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Hands-on Training: eTFL Portal & TFL Designer Community

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ABSTRACT

With the introduction of CDISC Analysis Results Standards (ARS) and Analysis Results Data (ARD), the industry is moving toward greater standardization and automation in Tables, Figures, and Listings (TFLs). This hands-on training session will introduce participants to the eTFL Portal, a CDISC-hosted repository launched in October 2024 that provides examples and guidance for implementing ARS, and the Community version of TFL Designer, which was used to generate machine-readable mock-up shells and ARS metadata for eTFL artifacts.

The eTFL Portal serves as a reference hub, offering standardized TFL templates, ARS metadata artifacts, and implementation examples to help organizations operationalize CDISC standards. Attendees will explore how to leverage these resources to align their workflows with ARS and ARD.

The TFL Designer Community portion of the training will focus on using templates from the eTFL Portal to generate study-specific artifacts, including machine-readable TFL mock-up shells and ARS metadata. Participants will gain hands-on experience applying these artifacts to automate TFL development.

At the end of this session, attendees will have practical insights into using the eTFL Portal as a reference for ARS and ARD adoption and the Community version of TFL Designer as a tool for generating study artifacts, streamlining TFL standardization and automation.

INTRODUCTION

In April 2024, CDISC published the Analysis Results Standard (ARS) to support automation, consistency, traceability, and reuse of results data. In order to promote the adoption and implementation of ARS, CDISC is developing an eTFL portal that will reside within the CDISC Knowledge Base on the CDISC website. The eTFL portal will be comprised of packages containing informative examples showing how to implement ARS for a specific analysis concept. Each package will contain a definition of an analysis concept and examples of display shell representation, ADaM dataset and metadata, analysis results metadata, and an analysis results dataset. This hands-on-training will provide an overview of the eTFL portal, associated assets, and future development.

Analysis results play a crucial role in the drug development process, providing essential information for regulatory submission and decision-making. However, the current state of analysis results reporting is suboptimal, with limited standardization, lack of automation, and poor traceability. Currently, analysis results (tables, figures, and listings) are often presented in static, PDF-based reports that are difficult to navigate and vary between sponsors. Moreover, these reports are expensive to generate and offer limited reusability. To address these issues, the CDISC Analysis Results Standard (ARS) Model [1] and accompanying user guide [2] have been developed to support automation, consistency, traceability, and reuse of results data.

Analysis Results Standard

The goal for the future state of analysis results is that they are machine-readable, easily navigable, and highly reusable [3]. The aim in creating the ARS was to provide a logical model that fully described analysis results and associated metadata to support:

- automated generation of machine-readable results data;
- improved navigation and reusability of analysis and results data;
- storage, access, processing, and reproducibility of results data; and
- traceability to the study protocol, statistical analysis plan (SAP), and to the input ADaM dataset.

The ARS Model has several possible implementations, including leveraging analysis results metadata to aid in automation as well as representing analysis results as data in a dataset structure. The creation of an ARS technical specification could be used to support automation, traceability, and the creation of data displays. An analysis results dataset could support reuse and reproducibility of results data. Figure 1 is an example of how the ARS Model could be used in a modernized workflow that shifts the focus from retrospective reporting to prospective planning.

First, an end user could use the ARS Model to guide the generation of a technical specification prior to generating a display, rather than after the display has been created. This approach allows for better planning and standardization of the analysis process, resulting in more consistent and traceable reporting. The technical specification could include metadata about the statistical methods, data sources, and displays to be generated. This technical specification could then be used to generate an analysis results dataset containing the results data needed to generate the display. The analysis results dataset could be designed to support reuse and reproducibility of the results data, enabling more efficient and effective analysis reporting.

Finally, the machine-readable analysis results dataset serves as the "single source of truth" capturing the analysis results metadata and results data in a standardized format. This dataset can then be used to generate displays for multiple reporting purposes, such as traditional analysis reporting for the clinical study report (CSR), in-text tables for the CSR, safety reporting, meta-analyses, dynamic applications, ClinicalTrials.gov, publications, and presentations. This streamlined approach ensures consistency and accuracy in the generation of displays across various deliverables, making it more efficient and reliable for reporting and communication of analysis results.

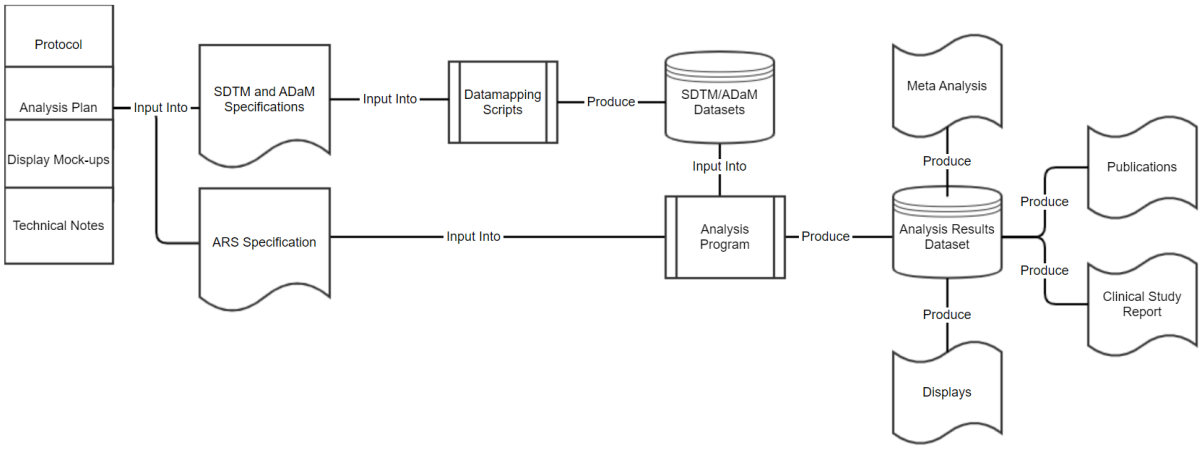


Figure 1: Example of Potential Future Workflow

Overall, this new workflow allows end users to generate analysis results metadata prospectively, with greater standardization, consistency, and traceability of analysis results reporting, which in turn enables better decision making and regulatory submissions. Shifting the focus from retrospective reporting to prospective planning helps to address many of the current limitations of analysis results reporting and supports the development of more efficient and effective analysis standards.

In our vision for the future state, we anticipate the availability of open-source or community tools in the industry, such as TFL Designer Community [4] and R package: {siera} [5]. These tools will empower users to create machine-readable analysis metadata, which can automate the generation of analysis results data and displays. We also hope that such a tool can seamlessly integrate with existing analysis programs and report creation tools, enabling an end-to-end automation of the analysis and reporting process.

CDISC 360: The Art of the Possible

One of the CDISC's transformative initiatives is CDISC 360, a project that was launched with the vision of enhancing clinical data standards and facilitating greater automation in data analysis, submission, and

reporting. The CDISC 360 white paper [6], published in 2021, outlines a future where clinical trial data can be seamlessly automated, analyzed, and displayed through an integrated metadata-driven process. This vision seeks to transform the traditionally manual and labor-intensive generation of TFLs into an automated system where analysis results metadata and datasets are pulled from a centralized library.

The "art of the possible" envisioned in the CDISC 360 project aimed to enable industry users to select a study endpoint and the desired analysis from the CDISC library [7]. After making a selection, users could instantly download the analysis display shell, relevant analysis results metadata, sample analysis datasets, and associated analysis dataset define files [Figure 2]. These artifacts would then serve as standardized templates that could be incorporated into a study, allowing users to generate the necessary analysis results and outputs efficiently.

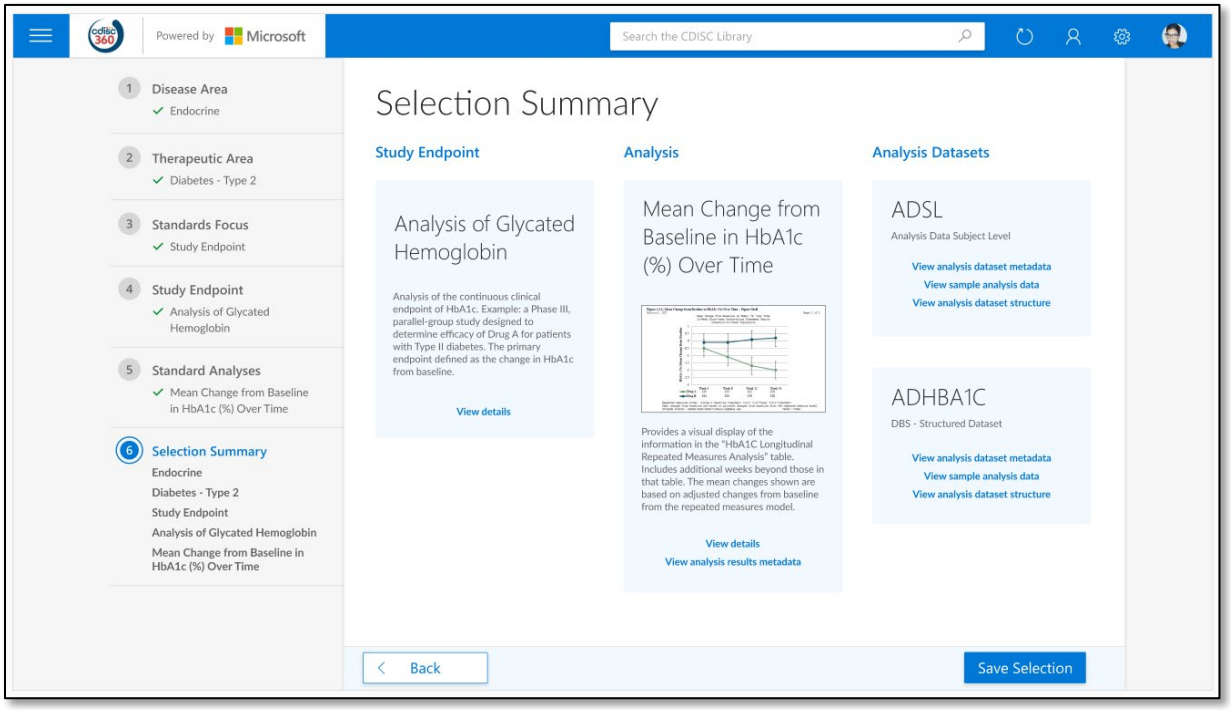


Figure 2: The "Art of the Possible" user interface envisioned during CDISC 360

THE eTFL PORTAL: NEXT STEP AFTER ARS

To support the adoption of ARS and promote industry-wide implementation, in alignment with the CDISC 360 vision, CDISC is collaborating with Clymb Clinical to develop the eTFL portal [8]. This portal, housed within the CDISC Knowledge Base, will serve as a centralized resource where users can access example-driven, informative packages that demonstrate how to implement ARS for various analysis concepts.

The eTFL portal is the natural extension of the CDISC ARS standards and represents the next phase in the evolution of TFL automation. Its purpose is to simplify the complexities of ARS by offering an easy-to-use, standardized library of TFLs, complete with the necessary metadata and example ADaM datasets. This portal will help users navigate through the intricacies of ARS implementation while promoting consistency and traceability, which are critical for regulatory submissions.

Components of the eTFL Portal

The eTFL Portal is designed to support the implementation of ARS through a structured, example-driven approach [Figures 3, 4, 5, and 6]. The key components of the portal include:

- Overview of Analysis Concepts: Each package will start with a clear definition of an analysis concept (e.g., a safety analysis).
- Display Shells: Example display shells will demonstrate how analysis concepts are visually represented in tables, figures, or listings.
- ADaM Datasets and Metadata: For each analysis concept, example ADaM datasets and their associated metadata will be provided, illustrating how analysis-ready data can be structured.
- Analysis Results Metadata: Detailed metadata will be available, specifying how analysis results were derived, ensuring transparency and traceability in the analysis process.
- Analysis Results Datasets: Example datasets containing the final analysis results, showing how these outputs should be structured for submission.

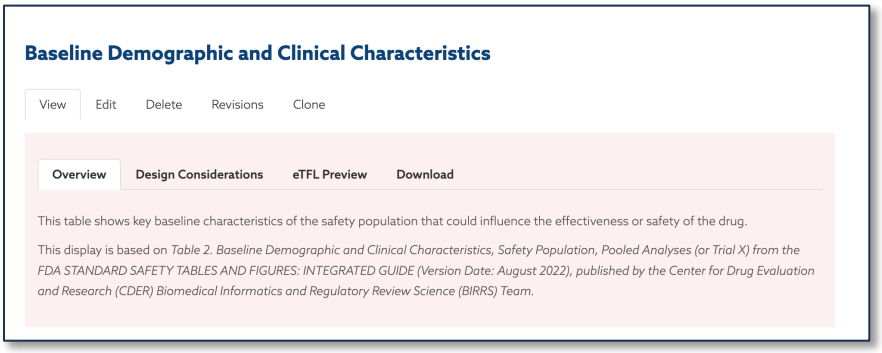


Figure 3: Overview section of the Baseline Demographic and Clinical Characteristics package on eTFL Portal

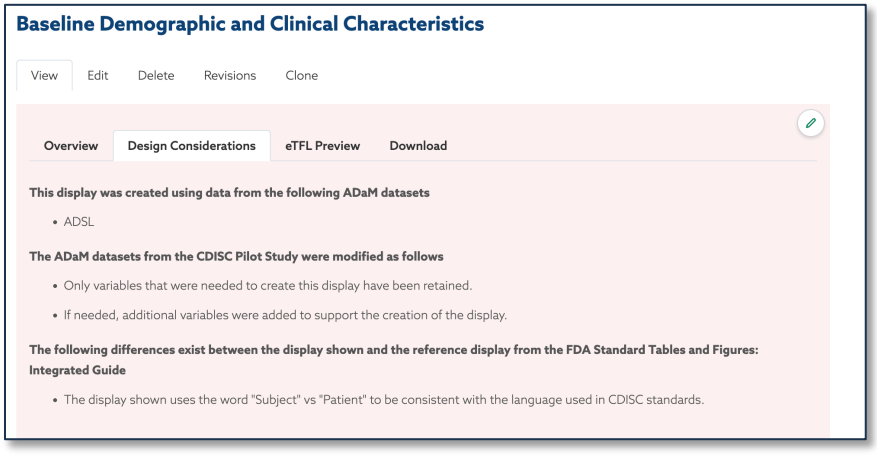
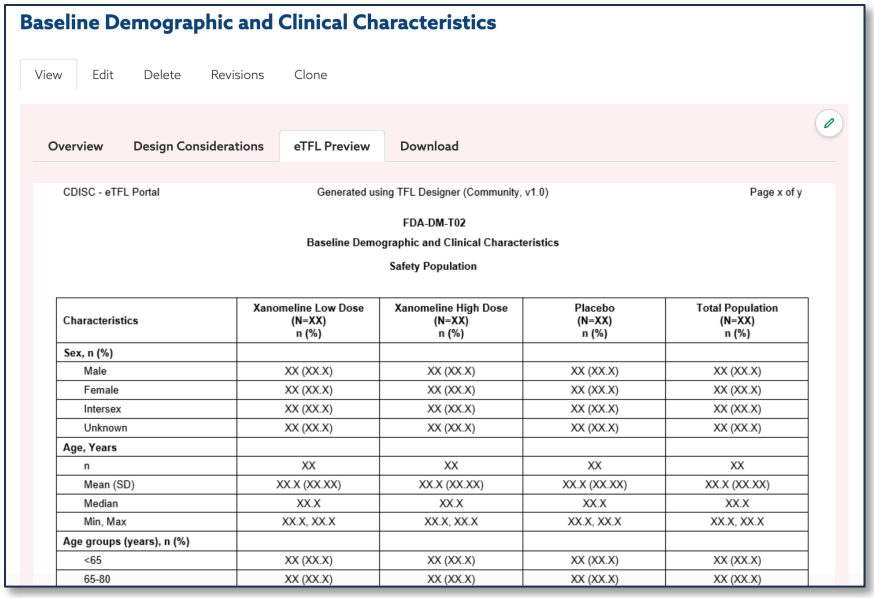


Figure 4: Design Considerations section of the Baseline Demographic and Clinical Characteristics package on eTFL Portal



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)

Figure 5: eTFL Preview section of the Baseline Demographic and Clinical Characteristics package on eTFL Portal

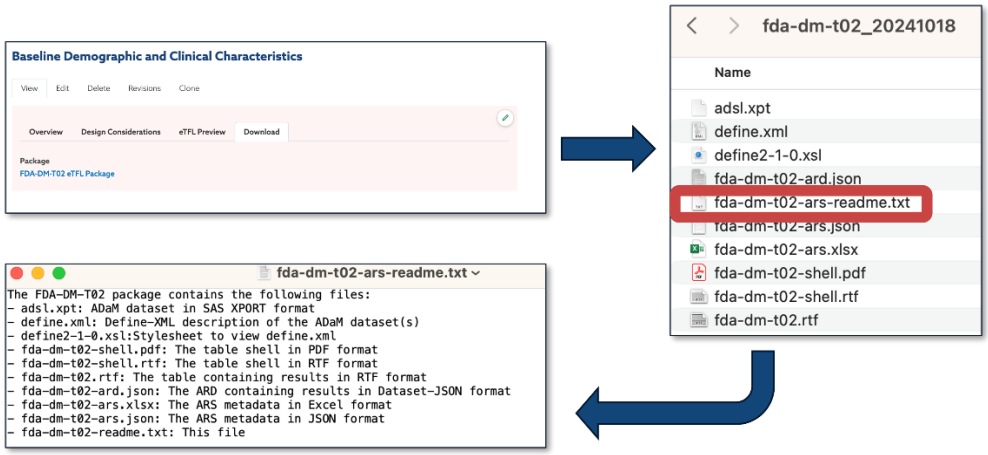


Figure 6: Download section of the Baseline Demographic and Clinical Characteristics package on eTFL Portal

These packages are intended as informative examples and are not meant to imply a preferred layout or analysis plan. The first set of packages was developed based on safety analysis displays, using content from the ARS v1.0 User Guide [2] and the FDA Standard Safety Tables and Figures Integrated Guide [9].

The eTFL Portal currently holds 12 safety examples, which include:

1. Baseline Demographic and Clinical Characteristics
2. Subject Disposition
3. Duration of Treatment Exposure
4. Overview of Adverse Events
5. Subjects With Adverse Events by System Organ Class and Preferred Term

6. Subjects With Adverse Events Leading to Treatment Discontinuation by System Organ Class and Preferred Term
7. Subjects With Serious Adverse Events by System Organ Class and Preferred Term
8. Deaths
9. Subjects With Common Adverse Events Occurring at ≥X% Frequency
10. Summary of Observed and Change from Baseline by Scheduled Visits - Chemistry Laboratory Test
11. Summary of Observed and Change from Baseline by Scheduled Visits - Hematology Laboratory Test
12. Summary of Observed and Change from Baseline by Scheduled Visits - Vital Signs

Guiding Principles for eTFL Package Development

The initial packages were created with Version 1.0 of the Analysis Data Model Metadata Submission Guidelines (ADaM-MSG) [10] as the reference implementation. ADaM datasets were adapted from the CDISC Pilot Study [11] to meet the specific requirements of each display and analysis concept. This approach ensures that the packages align with regulatory expectations while providing flexibility for broad use across different studies.

CDISC has partnered with Clymb Clinical to bring the first ARS-compliant packages within the eTFL Portal. The CDISC eTFL Portal Team utilizes the Community version of the TFL Designer [4] to generate system-agnostic ARS metadata, ensuring that the portal can integrate seamlessly with various systems and platforms.

By offering these ready-to-use examples, the eTFL Portal significantly simplifies the implementation of the ARS model and accelerates the industry's shift toward automated, metadata-driven TFL generation. These examples are designed to help users implement ARS for safety analyses more effectively.

Key Benefits of the eTFL Portal

The development of the eTFL portal offers numerous benefits to stakeholders in the clinical trial industry:

- Simplifying ARS Implementation: The ARS model and its documentation are inherently complex, and the eTFL portal will simplify this complexity by providing easily accessible, example-driven content that focuses on practical implementation.
- Standardized TFL Library: The portal will include a standardized library of TFLs that can be reused across studies, promoting consistency and traceability.
- Integration with Metadata: The eTFL portal supports integration with ADaM and Analysis Results Metadata, facilitating the automation of TFL generation. Future updates may include integration with other CDISC standards, such as SDTM and CDASH, making the portal even more comprehensive.
- Regulatory Alignment: The eTFL portal aligns with regulatory expectations, such as the FDA's Study Data Technical Conformance Guide (STF-IG) and is built following best practices defined by organizations like PHUSE. This ensures that outputs created through the portal meet the standards required for regulatory submissions.
- Support for Therapeutic Areas: While the initial focus is on safety analyses, future iterations of the portal will include efficacy and therapeutic area-specific templates, expanding its scope to cover a broader range of clinical trial data.
- Automation and Efficiency: By providing predefined analysis concepts, display shells, and metadata, the eTFL portal significantly reduces the time and effort required to generate TFLs, improving efficiency and lowering costs for sponsors and CROs.

- Collaboration and Knowledge Sharing: The eTFL portal will facilitate collaboration among industry stakeholders by providing a common platform for sharing standardized analysis templates and methodologies.

TFL DESIGNER (COMMUNITY)

To support the broader adoption of CDISC ARS and promote community-driven innovation, Clymb Clinical has launched the TFL Designer Community - an open-access, web-based tool designed to enable metadata-driven TFL development. The community version complements the eTFL Portal by offering users a hands-on environment to create, edit, and manage machine-readable TFL mock-up shells using ARS-compliant metadata.

TFL Designer Community is freely available at https://tfldesigner.org and serves as a practical entry point for organizations and individuals seeking to explore ARS implementation. Users can start with standardized templates published in the eTFL Portal and customize them to generate study-specific shells and metadata without needing proprietary software or coding expertise.

This hands-on training on TFL Designer will help attendees gain a better understanding of using the artifacts published on the eTFL Portal and assist them in operationalizing the CDISC ARS/ARD standards.

CONCLUSION

As the industry moves toward greater standardization and automation in clinical reporting, the CDISC eTFL Portal and TFL Designer Community offer practical solutions to support the adoption of the Analysis Results Standard (ARS) and Analysis Results Data (ARD). The eTFL Portal provides example-driven, ARS-compliant packages that simplify the implementation of analysis metadata and promote reuse and traceability. In parallel, the TFL Designer Community empowers users to generate study-specific TFL shells and metadata in a machine-readable format.

This hands-on training equips attendees with the knowledge and tools needed to operationalize ARS and ARD standards in real-world settings - bridging the gap between CDISC guidance and implementation.

REFERENCES

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10. CDISC ADaM Metadata Submission Guidelines v1.0: https://www.cdisc.org/standards/foundational/adam/adam-metadata-submission-guidelines-v1-0
11. CDISC Pilot Study package: https://github.com/cdisc-org/sdtm-adam-pilot-project

Additional Resources:

12. CDISC Analysis Results Standard landing page: https://www.cdisc.org/standards/foundational/analysis-results-standards
13. Busa, Bhavin; LeRoy, Bess; 'Pre-launching CDISC Analysis Results Standards' at PHUSE US Connect (Mar 2023) Presentation Link, Video Link
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