The Development of the CDISC eTFL Portal to Support the Adoption and Implementation of the Analysis Result Standard

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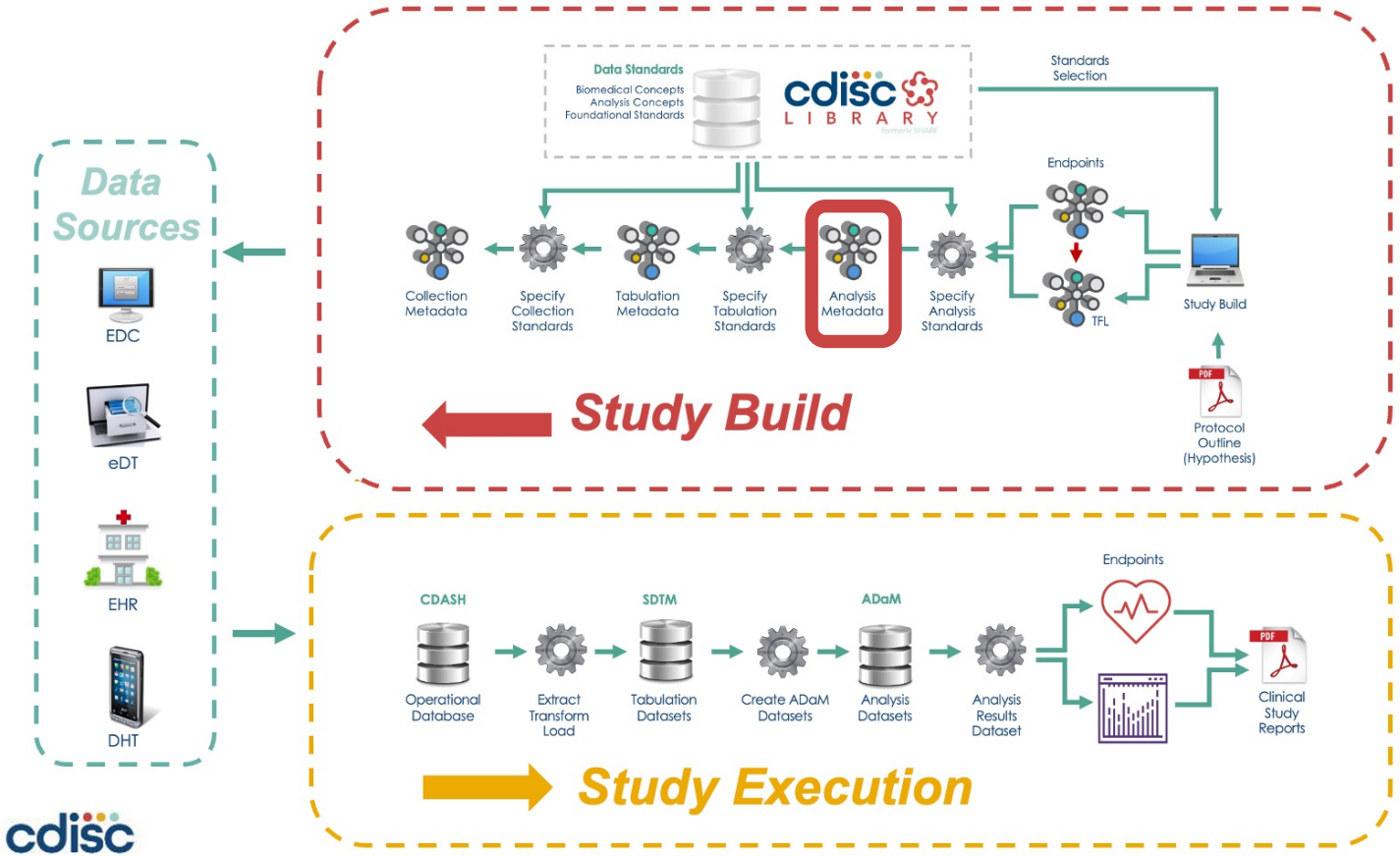
Agenda

- Where we started
- Development of the Analysis Results Standard (ARS)
- Expanding content through the eTFL Portal
- Q&A

Standardizing Analysis Metadata



CDISC 360

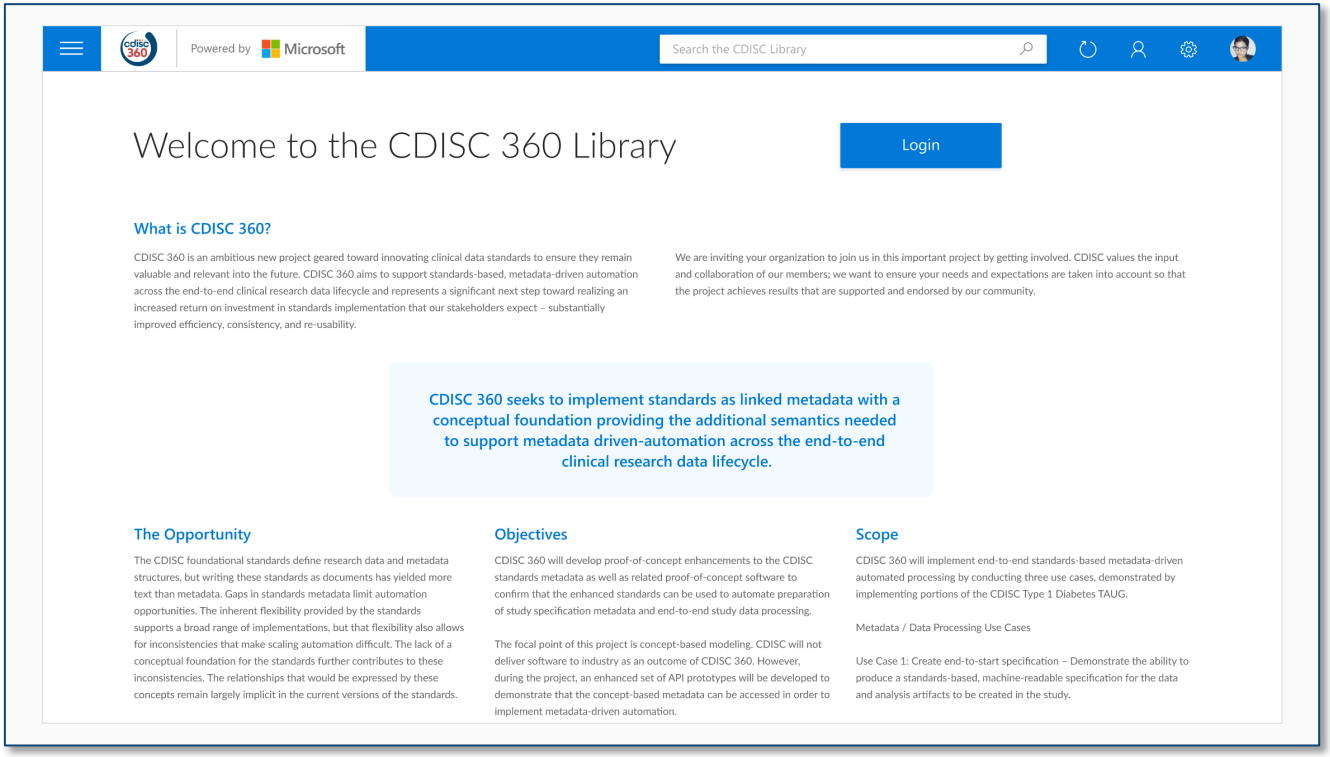
- CDISC 360 was a proof of concept that sought to implement standards as linked metadata with a conceptual foundation providing the additional semantics needed to support metadata-driven automation across the end-to-end clinical research data lifecycle.

- This will enable software developers to develop new tools (proprietary and open source) that consume this novel metadata to ease standards' implementations, while increasing data processing efficiencies.

- Reduce unnecessary variation and lower the barrier to adoption.

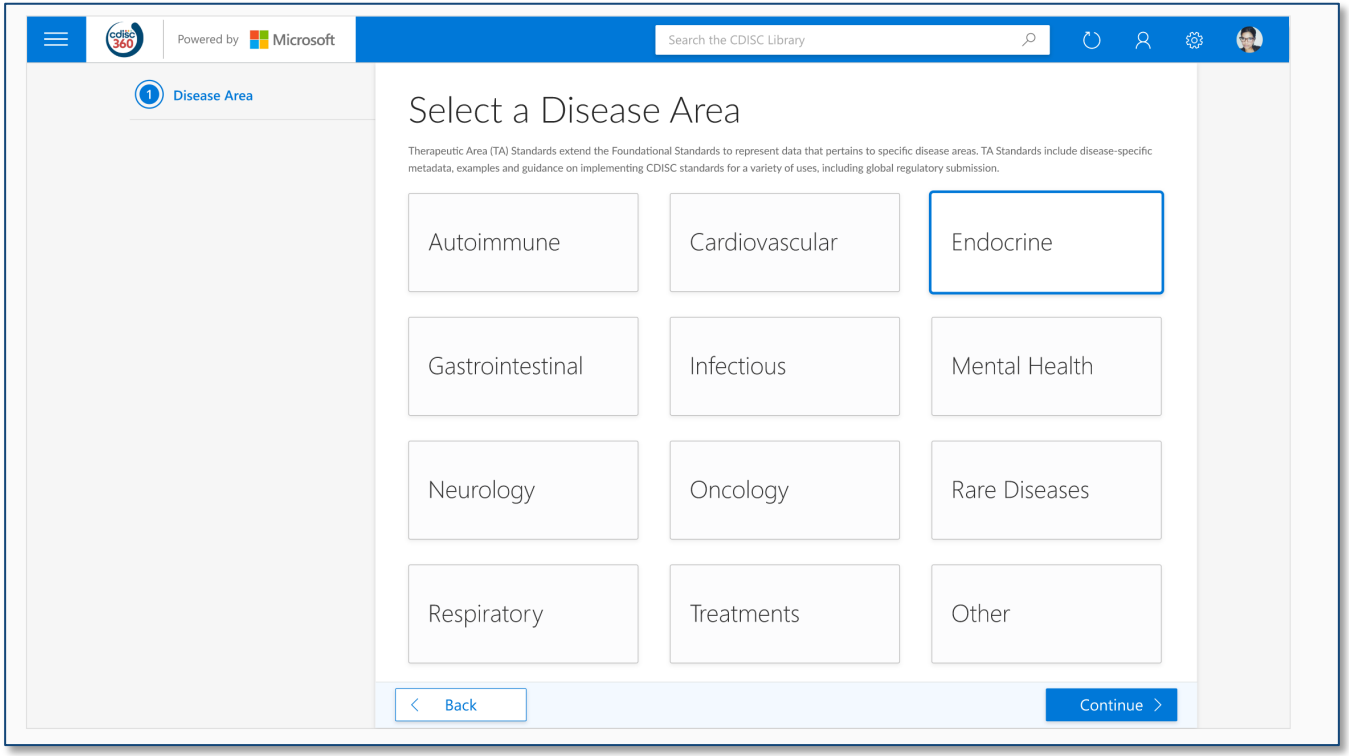
White Paper: https://www.cdisc.org/sites/default/files/2021-06/CDISC_360_Project_White_Paper.pdf

CDISC 360: The Art of the Possible

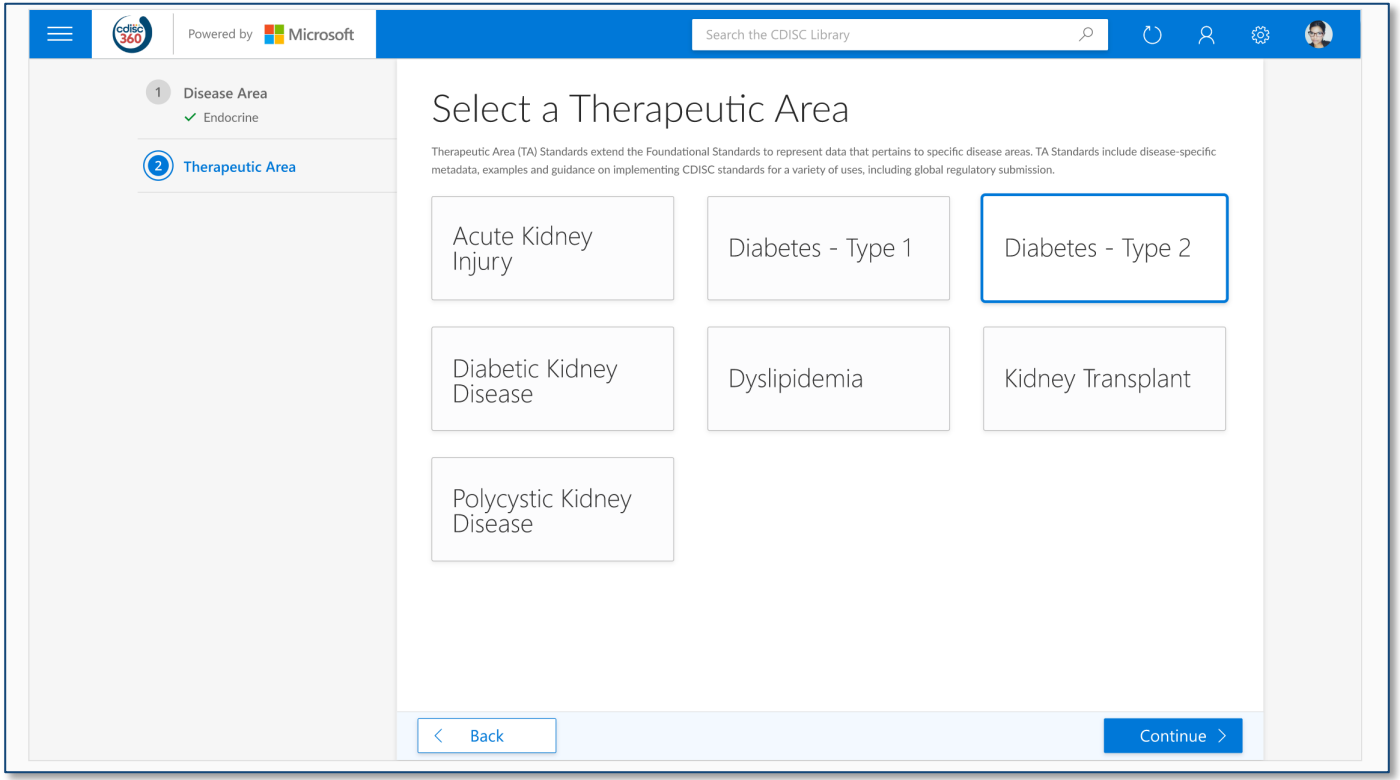


Reference: '*CDISC 360 - The Journey so Far and the Road Ahead', Peter Van Reusel, 28th April 2020*

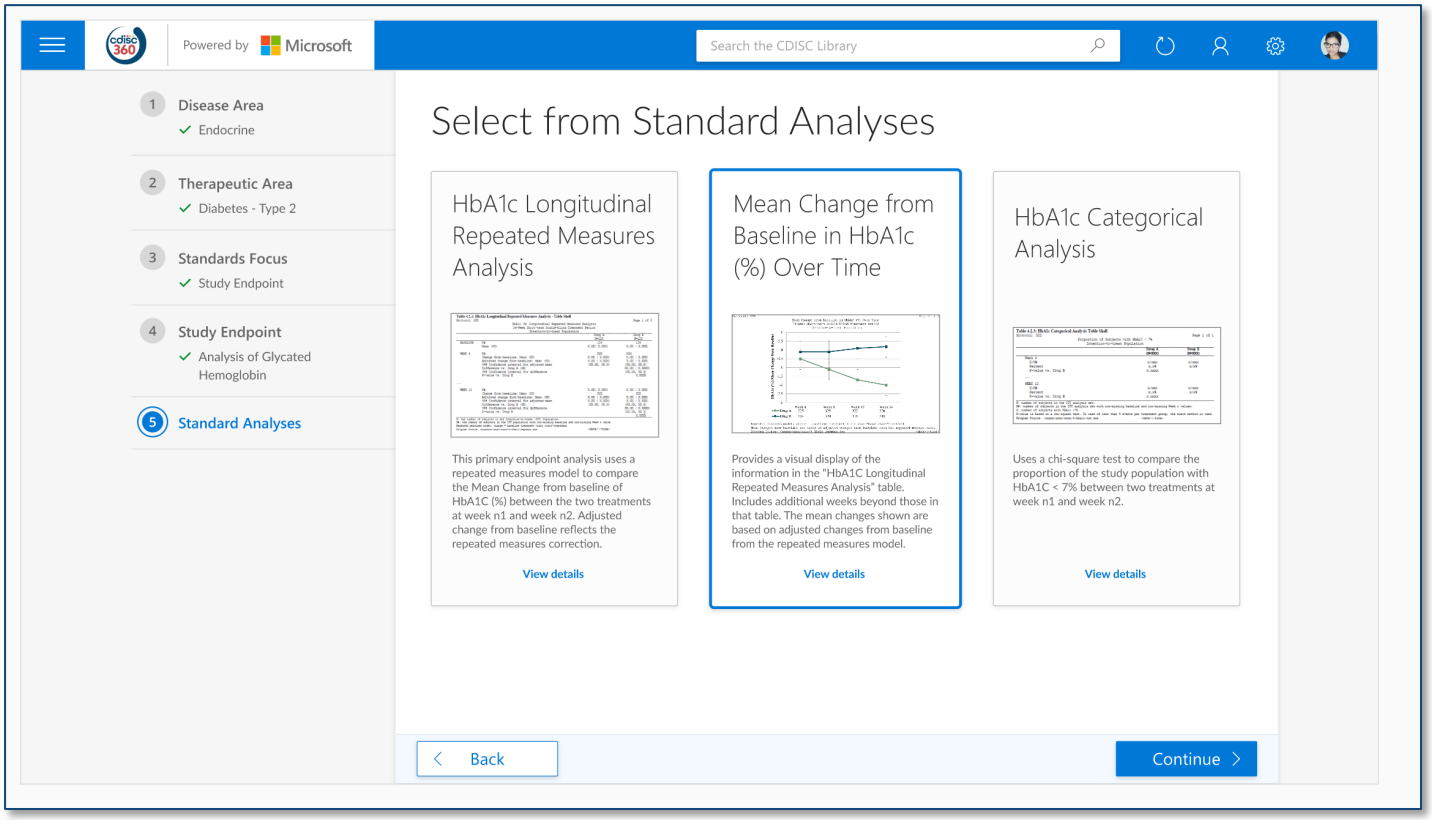
CDISC 360: The Art of the Possible



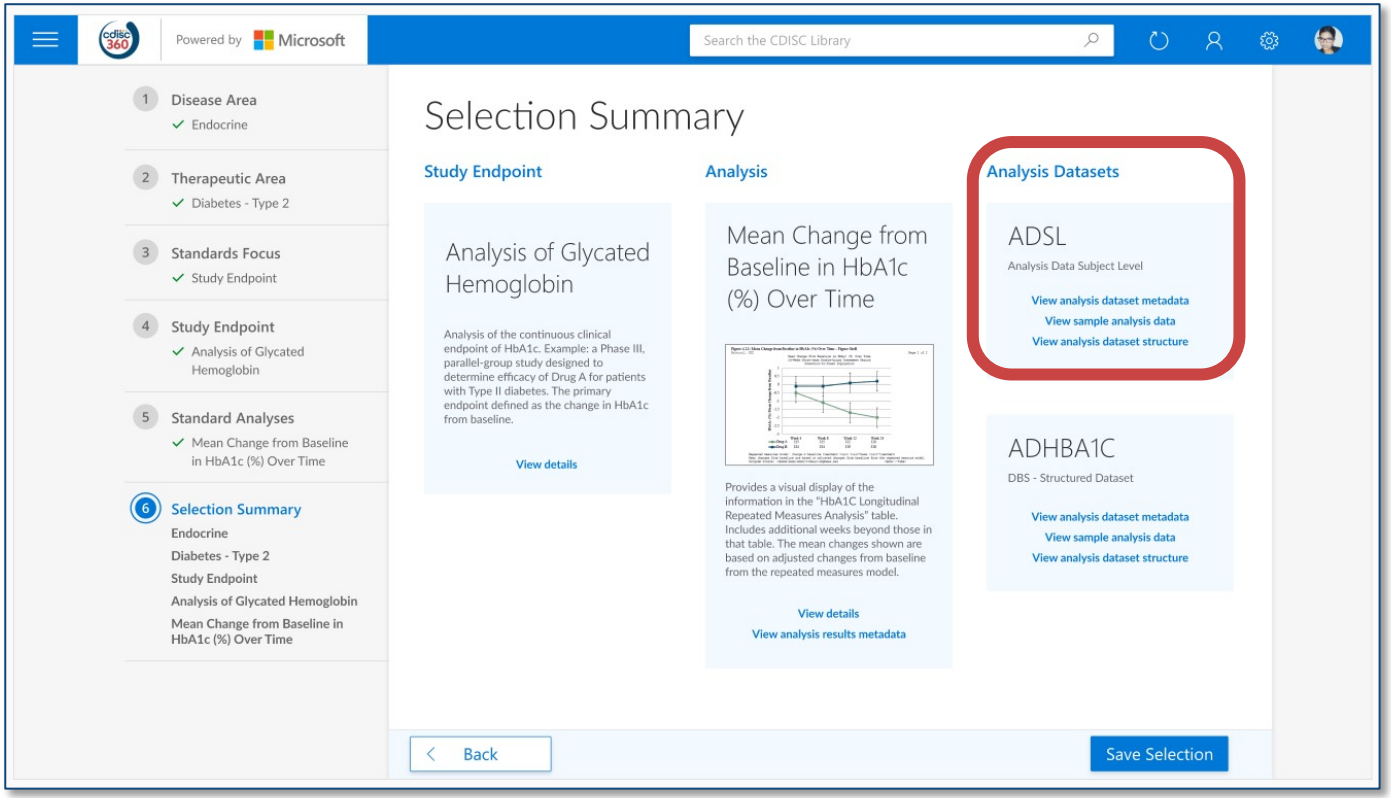
CDISC 360: The Art of the Possible

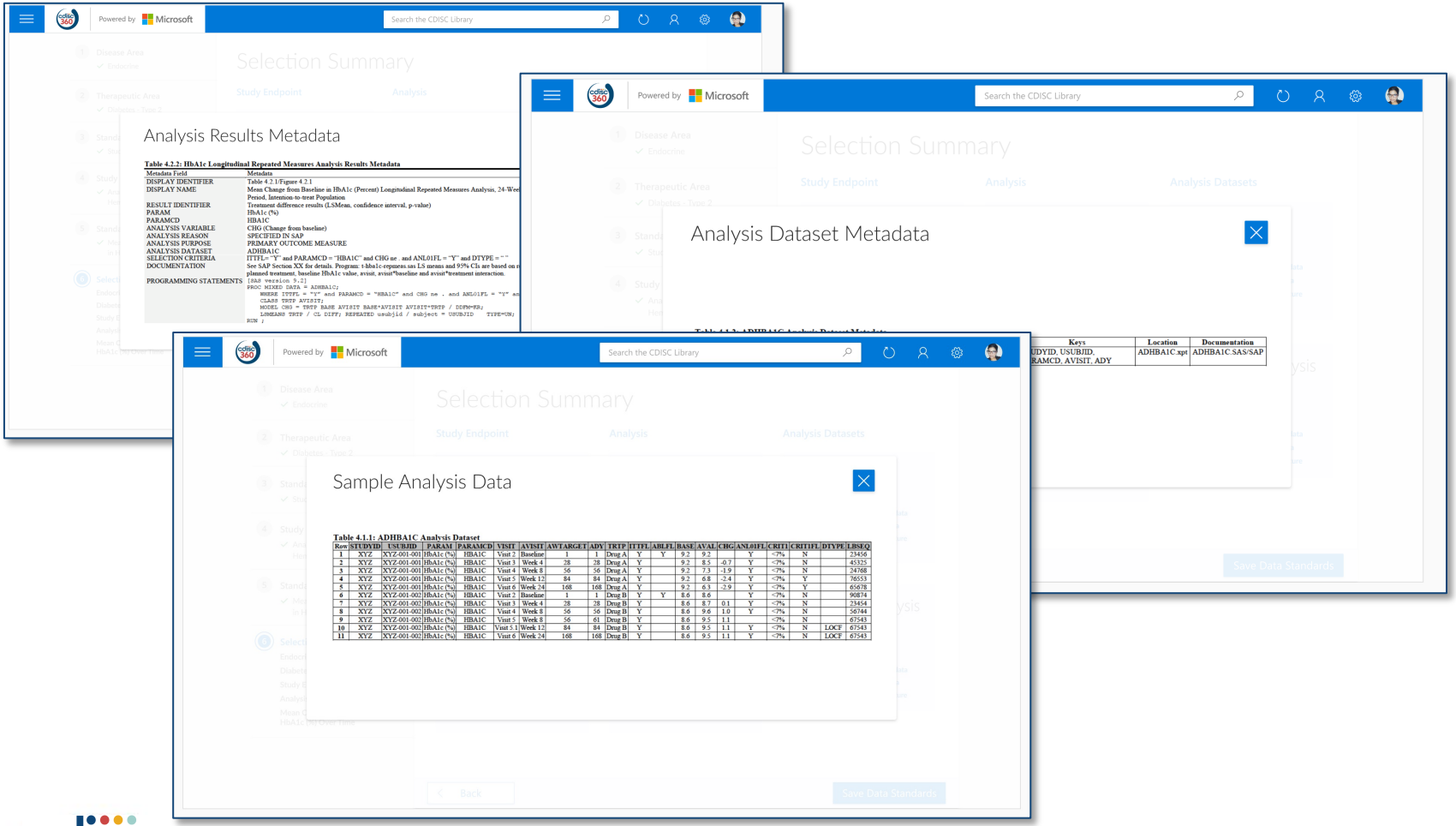


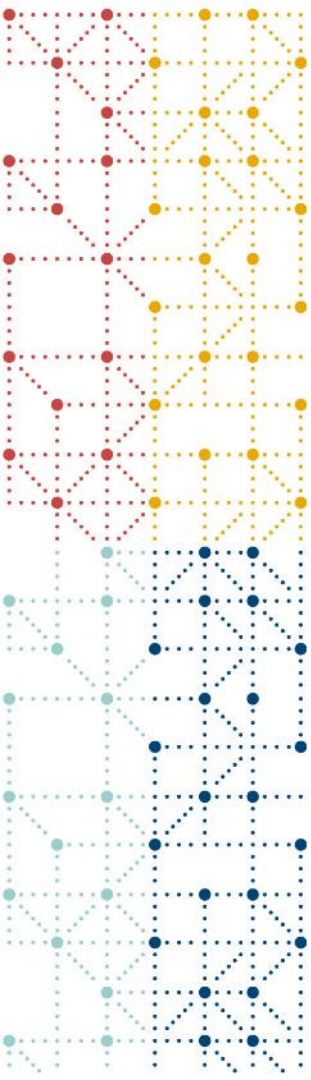
CDISC 360: The Art of the Possible



CDISC 360: The Art of the Possible

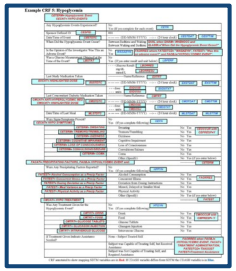



Powered by Microsoft
Search the CDISC Library
Selection Summary
Analysis Results Metadata
Table 4.2.2: HbA1c Longitudinal Repeated Measures Analysis Results Metadata
Metadata Field
Metadata
DISPLAY IDENTIFIER
Table 4.2.1/Figure 4.2.1
DISPLAY NAME
Mean Change from Baseline in HbA1c (Percent) Longitudinal Repeated Measures Analysis, 24-Wee
Period, Intention-to-treat Population
RESULT IDENTIFIER
Treatment difference results (LSMean, confidence interval, p-value)
PARAM
HbA1c (%)
PARAMCD
HBA1C
ANALYSIS VARIABLE
CHG (Change from baseline)
ANALYSIS REASON
SPECIFIED IN SAP
ANALYSIS PURPOSE
PRIMARY OUTCOME MEASURE
ANALYSIS DATASET
ADHBA1C
SELECTION CRITERIA
ITTFL= "Y" and PARAMCD = "HBA1C" and CHG ne . and ANL01FL = "Y" and DTYPE = " "
DOCUMENTATION
See SAP Section XX for details. Program: t-hba1c-repmeas.sas LS means and 95% CIs are based on r
planned treatment, baseline HbA1c value, avisit, avisit*baseline and avisit*treatment interaction.
PROGRAMMING STATEMENTS
[SAS version 9.2]
PROC MIXED DATA = ADHBA1C;
WHERE ITTFL = "Y" and PARAMCD = "HBA1C" and CHG ne . and ANL01FL = "Y" an
CLASS TRTP AVISIT;
MODEL CHG = TRTP BASE AVISIT BASE*AVISIT AVISIT*TRTP / DDFM=KR;
LSMEANS TRTP / CL DIFF; REPEATED usubjid / subject = USUBJID TYPE=UN;
RUN ;
Analysis Dataset Metadata
Keys
Location
Documentation
UDYID, USUBJID,
RAMCD, AVISIT, ADY
ADHBA1C.xpt
ADHBA1C.SAS/SAP
Sample Analysis Data
Table 4.1.1: ADHBA1C Analysis Dataset
Row STUDYID USUBJID PARAM PARAMCD VISIT AVISIT AWTARGET ADY TRTP ITTFL ABLFL BASE AVAL CHG ANL01FL CRIT1 CRIT1FL DTYPE LBSEQ
1 XYZ XYZ-001-001 HbA1c (%) HBA1C Visit 2 Baseline 1 1 Drug A Y Y 9.2 9.2 Y <7% N 23456
2 XYZ XYZ-001-001 HbA1c (%) HBA1C Visit 3 Week 4 28 28 Drug A Y 9.2 8.5 -0.7 Y <7% N 45325
3 XYZ XYZ-001-001 HbA1c (%) HBA1C Visit 4 Week 8 56 56 Drug A Y 9.2 7.3 -1.9 Y <7% N 24708
4 XYZ XYZ-001-001 HbA1c (%) HBA1C Visit 5 Week 12 84 84 Drug A Y 9.2 6.8 -2.4 Y <7% Y 76553
5 XYZ XYZ-001-001 HbA1c (%) HBA1C Visit 6 Week 24 168 168 Drug A Y 9.2 6.3 -2.9 Y <7% Y 65678
6 XYZ XYZ-001-002 HbA1c (%) HBA1C Visit 2 Baseline 1 1 Drug B Y Y 8.6 8.6 Y <7% N 90874
7 XYZ XYZ-001-002 HbA1c (%) HBA1C Visit 3 Week 4 28 28 Drug B Y 8.6 8.7 0.1 Y <7% N 23454
8 XYZ XYZ-001-002 HbA1c (%) HBA1C Visit 4 Week 8 56 56 Drug B Y 8.6 9.6 1.0 Y <7% N 56744
9 XYZ XYZ-001-002 HbA1c (%) HBA1C Visit 5 Week 8 56 61 Drug B Y 8.6 9.5 1.1 <7% N 67543
10 XYZ XYZ-001-002 HbA1c (%) HBA1C Visit 5.1 Week 12 84 84 Drug B Y 8.6 9.5 1.1 Y <7% N LOCF 67543
11 XYZ XYZ-001-002 HbA1c (%) HBA1C Visit 6 Week 24 168 168 Drug B Y 8.6 9.5 1.1 Y <7% N LOCF 67543



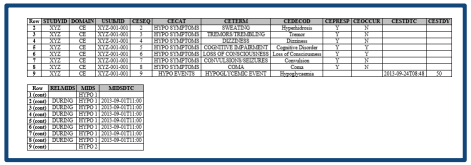
What did we learn from CDISC 360?

CDISC Foundational Standards



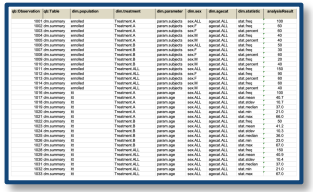
Data Collection

CDASH



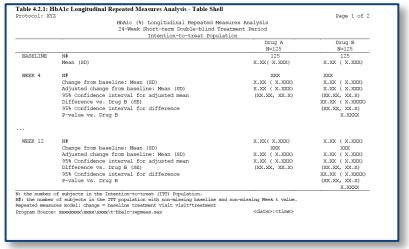
Data Aggregation

SDTM



Analysis

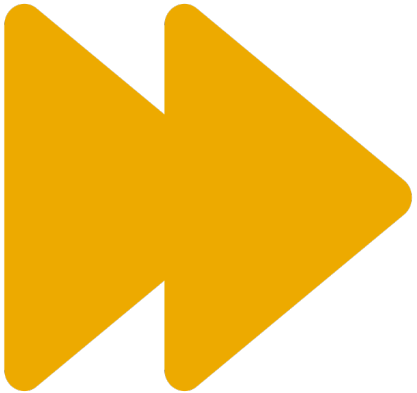
ADaM



Results

???

Fast Forward
Q1 2021 to Q1 2024



CDISC Analysis Result Standards – Released April 19, 2024!

cdisc
Clear data. Clear impact

Analysis Results Standard (ARS) v1.0

cdisc ARS ANALYSIS RESULTS STANDARD

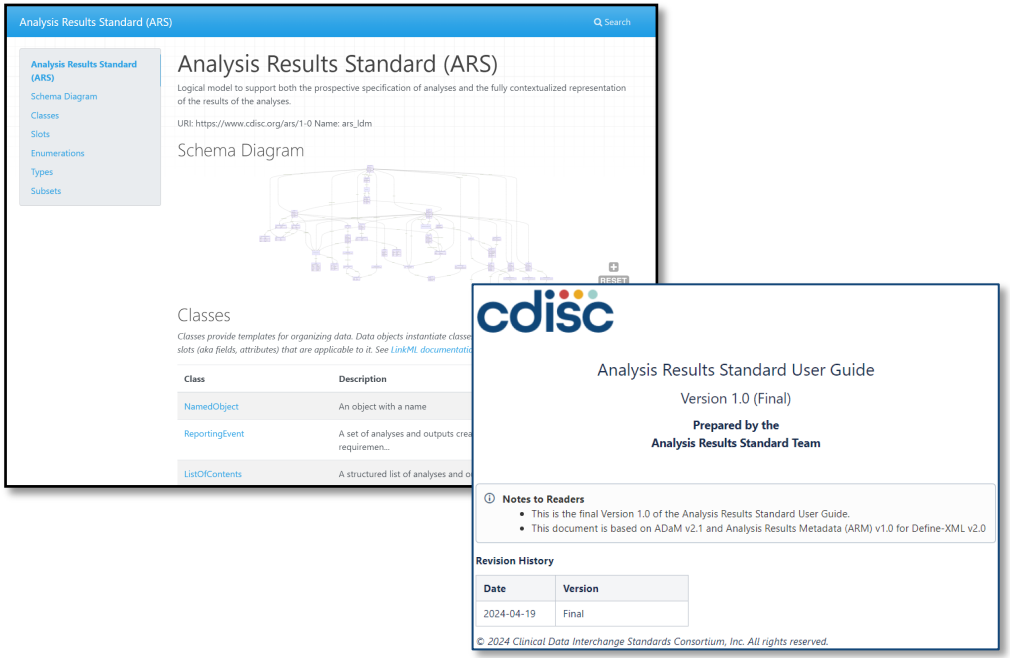
Large trials generate many analysis results in the form of tables, figures, and written reports, yet these results are rarely output in a form that is machine-readable. Previously, there has been no standard way of describing and organizing these results, making it difficult to automate their generation, make them reproducible, trace their origin, or enable them to be reused in other outputs.

To address these inefficiencies, CDISC has developed the Analysis Results Standard (ARS), which aim to facilitate automation, reproducibility, reusability, and traceability of analysis results data.

Features of ARS v1.0

- A Logical Data Model that describes analysis results and associated metadata.
- A User Guide to illustrate and exercise the model with common safety displays.

https://cdisc-org.github.io/analysis-results-standard/



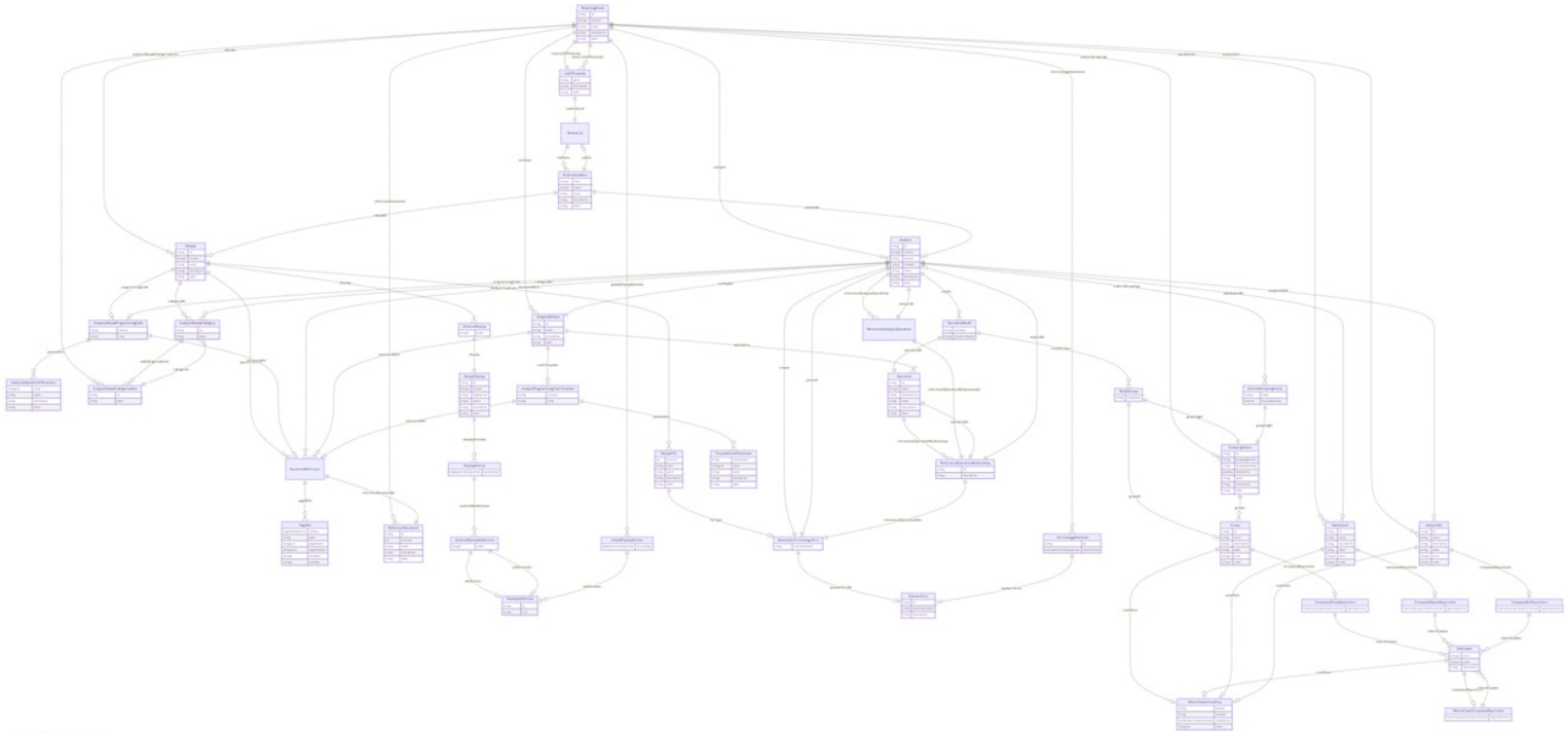
https://wiki.cdisc.org/display/ARSP/Analysis+Results+Standard+User+Guide+v1.0

Analysis Results Key Objectives

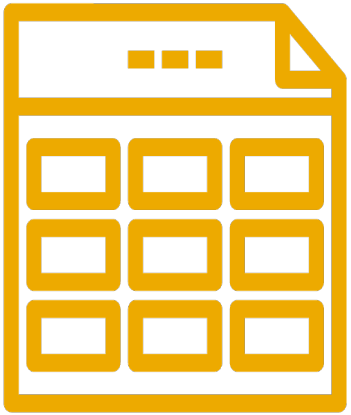
Leverage analysis results metadata to drive the automation of results

Support storage, access, processing, traceability and reproducibility of results

ARS Logical Model Schema Diagram



ARS User Guide Reporting Events Example



- Common Safety Displays
  - Summary of Demographics
  - Overall Summary of Treatment-Emergent Adverse Events
  - Summary of TEAE by System Organ Class and Preferred Term
  - Summary of Observed and Change from Baseline by Scheduled Visits - Vital Signs
  - Summary of Observed and Change from Baseline by Scheduled Visits - Vital Signs <Vertical Layout>
- FDA Standard Safety Tables and Figures
  - Table 2: Baseline Demographic and Clinical Characteristics, Safety Population

Creating Analysis Results Metadata: JSON

Table 2. Baseline Demographic and Clinical Characteristics, Safety Population, Pooled Analyses (or Trial X)

Characteristic	Drug Name Dosage X N = XXX	Drug Name Dosage Y N = XXX	Placebo N = XXX	Active Control N = XXX	Total Population N = XXX
	n (%)	n (%)	n (%)	n (%)	n (%)
Sex, n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Male	n (%)	n (%)	n (%)	n (%)	n (%)
Female	n (%)	n (%)	n (%)	n (%)	n (%)
Age, years	**X.X (Y.Y)**	**X.X (Y.Y)**	**X.X (Y.Y)**	**X.X (Y.Y)**	**X.X (Y.Y)**
Mean (SD)	X.X (Y.Y)	X.X (Y.Y)	X.X (Y.Y)	X.X (Y.Y)	X.X (Y.Y)
Median (min, max)	X.X (Y.Y, Z.Z)	X.X (Y.Y, Z.Z)	X.X (Y.Y, Z.Z)	X.X (Y.Y, Z.Z)	X.X (Y.Y, Z.Z)
Age groups (years), n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
≥17 to <65	n (%)	n (%)	n (%)	n (%)	n (%)
≥65	n (%)	n (%)	n (%)	n (%)	n (%)
≥65 to <75	n (%)	n (%)	n (%)	n (%)	n (%)
≥75	n (%)	n (%)	n (%)	n (%)	n (%)
Race, n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
American Indian or Alaska Native Asian	n (%)	n (%)	n (%)	n (%)	n (%)
Black or African American	n (%)	n (%)	n (%)	n (%)	n (%)
Native Hawaiian or Other Pacific Islander	n (%)	n (%)	n (%)	n (%)	n (%)
White	n (%)	n (%)	n (%)	n (%)	n (%)
Other	n (%)	n (%)	n (%)	n (%)	n (%)

Source: [include Applicant source, datasets and/or software tools used].
[1] Difference is shown between [treatment arms] (e.g., difference is shown between Drug Name dosage X vs. placebo).
Abbreviations: N, number of patients in treatment arm; n, number of patients with given characteristic; SD, standard deviation

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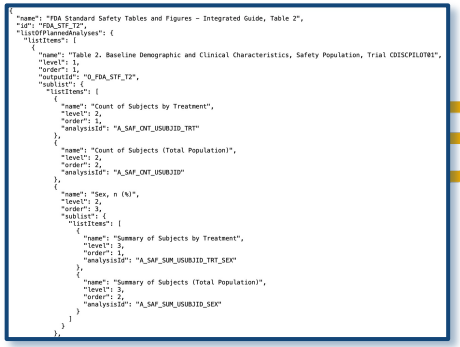
Leveraging ARS Metadata to Drive Results Automation

ARS Metadata



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         }
        ]
       }
      }
```

ADaM Dataset

USUBJID	ARM	AGE	AGEGR1	AGEU	RACE	SEX
01-701-1015	Placebo	63	<65	YEARS	WHITE	F
01-701-1023	Placebo	64	<65	YEARS	WHITE	M
01-701-1028	Xanomeline High Dose	71	65+	YEARS	WHITE	M
01-701-1033	Xanomeline Low Dose	74	65+	YEARS	WHITE	M
01-701-1034	Xanomeline High Dose	77	65+	YEARS	WHITE	F
01-701-1047	Placebo	85	65+	YEARS	WHITE	F

id	operation_id	resultGroup1_groupingId	resultGroup1_groupId	resultGroup2_groupingId	resultGroup2_groupId	rawValu	formattedVal
An03.02_AgeGrp_ByTrt	Mth01_CatVar_ByGrp_1_n	AnlsGrouping_02_Trt	AnlsGrouping_02_Trt_1	AnlsGrouping_03_AgeGp	AnlsGrouping_03_AgeGp_1	14	14
An03.02_AgeGrp_ByTrt	Mth01_CatVar_ByGrp_1_n	AnlsGrouping_02_Trt	AnlsGrouping_02_Trt_1	AnlsGrouping_03_AgeGp	AnlsGrouping_03_AgeGp_2	72	72
An03.02_AgeGrp_ByTrt	Mth01_CatVar_ByGrp_1_n	AnlsGrouping_02_Trt	AnlsGrouping_02_Trt_2	AnlsGrouping_03_AgeGp	AnlsGrouping_03_AgeGp_1	8	8
An03.02_AgeGrp_ByTrt	Mth01_CatVar_ByGrp_1_n	AnlsGrouping_02_Trt	AnlsGrouping_02_Trt_2	AnlsGrouping_03_AgeGp	AnlsGrouping_03_AgeGp_2	76	76
An03.02_AgeGrp_ByTrt	Mth01_CatVar_ByGrp_1_n	AnlsGrouping_02_Trt	AnlsGrouping_02_Trt_3	AnlsGrouping_03_AgeGp	AnlsGrouping_03_AgeGp_1	11	11
An03.02_AgeGrp_ByTrt	Mth01_CatVar_ByGrp_1_n	AnlsGrouping_02_Trt	AnlsGrouping_02_Trt_3	AnlsGrouping_03_AgeGp	AnlsGrouping_03_AgeGp_2	73	73
An03.02_AgeGrp_ByTrt	Mth01_CatVar_ByGrp_2_pct	AnlsGrouping_02_Trt	AnlsGrouping_02_Trt_1	AnlsGrouping_03_AgeGp	AnlsGrouping_03_AgeGp_1	16.27907	(16.3)
An03.02_AgeGrp_ByTrt	Mth01_CatVar_ByGrp_2_pct	AnlsGrouping_02_Trt	AnlsGrouping_02_Trt_1	AnlsGrouping_03_AgeGp	AnlsGrouping_03_AgeGp_2	83.72093	(83.7)
An03.02_AgeGrp_ByTrt	Mth01_CatVar_ByGrp_2_pct	AnlsGrouping_02_Trt	AnlsGrouping_02_Trt_2	AnlsGrouping_03_AgeGp	AnlsGrouping_03_AgeGp_1	9.52381	(9.5)
An03.02_AgeGrp_ByTrt	Mth01_CatVar_ByGrp_2_pct	AnlsGrouping_02_Trt	AnlsGrouping_02_Trt_2	AnlsGrouping_03_AgeGp	AnlsGrouping_03_AgeGp_2	90.47619	(90.5)
An03.02_AgeGrp_ByTrt	Mth01_CatVar_ByGrp_2_pct	AnlsGrouping_02_Trt	AnlsGrouping_02_Trt_3	AnlsGrouping_03_AgeGp	AnlsGrouping_03_AgeGp_1	13.09524	(13.1)
An03.02_AgeGrp_ByTrt	Mth01_CatVar_ByGrp_2_pct	AnlsGrouping_02_Trt	AnlsGrouping_02_Trt_3	AnlsGrouping_03_AgeGp	AnlsGrouping_03_AgeGp_2	86.90476	(86.9)

Analysis Results Dataset

Analysis Results: Write Once, Read Many

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An03.02_AgeGrp_ByTrt	Mth01_CatVar_ByGrp_2_pct	AnlsGrouping_02_Trt	AnlsGrouping_02_Trt_1	AnlsGrouping_03_AgeGp	AnlsGrouping_03_AgeGp_1	16.27907	(16.3)
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An03.02_AgeGrp_ByTrt	Mth01_CatVar_ByGrp_2_pct	AnlsGrouping_02_Trt	AnlsGrouping_02_Trt_2	AnlsGrouping_03_AgeGp	AnlsGrouping_03_AgeGp_1	9.52381	(9.5)
An03.02_AgeGrp_ByTrt	Mth01_CatVar_ByGrp_2_pct	AnlsGrouping_02_Trt	AnlsGrouping_02_Trt_2	AnlsGrouping_03_AgeGp	AnlsGrouping_03_AgeGp_2	90.47619	(90.5)
An03.02_AgeGrp_ByTrt	Mth01_CatVar_ByGrp_2_pct	AnlsGrouping_02_Trt	AnlsGrouping_02_Trt_3	AnlsGrouping_03_AgeGp	AnlsGrouping_03_AgeGp_1	13.09524	(13.1)
An03.02_AgeGrp_ByTrt	Mth01_CatVar_ByGrp_2_pct	AnlsGrouping_02_Trt	AnlsGrouping_02_Trt_3	AnlsGrouping_03_AgeGp	AnlsGrouping_03_AgeGp_2	86.90476	(86.9)

Displays

Publications

Clinical Study Report

Meta Analysis

What's Next?

eTFL Portal!

Expanding Content through CDISC eTFL Portal

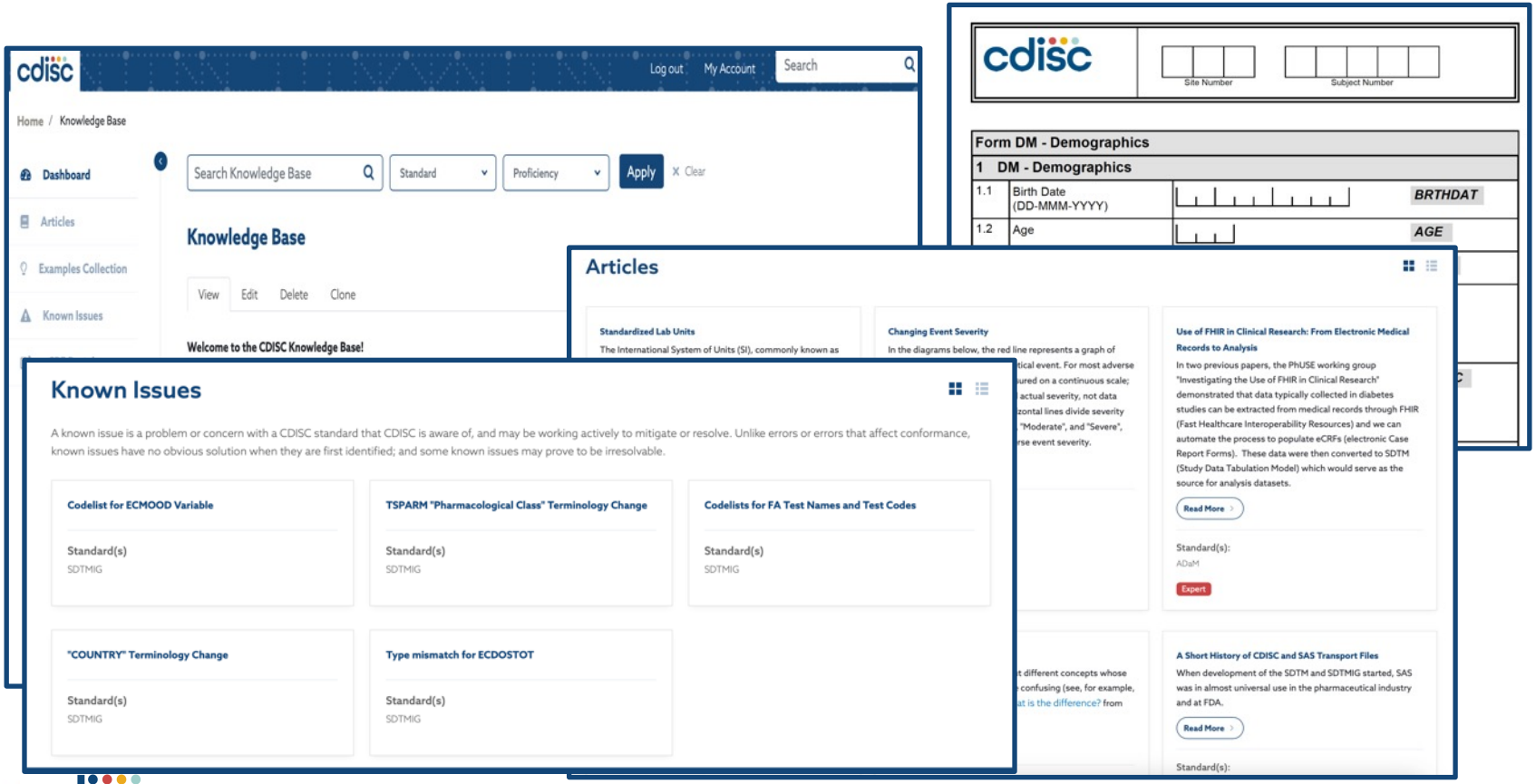
- ARS model and documentation is complex, the eTFL portal will promote implementation.
- Informative content (example driven) not normative
  - Standard library of TFLs
    - Safety
    - Therapeutic Area-specific (future addition)
  - Components
    - Overview
    - Display
    - ADaM Dataset and associated Metadata
    - Analysis Results Metadata
    - Analysis Results Dataset

Launching the eTFL Portal

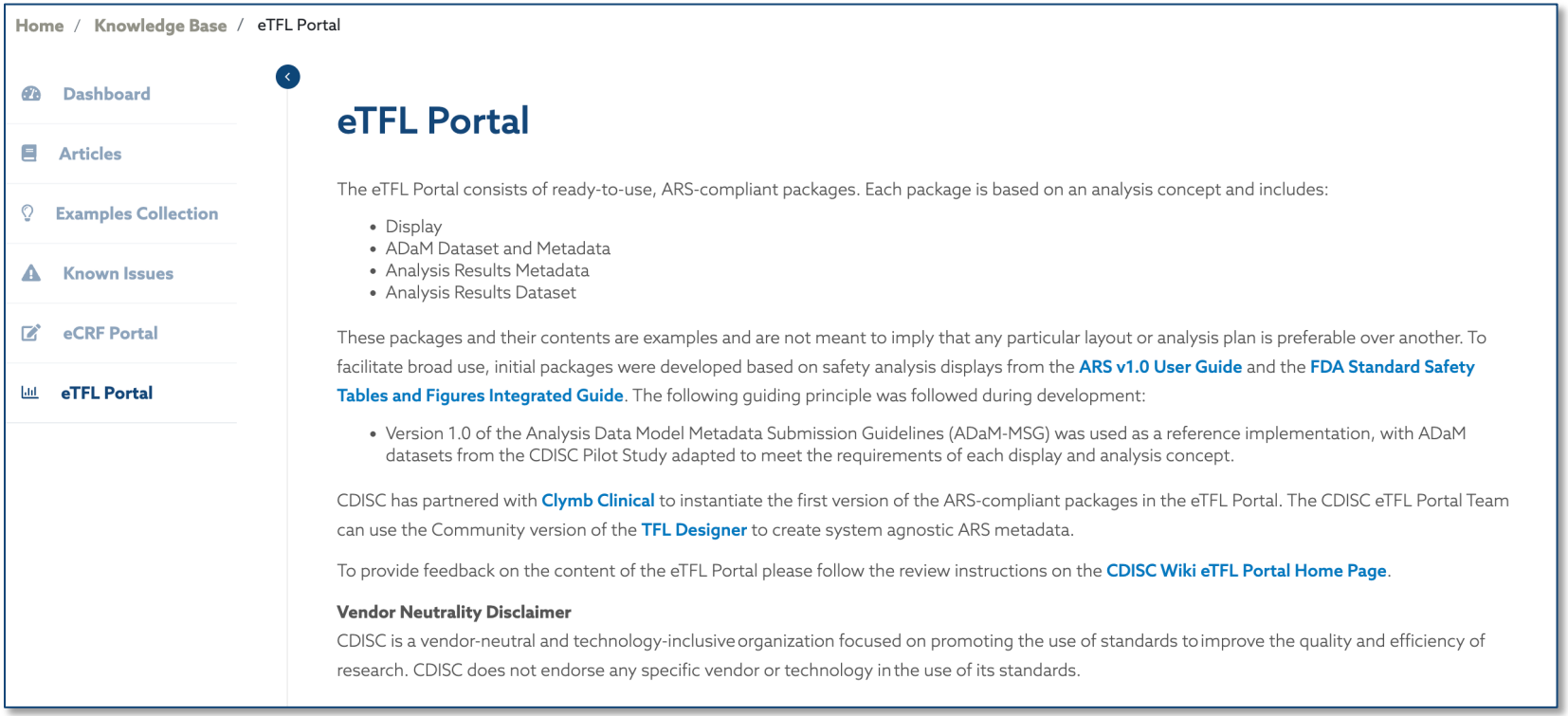
- CDISC has partnered with Clymb Clinical to instantiate the first version of the ARS-compliant packages in the eTFL Portal.

- The CDISC eTFL Portal Team will use the Community version of the TFL Designer to create system agnostic ARS metadata.

CDISC Knowledge Base



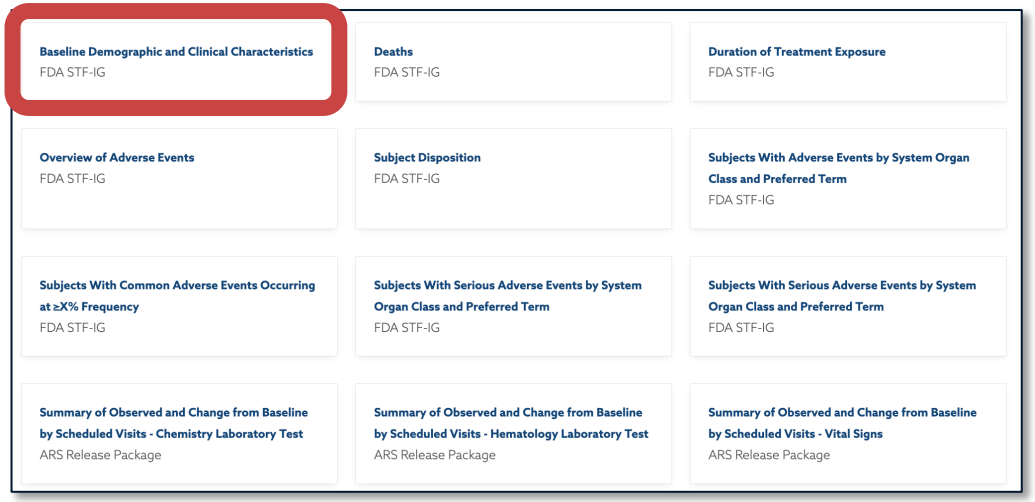
eTFL Portal in the CDISC Knowledge Base



https://cdisc.org/kb/etfl

eTFL Portal

- Each Package contains
  - Analysis overview, design considerations, and TFL preview
  - Download
    - ADaM Dataset and Metadata
    - ARS Metadata
    - Analysis Results Dataset
    - Display



Overview

Baseline Demographic and Clinical Characteristics

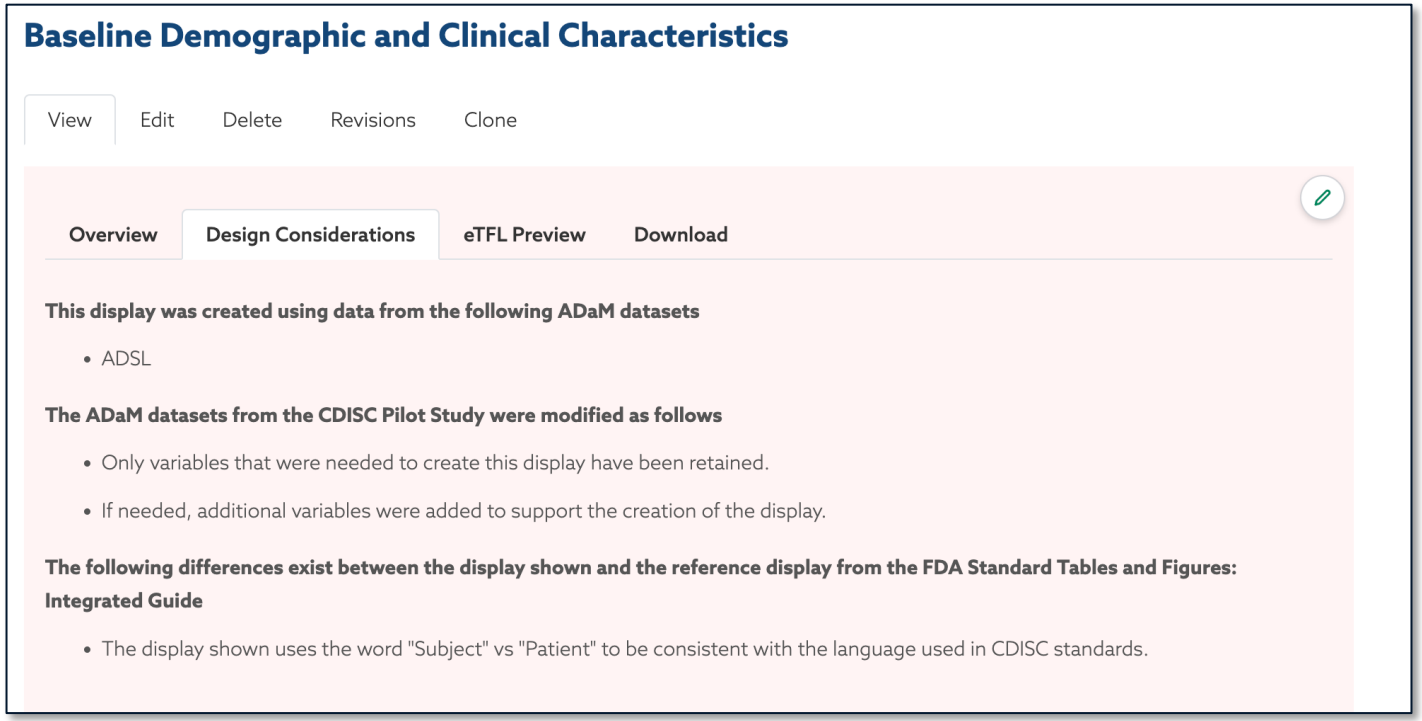
View | Edit | Delete | Revisions | Clone

Overview | **Design Considerations** | **eTFL Preview** | **Download**

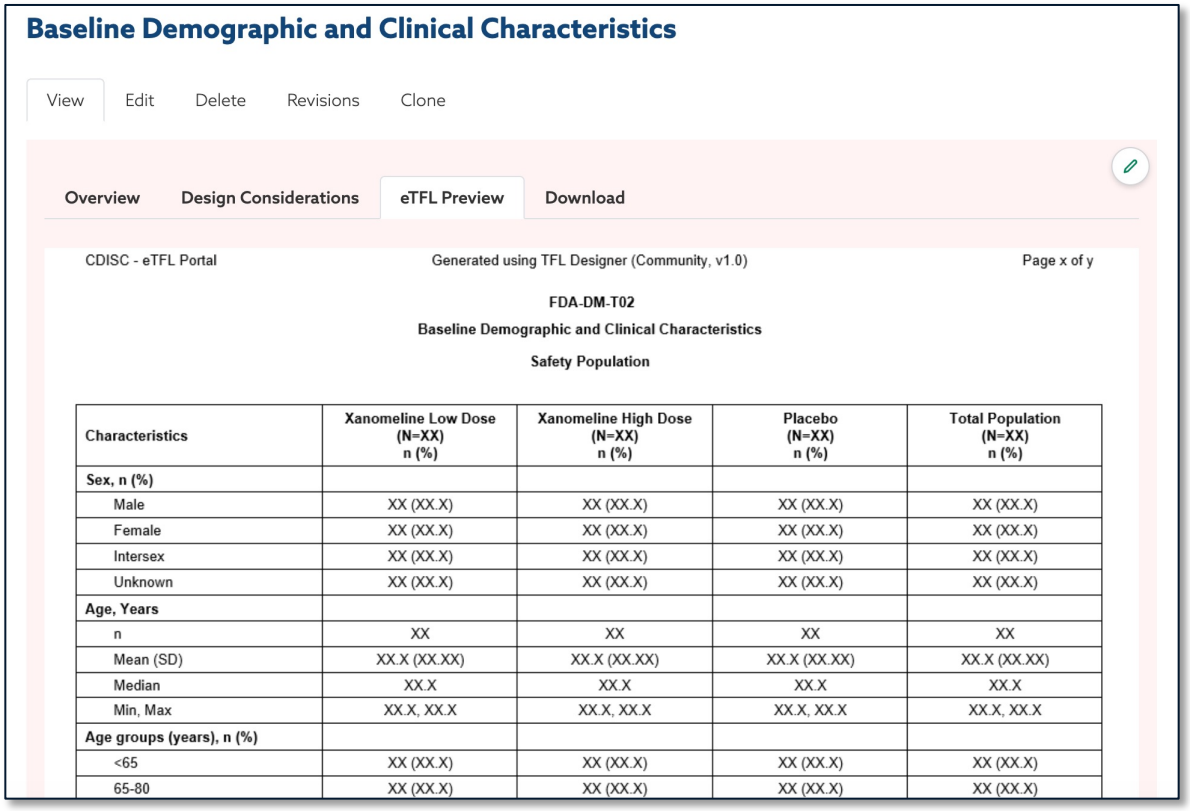
This table shows key baseline characteristics of the safety population that could influence the effectiveness or safety of the drug.

This display is based on *Table 2. Baseline Demographic and Clinical Characteristics, Safety Population, Pooled Analyses (or Trial X) from the FDA STANDARD SAFETY TABLES AND FIGURES: INTEGRATED GUIDE (Version Date: August 2022), published by the Center for Drug Evaluation and Research (CDER) Biomedical Informatics and Regulatory Review Science (BIRRS) Team.*

Design Considerations



eTFL Preview



Baseline Demographic and Clinical Characteristics

View | Edit | Delete | Revisions | Clone

Overview | Design Considerations | eTFL Preview | Download

CDISC - eTFL Portal | Generated using TFL Designer (Community, v1.0) | Page x of y

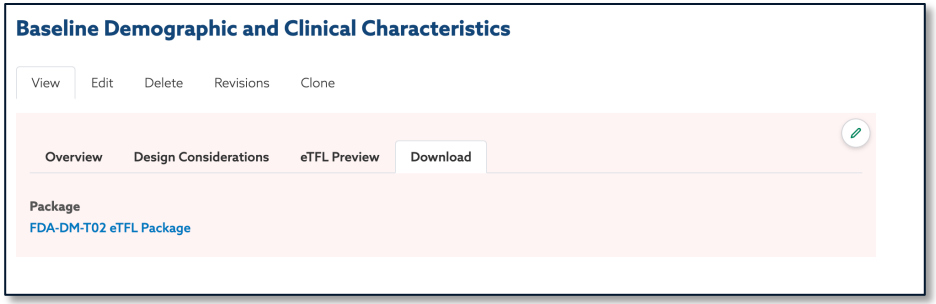
FDA-DM-T02

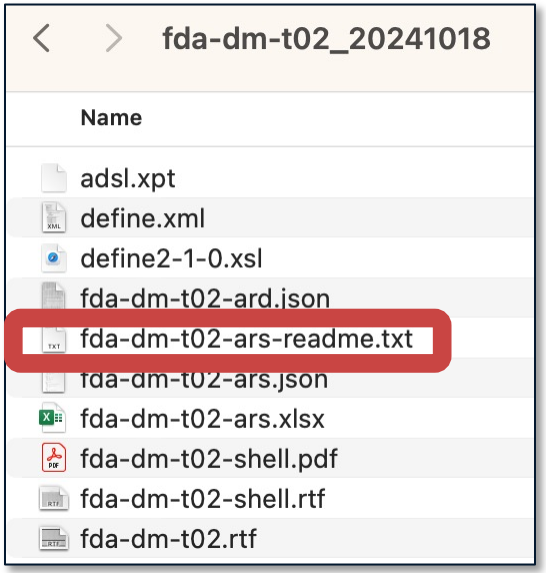
Baseline Demographic and Clinical Characteristics

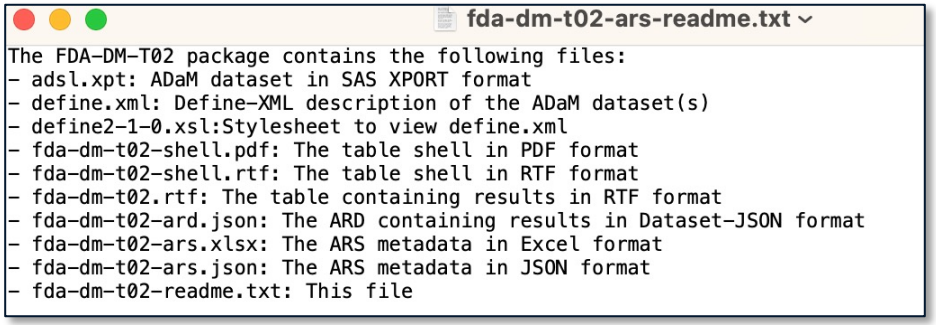
Safety Population

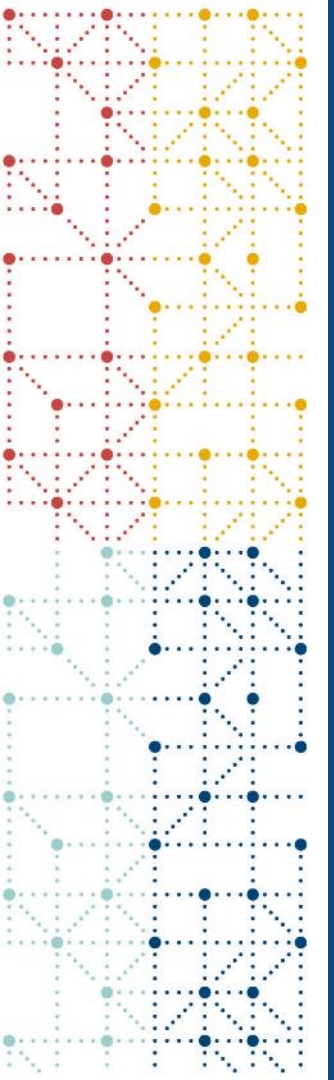
Characteristics	Xanomeline Low Dose (N=XX) n (%)	Xanomeline High Dose (N=XX) n (%)	Placebo (N=XX) n (%)	Total Population (N=XX) n (%)
Sex, n (%)				
Male	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Female	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Intersex	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Unknown	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Age, Years				
n	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Age groups (years), n (%)				
<65	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
65-80	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

Package Download







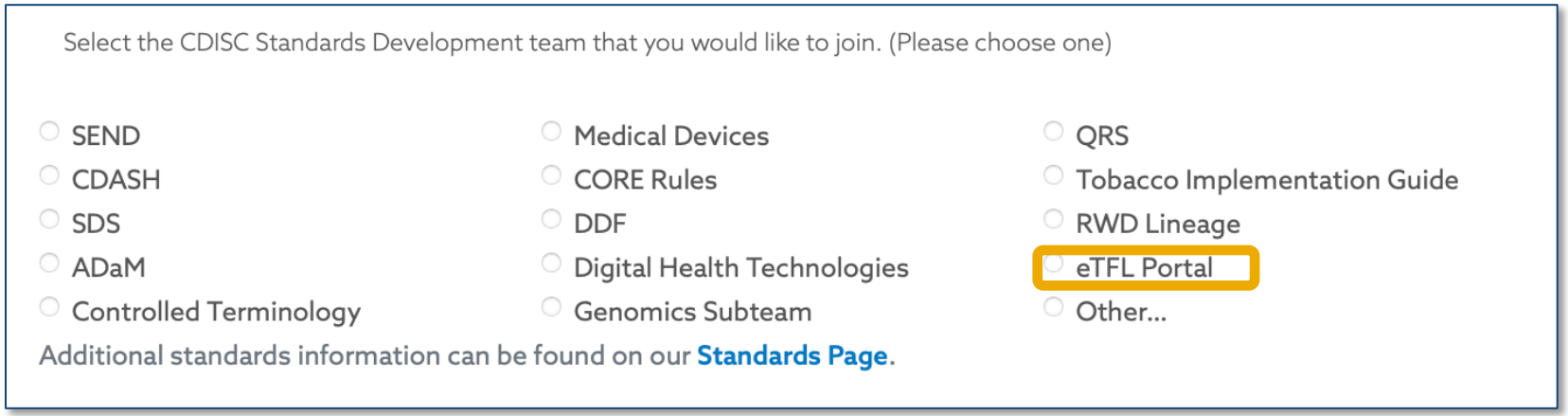


Next Steps for Development

Expanding the eTFL Portal Content

- Joint effort with PHUSE Safety Analytics Working Group to complete eTFL packages for the FDA Standard Safety Tables and Figures: Integrated Guide over the next three years
- Content to support the CDISC 360i initiative
- We are looking for volunteers!

Volunteer!



https://www.cdisc.org/volunteer/form

Thank you!

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