# Library Navigator: A Novel Approach to Standard Library Presentation in Clinical Trials Using Define.xml

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# Library Navigator: A Novel Approach to Standard Library Presentation in Clinical Trials Using Define.xml

Presented by Catherine Laugel, PhD, Senior Data Standards Expert,
DMMI, Merck KGaA

# Meet the Speaker

## Catherine Laugel

Title: Senior Data Standards Expert

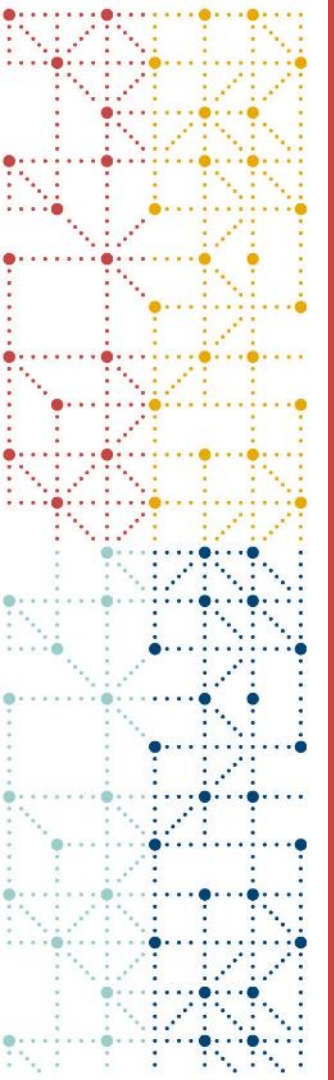
Organization: Merck KGaA

- At Merck: Reference for data collection Standards, involved in study set-up and co-leading a trans functional Governance group for the review and approval of Merck KGaA Standard Library.
- 14+ years' experience in end-to-end data management of clinical trials, including database design, data collection and quality control, in both CRO and pharma companies.
- Education : PhD in Organic Chemistry in Fundamental Research from Strasbourg (France) and 2 years post-doctoral position in Berlin (Germany).
- Hobbies : If time permits between work and my 2 kids, spending remaining energy in training for semi-marathon !

# Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC or Merck KGaA.*

- *The author(s) have no real or apparent conflicts of interest to report.*

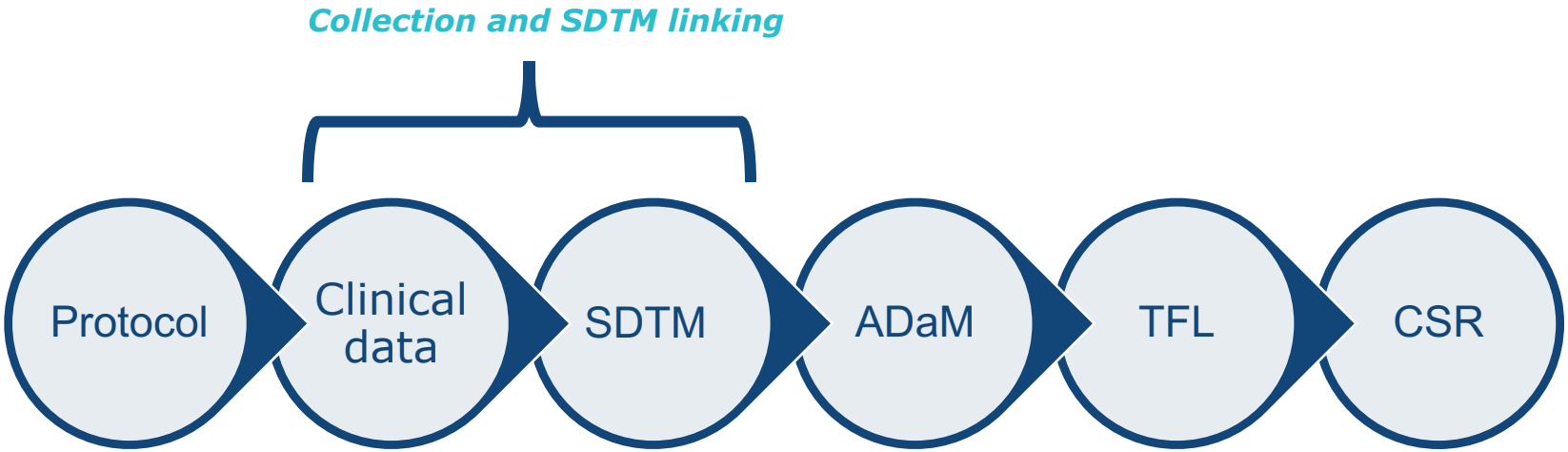


# Agenda

1. Merck KGaA Standard Library Innovative Approach
2. Merck KGaA Standard Library Overview
3. Presentation of the Library Navigator
4. How to implement the Library Navigator?
5. Conclusion

# Merck KGaA Standard Library Innovative Approach

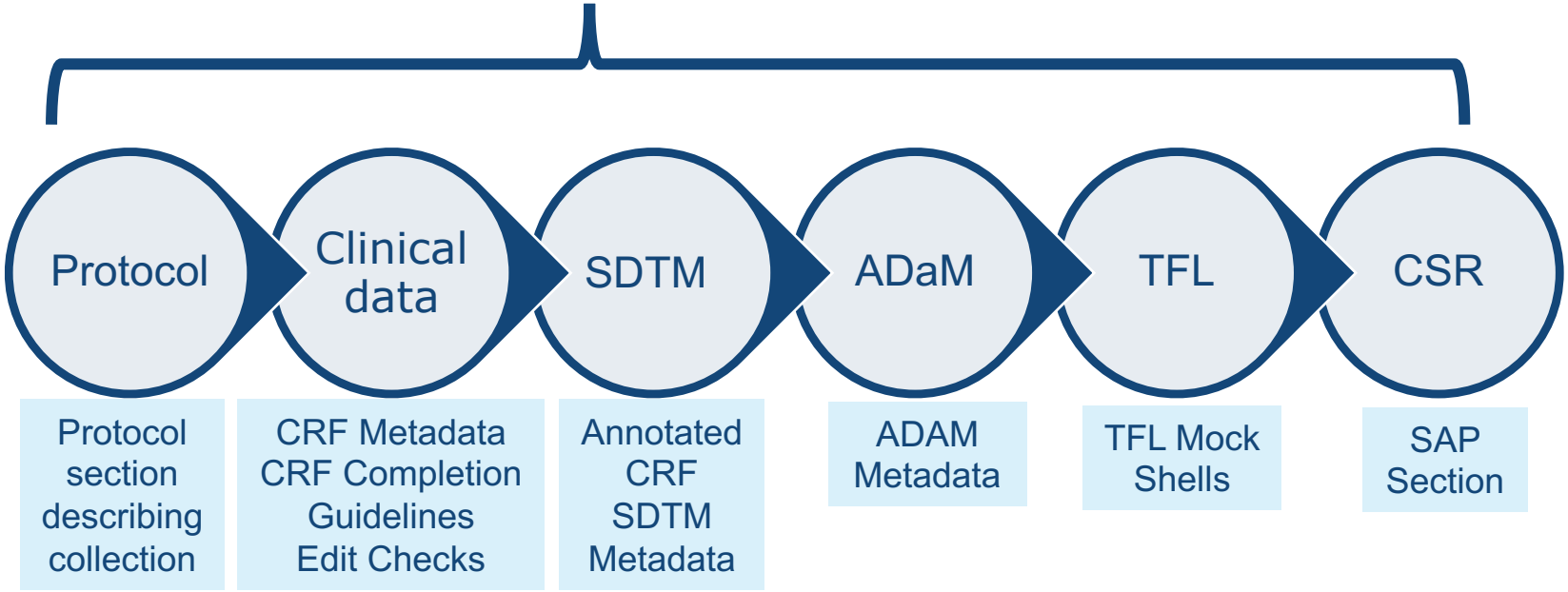
# End-To-End Approach : Connect Elements together




- ✓ Smoother connectivity
- ✓ Less transformation effort
- ✓ Accelerate the setup and conduct activities of clinical trials, ensuring submission-ready data soon after database lock

# Concept of Standard Element

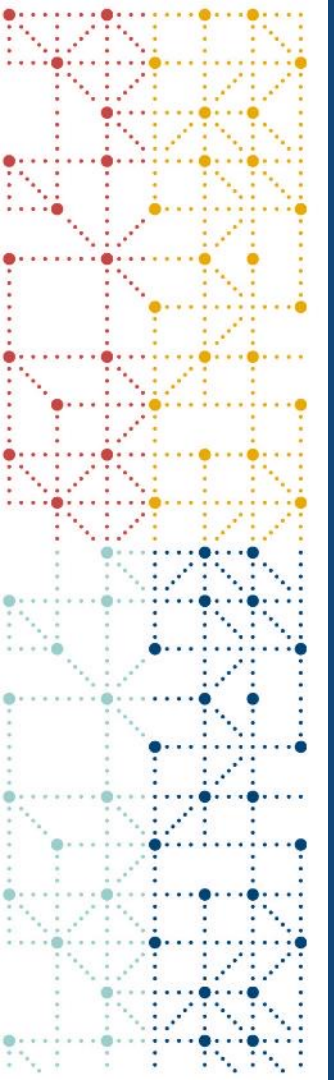
A **Standard Element** provides a **“Topic”** in the clinical trial with all the information and “elements” needed for setup, conduct, and submission.



# Development of the Standard Library

For each “Topic,” we defined a series of “objects” needed for the definition of setup, conduct, and submission of that topic : all accessible in one place with a single click !

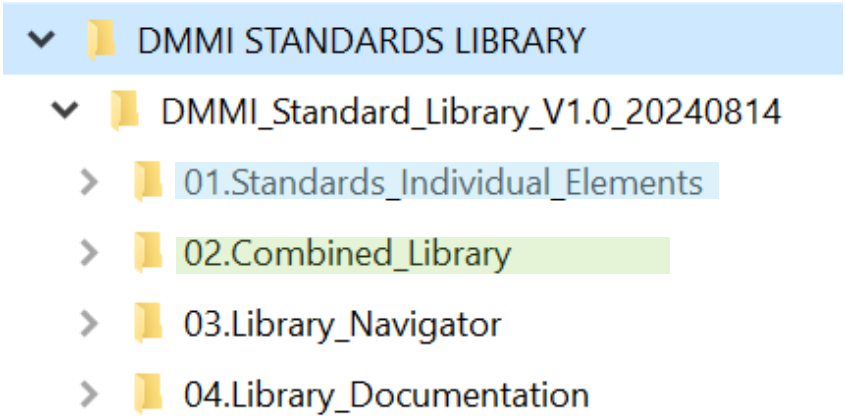
The user will “**pick**” the standard elements needed for their trials from the standard library, which will provide them with the full eDC, SDTM, etc., for their study



# Merck KGaA Standard Library Overview

# Overview of Merck Standard Library

Flexible Access Options : we understand the need for flexibility, which is why we offer access to the library in **two formats**



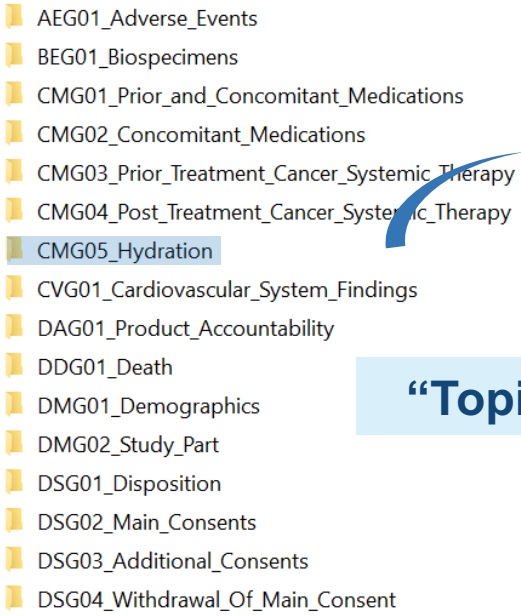

**Individual Standard Elements:** Compiling multiple standard elements to support the eDC setup, SDTM, and submission readiness.

**Standard Combined Library:** This includes, for example, a combined CRF with all the standard CRF forms bookmarked, the full eDC metadata, the full SDTM metadata, etc.

# Individual Standard Elements

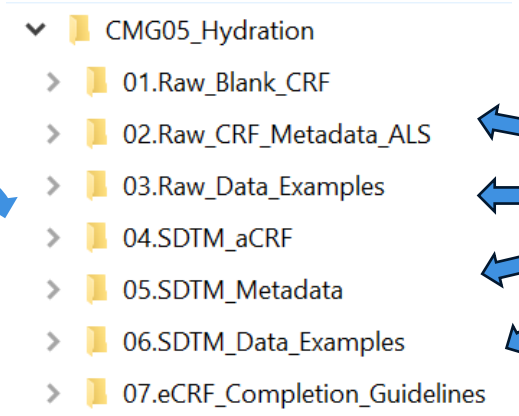
- AEG01_Adverse_Events
- BEG01_Biospecimens
- CMG01_Prior_and_Concomitant_Medications
- CMG02_Concomitant_Medications
- CMG03_Prior_Treatment_Cancer_Systemic_Therapy
- CMG04_Post_Treatment_Cancer_Systemic_Therapy
- CMG05_Hydration
- CVG01_Cardiovascular_System_Findings
- DAG01_Product_Accountability
- DDG01_Death
- DMG01_Demographics
- DMG02_Study_Part
- DSG01_Disposition
- DSG02_Main_Consents
- DSG03_Additional_Consents
- DSG04_Withdrawal_Of_Main_Consent

# From Standard Library Topics to Elements




**1 Folder per Form**

**"Topic"**



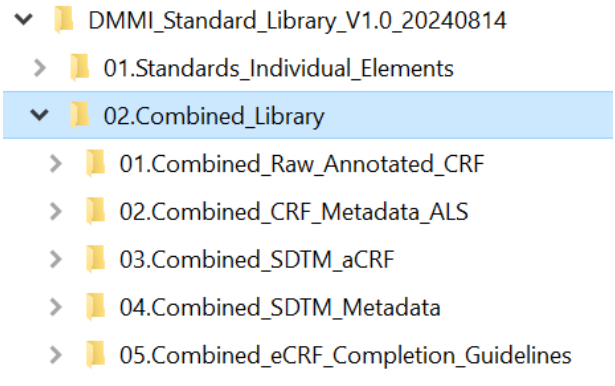

**Several sub-folders per Form**

**"Standard Library Element"**

Browsing through folders and files individually can be cumbersome and not user-friendly. **We began exploring ways to enhance the user experience…**

# Combined Standard Library

All these Standards Individual Elements are also present as **combined version.**




- **Holistic View:** Access a comprehensive, combined view of all objects, including CRF forms, full eDC metadata, and complete SDTM metadata.
- **Enhanced Browsing:** Easily navigate through the combined library to find all relevant information in one place, providing a seamless and efficient user experience.
- **Comprehensive Documentation:** Includes all related documentation, such as CRF completion guidelines and metadata, ensuring you have all the information you need at your fingertips.

# Brainstorming…

Despite having both combined and individual standard elements in our library, users still need to navigate through folders to access each different object.

How could we **enhance** the user experience ?

- ✓ Enable users to visualize the library and access its content effortlessly
- ✓ Allow users to retrieve both structured (excel files) and unstructured objects (PDF, word) with a single click.

=> Introduction of our **Library Navigator**

# Presentation of the Library Navigator

# Repurposing the Define.xml

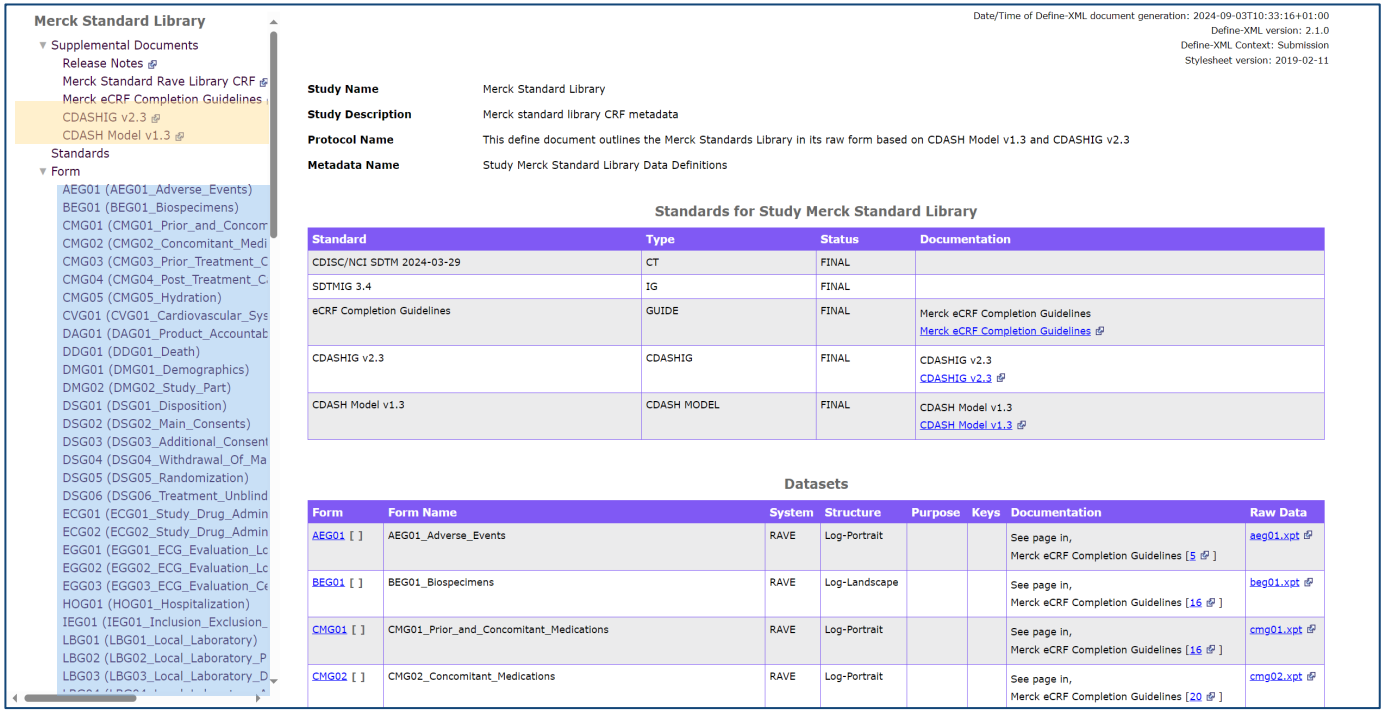

Part of the Clinical Data Interchange Standards Consortium (CDISC) standards, the **define.xml** facilitates data sharing and submission to **regulatory authorities**.

The define.xml file is a **standardized document** used in clinical trials to represent at the study level both structured information like data and metadata for Study SDTM and ADaM and unstructured data like the aCRF, SAP.

However, the Define.xml was not originally designed to represent CRF (raw) data.

**=> Repurposing the Define.xml to effectively represent CRF data**

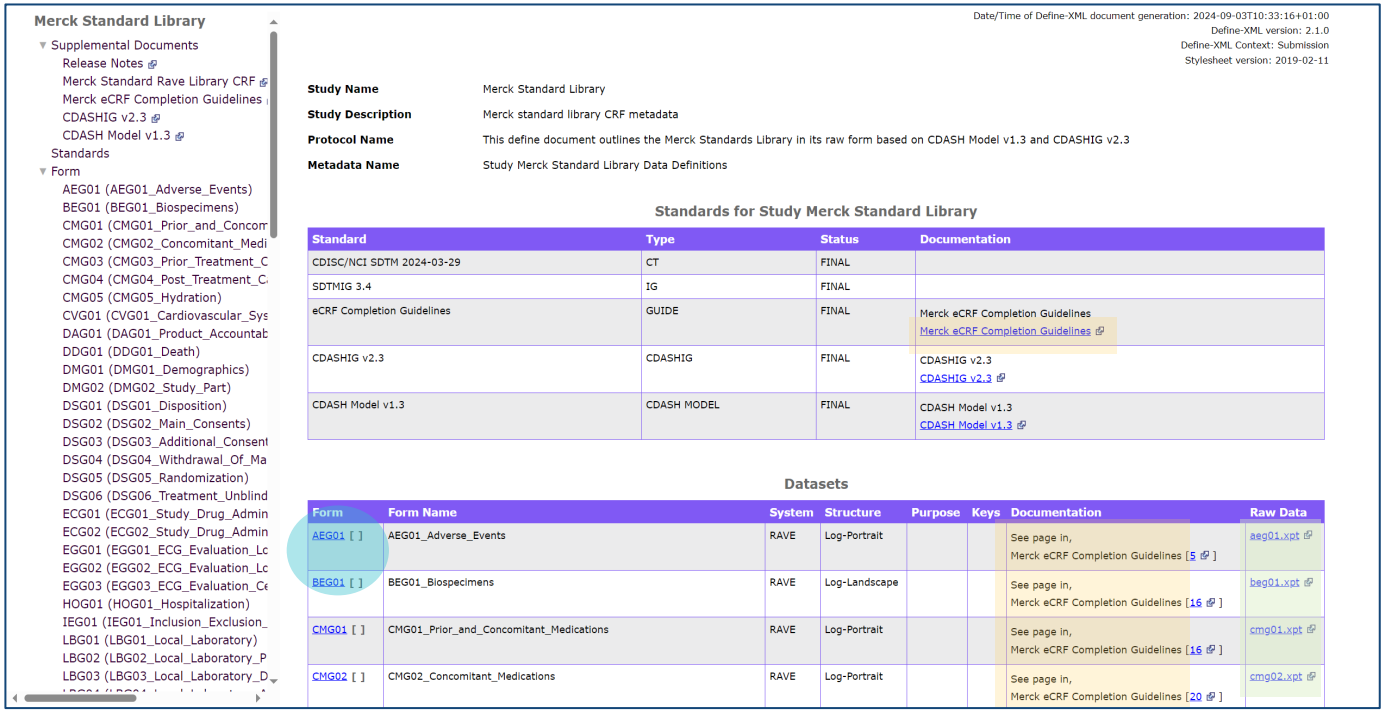
# Navigating through the Library with Define.html - CRF




References to **Standards used to create the library**.

The user can **browse all the forms and documentation available in the library** and click on them for more details.

# Navigating through the Library with Define.html - CRF




Library Navigator presentation for CRF forms, with hyperlinks to:

CRF completion guideline PDF files

Raw data example in XPT files

**When the Form is selected…**

# Navigating through the Library with Define.html - CRF

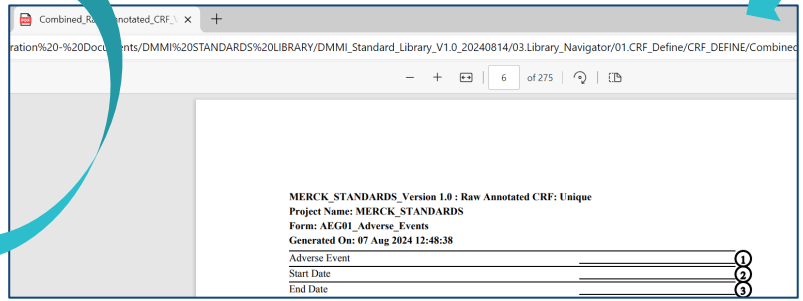
**When the Form is selected…** it will display the list of variables, with type, format and more details :

AEG01 (AEG01_Adverse_Events) - [ ]

Location: aeg01.xpt

| Variable | Label / Description | Type | Length or Display Format | Controlled Terms or ISO Format | Origin / Source / Method / Comment |
|---|---|---|---|---|---|
| AETERM | Adverse Event | text | 200 | | Collected (Source: Investigator)<br>See page in,<br>Merck Standard Rave Library CRF [6 7 8 9 10 11 12 13] |
| AESTDAT | Start Date | date9 | | | Collected (Source: Investigator)<br>See page in,<br>Merck Standard Rave Library CRF [6 7 8 9 10 11 12 13] |
| AEENDAT | End Date | date9 | | | Collected (Source: Investigator)<br>See page in,<br>Merck Standard Rave Library CRF [6 7 8 9 10 11 12 13] |
| AEONGO | Is the adverse event ongoing? | text | 1 | CL_C66742_NY<br>• "Y" = "Yes"<br>• "N" = "No" | Collected (Source: Investigator)<br>See page in,<br>Merck Standard Rave Library CRF [6 7 8 9 10 11 12 13] |
| AEOUT | Outcome | text | 50 | CL_C66768_OUT<br>[6 Terms] | Collected (Source: Investigator)<br>See page in,<br>Merck Standard Rave Library CRF [6 7 8 9 10 11 12 13] |

**Opening of the Rave Raw PDF**

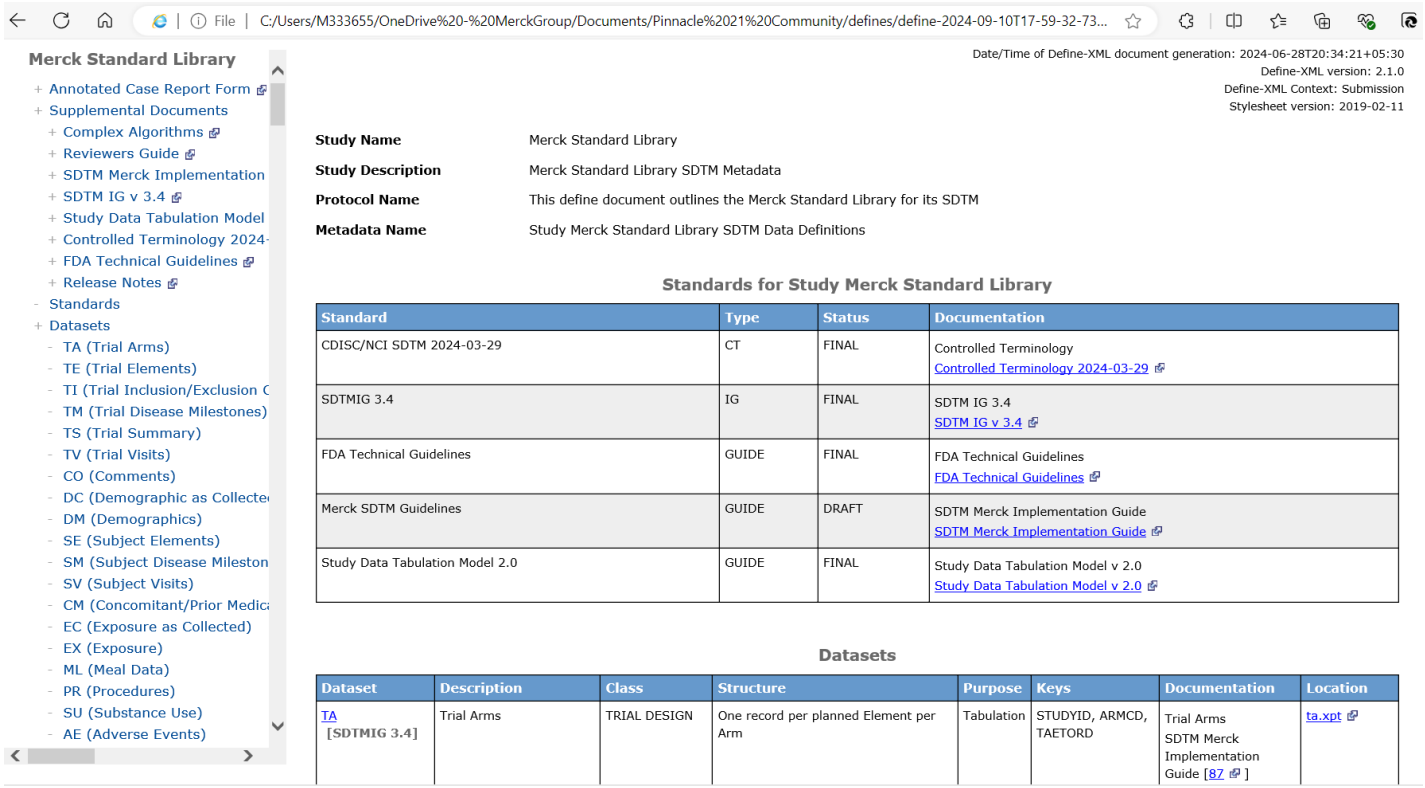



CL_C66768_OUT [*C66768*] [CDISC/NCI SDTM 2024-03-29]

| Permitted Value (Code) | Display Value (Decode) |
|---|---|
| RECOVERED/RESOLVED [*C49498*] | Recovered or Resolved |
| RECOVERED/RESOLVED WITH SEQUELAE [*C49495*] | Recovered or Resolved with Sequelae |
| RECOVERING/RESOLVING [*C49496*] | Recovering or Resolving |
| NOT RECOVERED/NOT RESOLVED [*C49494*] | Not Recovered or Not Resolved |
| UNKNOWN [*C17998*] | Unknown |
| FATAL [*C48275*] | Fatal |

**Display of the codelist details**

# Navigating through the Library with Define.html - SDTM



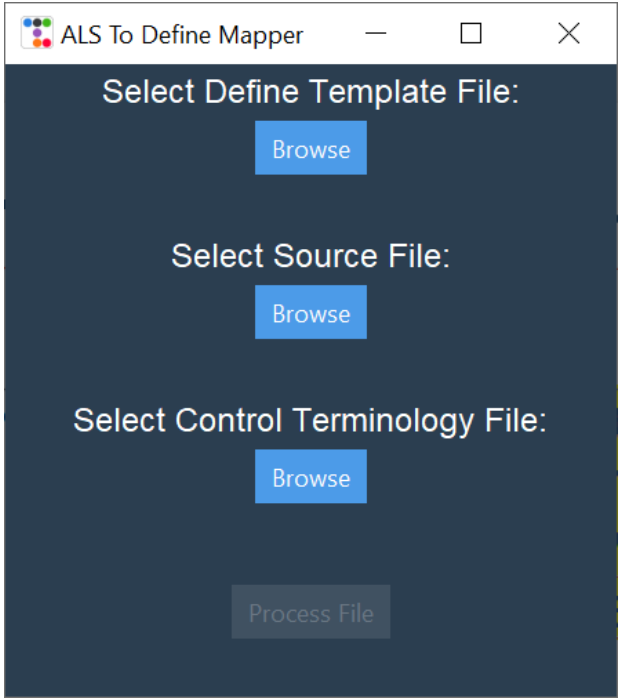

Same principle for SDTM data

# How to implement the Library Navigator?

# Technical implementation – CRF Library Navigator

- Taking the Merck Library Combined ALS Metadata this file is transformed into the define.xml format using an in-house Python developed tool which will convert almost entirely the ALS structure, including Rave centric length, format types into the required format.

- Using the ALS, and CDISC CT to fill in any gaps with NCI codes for Codelists.



# Technical implementation - CRF Library Navigator

| FormOID | FieldOID | Ordinal | DraftFieldNumber | DraftFieldName | DraftFieldActive | VariableOID | DataFormat | DataDictionaryName |
|---|---|---|---|---|---|---|---|---|
| AEG01 | AETERM | 1 | | AETERM | TRUE | AETERM | $200 | |
| AEG01 | AESTDAT | 2 | | AESTDAT | TRUE | AESTDAT | dd- MMM yyyy | |
| AEG01 | AEENDAT | 3 | | AEENDAT | TRUE | AEENDAT | dd- MMM yyyy | |
| AEG01 | AEONGO | 4 | | AEONGO | TRUE | AEONGO | $1 | CL_C66742_NY |
| AEG01 | AEOUT | 5 | | AEOUT | TRUE | AEOUT | $50 | CL_C66768_OUT |
| AEG01 | AETOXGR | 6 | | AETOXGR | TRUE | AETOXGR | $16 | CL_SP_AETOXGR |
| AEG01 | AESEV | 7 | | AESEV | TRUE | AESEV | $16 | CL_C66769_AESEV |

| Orde | Dataset | Variable | Label | Data Type | Length | Significant Digits | Forma | Mandator | Assigned Value | Codelist |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | AEG01 | AETERM | Adverse Event | text | 200 | | $200 | No | | |
| 2 | AEG01 | AESTDAT | Start Date | date9 | | | | No | | |
| 3 | AEG01 | AEENDAT | End Date | date9 | | | | No | | |
| 4 | AEG01 | AEONGO | Is the adverse event ongoing? | text | 1 | | $1 | No | | CL_C66742_NY |
| 5 | AEG01 | AEOUT | Outcome | text | 50 | | $50 | No | | CL_C66768_OUT |
| 6 | AEG01 | AETOXGR | Toxicity Grade | text | 16 | | $16 | No | | CL_SP_AETOXGR |
| 7 | AEG01 | AESEV | Severity | text | 16 | | $16 | No | | CL_C66769_AESEV |

As shown here you can see that the tool converts the ALS columns into columns that are suitable to convert to define.xml, including the adjustment of lengths, format and significant digits.

# Technical implementation - CRF Library Navigator

| DataDictionaryName | CodedData | Ordinal | UserDataString | Specify | Standard Team Instructions |
|---|---|---|---|---|---|
| CL_C66768_OUT | RECOVERED/RESOLVED | 1 | Recovered or Resolved | FALSE | |
| CL_C66768_OUT | RECOVERED/RESOLVED WITH SEQUELAE | 2 | Recovered or Resolved with Sequelae | FALSE | |
| CL_C66768_OUT | RECOVERING/RESOLVING | 3 | Recovering or Resolving | FALSE | |
| CL_C66768_OUT | NOT RECOVERED/NOT RESOLVED | 4 | Not Recovered or Not Resolved | FALSE | |
| CL_C66768_OUT | UNKNOWN | 5 | Unknown | FALSE | |
| CL_C66768_OUT | FATAL | 6 | Fatal | FALSE | |

| ID | Name | NCI Codelist Code | Data Type | Terminology | Comme | Orde | Term | NCI Term Code | Decoded Value |
|---|---|---|---|---|---|---|---|---|---|
| CL_C66768_OUT | CL_C66768_OUT | C66768 | text | SDTM 2024-09-27 | | 1 | RECOVERED/RESOLVED | C49498 | Recovered or Resolved |
| CL_C66768_OUT | CL_C66768_OUT | C66768 | text | SDTM 2024-09-27 | | 2 | RECOVERED/RESOLVED WITH SEQUELAE | C49495 | Recovered or Resolved with Sequelae |
| CL_C66768_OUT | CL_C66768_OUT | C66768 | text | SDTM 2024-09-27 | | 3 | RECOVERING/RESOLVING | C49496 | Recovering or Resolving |
| CL_C66768_OUT | CL_C66768_OUT | C66768 | text | SDTM 2024-09-27 | | 4 | NOT RECOVERED/NOT RESOLVED | C49494 | Not Recovered or Not Resolved |
| CL_C66768_OUT | CL_C66768_OUT | C66768 | text | SDTM 2024-09-27 | | 5 | UNKNOWN | C17998 | Unknown |
| CL_C66768_OUT | CL_C66768_OUT | C66768 | text | SDTM 2024-09-27 | | 6 | FATAL | C48275 | Fatal |

As shown here you can see how the Rave DataDictionaryEntries is converted to a usable Codelists sheet with all NCI Codelist Code and NCI Term Codes populated automatically. NCI Term Code is not part of Rave but our process brings this in.

# Technical implementation - CRF Library Navigator

**Datasets**

| Form | Form Name | System | Structure | Purpose | Keys | Documentation | Raw Data |
|---|---|---|---|---|---|---|---|
| AEG01 [ ] | AEG01_Adverse_Events | RAVE | Log-Portrait | | | See page in, Merck eCRF Completion Guidelines [5 ] | aeg01.xpt |
| BEG01 [ ] | BEG01_Biospecimens | RAVE | Log-Landscape | | | See page in, Merck eCRF Completion Guidelines [16 ] | beg01.xpt |

**Library Navigator for CRF**

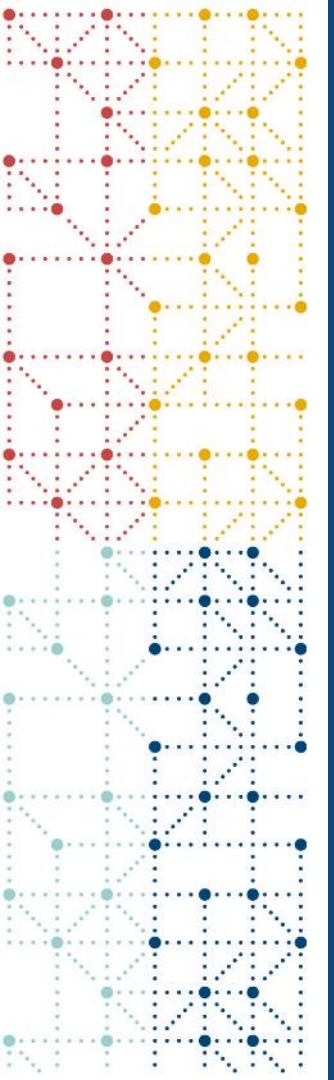
**Datasets**

| Dataset | Description | Class | Structure | Purpose | Keys | Documentation | Location |
|---|---|---|---|---|---|---|---|
| TA [SDTMIG 3.4] | Trial Arms | TRIAL DESIGN | One record per planned Element per Arm | Tabulation | STUDYID, ARMCD, TAETORD | Trial Arms SDTM Merck Implementation Guide [87 ] | ta.xpt |
| TE [SDTMIG 3.4] | Trial Elements | TRIAL DESIGN | One record per planned Element | Tabulation | STUDYID, ETCD | Trial Elements SDTM Merck Implementation Guide [86 ] | te.xpt |

**Library Navigator for SDTM**

For the Merck EDC Navigator we have created a custom stylesheet which provides **different colouring** to our SDTM Navigator.

It also **adjusts columns names** as seen here to suit the EDC, with columns such as, Form, Form Name, System & Raw data.



# Conclusion

# Take Home Message

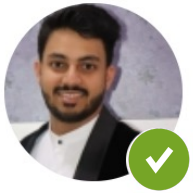

- **Holistic Access:** The repurposed Define.xml provides easy access to a wealth of interconnected data, offering a truly holistic view of every standard library object.

- **Individual Elements:** Users can explore individual elements that encapsulate all relevant information for specific topics, such as adverse events, ensuring you have everything you need in one place.

- **User-Friendly Navigation:** With a single click, you can visualize, browse, and retrieve all essential trial components, dramatically improving efficiency and reducing the time spent navigating through folders and files.

**The Library Navigator not only enhances users experience but also represents a significant advancement in how we manage and access standard library elements.**

# Thank You!



Krishna Shyam Narayan Gupta

Wafaa Jebert

Colm Smyth

# Back-up Slides

# Concept of Standard Element - Example