cdisc

2022
EUROPE
INTERCHANGE
27-28 APRIL | VIRTUAL EVENT

CDISC Analysis Results Standards - Approach and Development Update

Bess LeRoy, Head of Standards Development, CDISC
Bhavin Busa, VP Clinical Data Services & Operations, Vita Data Sciences

Meet the Speaker

Bess LeRoy

Title: Head of Standards Development

Organization: CDISC

Bess LeRoy is the Head of Standards Development at CDISC. Bess has been a CDISC team member since 2011. She is a member of the CDISC Technical Leadership Team and leads the CDISC Global Governance Group. Bess has over 15 years' experience working in public health research and has held positions at the Framingham Heart Study, the Rotterdam Study, the Arizona Cancer Center, and the Critical Path Institute.

Bess has a BS from the University of Michigan, an MPH from Boston University School of Public Health, and is currently pursuing a DrPH from Johns Hopkins Bloomberg School of Public Health

Meet the Speaker

Bhavin Busa

Title: VP, Clinical Data Services & Operations

Organization: Vita Data Sciences

Bhavin Busa is a thought leader in the areas of data standards, programming and regulatory submission. He is responsible for overseeing the group at VDS. He is very passionate about leveraging standards and technology to expedite data review, analysis, and submission processes. Along that line, he devotes much of his time outside of his day job to volunteer with PHUSE and CDISC. He is a Steering Committee member at PHUSE and is currently a board member of the CDISC Open-Source Alliance (COSA) team.

Agenda

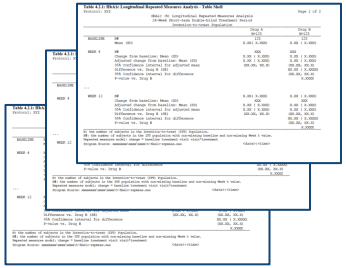
1. Analysis Results Current and Future State
2. Analysis Result Standards Goals
3. Analysis Results Standards Development Update
   - Analysis Results Concepts Selection
   - Extended ARM Elements of a Table/ARM Technical Specs
   - Analysis Results Dataset (VS Example)
4. COSA and Open-source TFL Designer
5. ARS Deliverables

Analysis Results Current State

Table 3.1.1: ADHYPO Analysis Dataset

Row	STUDYID	USUBJID	MIDS	CEDECOD	WASAEYN	ASTDTM
1	XYZ	000001	HYPO 1	Hypoglycemia	Y	07Sep2012 22:29:00
2	XYZ	000001	HYPO 2	Hypoglycemia	N	10Sep2012 09:12:00
3	XYZ	000001	HYPO 3	Hypoglycemia	N	10Sep2012 23:05:00
4	XYZ	000001	HYPO 4	Hypoglycemia	N	11Sep2012 15:24:00
5	XYZ	000001	HYPO 5	Hypoglycemia	N	18Sep2012 11:39:00
6	XYZ	000002	HYPO 1	Hypoglycemia	N	22Oct2012 13:28:00
7	XYZ	000002	HYPO 2	Hypoglycemia	N	25Oct2012 13:59:00
8	XYZ	000002	HYPO 3	Hypoglycemia	N	17Nov2012 05:01:00

ADaM Dataset



Analysis Results

Table 4.2.2: HbA1c Longitudinal Repeated Measures Analysis Results Metadata

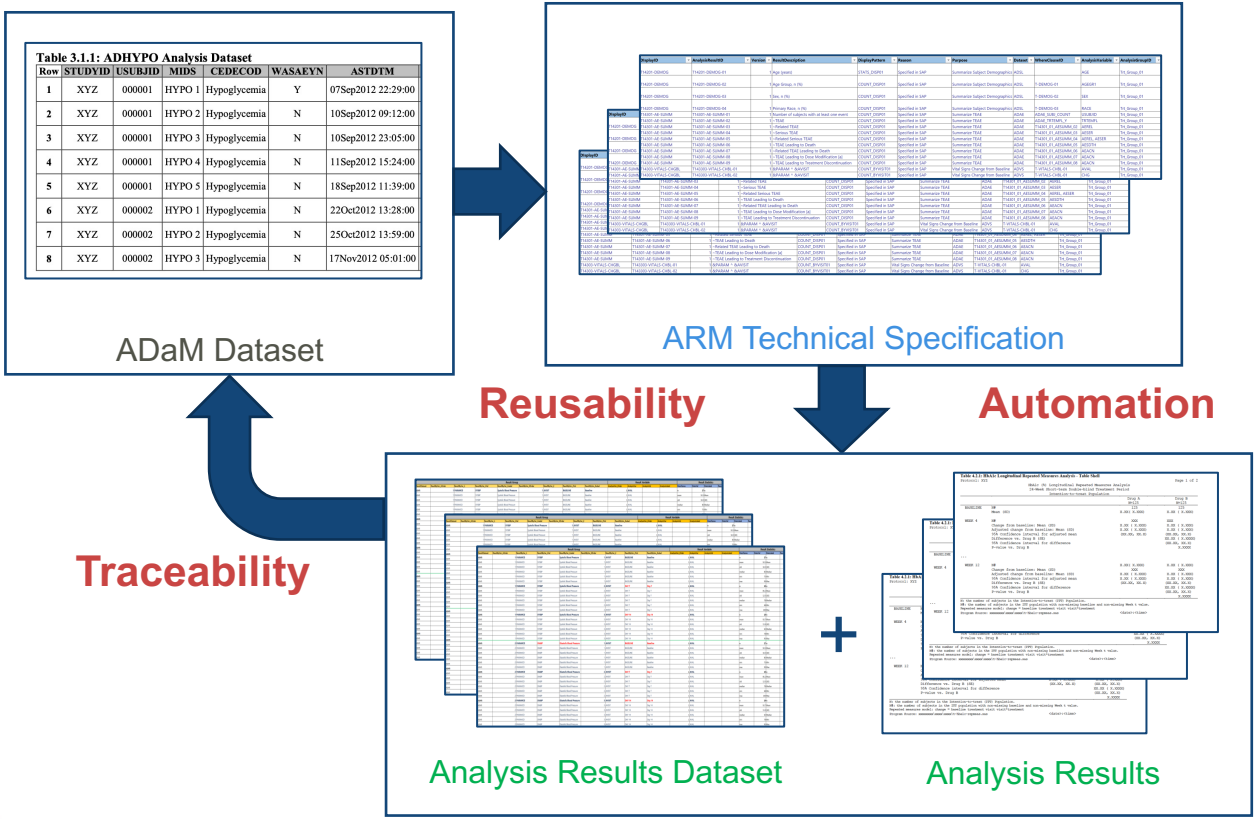
Metadata Field	Metadata
DISPLAY IDENTIFIER	Table 4.2.1/Figure 4.2.1
DISPLAY NAME	Mean Change from Baseline in HbA1c (Percent) Longitudinal Repeated Measures Analysis, 24-Week Short-term Double-blind Treatment Period, Intention-to-treat Population
RESULT IDENTIFIER	Treatment difference results (LSMean, 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

ARM for define.xml

Analysis Results Current State

- Static results created for Clinical Study Report
- May be hundred of tables in PDF format, often difficult to navigate
- No or limited traceability (e.g., to protocol, SAP, ADaM data)
- Expensive to generate and only used once, no or limited reusability
- ARM v1.0 describes *metadata* about displays (PDF) and results (at high level), no formal analysis and results model or results data.
- Lack of features to drive automation
- Limited regulatory use cases

Analysis Results Desired Future State



Analysis Results Desired Future State

- Formal model for describing analyses and results as data
- Facilitate automated generation of results
- From electronic (PDF) to machine readable results, with context and metadata to source
- Improved navigation and reusability of analyses and results
- Support storage, access, processing and reproducibility of results
- Traceability to Protocol/SAP and to input ADaM data
- Open-source tools to design, specify, build and generate analysis results

Principles for CDISC ARS Implementation

Analysis Results Standards Goals

Analysis Results Metadata Technical Specification (ARM-TS), to support automation, traceability, and creation of data displays

Define an Analysis Results Data (ARD) structure, to support reuse and reproducibility of results data

Illustrate and exercise ARD and ARM-TS with a set of common data displays

Concepts Team Consulted Published Layouts

- PH
- JPI
- Re
- Sub-team

Scatterplot and Shift Table Summary of Absolute Lab values – Lab Test 1 Minimum Baseline vs Minimum Post-baseline

Treatment
T1 (N = xxx)
T2 (N = xxx)
PL (N = xxx)

N = number of su
of subjects in ea
using the referer
demographics.

3.14安全性の解析（バイタルサイン、身体的所見及び安全性に関連する

Table summary of vital signs by visit

<Prameter> *BDS*.PARAM
<Visit> *BDS*.AVISIT
n
Mean (SD) *BDS*.AVAL
Median
Min - Max

上記例は、絶対値の集計の場合。
バイタルサインのベースラインからの変化量を集計する必要がある場合
る場合は *BDS*.PCHG を使用する

Table 3. Laboratory Abnormalities that Worsened from Baseline to Grade 3 or 4 Occurring in ≥1% of Patients with dMMR Endometrial Cancer Receiving Product in Study

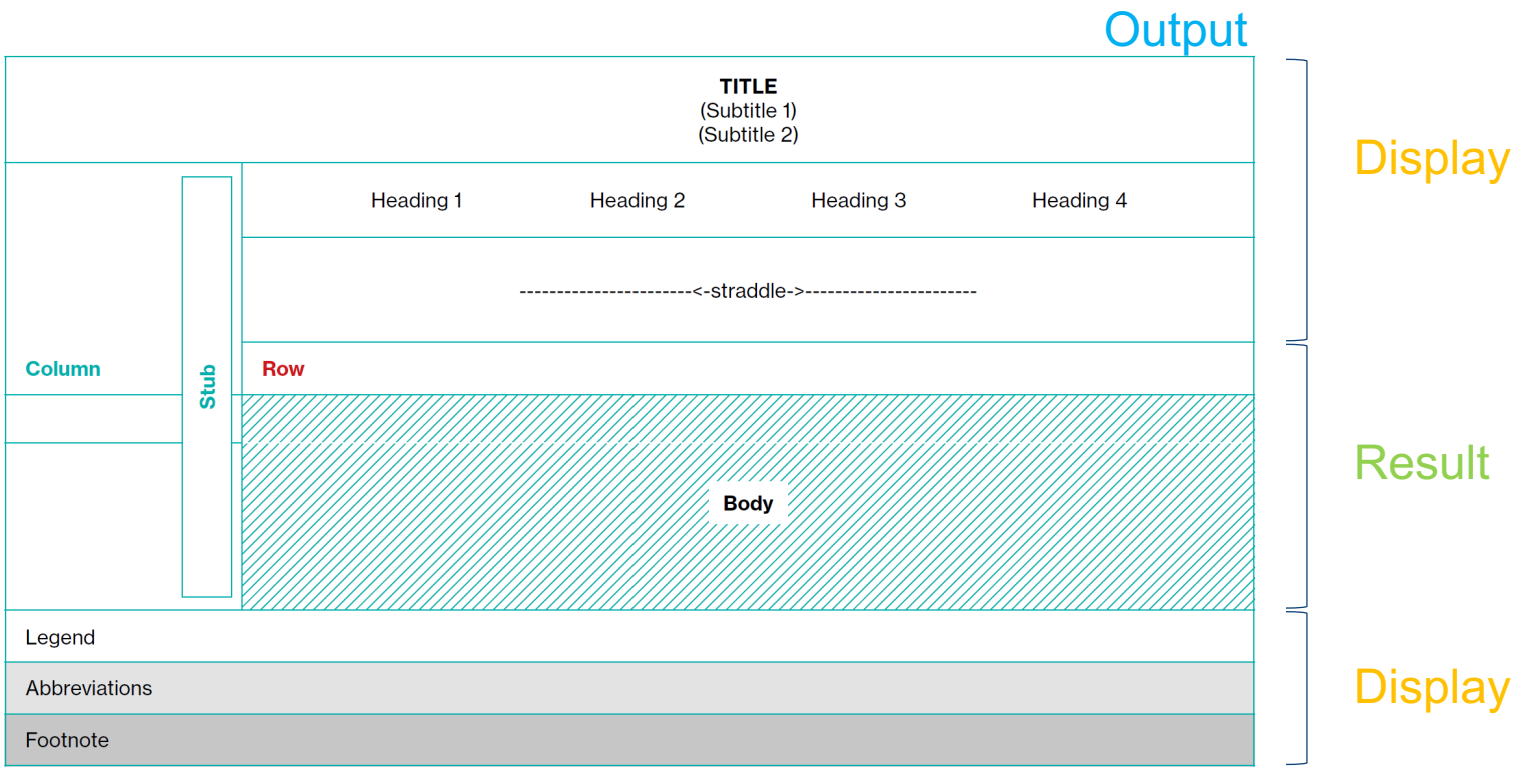
Laboratory Test	Product N = 104 All Grades[a] %	Product N = 104 Grade 3 or 4[a] %
Hematology		
Decreased lymphocytes	37	9
Decreased leukocytes	21	2.9
Chemistry		
Decreased albumin	30	2.9
Increased creatinine	27	2.9
Increased alkaline phosphatase	25	2.9
Increased aspartate aminotransferase	16	1.9
Increased alanine aminotransferase	15	2.9
Electrolytes		
Decreased sodium	26	4.8
Increased calcium	15	1.9
Decreased potassium	15	1.9

[a] Consists of new onset of laboratory abnormality or worsening of baseline laboratory abnormality.

List of Analysis Display, Concepts - Illustration

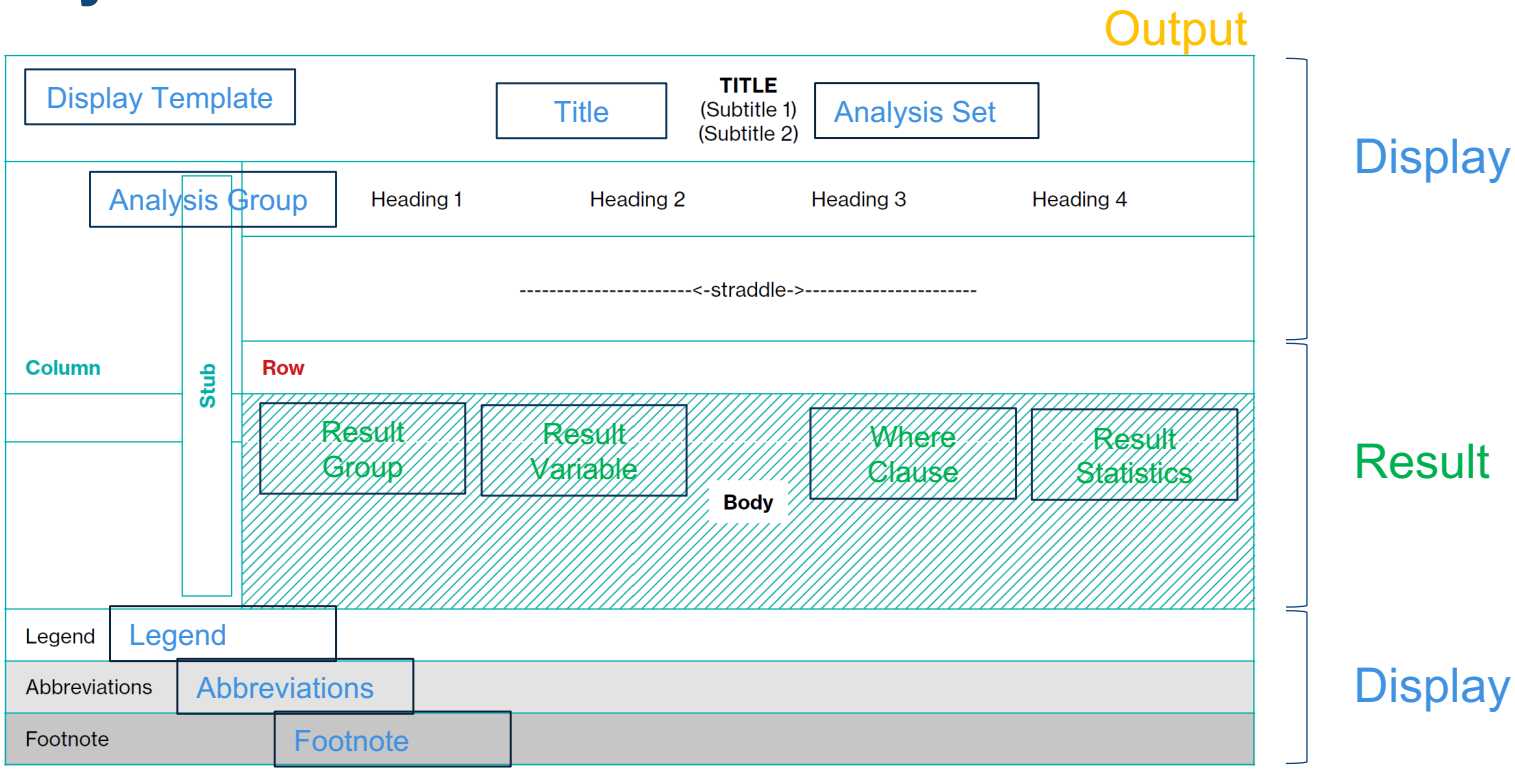
Analysis Title
• Summary of Analysis Populations and Subject Disposition
• Summary of Demographics
• Summary of Protocol Deviations
• Summary of Medical History by System Organ Class and Preferred Term
• Summary of Concomitant Medications by Anatomic Classification and Preferred Term
• Overall Summary of Treatment-Emergent Adverse Events
• Summary of Treatment Emergent Adverse Events by SOC and PT
• Summary of TEAE System Organ Class and Preferred Term by Maximum Severity
• Summary of Observed and Change from Baseline by Scheduled Visits – <Lab Panel Name>
• Shift from Baseline for Laboratory Tests by Treatment Group - <Lab Panel Name>
• Summary of ECG Overall Interpretation Findings by Visit
• Summary of Observed and Change from Baseline by Scheduled Visits – Vital Signs

Parts of a Table



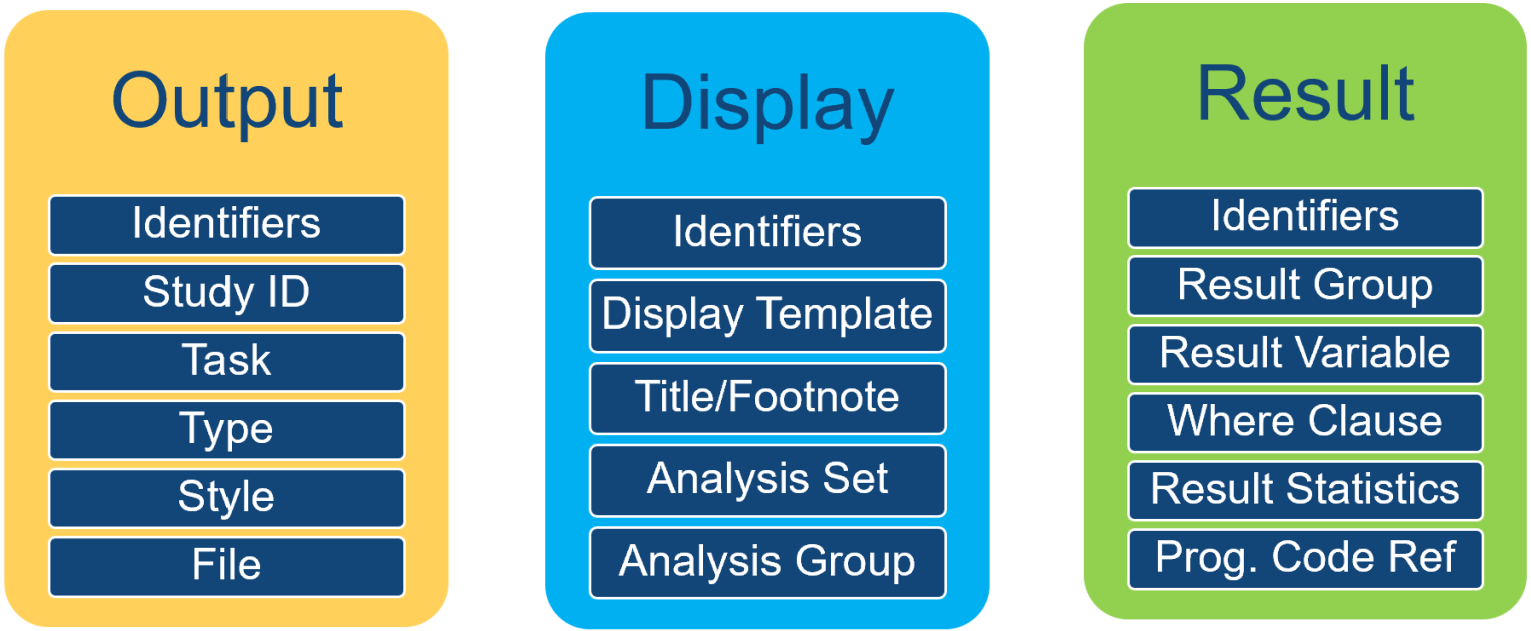
Reference: PHUSE White Paper "*General Output Tips and Considerations*", Doc ID: WP-034, Version 1.0, Aug 2020

Key Metadata Elements of a Table



Reference: PHUSE White Paper "*General Output Tips and Considerations*", Doc ID: WP-034, Version 1.0, Aug 2020

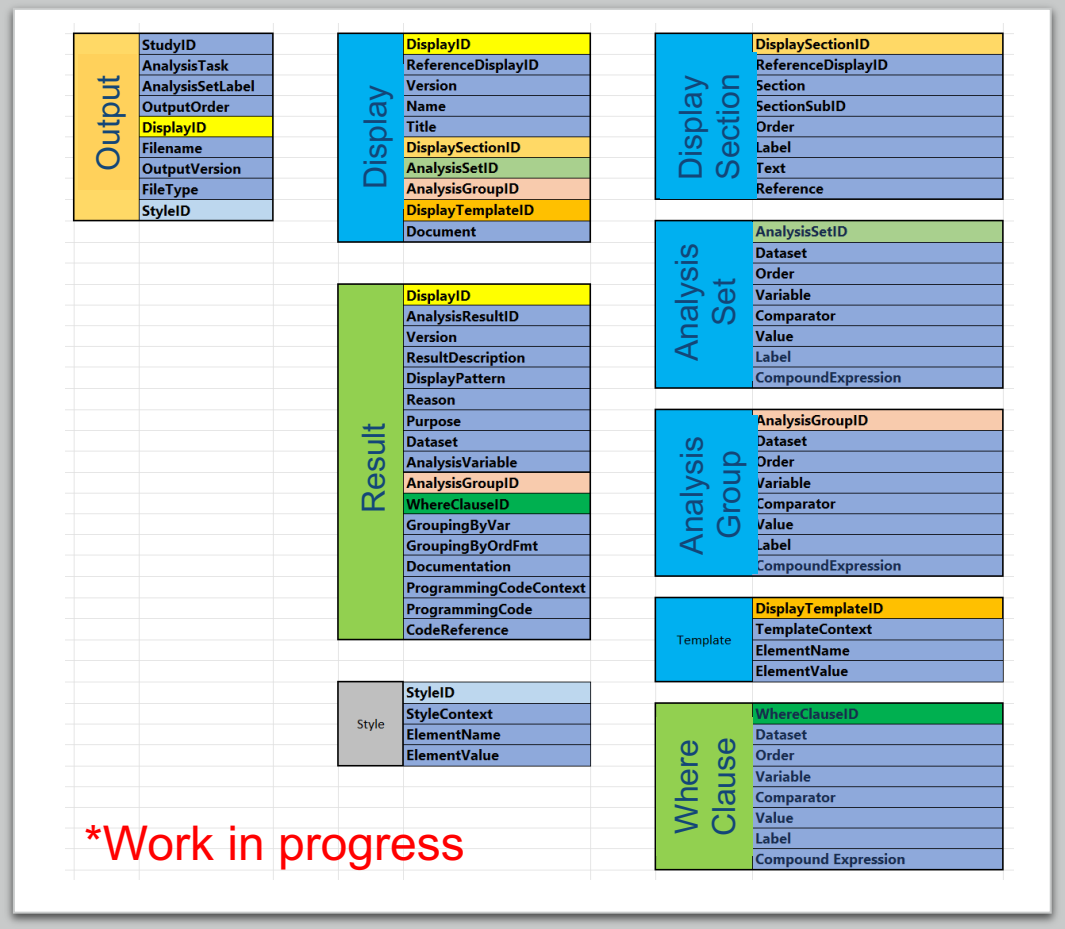
Extended ARM Elements for a Table Development*



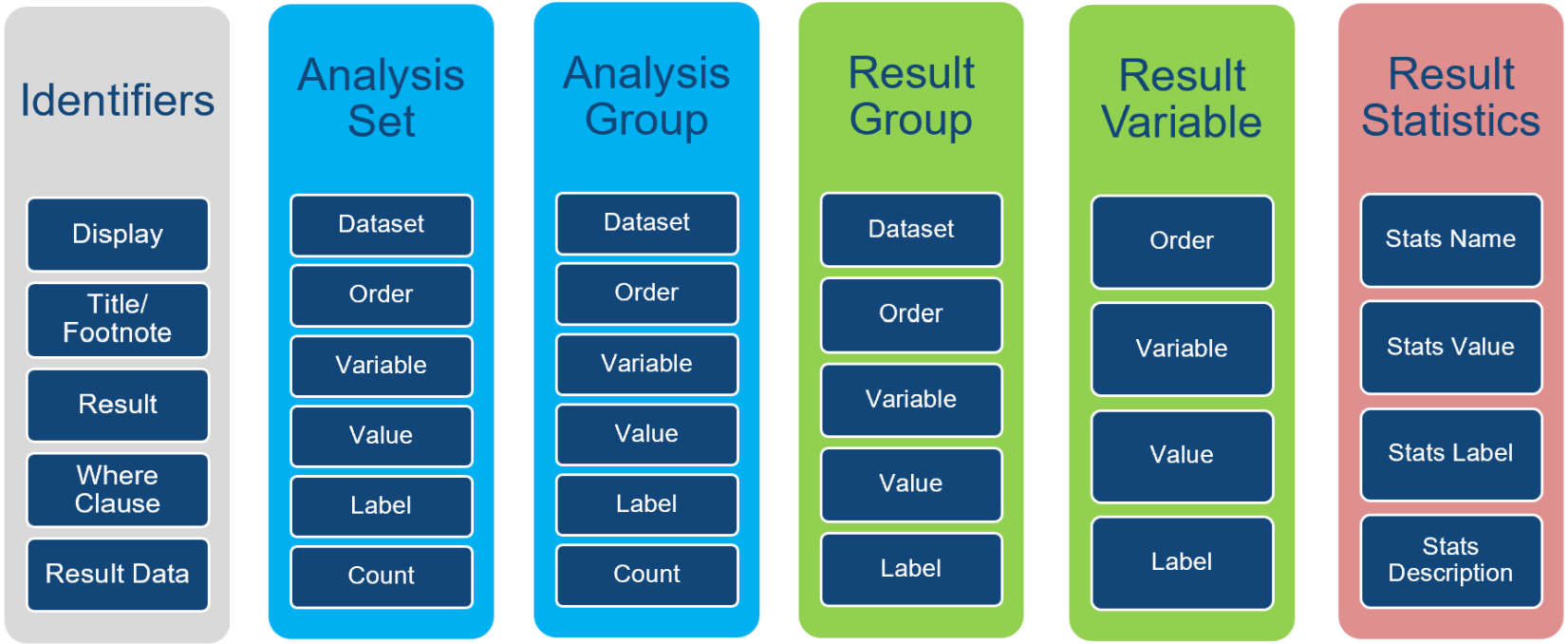
* Work in progress

ARM Technical Specification*

- Prospective focus on automation, traceability, and creation of data displays
- Linked, modular, flexible and tool agnostics
- Supports meta-programming
- Serves a different purpose than ARM for Define-XML



Analysis Result Dataset Model – Key Elements*



* Work in progress

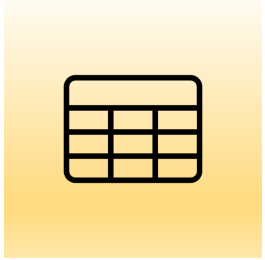
Analysis Results Data – Vital Signs Example*

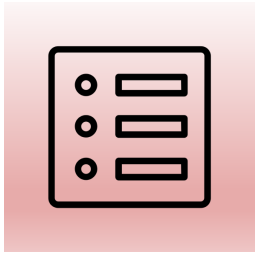
Analysis Set						Analysis Group						
AnalysisSetDataset	AnalysisSetOrder	AnalysisSetVar_1	AnalysisSetVar_1Val	AnalysisSetVar_1Label	AnalysisSetVar_1Cnt	AnalysisGrpDataset	AnalysisGrpOrder	AnalysisGrpVar_1	AnalysisGrpVar_1Val	AnalysisGrpVar_1Label	AnalysisGrpVar_1Cnt	ResultDataset
ADSL	**1**	**SAFFL**	**Y**	**Safety Population**	**225**	**ADVS**	**1**	**TRT01A**	**Xanomeline High Dose**	**Xanomeline High Dose ^ (N=@N1)**	**58**	**ADVS**
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	**1**	**SAFFL**	**Y**	**Safety Population**	**225**	**ADVS**	**1**	**TRT01A**	**Xanomeline High Dose**	**Xanomeline High Dose ^ (N=@N1)**	**58**	**ADVS**
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	**1**	**SAFFL**	**Y**	**Safety Population**	**225**	**ADVS**	**1**	**TRT01A**	**Xanomeline High Dose**	**Xanomeline High Dose ^ (N=@N1)**	**58**	**ADVS**
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	**1**	**SAFFL**	**Y**	**Safety Population**	**225**	**ADVS**	**1**	**TRT01A**	**Xanomeline High Dose**	**Xanomeline High Dose ^ (N=@N1)**	**58**	**ADVS**
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	**1**	**SAFFL**	**Y**	**Safety Population**	**225**	**ADVS**	**1**	**TRT01A**	**Xanomeline High Dose**	**Xanomeline High Dose ^ (N=@N1)**	**58**	**ADVS**
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS
ADSL	1	SAFFL	Y	Safety Population	225	ADVS	1	TRT01A	Xanomeline High Dose	Xanomeline High Dose ^ (N=@N1)	58	ADVS

* Work in progress

Need for Open-Source Tools

- Need for tool that can leverage available CDISC analysis results standards/templates
- The newly formed CDISC Open-Source Alliance supports, promotes, and sometimes sponsors open-source software projects that create tools for implementing or developing CDISC standards to drive innovation in the CDISC community





TFL Designer

- The TFL Designer has been approved under COSA as a tool to be developed that can leverage available CDISC analysis results standards/templates and accelerate generation of the TFL shells and support metadata driven automation in development of ADaM and TFLs

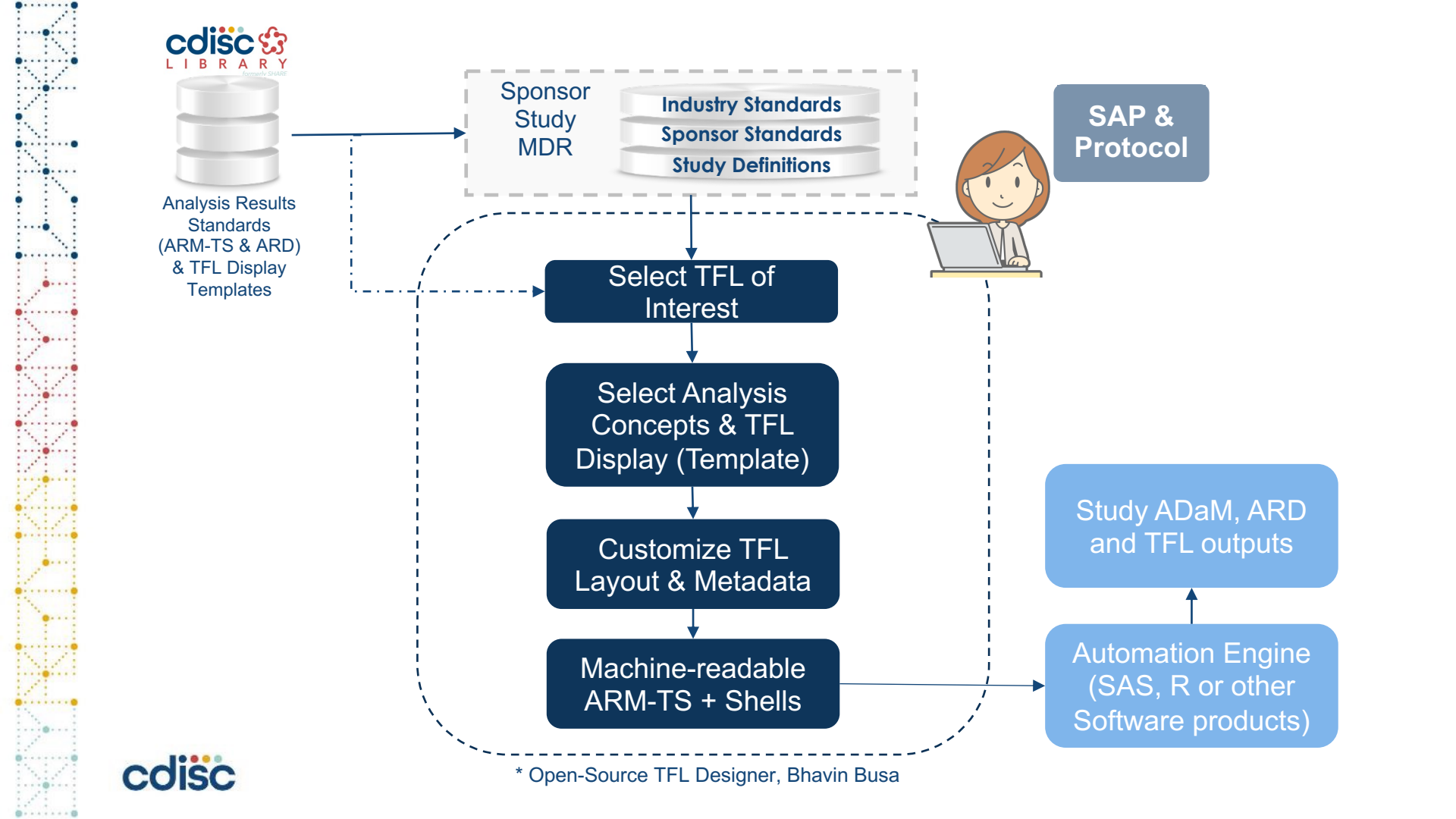
- Open-source tool to design tables, figures, and listings (TFL) and generate associated metadata to support clinical trial data analysis and reporting

https://github.com/bhavinbusa/tfldesigner/

Analysis Results Standards Deliverables

- Content Scope: common safety analyses
- Deliverables for v1.0
  - Machine readable mock displays made accessible through an “eTFL portal”
  - ARM Technical Specification
  - New Model and Implementation Guide to represent analysis results
  - Terminology
  - Identification of Conformance Rules
- Internal Review target Q2, 2022

Back-up Slides


cdisc LIBRARY
Analysis Results Standards (ARM-TS & ARD) & TFL Display Templates
Sponsor Study MDR
Industry Standards
Sponsor Standards
Study Definitions
SAP & Protocol
Select TFL of Interest
Select Analysis Concepts & TFL Display (Template)
Customize TFL Layout & Metadata
Machine-readable ARM-TS + Shells
Study ADaM, ARD and TFL outputs
Automation Engine (SAS, R or other Software products)
* Open-Source TFL Designer, Bhavin Busa
cdisc