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Tables, Listings and Figures Metadata and Traceability

SI12

Judith Goud, Nurocor

Agenda

Introduction

TLF Generation Process

Role of Metadata

Traceability

Using an MDR to generate TFLs

Conclusion

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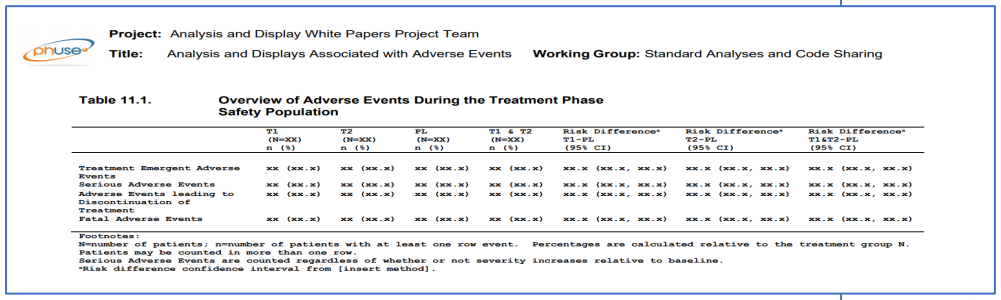
Introduction

- Tables, Listings and Figures (TFLs) are required part of Clinical Study Report

- PhUSE CSS Working Group has developed standard shells

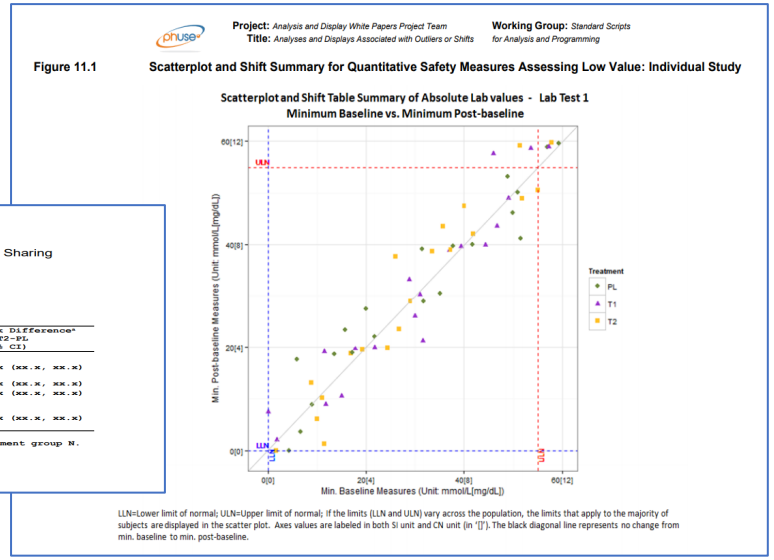


Project: Analysis and Display White Papers Project Team
Title: Analysis and Displays Associated with Adverse Events **Working Group:** Standard Analyses and Code Sharing

Table 11.1. **Overview of Adverse Events During the Treatment Phase**
Safety Population

	T1 (N=XX) n (%)	T2 (N=XX) n (%)	PL (N=XX) n (%)	T1 & T2 (N=XX) n (%)	Risk Difference* T1-PL (95% CI)	Risk Difference* T2-PL (95% CI)	Risk Difference* T1&T2-PL (95% CI)
Treatment Emergent Adverse Events	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
Serious Adverse Events	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
Adverse Events leading to Discontinuation of Treatment	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
Fatal Adverse Events	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)

Footnotes:
N=number of patients; n=number of patients with at least one row event. Percentages are calculated relative to the treatment group N.
Patients may be counted in more than one row.
Serious Adverse Events are counted regardless of whether or not severity increases relative to baseline.
*Risk difference confidence interval from [insert method].



Project: Analysis and Display White Papers Project Team
Title: Analyses and Displays Associated with Outliers or Shifts **Working Group:** Standard Scripts for Analysis and Programming

Figure 11.1 **Scatterplot and Shift Summary for Quantitative Safety Measures Assessing Low Value: Individual Study**

LLN=Lower limit of normal; ULN=Upper limit of normal; if the limits (LLN and ULN) vary across the population, the limits that apply to the majority of subjects are displayed in the scatter plot. Axes values are labeled in both SI unit and CN unit (in '[]'). The black diagonal line represents no change from min. baseline to min. post-baseline.

- Regulatory Authorities require traceability

> *"it is very important that the results presented in the accompanying study report be traceable back to the original data collected"*

FDA Study Data Technical Conformance Guide section 4.1.3.2.1

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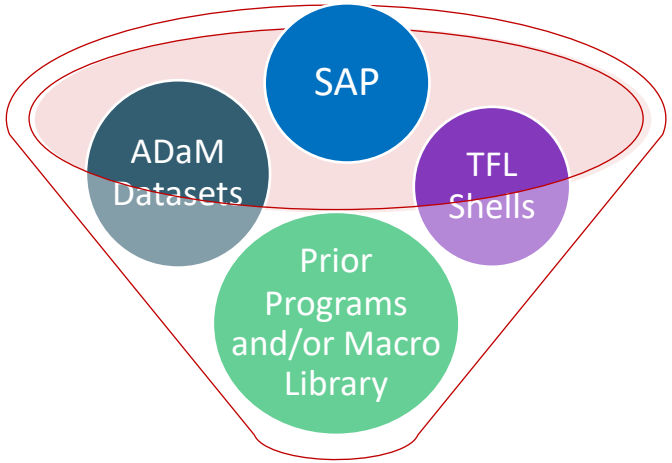
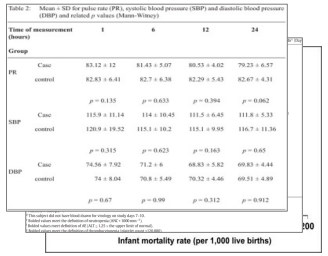
Current TFL Generation Process



Statistical Programmer



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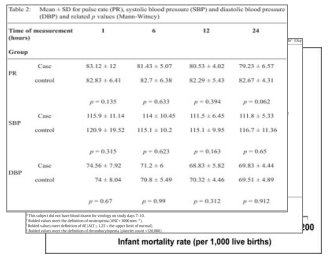
2nd Statistical Programmer



Validated Tables, Listings and Figures

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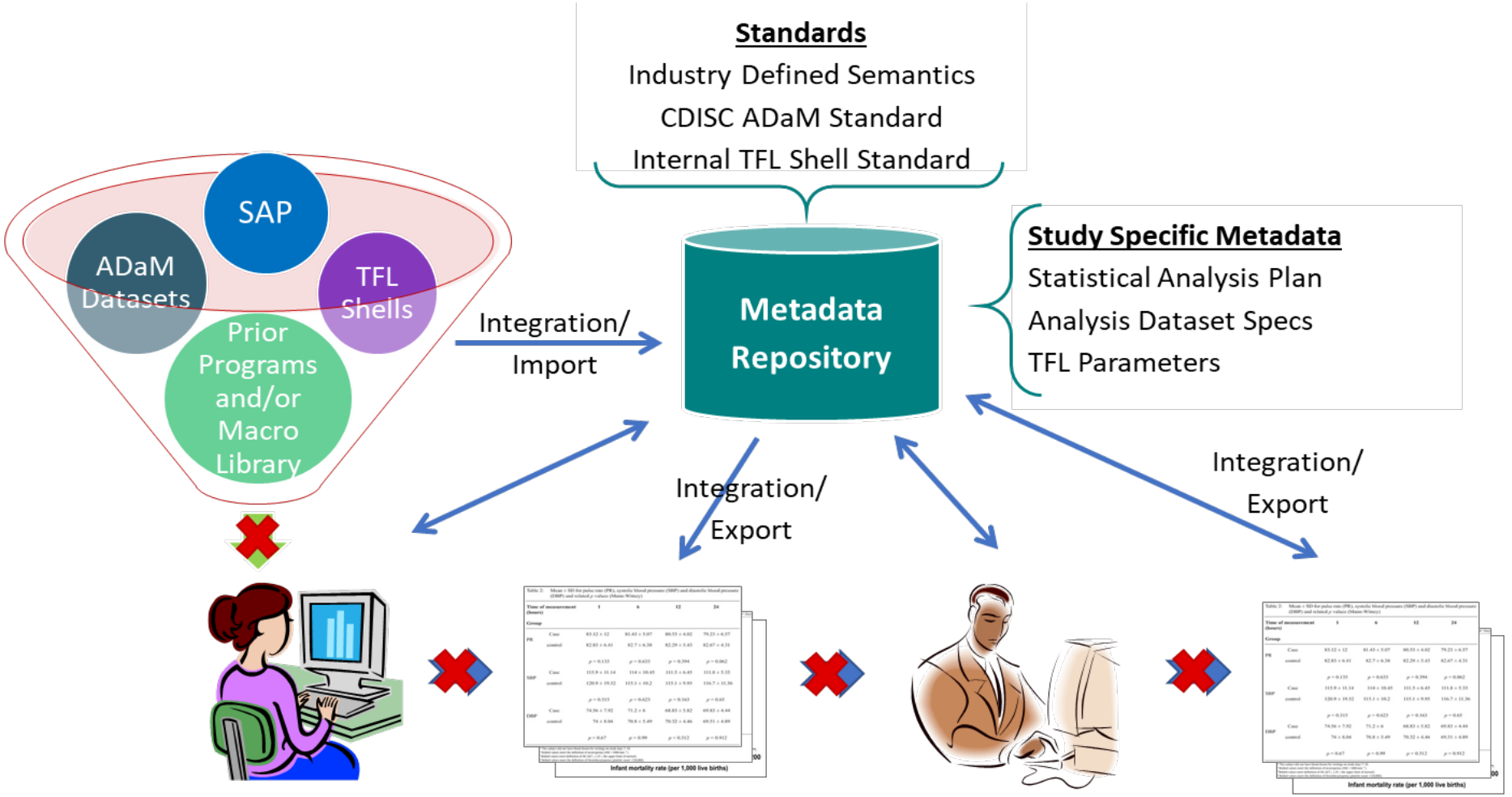
TFL Generation Process using an MDR



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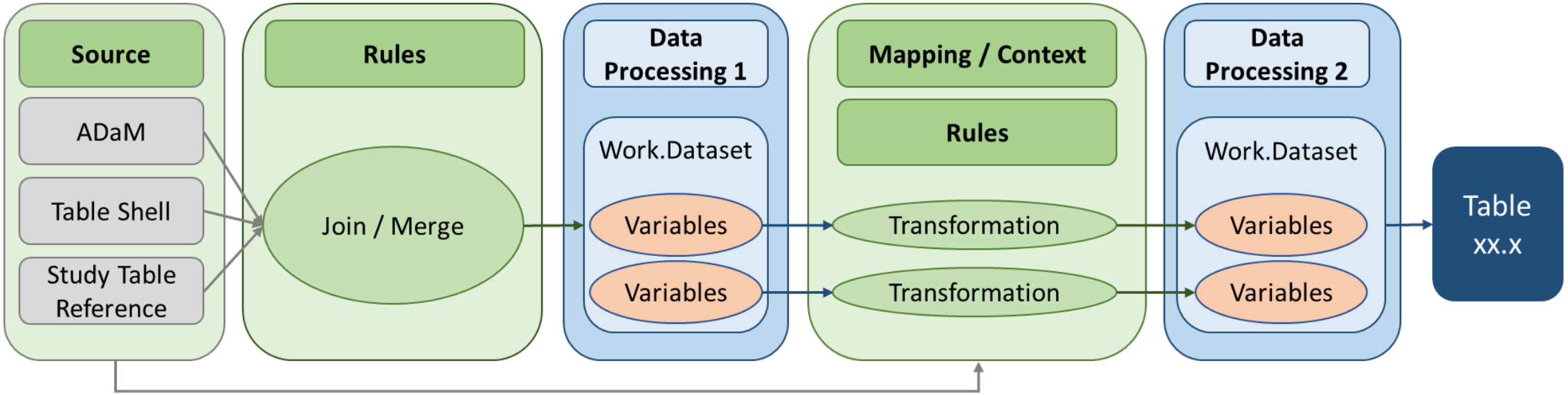
Example Process Flow for Creating a Table



Domain, Variable, Table, Reference

Dataset level Transformation: Instruction & SQL

Variable (row, column, cell) level Transformation: Instruction & SAS (Pseudo) Code

Output: Approved table

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Example : Table Shell using Macro Calls

Company Header(s)

Titles

Description

Row Variable 1

Row Variable 2

Footnote(s)

- Table Name
- Table ID
- Macro Name
- Description
- Titles
- Footnotes
- Input Data
- Filter (i.e. Pop Flag)
- Column Variable
- Row Variable 1
- Row Variable 2…
- Row Variable n

- Table Type
- Data Join(s)
- Output Format (i.e. PDF)
- Orientation
- Project
- Study
- Company Headers
- Column Format
- Column n %
- Page By
- Row Labels 1 - n
- Row Formats 1 - n
- Row Statistics 1 - n
- Categorical Continuous 1 - n

MDR
- ADaM
- TFL metadata
- Study Reference

SAS
- Data
- Macros
- Output

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Example : Table Shell / Metadata Defined

Company Header(s)		
Titles		Column Variable
Description	• Table Name • Table ID	• Column Variable • Column Variable Values
Row Variable	• Table Type • Description • Titles • Footnotes • Input Data	• Column Format • Column n % • Page By • Row Variable 1 • Values, Label, Format, Stats, Categorical or Continuous
Row Variable	• Data Join(s) • Filter (i.e. Pop Flag) • Output Format (i.e. PDF) • Orientation • Project • Study	• Row Var Value 1 x Col 1 Algorithm • Row Var Value 1 x Col 2… Algorithm • Row Var Value 2 x Col 1 Algorithm • Row Var Value 2 x Col 2… Algorithm
Footnote(s)	• Company Headers	• Row Variable n …

MDR
- ADaM
- TFL metadata
- Study Reference

SAS
- Data
- Macros
- Output

Combined
- TFL metadata
- Output

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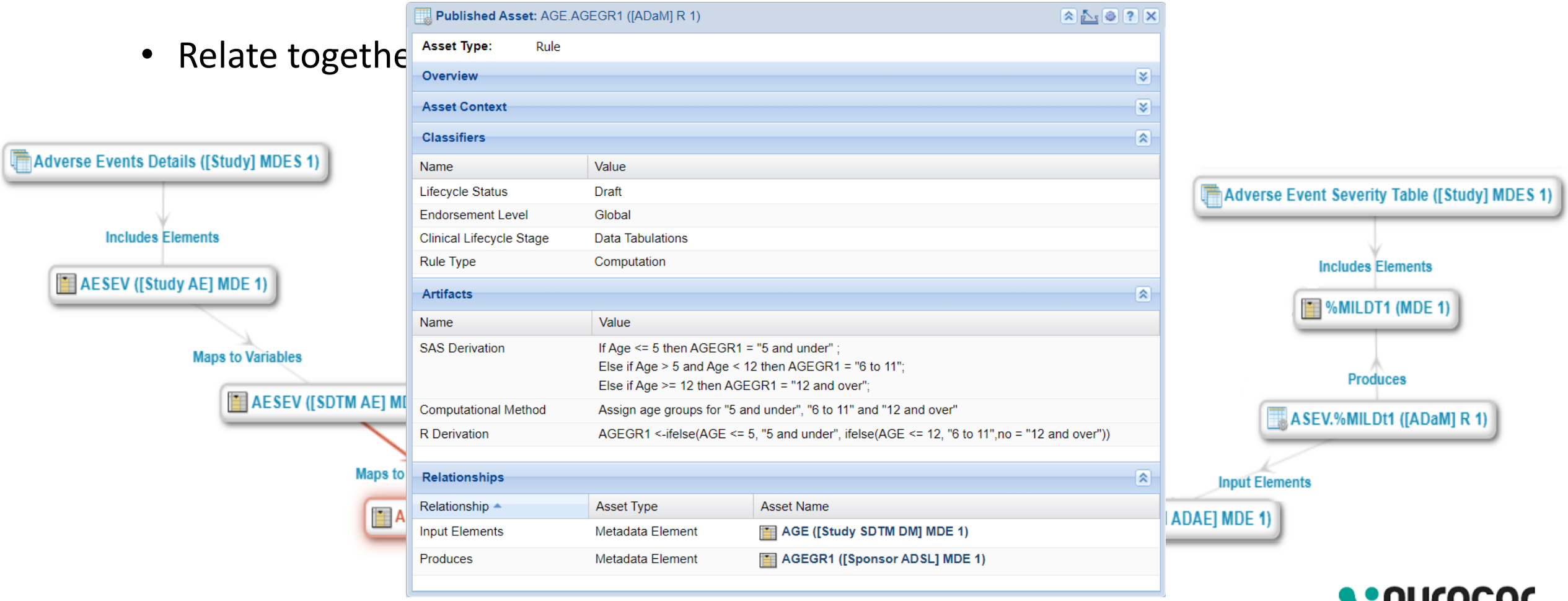
Traceability

- Define study Source and Target metadata and Mapping / Context Rules
- Relate togethe



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Providing Metadata for Consumption

- API Calls
- MDR Exports
- SQL Queries

TARGET DOMAIN	TARGET FIELD	DESCRIPTION	ROLE	TYPE	FIELD TYPE	SOURCE DATA MODEL	SOURCE DOMAIN	SOURCE FIELD	Transformation
AE Severity Table	Unique_Subject_ID	Unique Subject Identifier			Analysis	ADaM	ADAE	USUBJID	Direct
AE Severity Table	Treatment_Group	Treatment Group			Analysis	ADaM	ADAE	ARM	Direct
AE Severity Table	Severity_T1	Total number of Adverse Events for treatment group 1			Analysis	ADaM	ADAE	ASEV, ARM	Count of adverse events within treatment group 1
AE Severity Table	Mild_T1	Total number of Mild Adverse Events for treatment group 1			Analysis	ADaM	ADAE	ASEV, ARM	Count of adverse events within treatment group 1 where severity = Mild
AE Severity Table	Mild%_T1	Percentage of Mild Adverse Events for treatment group 1			Analysis	ADaM	ADAE	Mild_T1, Severity_T1	Count of adverse events within treatment group 1 where severity = Mild divided by total number of adverse events within treatment group 1
AE Severity Table	Moderate_T1	Total number of Moderate Adverse Events for treatment group 1			Analysis	ADaM	ADAE	ASEV, ARM	Count of adverse events within treatment group 1 where severity = Moderate
AE Severity Table	Moderate%_T1	Percentage of Moderate Adverse Events for treatment group 1			Analysis	ADaM	ADAE	Moderate_T1, Severity_T1	Count of adverse events within treatment group 1 where severity = Moderate divided by total number of adverse events within treatment group 1
AE Severity Table	Severe_T1	Total number of Severe Adverse Events for treatment group 1			Analysis	ADaM	ADAE	ASEV, ARM	Count of adverse events within treatment group 1 where severity = Severe
AE Severity Table	Severe%_T1	Percentage of Severe Adverse Events for treatment group 1			Analysis	ADaM	ADAE	Severe_T1, Severity_T1	Count of adverse events within treatment group 1 where severity = Severe divided by total number of adverse events within treatment group 1
AE Severity Table	Missing_T1	Total number of Missing Values for treatment group 1			Analysis	ADaM	ADAE	ASEV, ARM	Count of adverse events within treatment group 1 where severity = Missing

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Conclusion

- TFL metadata includes source dataset standards, TFL shell content, and transformational instructions/code
- An MDR should be able to manage TFL metadata on a global as well as study level
- If the MDR can manage all above-mentioned metadata, this can provide full data traceability and it can be fed to executional software to automate the generation of TFL output

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Any questions?

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