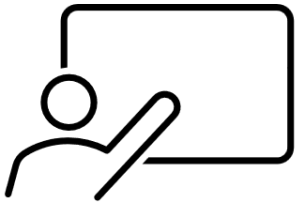
cdisc


2024 CDISC + TMF
US INTERCHANGE
PHOENIX/SCOTTSDALE
23-24 OCTOBER: CONFERENCE & EXPO | 21, 22, 25 OCTOBER: TRAININGS

Driving Efficiency and Automation in TFL Generation: A Case Study of Establishing an Oncology TFL Library and Analysis Results Metadata Repository

CDISC US Interchange 2024
October 24th, 2024 [Session 6C: Analysis Results Standards – eTFL]
Bhavin Busa (Clymb Clinical) & Salil Parab (Xencor, Inc)

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% organization 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

CDISC Analysis Result Standards – Released April 19, 2024!

cdisc
Clear data. Clear impact

Analysis Results Standard (ARS) v1.0

cdisc ARS ANALYSIS RESULTS STANDARD

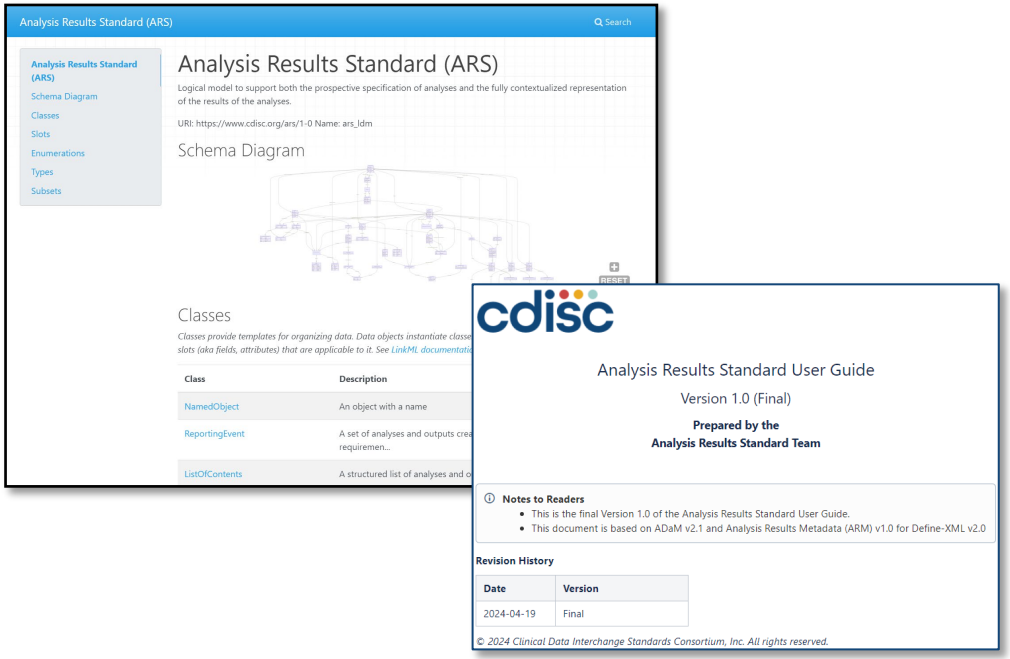
Large trials generate many analysis results in the form of tables, figures, and written reports, yet these results are rarely output in a form that is machine-readable. Previously, there has been no standard way of describing and organizing these results, making it difficult to automate their generation,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

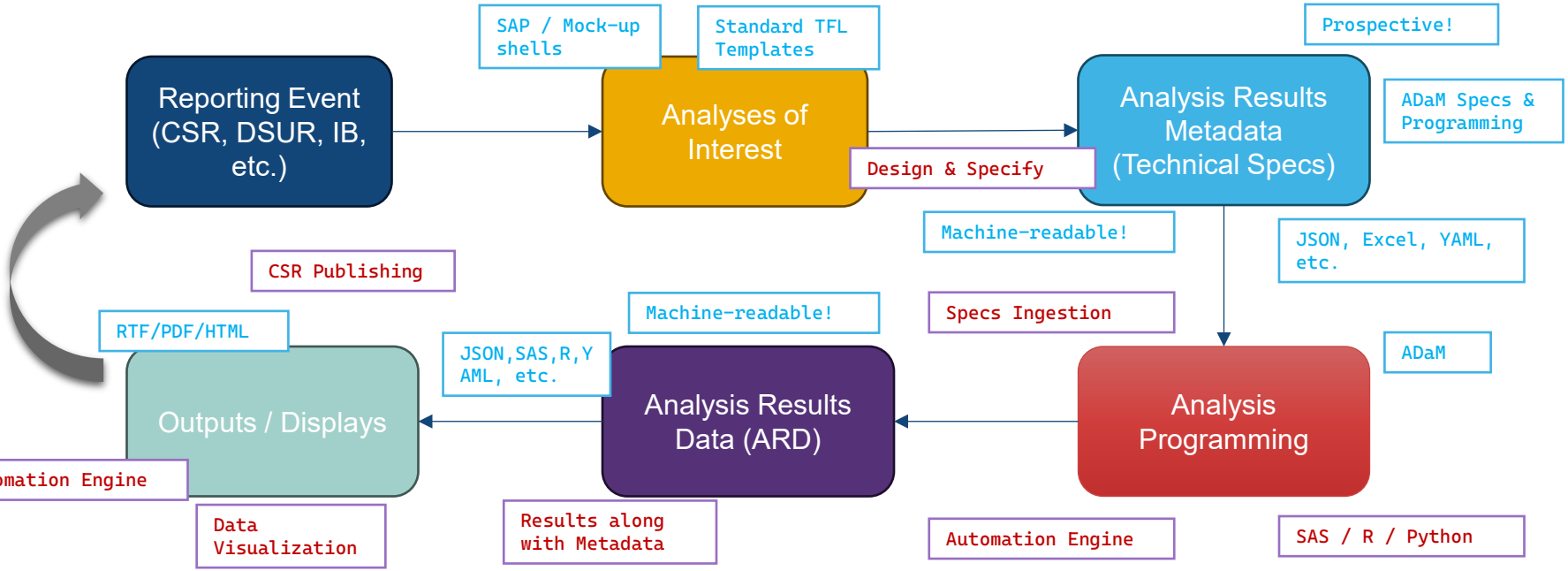
- A Logical Data Model that describes analysis results and associated metadata.
- A User Guide to illustrate and exercise the model with common safety displays.

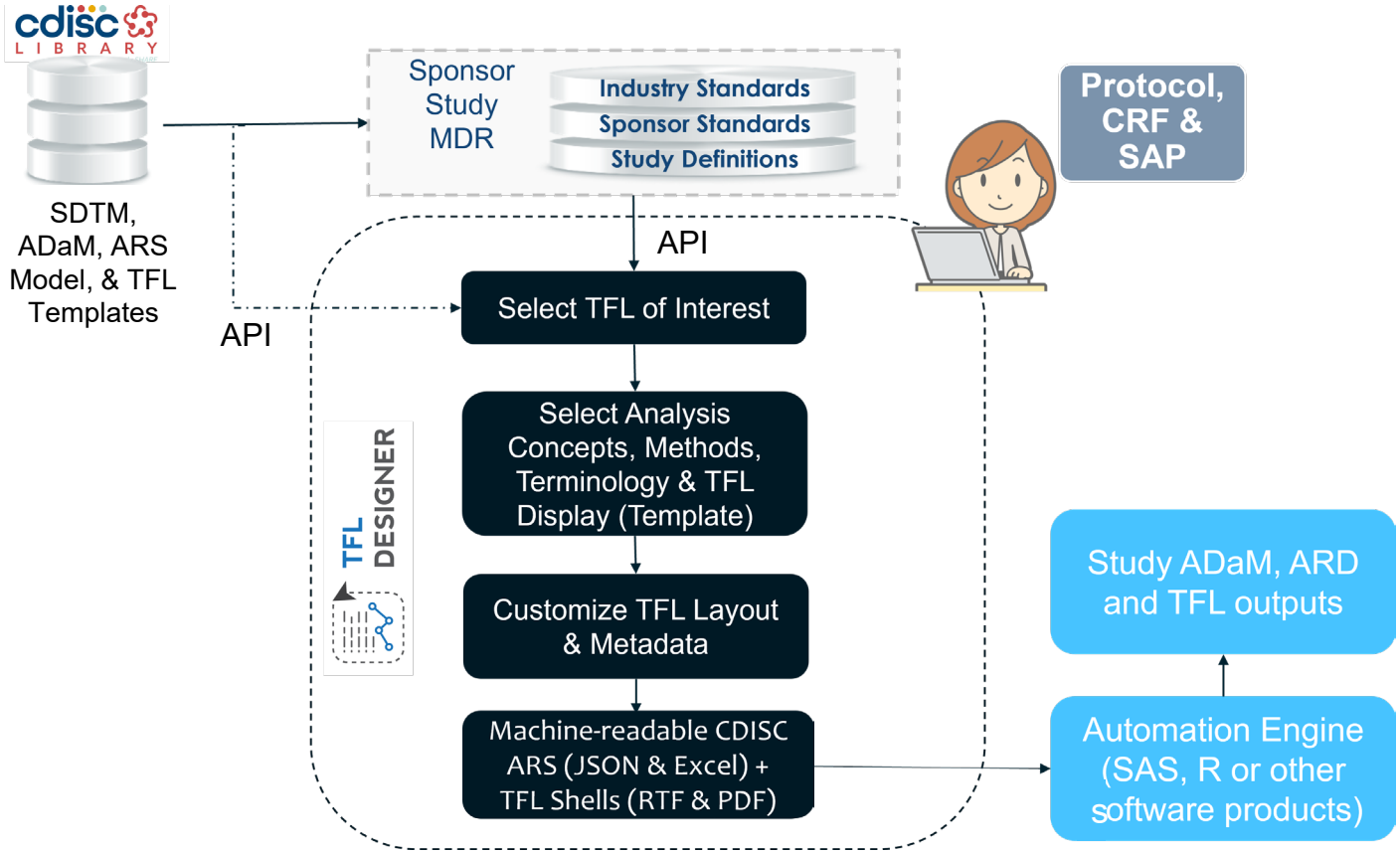
https://cdisc-org.github.io/analysis-results-standard/



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

ARS Model Supported Workflow and Entry Points

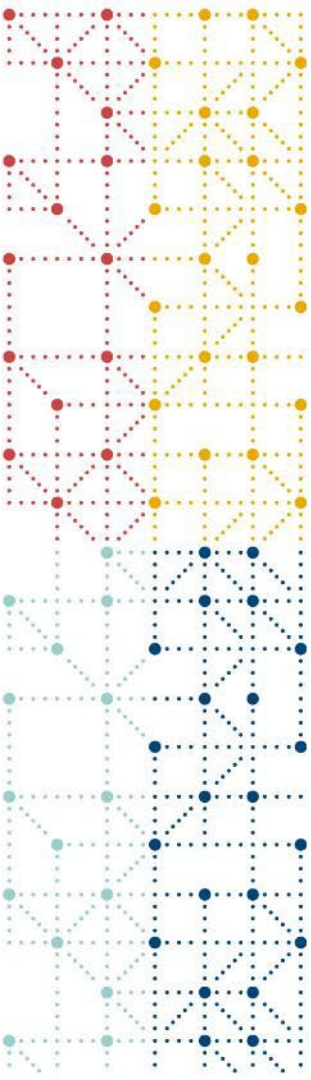



cdisc LIBRARY
SDTM, ADaM, ARS Model, & TFL Templates
Sponsor Study MDR
Industry Standards
Sponsor Standards
Study Definitions
Protocol, CRF & SAP
API
API
Select TFL of Interest
Select Analysis Concepts, Methods, Terminology & TFL Display (Template)
Customize TFL Layout & Metadata
Machine-readable CDISC ARS (JSON & Excel) + TFL Shells (RTF & PDF)
TFL DESIGNER
Study ADaM, ARD and TFL outputs
Automation Engine (SAS, R or other software products)

TFL
DESIGNER

TFL Designer – Key Highlights

- Digitizing your analysis results (TFL)
- Community & Enterprise versions
- Aligned with CDISC Analysis Results Standard (ARS)
- Automate generation of TFL shells and provides machine-readable metadata
- Support downstream automation (TFL code and output generation)
- CDISC 360 Vision: From PoC to Reality



Case Study Background

- Biotech using plug and play technology to create powerful & effective antibodies
- Pasadena and San Diego, CA based
- Primary focus on Oncology and Autoimmune indications

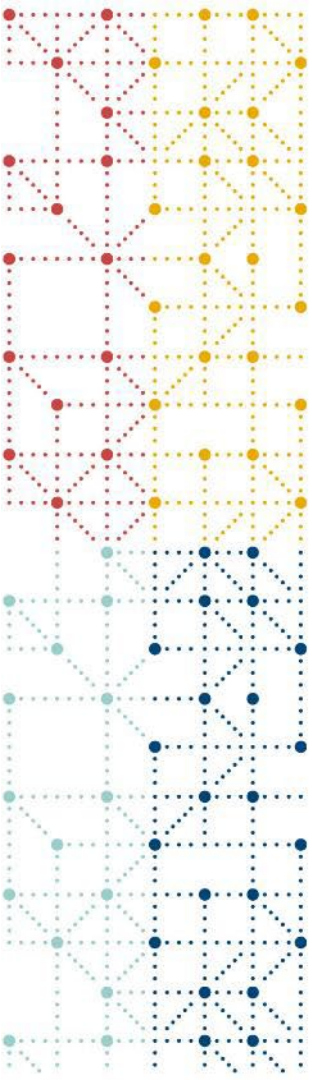
Biostats and Statistical Programming at Xencor

- Small team supporting regulatory fillings including DERC, DSUR, IB, Publications, CSR, Exploratory analysis, etc., and hybrid outsourcing with collaborative production work
- Focus is to maximize standardization & automation to gain efficiencies

Mock shell preparation was manual

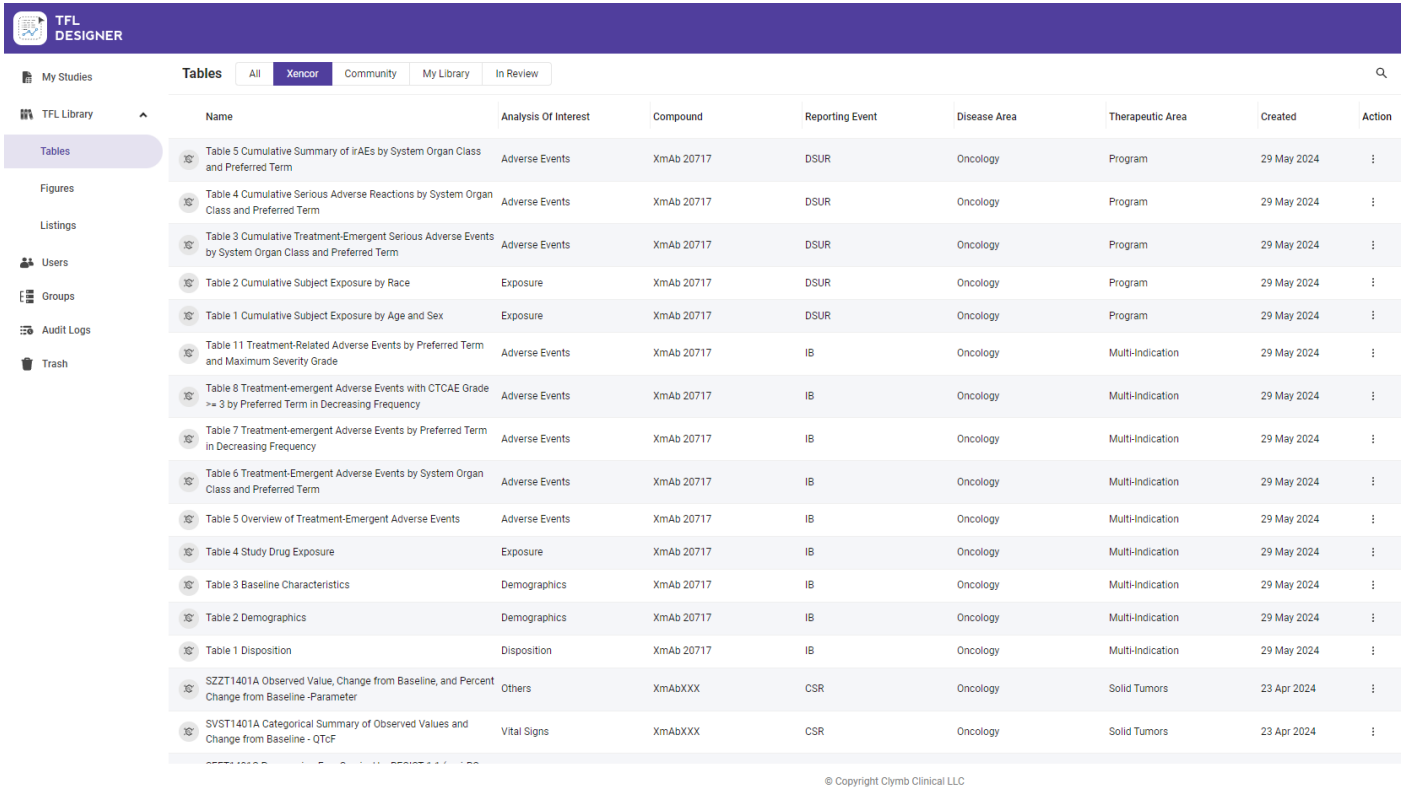
- Primary tool is MS Word
- Considerable time spent on formatting
- Copy and paste of repeat TFLs
- TOC and hyperlinks
- Annotation of TFLs/ ADaM metadata
- Team would enter feedback in Word document resulting in a tedious process to review and respond to feedback

All the above needs to be repeated to insert/ delete TFLs after team review



Establishing Safety & Oncology Specific TFL Library and Analysis Results Metadata Repository

Xencor Template Library (for DSUR, IB and CSR)

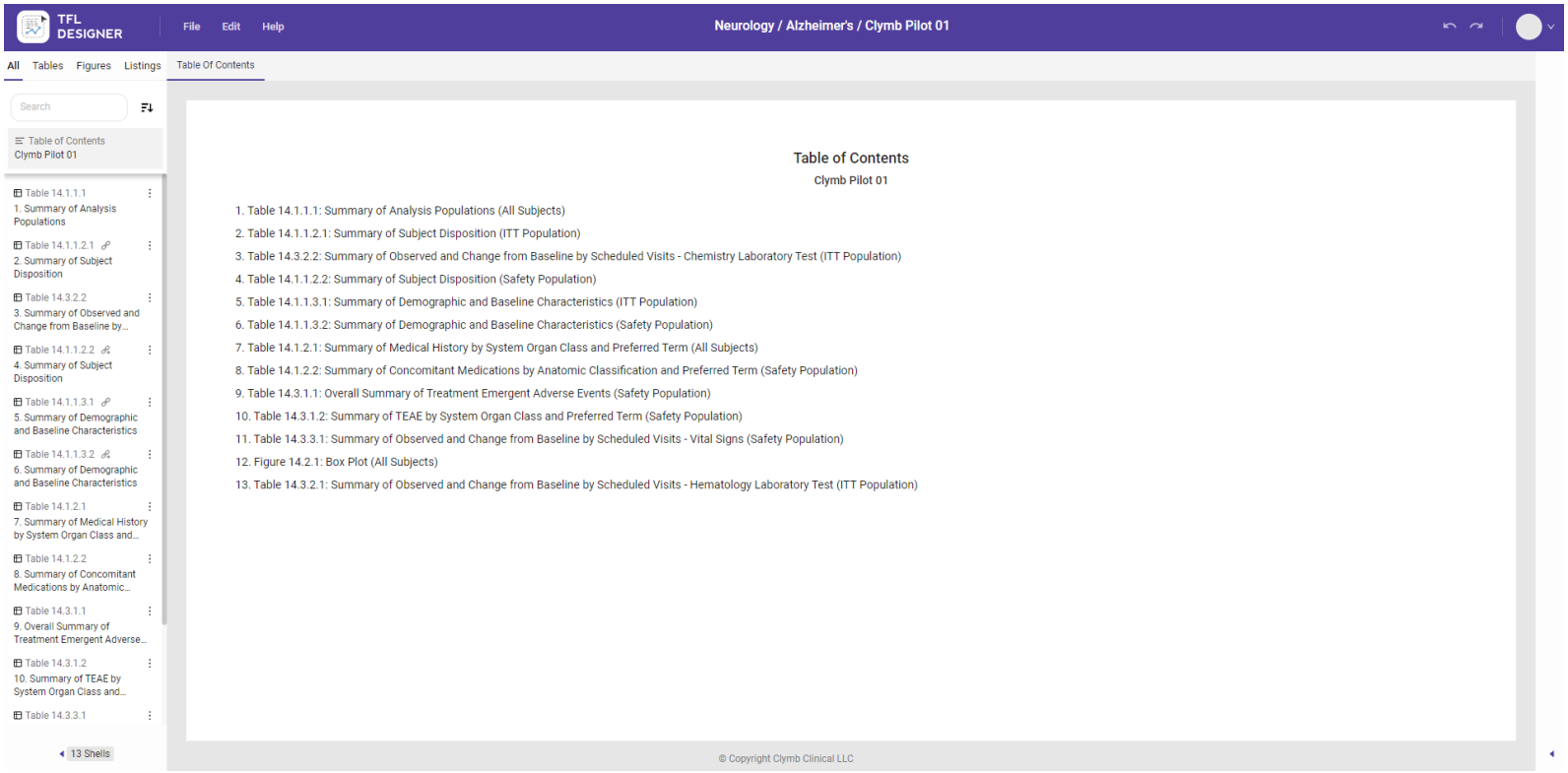


Name	Analysis Of Interest	Compound	Reporting Event	Disease Area	Therapeutic Area	Created	Action
Table 5 Cumulative Summary of irAEs by System Organ Class and Preferred Term	Adverse Events	XmAb 20717	DSUR	Oncology	Program	29 May 2024	
Table 4 Cumulative Serious Adverse Reactions by System Organ Class and Preferred Term	Adverse Events	XmAb 20717	DSUR	Oncology	Program	29 May 2024	
Table 3 Cumulative Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term	Adverse Events	XmAb 20717	DSUR	Oncology	Program	29 May 2024	
Table 2 Cumulative Subject Exposure by Race	Exposure	XmAb 20717	DSUR	Oncology	Program	29 May 2024	
Table 1 Cumulative Subject Exposure by Age and Sex	Exposure	XmAb 20717	DSUR	Oncology	Program	29 May 2024	
Table 11 Treatment-Related Adverse Events by Preferred Term and Maximum Severity Grade	Adverse Events	XmAb 20717	IB	Oncology	Multi-Indication	29 May 2024	
Table 8 Treatment-emergent Adverse Events with CTCAE Grade >= 3 by Preferred Term in Decreasing Frequency	Adverse Events	XmAb 20717	IB	Oncology	Multi-Indication	29 May 2024	
Table 7 Treatment-emergent Adverse Events by Preferred Term in Decreasing Frequency	Adverse Events	XmAb 20717	IB	Oncology	Multi-Indication	29 May 2024	
Table 6 Treatment-Emergent Adverse Events by System Organ Class and Preferred Term	Adverse Events	XmAb 20717	IB	Oncology	Multi-Indication	29 May 2024	
Table 5 Overview of Treatment-Emergent Adverse Events	Adverse Events	XmAb 20717	IB	Oncology	Multi-Indication	29 May 2024	
Table 4 Study Drug Exposure	Exposure	XmAb 20717	IB	Oncology	Multi-Indication	29 May 2024	
Table 3 Baseline Characteristics	Demographics	XmAb 20717	IB	Oncology	Multi-Indication	29 May 2024	
Table 2 Demographics	Demographics	XmAb 20717	IB	Oncology	Multi-Indication	29 May 2024	
Table 1 Disposition	Disposition	XmAb 20717	IB	Oncology	Multi-Indication	29 May 2024	
SZZT1401A Observed Value, Change from Baseline, and Percent Change from Baseline -Parameter	Others	XmAbXXX	CSR	Oncology	Solid Tumors	23 Apr 2024	
SVST1401A Categorical Summary of Observed Values and Change from Baseline - QTcF	Vital Signs	XmAbXXX	CSR	Oncology	Solid Tumors	23 Apr 2024	

Examples of Oncology Templates Developed

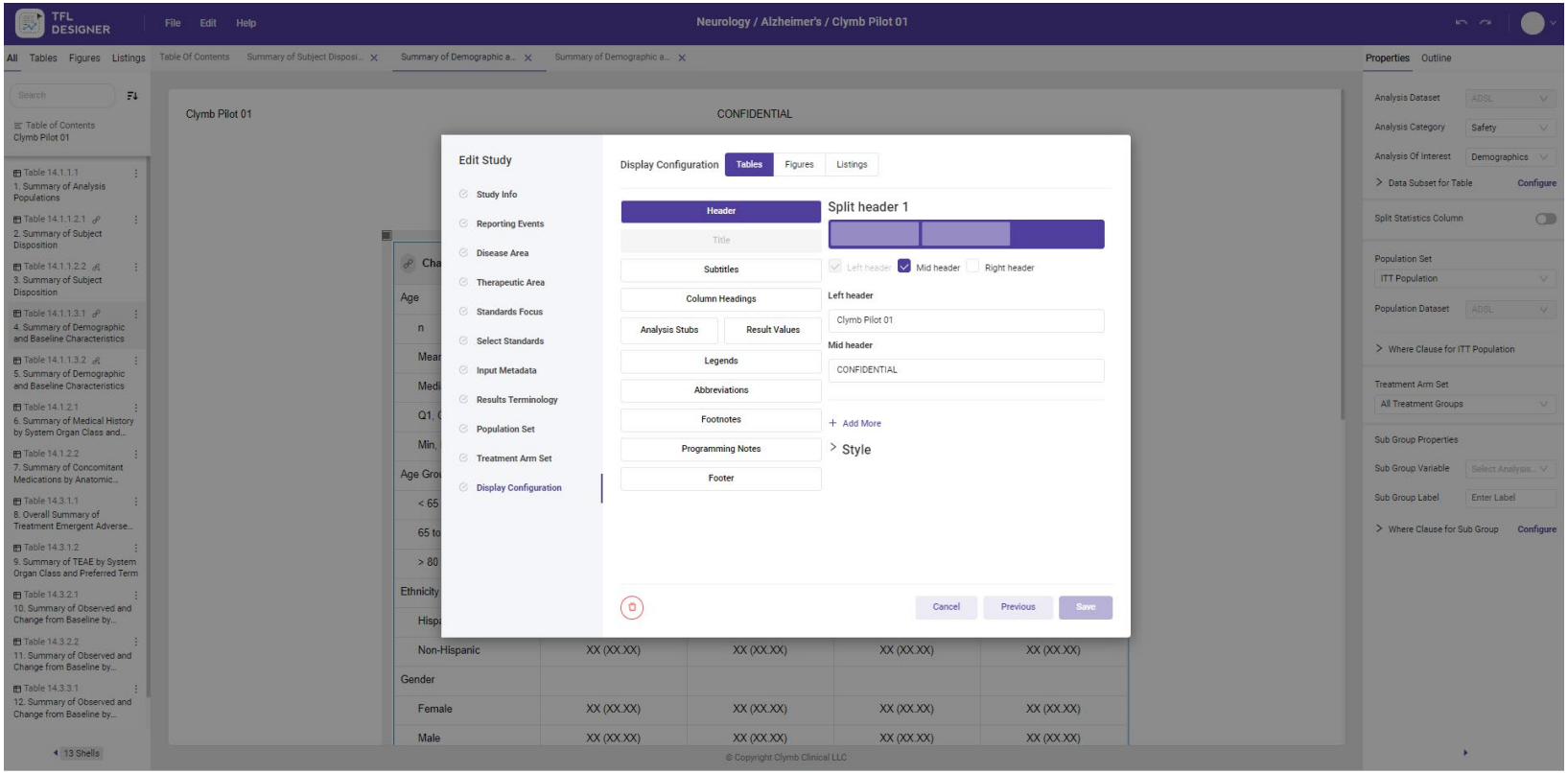
- ECOG: Observed Values, Change from Baseline, and Percent Change from Baseline
- RECIST 1.1 (irRC or imRECIST): Best Overall Responses, Time to Response, Duration of Response, Progression-Free Survival, Overall Survival
- Tumor Burden by RECIST 1.1
- Kaplan-Meier Plots for Progression-Free Survival and Overall Survival
- Best Percent Change in RECIST 1.1 Sum of Diameters
- Swimmer Plots for Subject Disposition and Response

Automation for Biostats and Stat Programmers

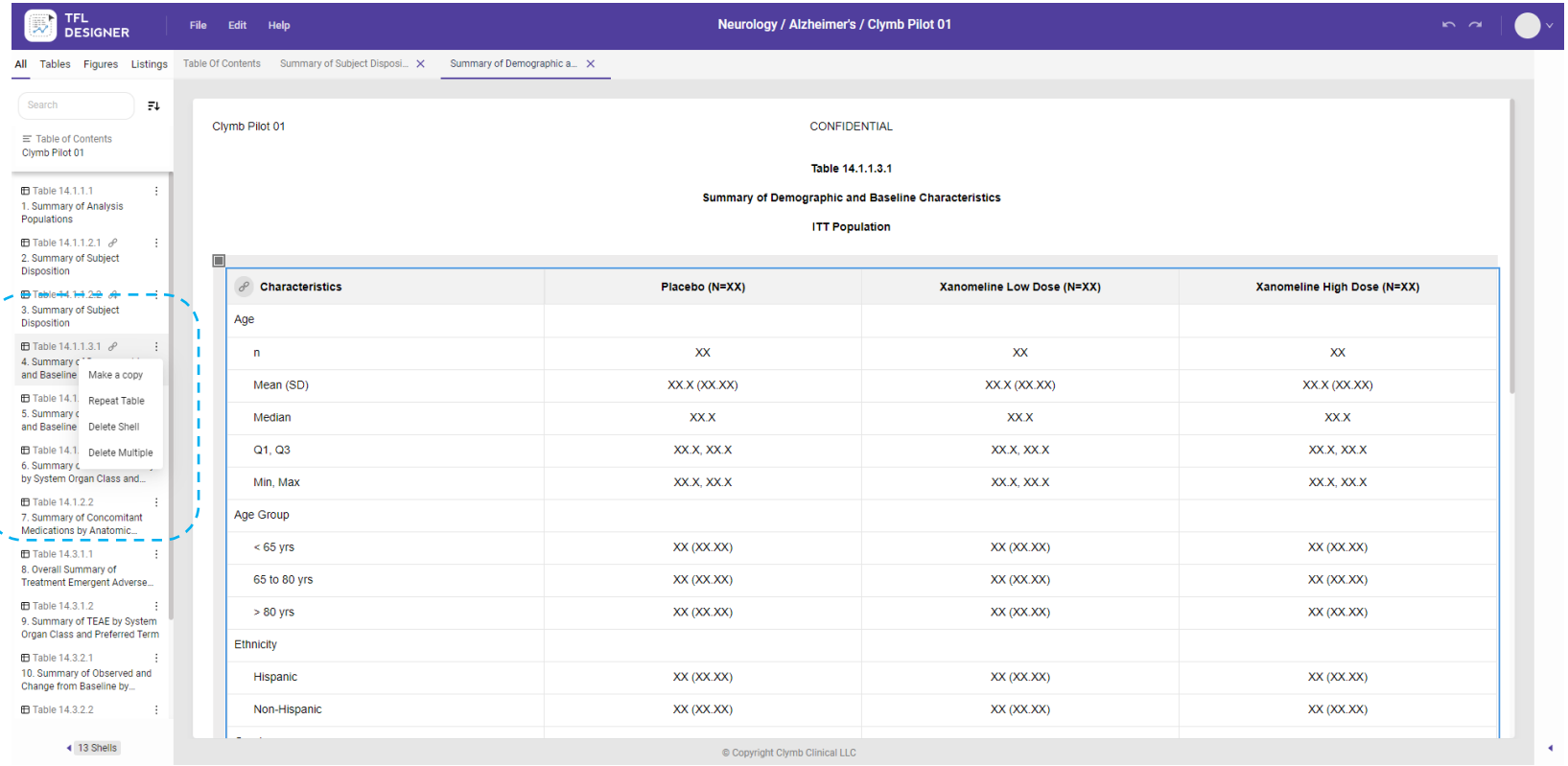


cdisc

Automation for Biostats and Stat Programmers

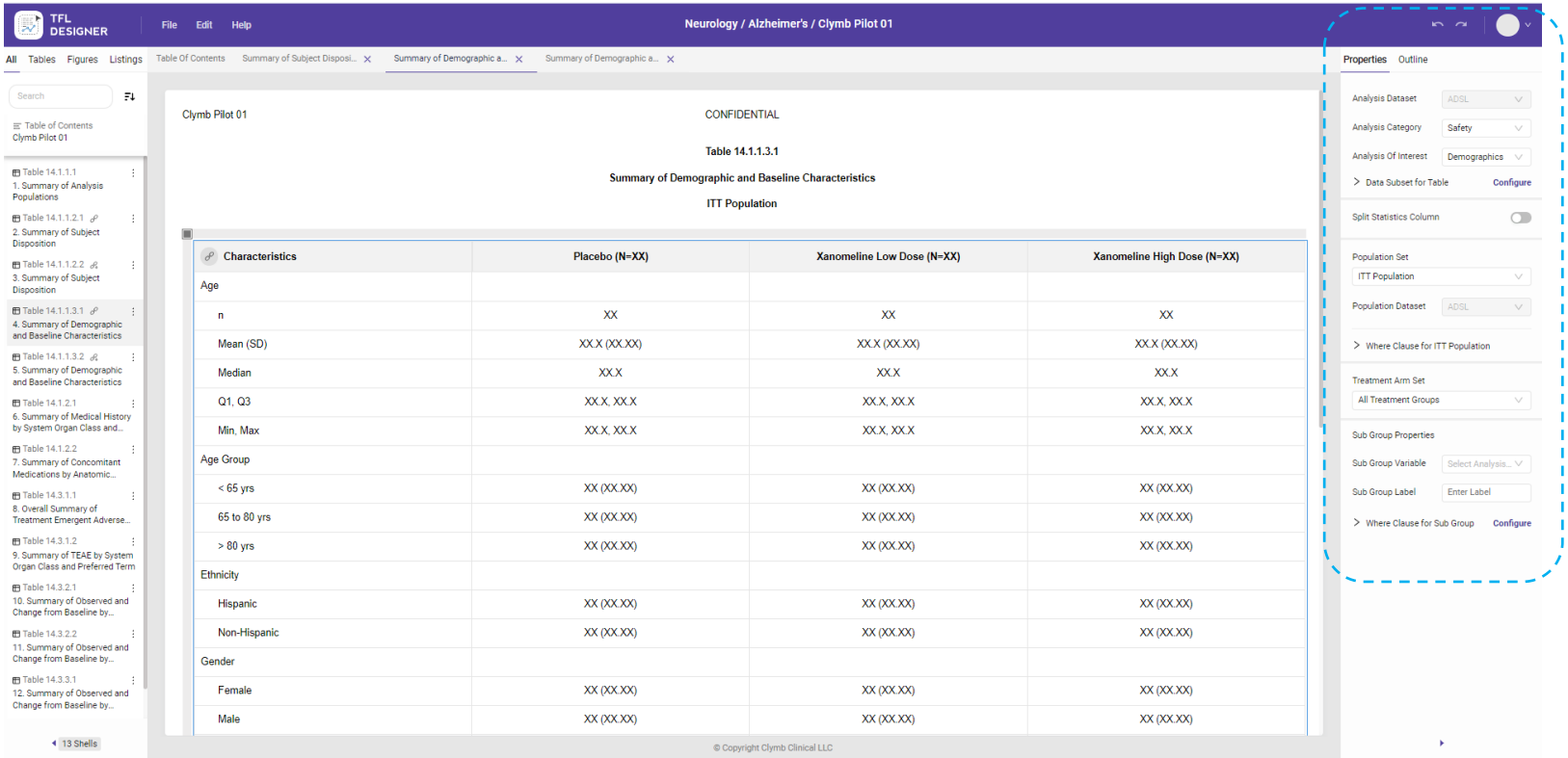


Automation for Biostats and Stat Programmers

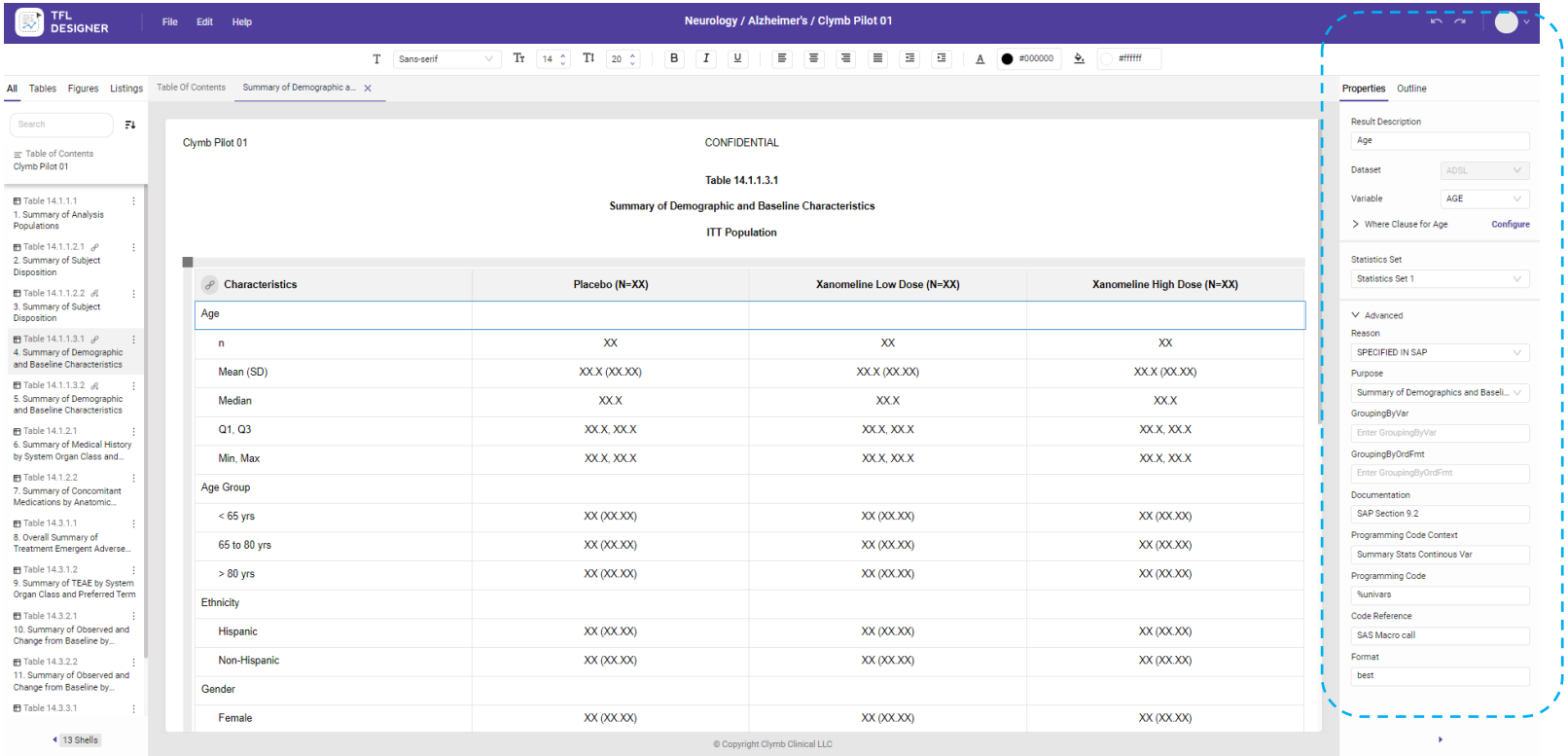


cdisc

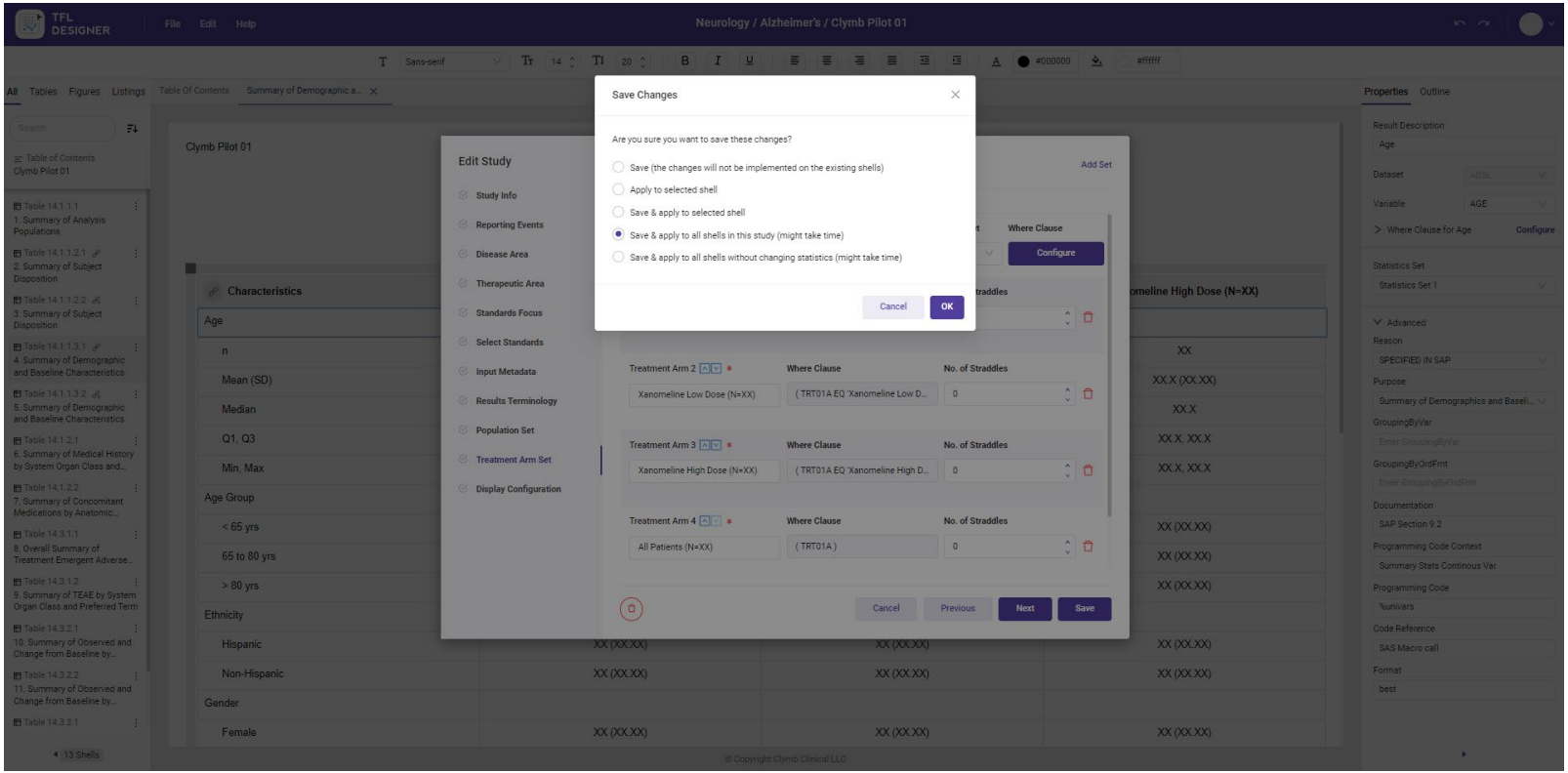
Automation for Biostats and Stat Programmers



Automation for Biostats and Stat Programmers

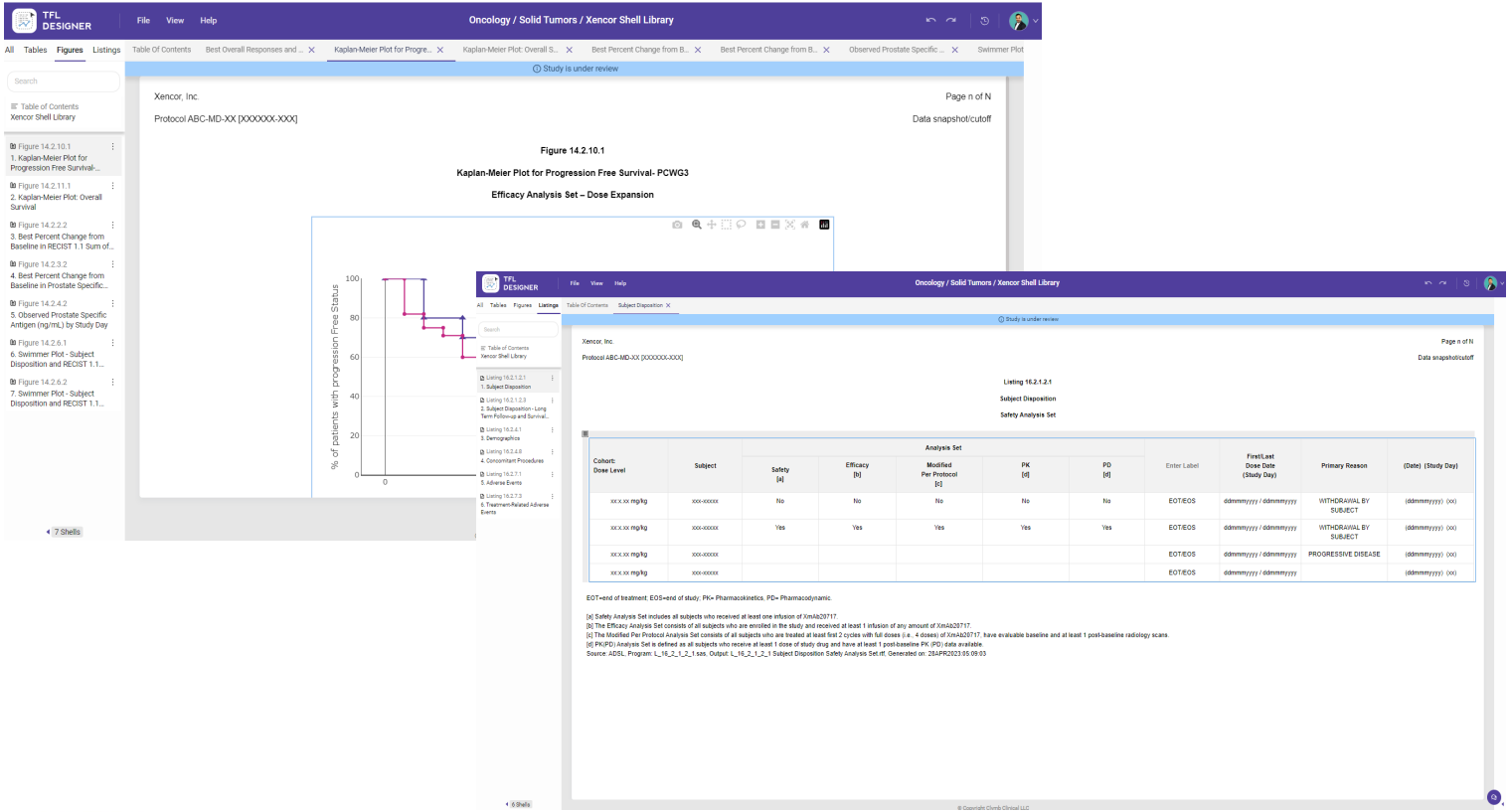


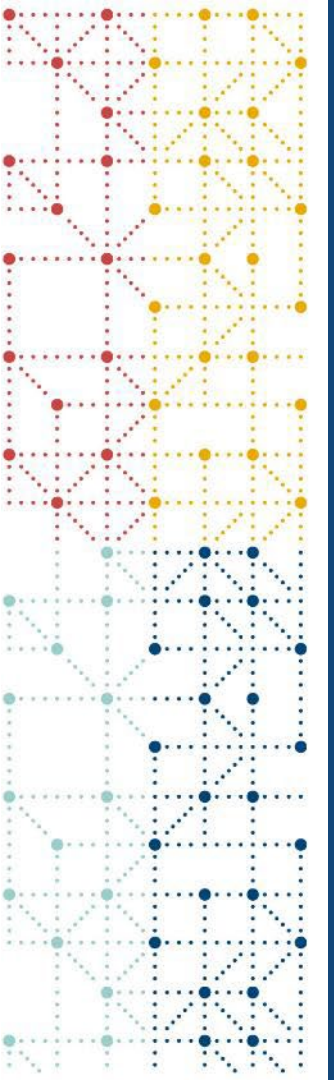
Automation for Biostats and Stat Programmers



cdisc

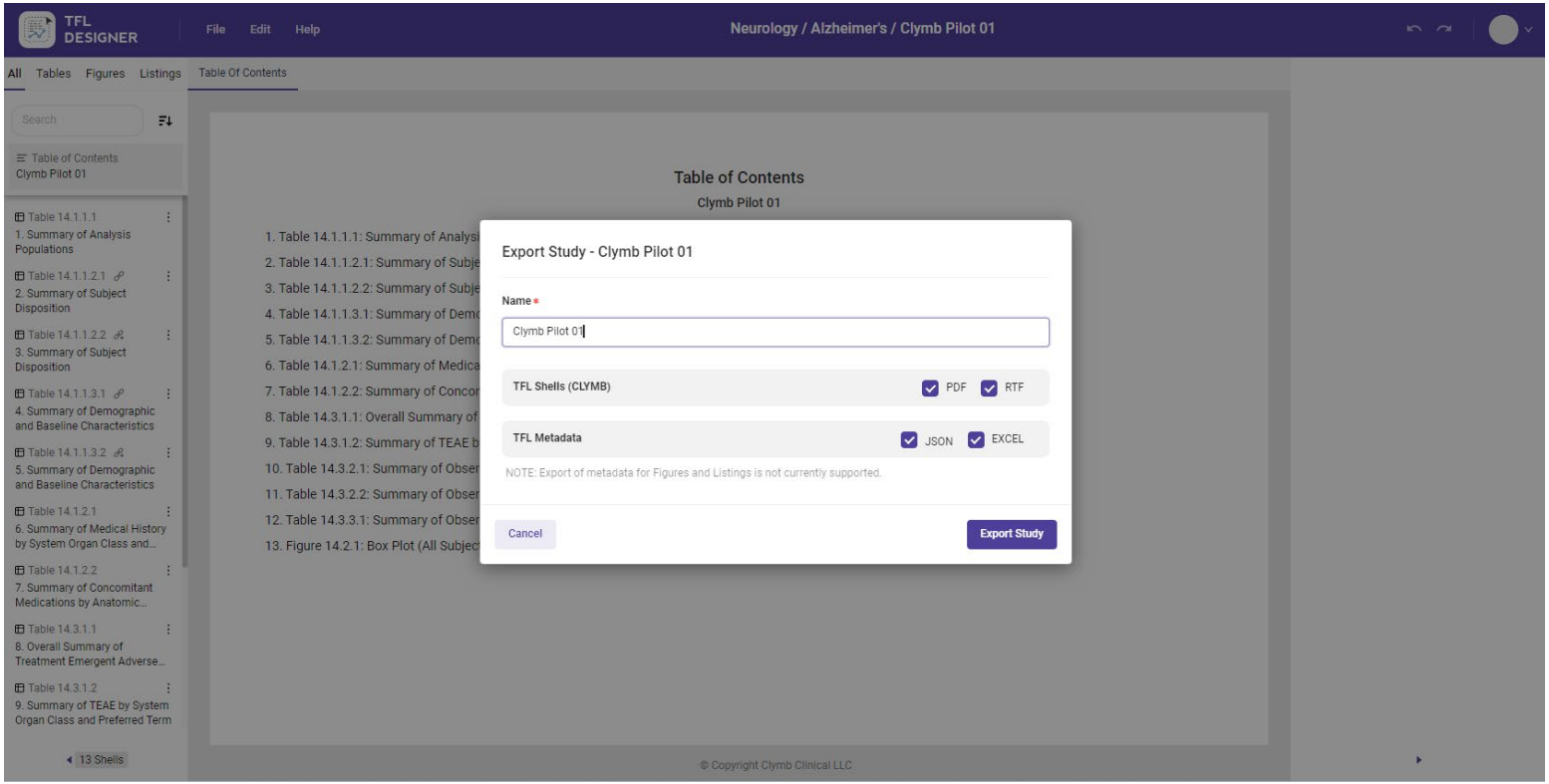
Figures and Listings Mock-ups



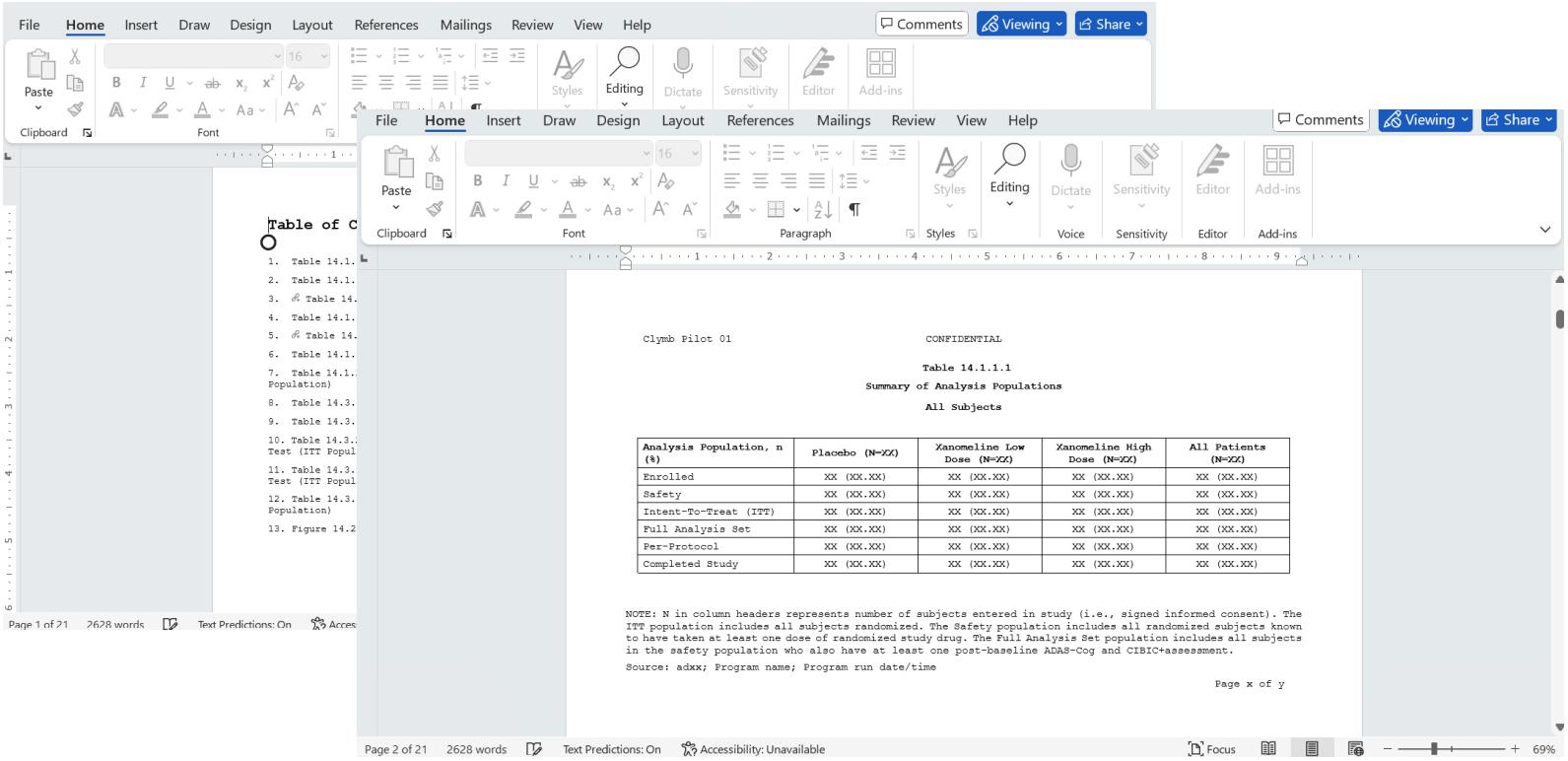


Export TFL Shells and Metadata

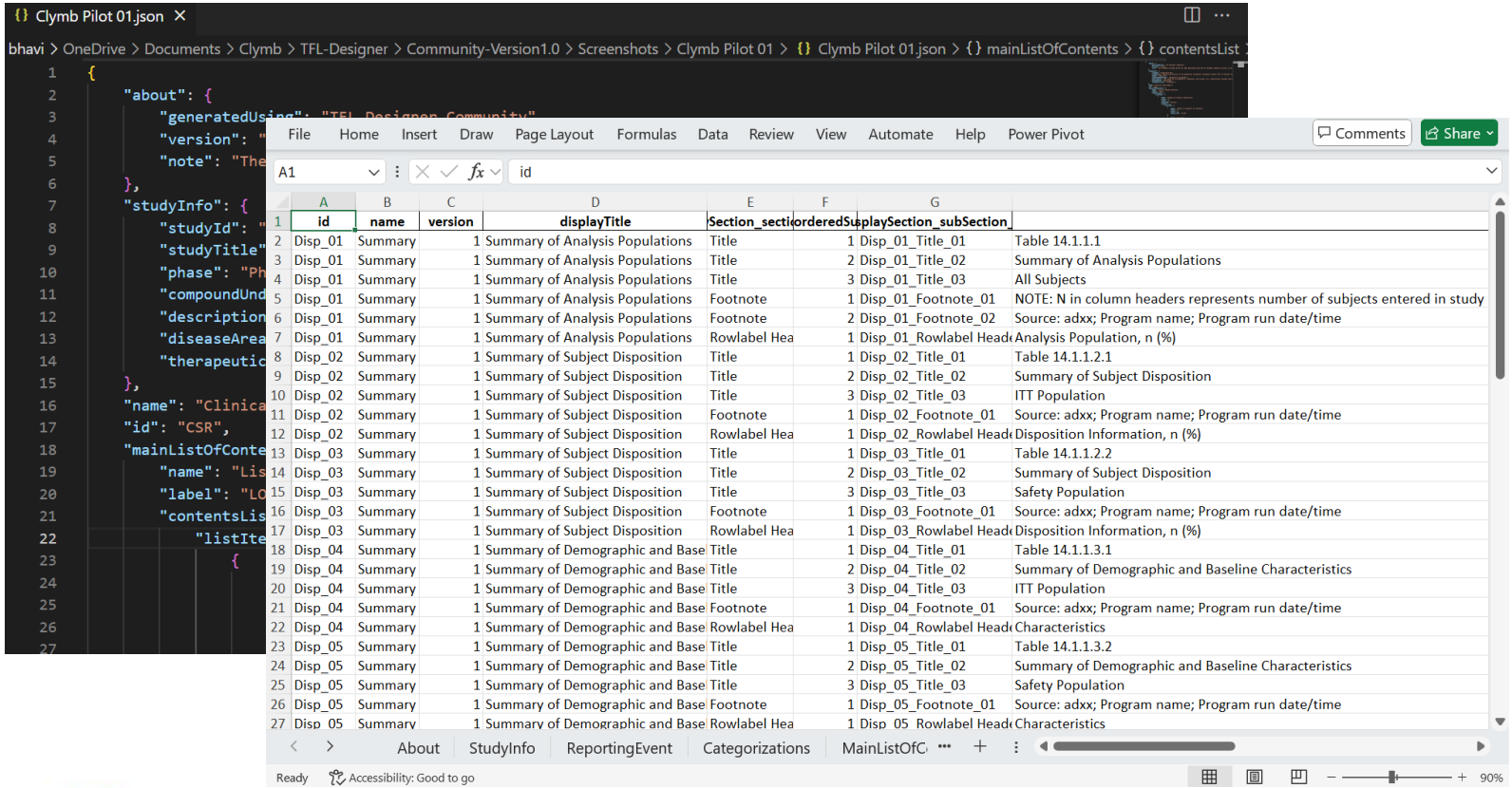
Export TFL Shells and ARS Metadata



Export TFL Shells and ARS Metadata



Export TFL Shells and ARS Metadata

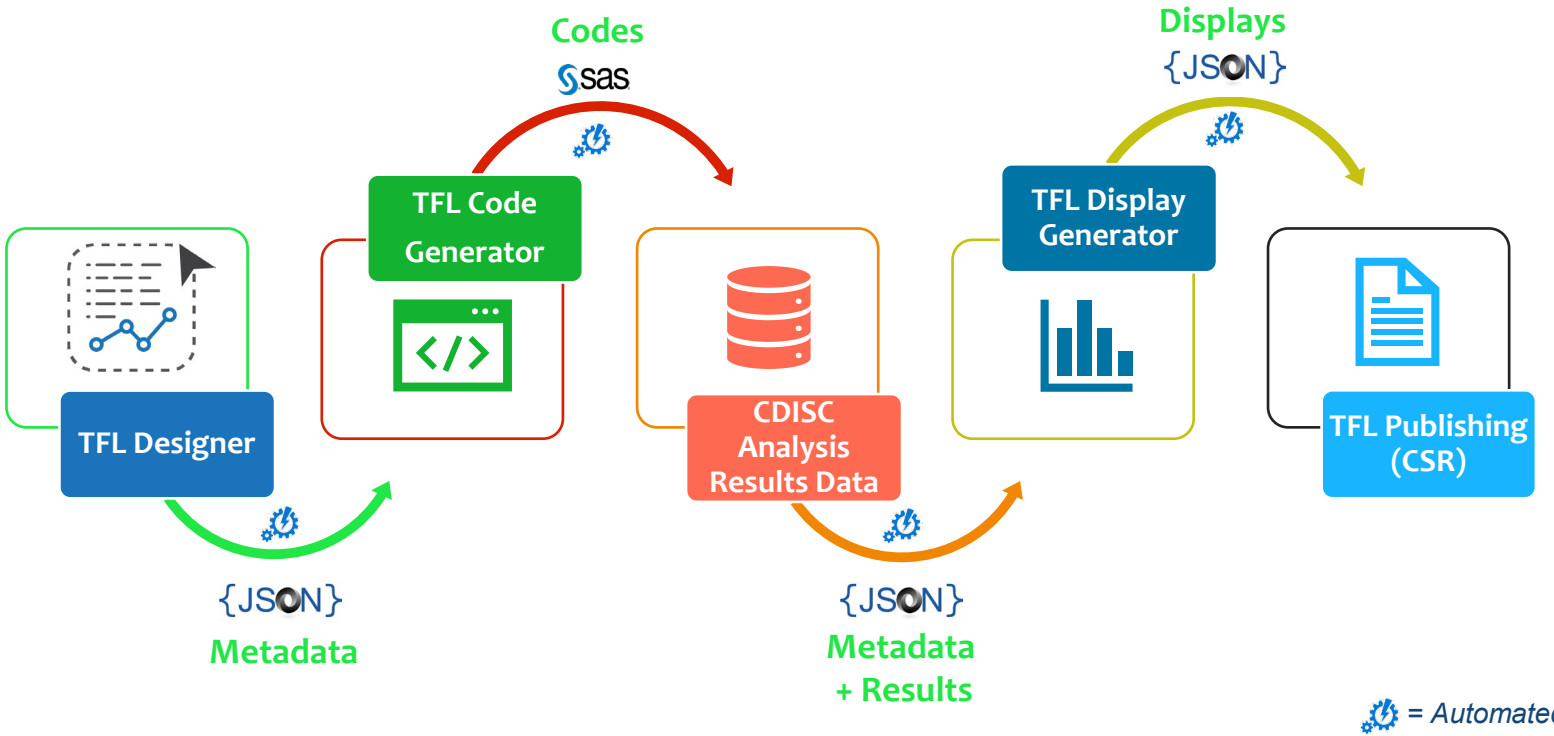


	A	B	C	D	E	F	G	
1	id	name	version	displayTitle	Section_sectio	orderedSu	playSection_subSection_	
2	Disp_01	Summary	1	Summary of Analysis Populations	Title	1	Disp_01_Title_01	Table 14.1.1.1
3	Disp_01	Summary	1	Summary of Analysis Populations	Title	2	Disp_01_Title_02	Summary of Analysis Populations
4	Disp_01	Summary	1	Summary of Analysis Populations	Title	3	Disp_01_Title_03	All Subjects
5	Disp_01	Summary	1	Summary of Analysis Populations	Footnote	1	Disp_01_Footnote_01	NOTE: N in column headers represents number of subjects entered in study
6	Disp_01	Summary	1	Summary of Analysis Populations	Footnote	2	Disp_01_Footnote_02	Source: adxx; Program name; Program run date/time
7	Disp_01	Summary	1	Summary of Analysis Populations	Rowlabel Hea	1	Disp_01_Rowlabel Head	Analysis Population, n (%)
8	Disp_02	Summary	1	Summary of Subject Disposition	Title	1	Disp_02_Title_01	Table 14.1.1.2.1
9	Disp_02	Summary	1	Summary of Subject Disposition	Title	2	Disp_02_Title_02	Summary of Subject Disposition
10	Disp_02	Summary	1	Summary of Subject Disposition	Title	3	Disp_02_Title_03	ITT Population
11	Disp_02	Summary	1	Summary of Subject Disposition	Footnote	1	Disp_02_Footnote_01	Source: adxx; Program name; Program run date/time
12	Disp_02	Summary	1	Summary of Subject Disposition	Rowlabel Hea	1	Disp_02_Rowlabel Head	Disposition Information, n (%)
13	Disp_03	Summary	1	Summary of Subject Disposition	Title	1	Disp_03_Title_01	Table 14.1.1.2.2
14	Disp_03	Summary	1	Summary of Subject Disposition	Title	2	Disp_03_Title_02	Summary of Subject Disposition
15	Disp_03	Summary	1	Summary of Subject Disposition	Title	3	Disp_03_Title_03	Safety Population
16	Disp_03	Summary	1	Summary of Subject Disposition	Footnote	1	Disp_03_Footnote_01	Source: adxx; Program name; Program run date/time
17	Disp_03	Summary	1	Summary of Subject Disposition	Rowlabel Hea	1	Disp_03_Rowlabel Head	Disposition Information, n (%)
18	Disp_04	Summary	1	Summary of Demographic and Base	Title	1	Disp_04_Title_01	Table 14.1.1.3.1
19	Disp_04	Summary	1	Summary of Demographic and Base	Title	2	Disp_04_Title_02	Summary of Demographic and Baseline Characteristics
20	Disp_04	Summary	1	Summary of Demographic and Base	Title	3	Disp_04_Title_03	ITT Population
21	Disp_04	Summary	1	Summary of Demographic and Base	Footnote	1	Disp_04_Footnote_01	Source: adxx; Program name; Program run date/time
22	Disp_04	Summary	1	Summary of Demographic and Base	Rowlabel Hea	1	Disp_04_Rowlabel Head	Characteristics
23	Disp_05	Summary	1	Summary of Demographic and Base	Title	1	Disp_05_Title_01	Table 14.1.1.3.2
24	Disp_05	Summary	1	Summary of Demographic and Base	Title	2	Disp_05_Title_02	Summary of Demographic and Baseline Characteristics
25	Disp_05	Summary	1	Summary of Demographic and Base	Title	3	Disp_05_Title_03	Safety Population
26	Disp_05	Summary	1	Summary of Demographic and Base	Footnote	1	Disp_05_Footnote_01	Source: adxx; Program name; Program run date/time
27	Disp_05	Summary	1	Summary of Demographic and Base	Rowlabel Hea	1	Disp_05_Rowlabel Head	Characteristics

Improvements after TFL Designer

- Reduction in manual formatting
- Create repository for TFL standardization
- Improved process for review and feedback of mock shell
- Automation of TFL metadata
- Improved collaboration with multiple vendors/CROs
- Ability to export to RTF/PDF

Next Steps: Utilizing Analysis Results Metadata to Automate Downstream Processes



Lessons Learned

- Be open to using newer tools that drive automation and efficiency
- Proactively train the team
- Available to answer questions
- Cost can be justified based on real improvements in efficiency, standardization, and automation of Biostatistics and programming processes, when other functions are implementing AI tools with uncertain benefits.

General Recommendations

- Involve stakeholders from the beginning to ensure buy-in and collaboration.
- Regularly update the TFL repository to incorporate the latest standards and lessons learned.
- Leverage machine learning and automation tools to further reduce manual effort and increase accuracy.

Thank You!

Bhavin Busa
Clymb Clinical
bhavin@clymbclinical.com

Salil Parab
Xencor, Inc
sparab@xencor.com