CLYMB CLINICAL

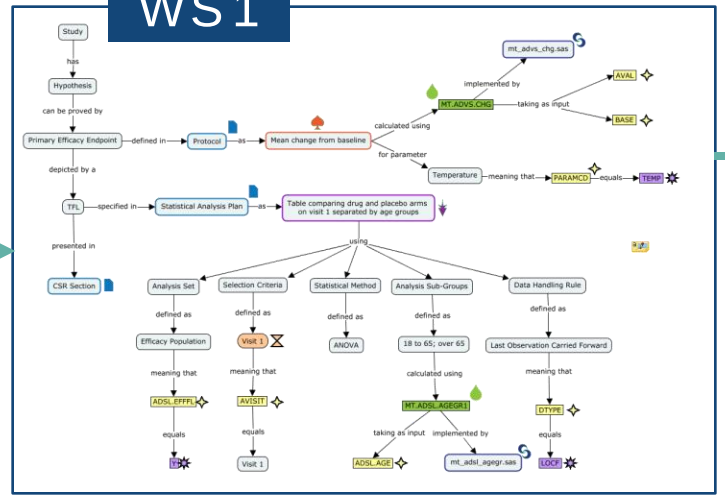
Integrating TFL Designer with CDISC 360: Advancing Automation and Concept-Based Standards in Clinical Trial Analysis & Reporting

Bhavin Busa

Oct 18, 2023

Session 4C: COSA Session - 360 & End-to-End

WS1



Create concepts in knowledge graphs

WS2

Transform concepts in machine readable form

Load into library

Biomedical Concepts
Analysis Concepts
Foundational Standards

cdisc LIBRARY
formerly SHARE

API

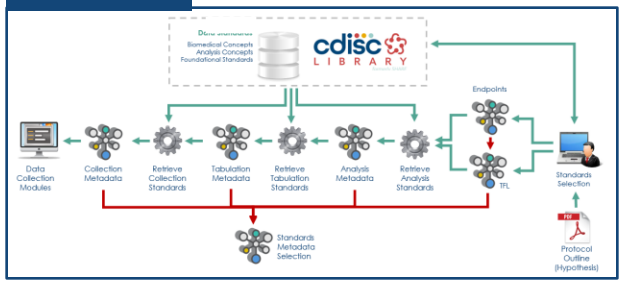
Extend API's

Use Case 1: Selecting standards concepts and linked metadata needed for a study
Use Case 2: Adding study design, concept configuration & generate artifacts
Use case 3: Automatic population of data into artifacts

WS3

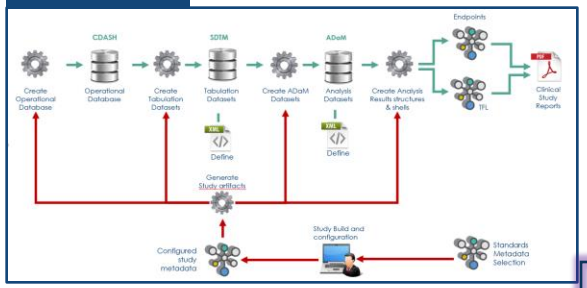
Add transformation semantics

WS4



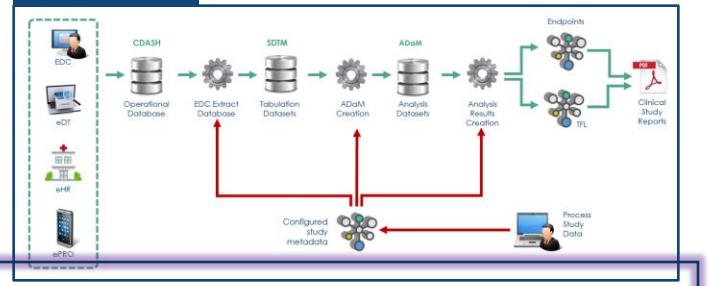
Identify and select standards specification (Use Case 1)

WS5



Configure study specification and create artifacts (Use Case 2)

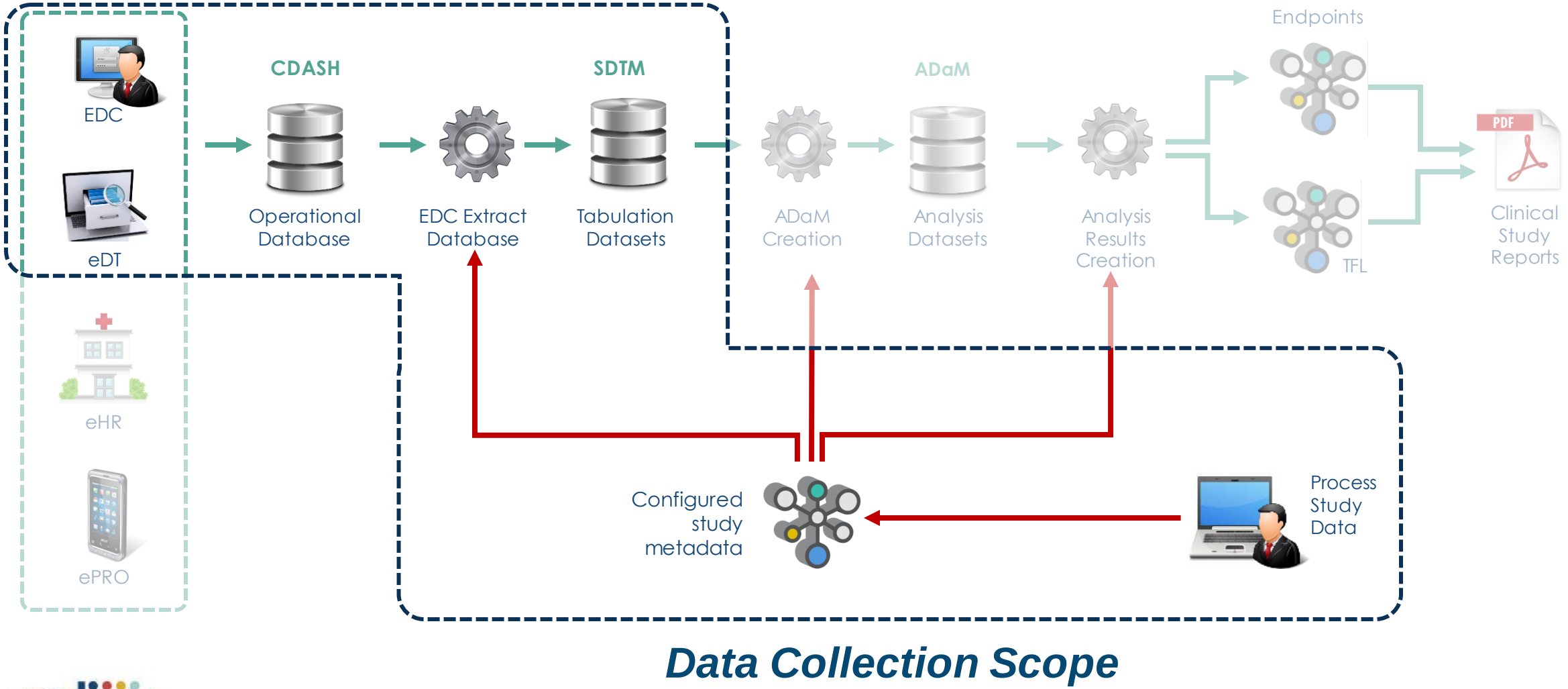
WS6



Automatically process and transform data (Use Case 3)

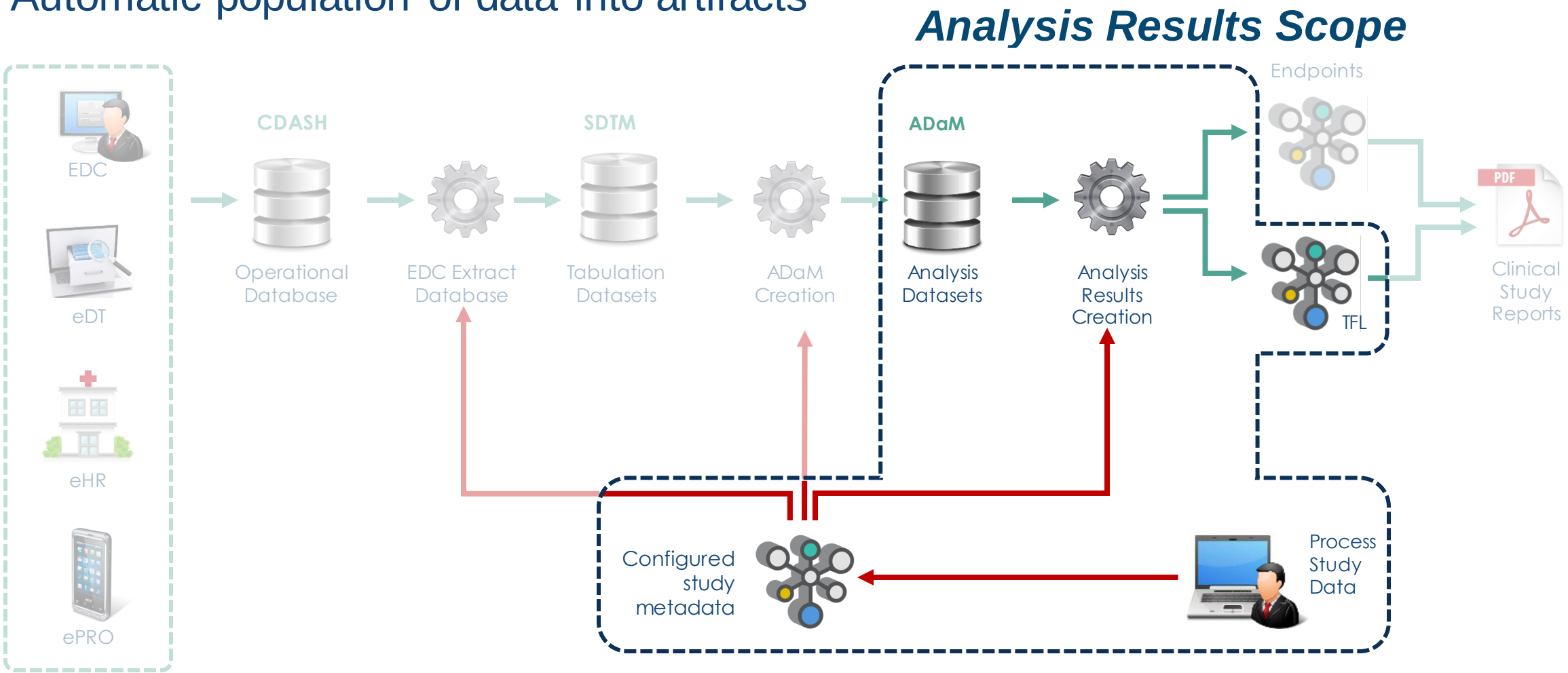
Use Case 3 : Execute

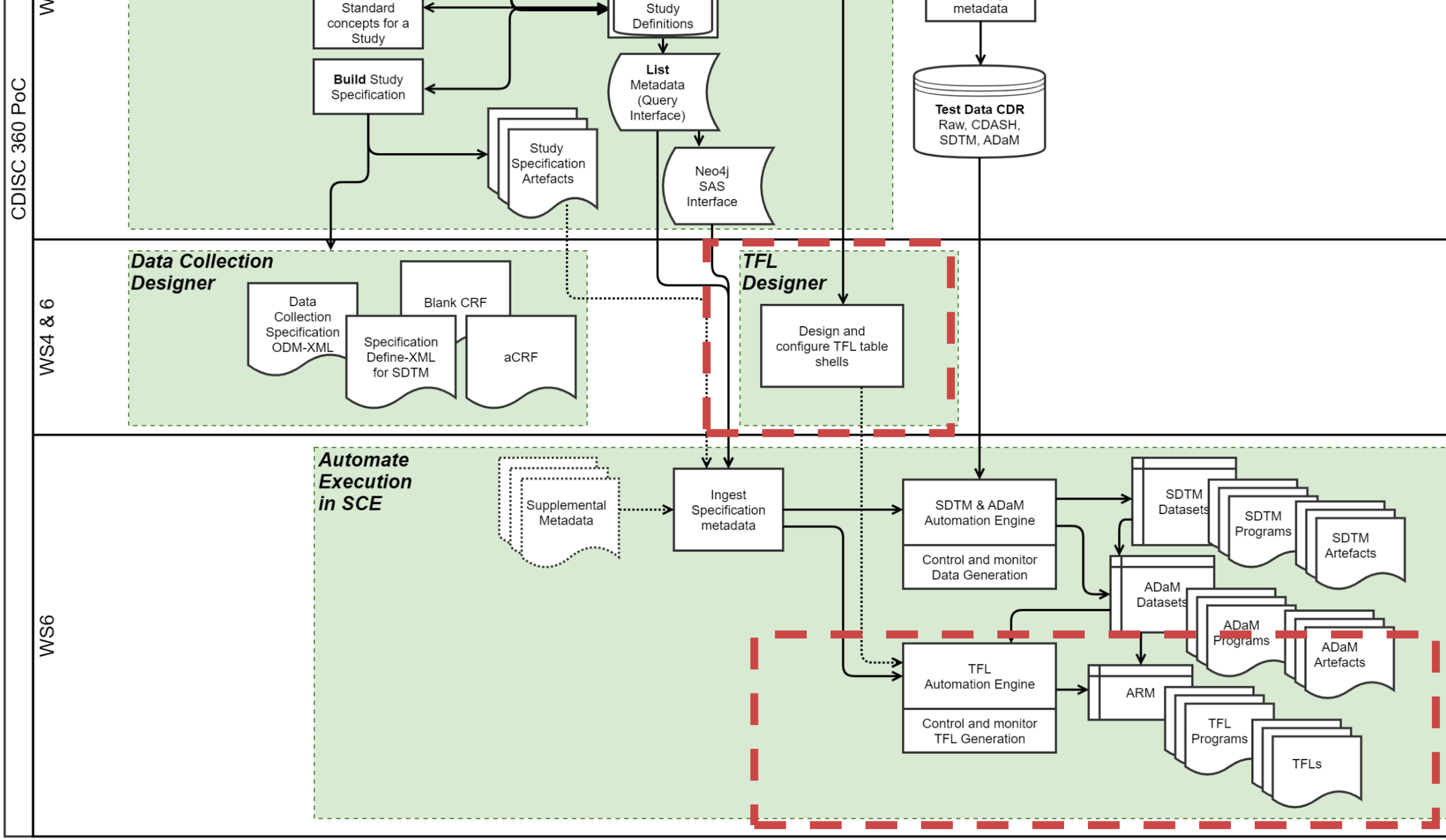
Automatic population of data into artifacts



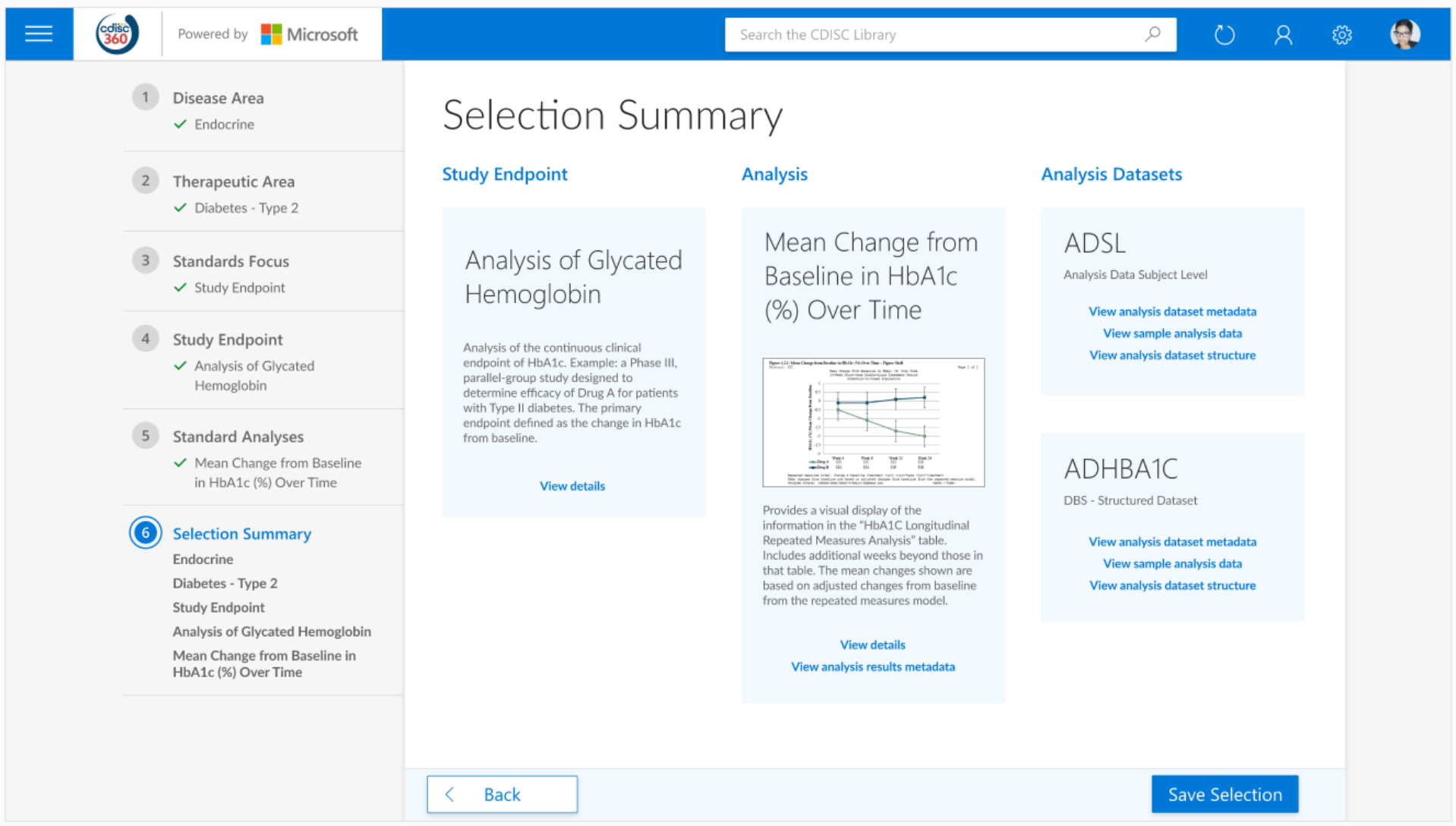
Use Case 3 : Execute

Automatic population of data into artifacts




CDISC 360 PoC
WS
Standard concepts for a Study
Study Definitions
Build Study Specification
List Metadata (Query Interface)
Study Specification Artefacts
Neo4j SAS Interface
metadata
Test Data CDR
Raw, CDASH, SDTM, ADaM
WS4 & 6
Data Collection Designer
Data Collection Specification ODM-XML
Blank CRF
Specification Define-XML for SDTM
aCRF
TFL Designer
Design and configure TFL table shells
WS6
Automate Execution in SCE
Supplemental Metadata
Ingest Specification metadata
SDTM & ADaM Automation Engine
Control and monitor Data Generation
SDTM Datasets
SDTM Programs
SDTM Artefacts
ADaM Datasets
ADaM Programs
ADaM Artefacts
TFL Automation Engine
Control and monitor TFL Generation
ARM
TFL Programs
TFLs

CDISC 360: The Art of the Possible

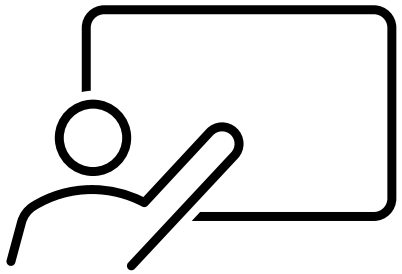


Reference: '*CDISC 360 - The Journey so Far and the Road Ahead', Peter Van Reusel, 28th April 2020*

Current State: Analysis Results Deliverables

- Manual process in designing TFL shells/layout and ADaM specifications
- Programmer writes the SAS code to generate analysis deliverables (sometime with macros or re-using the code)
- Too much variability across studies, disease areas, and organization
- Static results with no or limited linking facility (e.g., to Protocol, SAP, ADaM data)
- There is no industry standard for analysis results

Poll Summary*



** Results from the live poll (**n=253 responders**) conducted during the TFL Designer Virtual Design Thinking Workshop (Part I), 13th Sep 2022, Bhavin Busa*

Who attended the workshop:
- Clinical / Statistical Programmer (**63%**)
- Biostatisticians (**14%**)
- Data Standards Expert (**13%**)
- Other (**12%**)

Top 5 pain points:
1. Too much variability across studies / disease areas / organizations
2. No industry-wide standards exist
3. TFL metadata and shells are not machine-readable
4. Multiple manual steps in the process
5. Limited or no automation exist

Programming is more of a Science (**50%**) than it is an Art (**39%**)!

1

74% organizations have TFL standards or templates

Who generates TFL shells (mock-ups)?
57% - Biostatistician
31% - Biostats & Programmers

87% responders confirmed their TFL shells are NOT machine-readable

65% responders uses MS Word / RTF for TFL shells generation

40% annotate their TFL mock-up shells to provide results metadata information

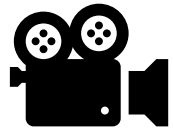
76% do not generate analysis results metadata prospectively to use in their TFL program

82% confirmed not having machine-readable TFL analysis results metadata

Out of the responders who use machine-readable ARM: MS Excel (**14%**) and SAS (**10%**) are top 2 format choices

CDISC Analysis Results Standard – Coming Soon!

All You Need to Know about the New CDISC Analysis Result Standards!

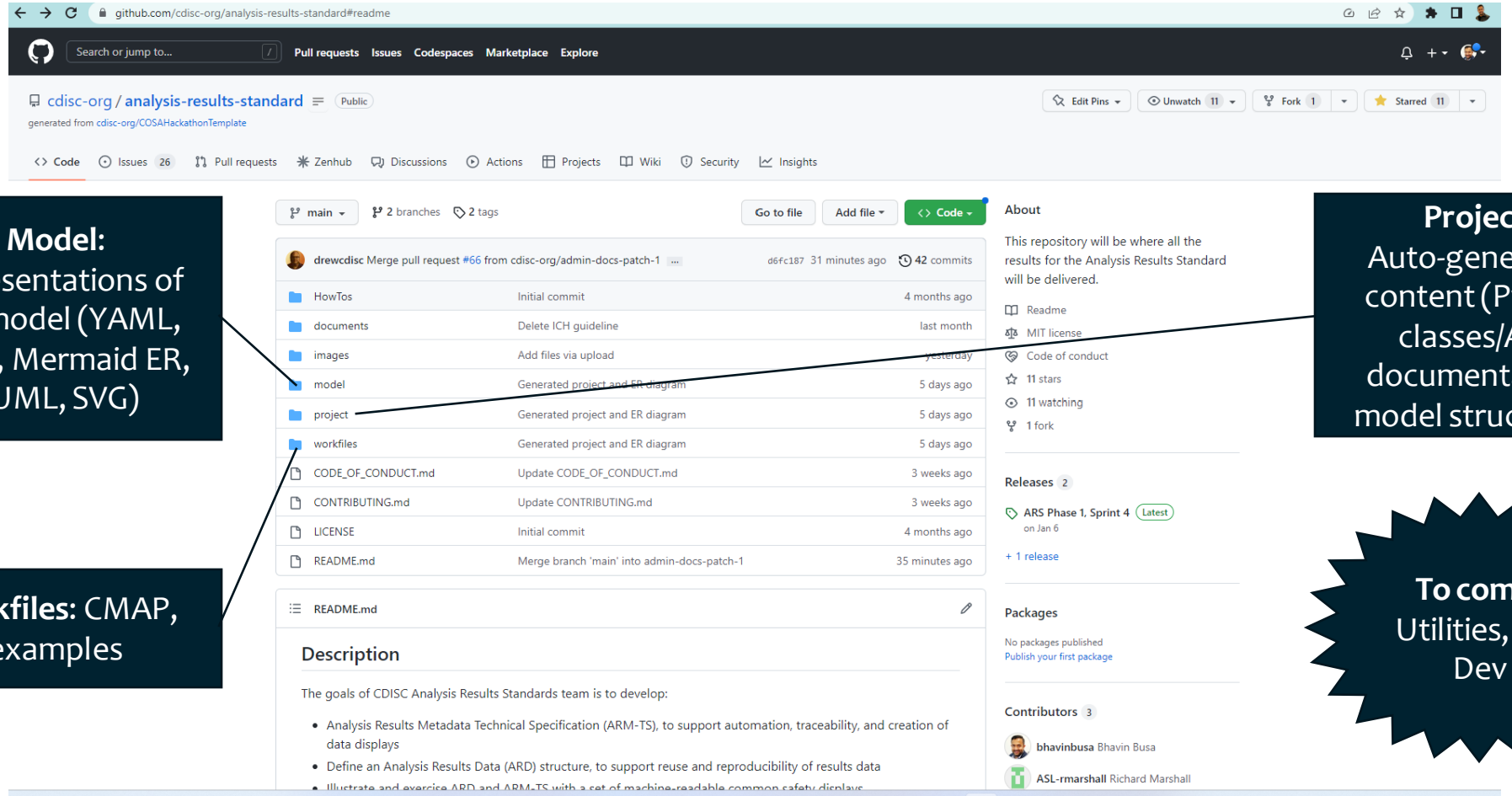


PharmaSUG 2023: Paper # MM327

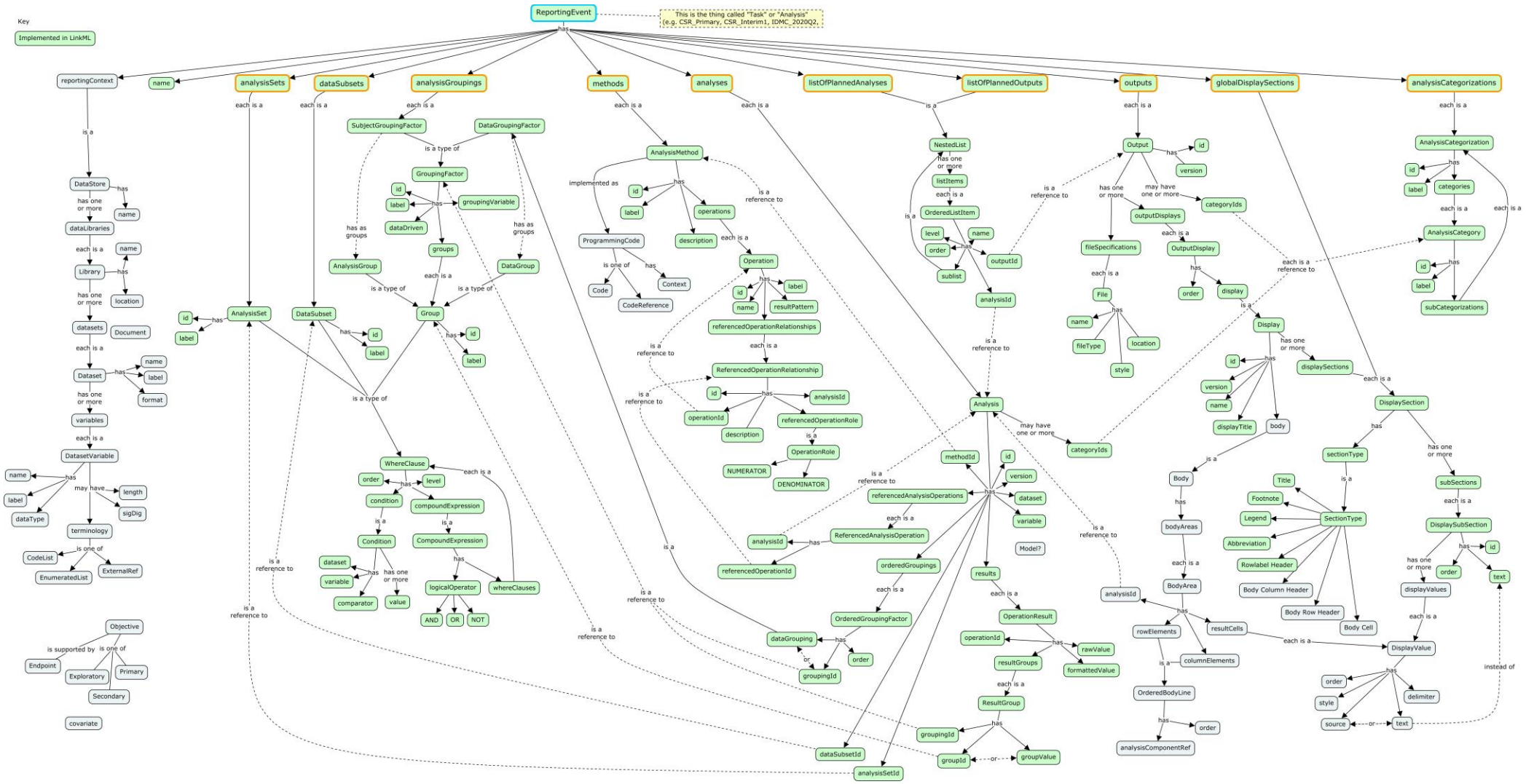
Bhavin Busa, Richard Marshall, Bess LeRoy

Analysis Results Standard Public Repo on GitHub

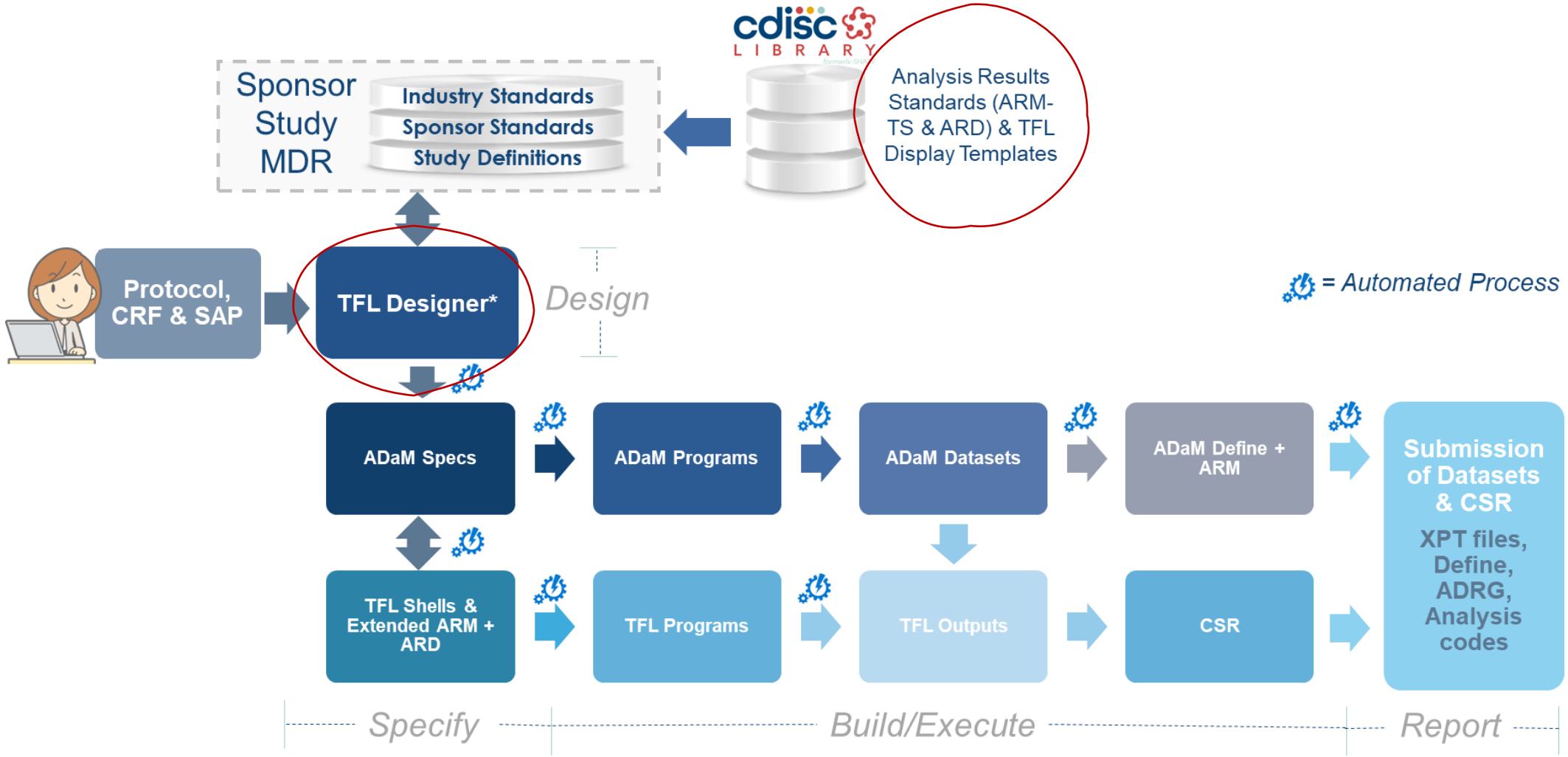
- https://github.com/cdisc-org/analysis-results-standard

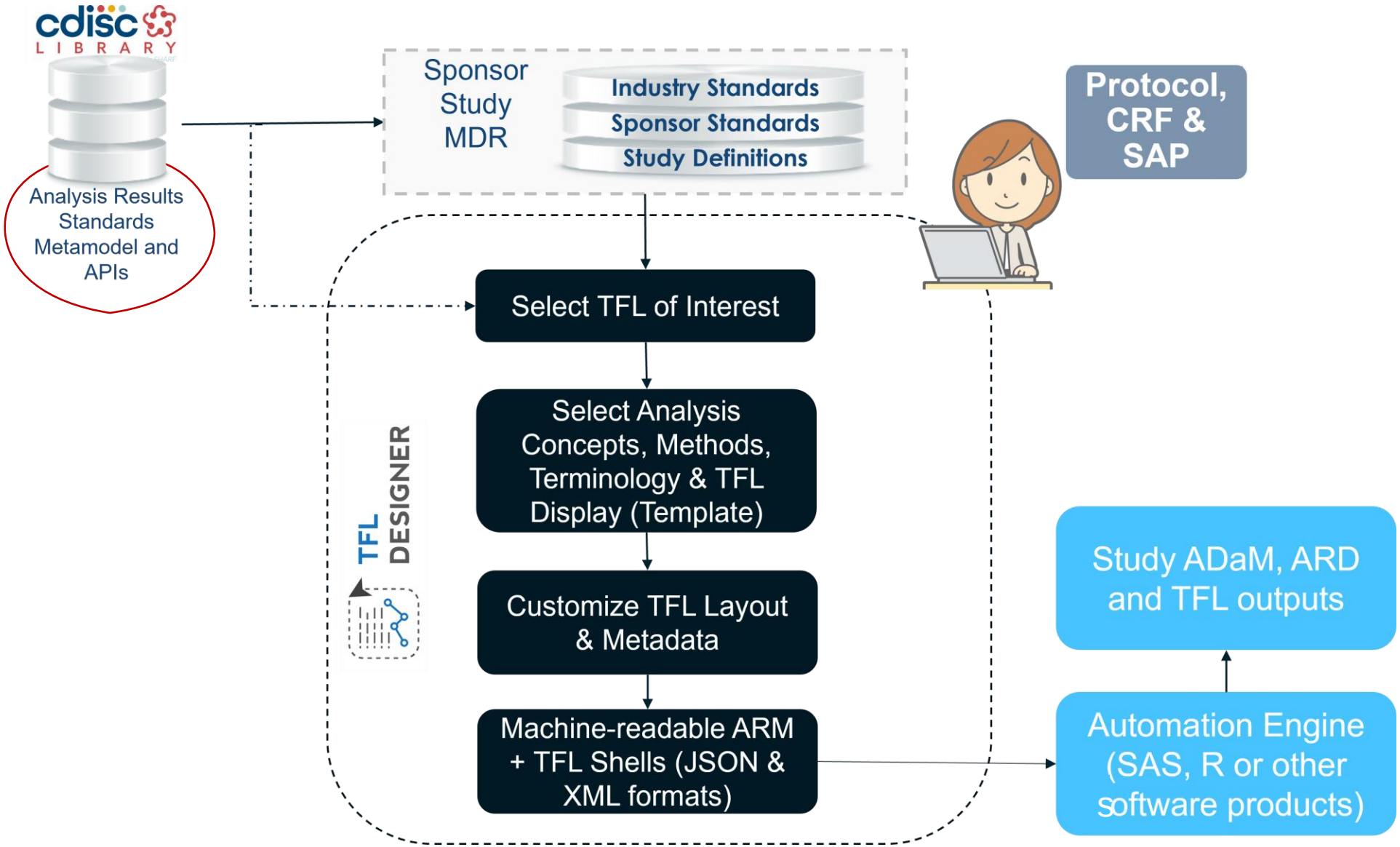


ARS Model Representation using CMAP*



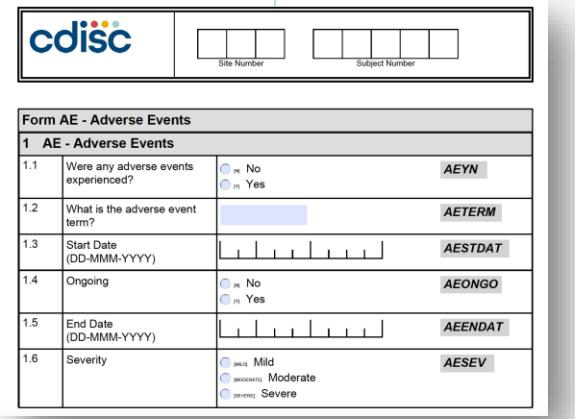
Future State: Analysis Results Deliverables




cdisc LIBRARY
Analysis Results Standards Metamodel and APIs
Sponsor Study MDR
Industry Standards
Sponsor Standards
Study Definitions
Protocol, CRF & SAP
Select TFL of Interest
Select Analysis Concepts, Methods, Terminology & TFL Display (Template)
Customize TFL Layout & Metadata
Machine-readable ARM + TFL Shells (JSON & XML formats)
TFL DESIGNER
Study ADaM, ARD and TFL outputs
Automation Engine (SAS, R or other software products)

Streamlining Analysis Data Flow

CDASH (Collection) ← SDTM (Tabulation) ← ADaM (Analysis) ← Analysis Results ← TFL



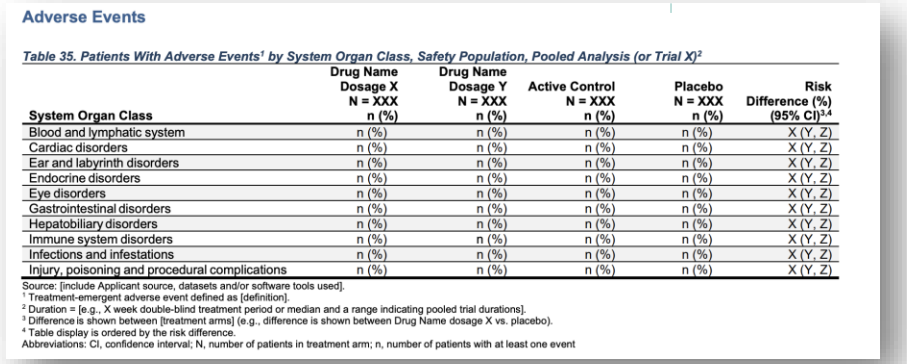
cdisc

Site Number | Subject Number

Form AE - Adverse Events

1 AE - Adverse Events

1.1	Were any adverse events experienced?	No / Yes	AEYN
1.2	What is the adverse event term?		AETERM
1.3	Start Date (DD-MMM-YYYY)		AESTDAT
1.4	Ongoing	No / Yes	AEONGO
1.5	End Date (DD-MMM-YYYY)		AEENDAT
1.6	Severity	Mild / Moderate / Severe	AESEV



Adverse Events

Table 35. Patients With Adverse Events[1] by System Organ Class, Safety Population, Pooled Analysis (or Trial X)[2]

System Organ Class	Drug Name Dosage X N = XXX n (%)	Drug Name Dosage Y N = XXX n (%)	Active Control N = XXX n (%)	Placebo N = XXX n (%)	Risk Difference (%) (95% CI)[3,4]
Blood and lymphatic system	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Cardiac disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Ear and labyrinth disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Endocrine disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Eye disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Gastrointestinal disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Hepatobiliary disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Immune system disorders	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Infections and infestations	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Injury, poisoning and procedural complications	n (%)	n (%)	n (%)	n (%)	X (Y, Z)

Source: [include Applicant source, datasets and/or software tools used].
[1] Treatment-emergent adverse event defined as [definition].
[2] Duration = [e.g., X week double-blind treatment period or median and a range indicating pooled trial durations].
[3] Difference is shown between [treatment arms] (e.g., difference is shown between Drug Name dosage X vs. placebo).
[4] Table display is ordered by the risk difference.
Abbreviations: CI, confidence interval; N, number of patients in treatment arm; n, number of patients with at least one event

Keeping End in Mind

TFL
DESIGNER

TFL Designer – Key Highlights

- Software as a Service (SaaS) Solution
- Digitizes your analysis results (TFL)
- Aligned with CDISC Analysis Results Standards
- Central repository for your TFL standards, display templates, conventions and metadata
- Automates generation of TFL shells and provides machine-readable metadata
- Community & Enterprise versions

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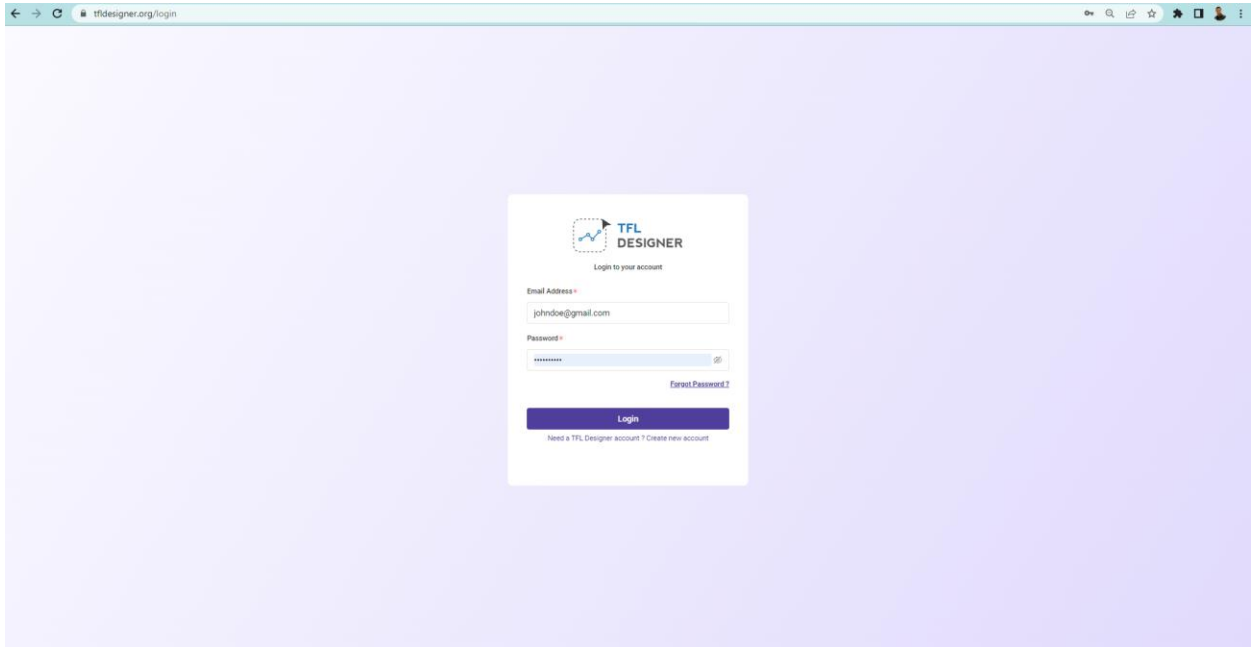
TFL DESIGNER®

Key Functionalities

- *Central repository for your TFL standards/templates, conventions and metadata*
- *Access to library of TFL templates (community and user generated) by disease areas, TA, and indication*
- *Access to CDISC Standards (SDTM, ADaM, CT) via API to CDISC Library*
- *Develop new mock-up shells, edit/delete items*
- *Automatically populate items based on user inputs*
- *Export TFL shells in RTF & PDF formats*
- *Export and import analysis results metadata in various machine-readable formats*

Visit Clymb or COSA Booth for TFL Designer (Community) Demo



Thursday, 19th Oct (Day 2)

@COSA Booth		@Clymb Booth	
10:30	11:00	14:00	14:30
11:00	11:30	14:30	15:00
11:30	12:00	15:00	15:30
12:00	12:30	15:30	16:00

What are we trying to accomplish?

- Build an industry leading software solution that automates TFL design and generation process [community & enterprise versions]
- Partner with companies to improve their internal TFL standards and processes
- Quantify process improvements and continue to build future state automation (target 40-50% efficiency)
- Accelerate study timelines to allow your team to get data quicker
- CDISC 360 Vision: From PoC to Reality

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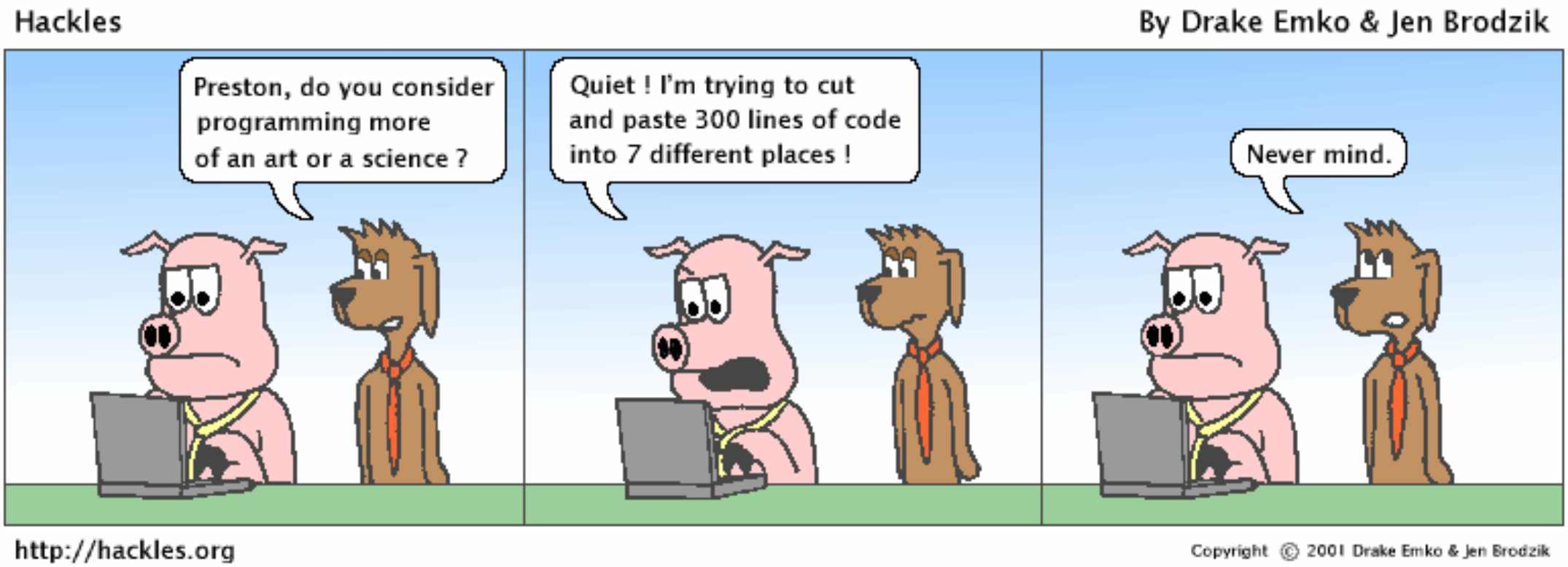
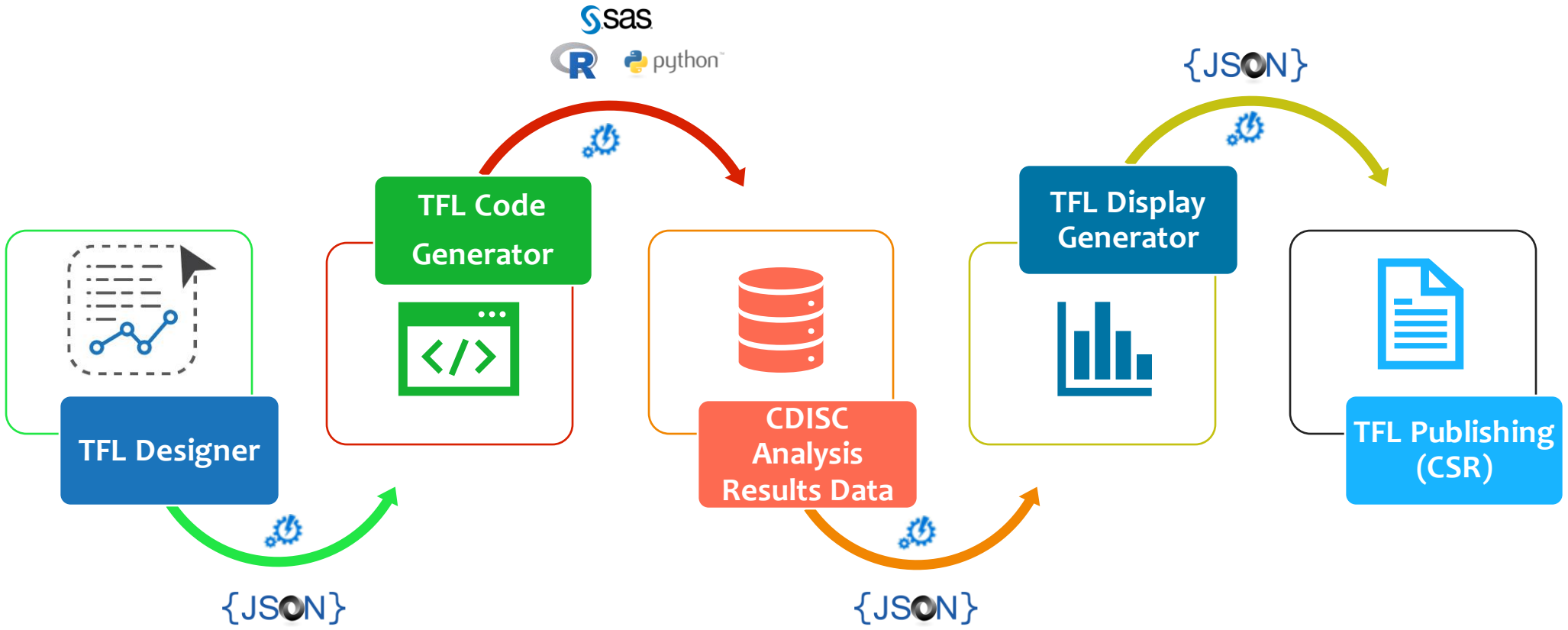
Challenging the Status Quo



"copy-paste programming" to "meta-programming"

TFL / Analysis Results – Clymb Vision



= Automated Process

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References

1. All You Need to Know about the New CDISC Analysis Result Standards!, PharmaSUG 2023: Paper # MM327, Bhavin Busa, Richard Marshall, Bess LeRoy

2. CDISC Analysis Results Standard GitHub, 2023: https://github.com/cdisc-org/analysis-results-standard

3. CDISC 360 White Paper

4. CDISC 360 - The Journey so Far and the Road Ahead, Peter Van Reusel, 28th April 2020