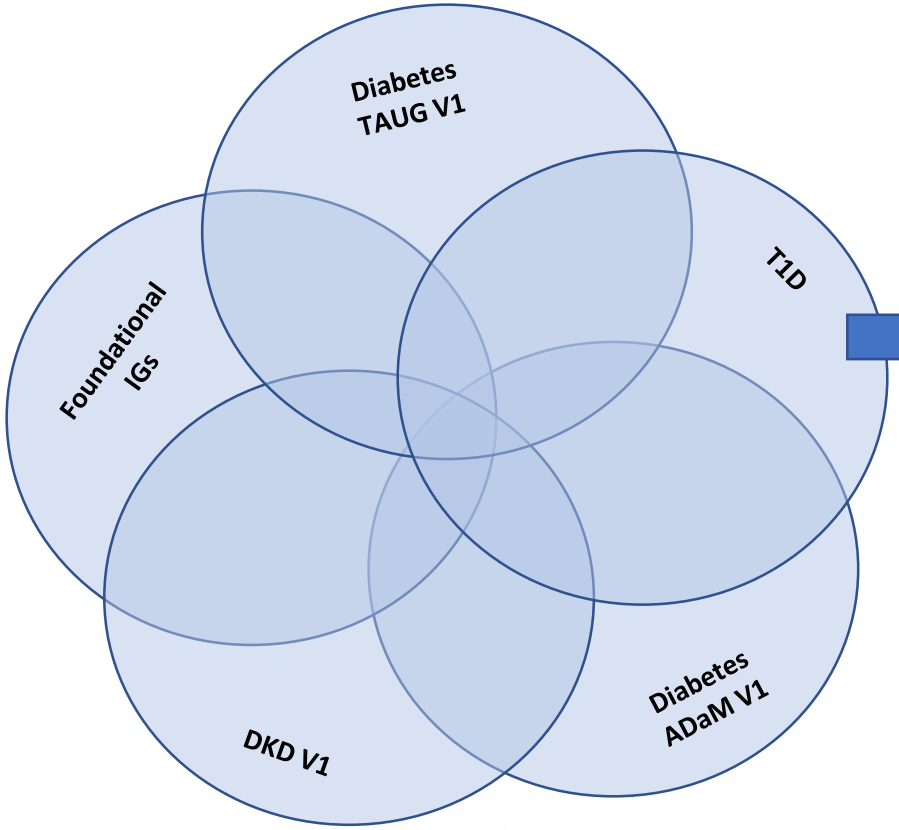
Concepts already covered in SDTMIG may only require discussion or development of examples (e.g., vital signs, conmeds, adverse events)

Concepts not covered in the IGs require development of new domains, variables, controlled terminology and examples

Diabetes Standards Already Developed



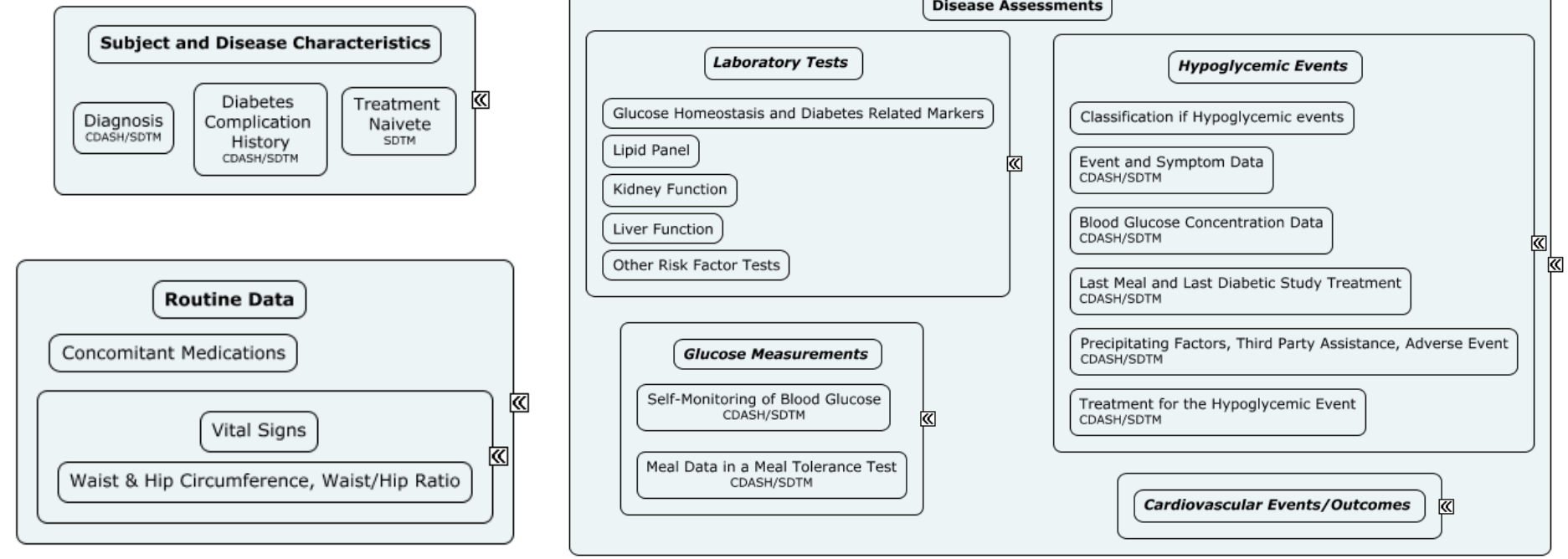
T1D Standards Development



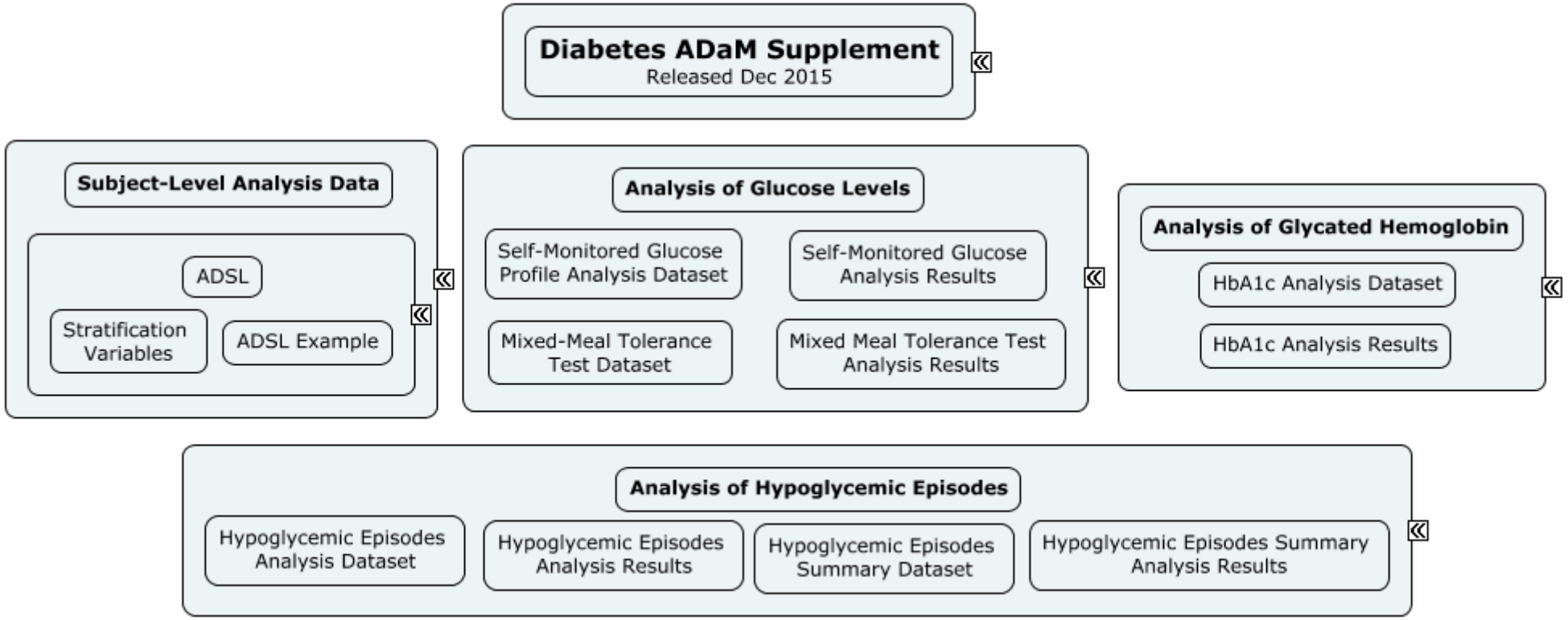
SCOPE = New T1D Concepts for
Pediatrics & Devices
and
Exercise & Prevention
(not already covered in previous guides)

Diabetes Concepts Already Developed

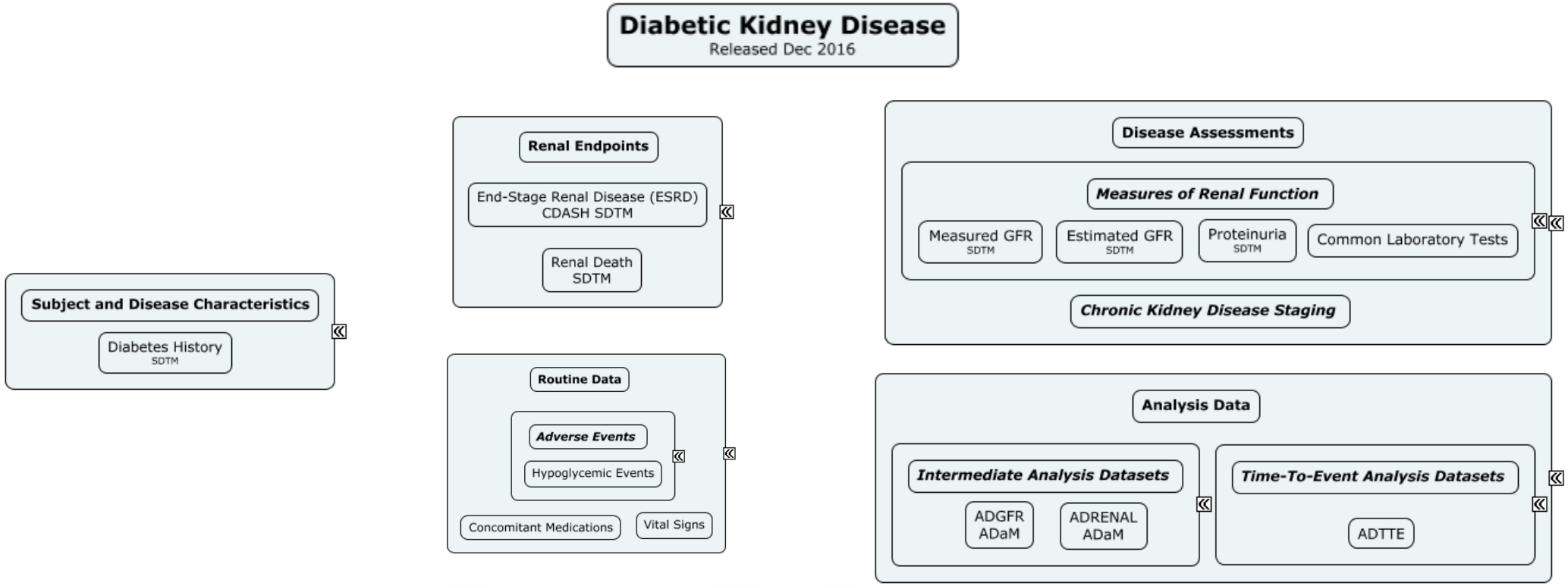
Diabetes Version 1.0
Released Aug 2014



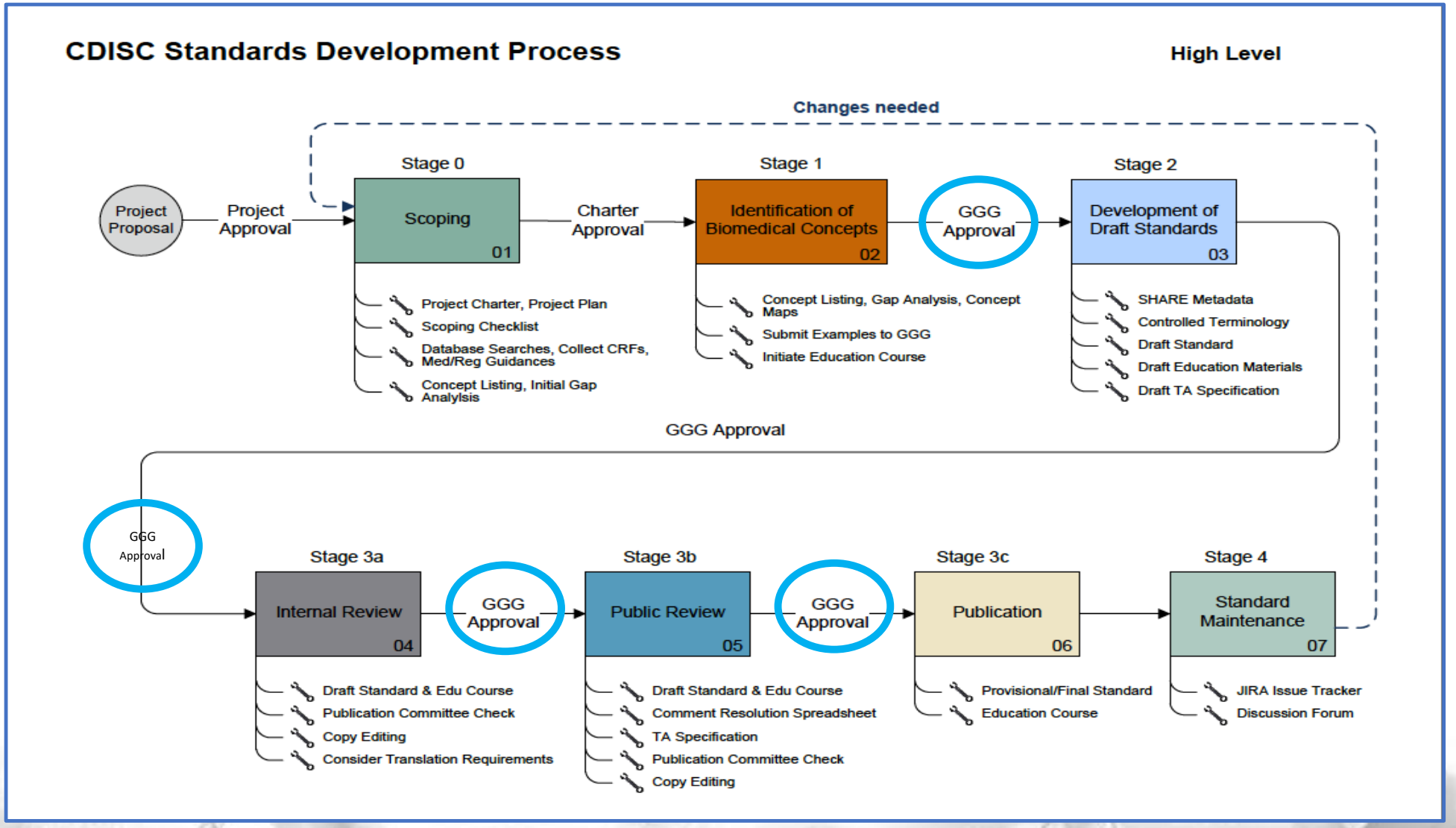
Diabetes Concepts Already Developed



Diabetes Concepts Already Developed



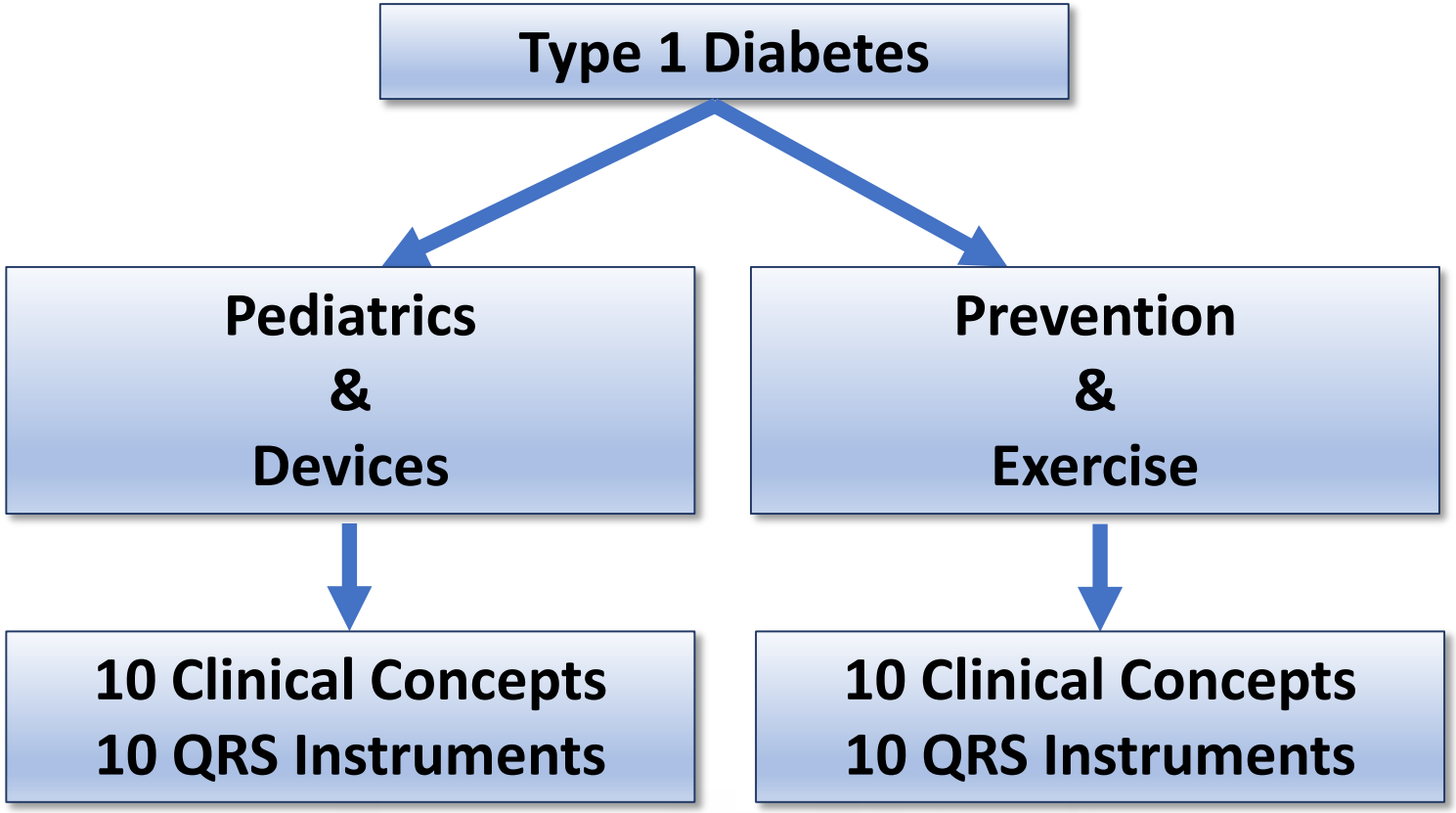
CDISC Standards Development Process



Scoping Process for T1D

- 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

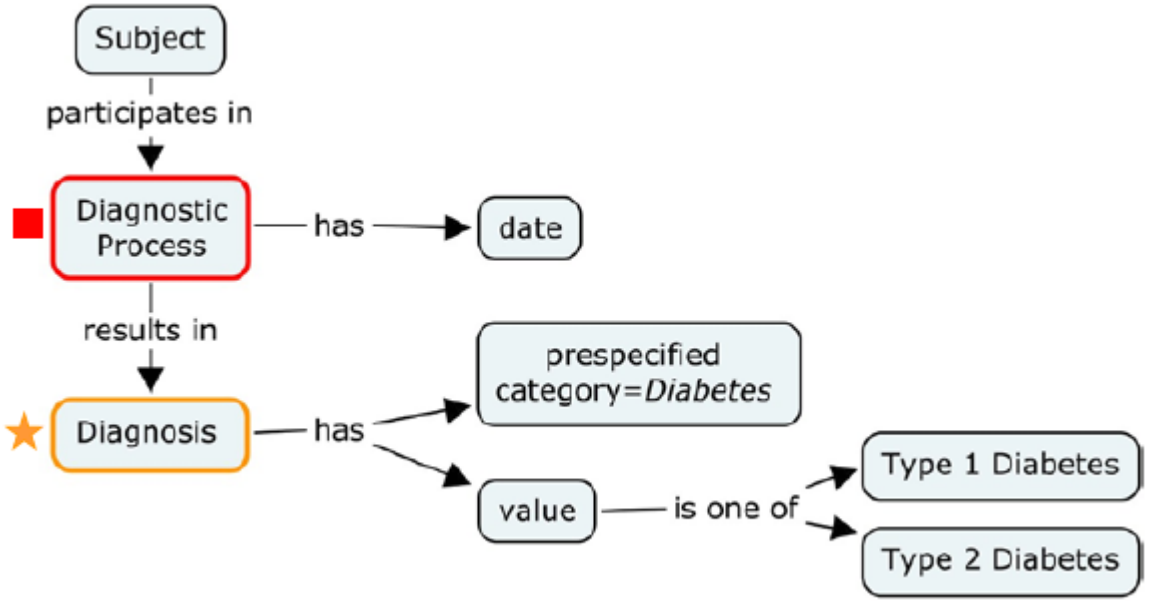
Scoping Aims



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

CDASH Example – Diabetes Diagnosis History

Annotated CRF: Diabetes History

Enter the date of diagnosis of diabetes.	Diagnosis Date MHSTDAT MHSTDTC	dd/mm/yyyy
	MHEVDTYP *Hidden/pre-populated*	DIAGNOSIS
Select the specific type of diabetes.	Type of Diabetes MHTERM	○ Type 1 Diabetes ○ Type 2 Diabetes
	MHPRESP *Hidden/pre-populated*	◉ Yes ○ No
	MHOCCUR *Hidden/pre-populated*	◉ Yes ○ No
	MHCAT *Hidden/pre-populated*	DIABETES

View CRF Metadata

Question Text	Prompt	Type	CDASH Variable Name	CDASH Core	SDTM Variable Name	SDTM Core	Case Report Form completion instructions	Mapping Instructions	Implementation Instructions	Permissible Values	Pre-specified Value	Hide?
Date of Diagnosis of Diabetes	Diagnosis Date	date	MHSTDAT	HR	MHSTDTC	Perm	Enter the date of diagnosis of diabetes.	Map directly to SDTM. Also maps to QVAL in SUPPMH with QNAM= MHDXDTC and QLABEL= Date of Diagnosis	Full Date Optional, Year expected.			
N/A	N/A	text	MHEVDTYP	O	MHEVDTYP	Perm			DIAGNOSIS		DIAGNOSIS	Y
Type of Diabetes		text	MHTERM	HR	MHTERM	Req	Select the specific type of diabetes.	Map directly to SDTM	Examples of codelist could be "Type 1 Diabetes" and "Type 2 Diabetes", which types to collect is a judgment to be made by the sponsor.	Type 1 Diabetes;Type 2 Diabetes		
N/A	N/A	boolean	MHPRESP	R/C	MHPRESP	Perm	Pre-specified = Y	Map directly to SDTM	When MHTERM is pre-specified, this value is "Y".		Y	Y
N/A	N/A	boolean	MHOCCUR	R/C	MHOCCUR	Perm		Map directly to SDTM	When MHTERM is pre-specified, this value is "Y".		Y	Y
N/A	N/A	text	MHCAT	R/C	MHCAT	Perm	Pre-specified = DIABETES	Map directly to SDTM			DIABETES	Y

SDTM Example – Diabetes Diagnosis History

mh.xpt

mh.xpt

Row	STUDYID	DOMAIN	USUBJID	MHSEQ	MHTERM	MHCAT	MHPRESP	MHOCCUR	MHDTC	MHSTDTC	EVDTYP
1	XYZ	MH	XYZ-001-001	1	TYPE 1 DIABETES	DIABETES	Y	Y	2010-09-26	2010-03-25	DIAGNOSIS
2	XYZ	MH	XYZ-001-002	1	TYPE 2 DIABETES	DIABETES	Y	Y	2010-10-26	2010-04-25	DIAGNOSIS

MH NSV Metadata

Variable	Label	Type	Role	Origin
EVDTYP	Event Date Type	text	Non-Standard Record Qualifier	CRF

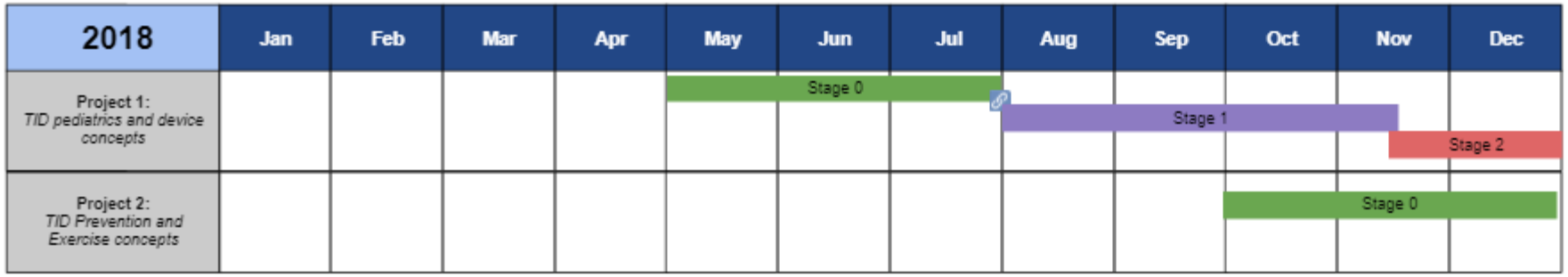
ADaM Example – Hypoglycemic events

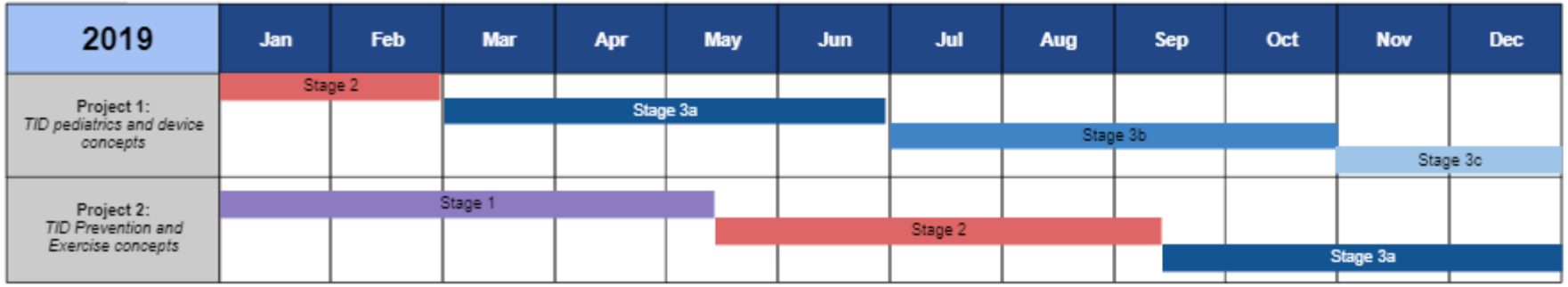
Table 3.1.1: ADHYPO Analysis Dataset

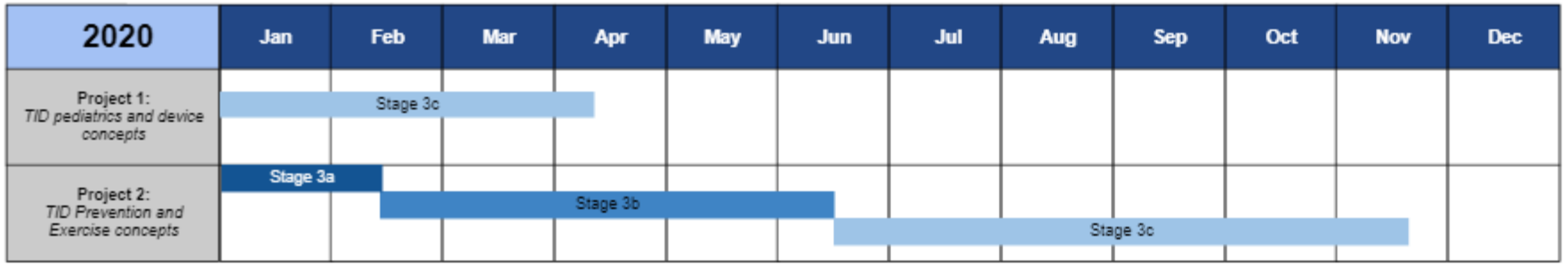
Row	STUDYID	USUBJID	MIDS	CEDECOD	WASAEYN	ASTDTM	TRTEMFL	SELFTRFL	SYMPFL	NOCTFL	GLUCSTD	GLUCCONV	ASTDY	LMLDTM
1	XYZ	000001	HYPO 1	Hypoglycemia	Y	07Sep2012 22:29:00	Y	N	Y	N	2.8	52	3	07Sep2012 20:33:00
2	XYZ	000001	HYPO 2	Hypoglycemia	N	10Sep2012 09:12:00	Y	Y	N	N	2.6	48	6	10Sep2012 08:15:00
3	XYZ	000001	HYPO 3	Hypoglycemia	N	10Sep2012 23:05:00	Y	Y	Y	Y	3.3	60	6	10Sep2012 21:06:00
4	XYZ	000001	HYPO 4	Hypoglycemia	N	11Sep2012 15:24:00	Y	Y	Y	N	3.9	71	7	11Sep2012 14:40:00
5	XYZ	000001	HYPO 5	Hypoglycemia	N	18Sep2012 11:39:00	Y	Y	N	N	3.9	71	14	18Sep2012 08:27:00
6	XYZ	000002	HYPO 1	Hypoglycemia	N	22Oct2012 13:28:00	Y	Y	N	N	3.4	62	6	22Oct2012 09:58:00
7	XYZ	000002	HYPO 2	Hypoglycemia	N	25Oct2012 13:59:00	Y	Y	Y	N	2.4	45	9	25Oct2012 10:50:00
8	XYZ	000002	HYPO 3	Hypoglycemia	N	17Nov2012 05:01:00	Y	N	N	Y	2.8	51	32	17Nov2012 03:30:00

Row	LMLRELTM	LMLRELTU	LEXDTM	LEXRELTM	LEXRELTU	ASEV	ASEVGR1	TRTA
1 (cont)	116	Minutes	07Sep2012 20:29:00	120	Minutes	Severe Hypoglycemia	Documented Symptomatic or Severe Hypoglycemia	Drug A
2 (cont)	57	Minutes	10Sep2012 8:12:00	60	Minutes	Severe Hypoglycemia	Documented Symptomatic or Severe Hypoglycemia	Drug A
3 (cont)	119	Minutes	10Sep2012 20:05:00	180	Minutes	Severe Hypoglycemia	Documented Symptomatic or Severe Hypoglycemia	Drug A
4 (cont)	44	Minutes	11Sep2012 14:26:00	58	Minutes	Severe Hypoglycemia	Documented Symptomatic or Severe Hypoglycemia	Drug A
5 (cont)	192	Minutes	18Sep2012 07:29:00	250	Minutes	Severe Hypoglycemia	Documented Symptomatic or Severe Hypoglycemia	Drug B
6 (cont)	210	Minutes	22Oct2012 09:31:00	237	Minutes	Pseudo-Hypoglycemia	Asymptomatic Hypoglycemia, Probable Symptomatic Hypoglycemia or Pseudo- Hypoglycemia	Drug B
7 (cont)	189	Minutes	25Oct2012 10:29:00	210	Minutes	Severe Hypoglycemia	Documented Symptomatic or Severe Hypoglycemia	Drug B
8 (cont)	91	Minutes	17Nov2012 03:25:00	96	Minutes	Severe Hypoglycemia	Documented Symptomatic or Severe Hypoglycemia	Drug B

Current Development Plan







Stage 0	Scoping and Planning
Stage 1	Identification/Modeling of Concepts
Stage 2	Standards Development
Stage 3a	**Internal Review**
Stage 3b	Public Review
Stage 3c	Publication
Stage 4	Educaton Course Development

The Global Team

Doers

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

Reviewers

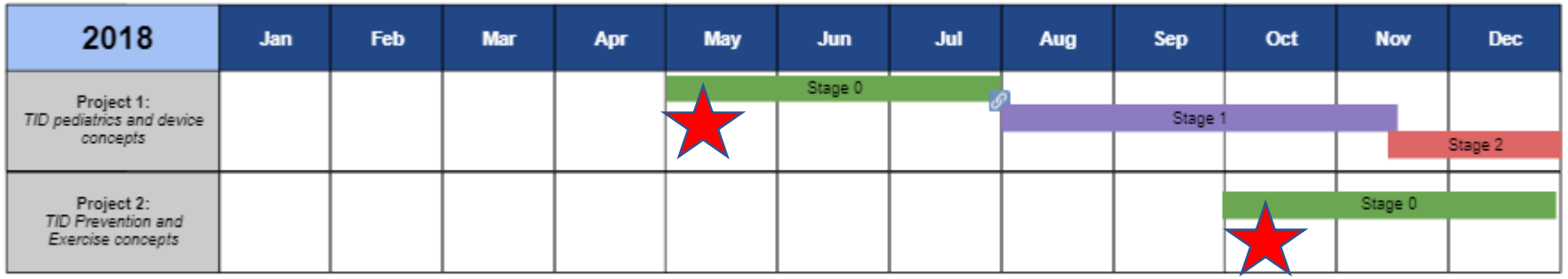
- Provide concepts from Real World Data
- Forms the global standards review community
- Leads to consensus based standards

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



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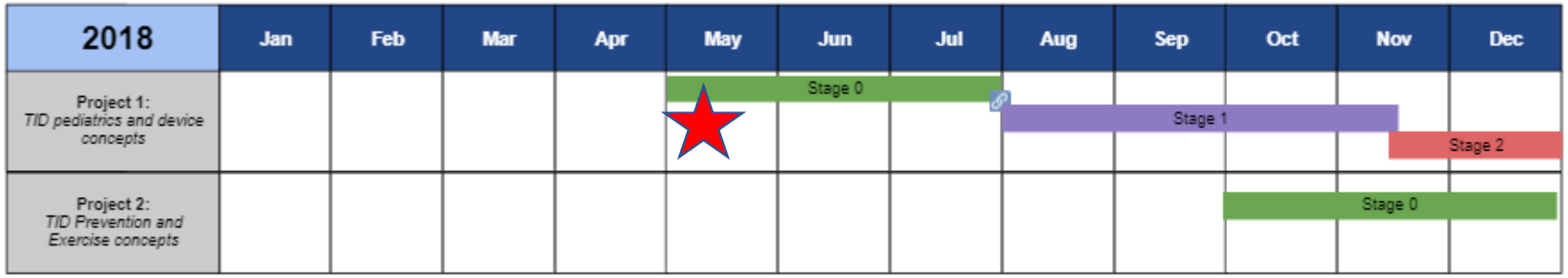
Scoping Process for T1D – Next steps

- 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



Stage 0	Scoping and Planning
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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)

Q&A Session