CDISC Strength Through Collaboration

How to Build and Manage CDISC Data and Create Analytical Reports with SAS

SAS® Clinical Standards Toolkit
SAS® Clinical Data Integration
JMP® Clinical

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Engagement Manager
Coordinateur Secteur Service et Industries

SAS – Aix en Provence

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Agenda

- How to Built and Manage your Clinical Data ?
  - SAS® Clinical Standards Toolkit
  - SAS® Clinical Data Integration
- How to Create Analytical Reports from your CDISC data ?
  - JMP® Clinical

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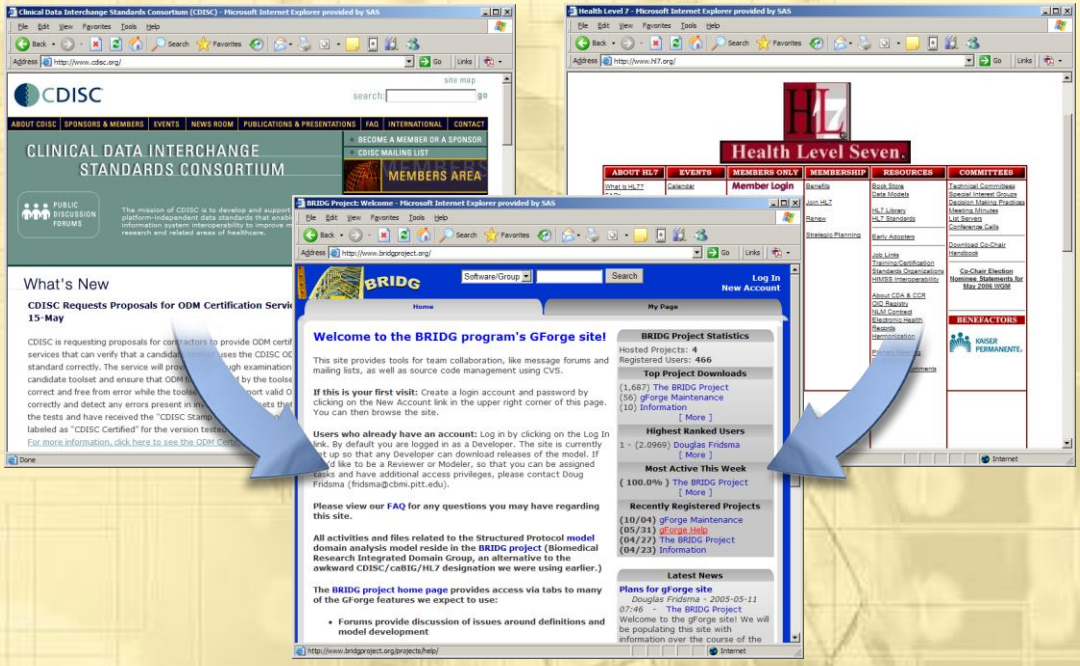
State of Standards

- CDISC
  - ODM
  - SDTM
  - ADaM
  - CRT-DDS (define.xml)
  - Etc.
- Other initiatives
  - Protocol Representation
  - BRIDG
  - Etc.



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Introduction to…

SAS Clinical Standards Toolkit

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SAS Clinical Standards Toolkit

- Set of macros designed to supersede Proc CDISC
- Free to existing SAS customers
- Built into Clinical Data Integration

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SAS Clinical Standards Toolkit Framework

V1.2

- CDISC SDTM Framework
- CDISC CRT-DDS Framework
- CDISC Terminology Framework
- Toolkit Utility Framework

Example Methods

```
%sdtm_validate(…);
%sdtm_report_validationResults();
%sdtm_create_cterms(…);
%sdtm_create_domainType(…);
%sdtm_create_domains(…);

%crtdds_validate(…);
%crtdds_report_validationResults(…);
%crtdds_create_cterms(…);
%crtdds_write(…);
%crtdds_read(…);

%cterms_create_package(…);
```


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SAS Clinical Standards Toolkit Pluggable Modules

V1.2
- CDISC SDTM Framework
- CDISC CRT-DDS Framework
- CDISC Terminology Framework
- Toolkit Utility Framework

SDTM V3.1.1 Module

SDTM V3.1.2 Module

CRT-DDS V1.0 Module

Terminology SDTM-1 Module

Terminology LABTEST Module

Terminology SDTM-2A Module

Terminology SDTM-2B Module

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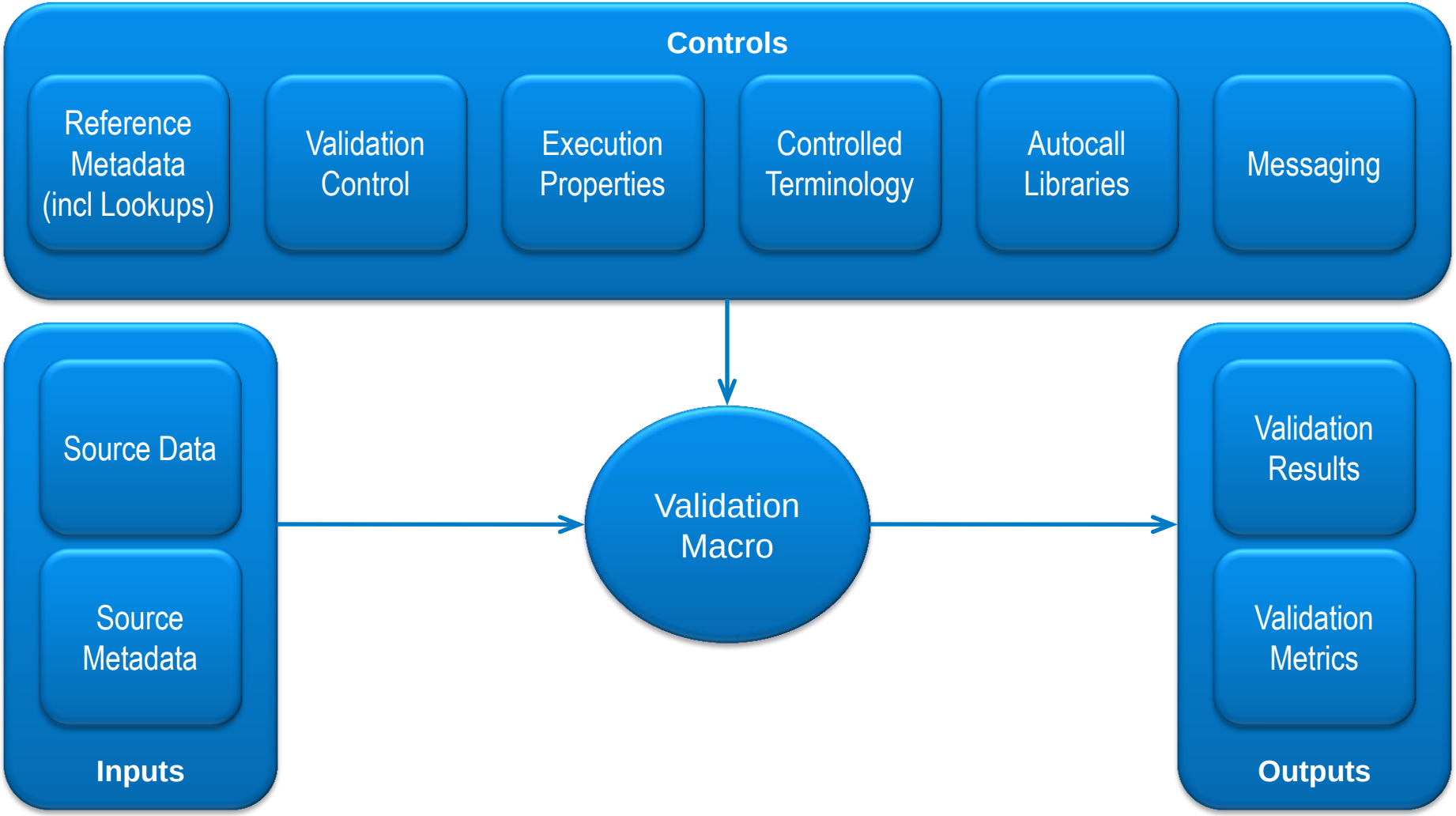
CDISC SDTM Validation



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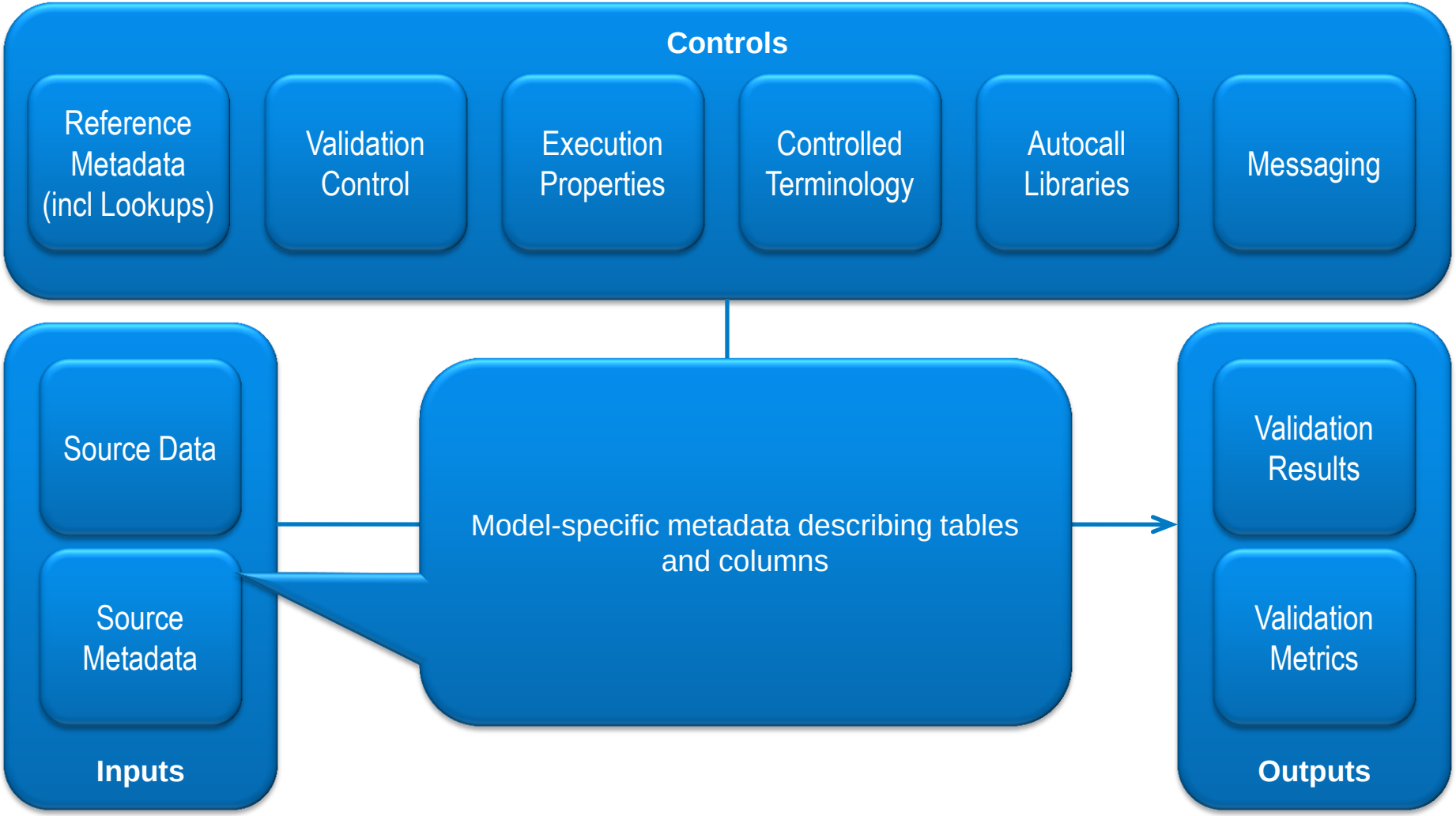

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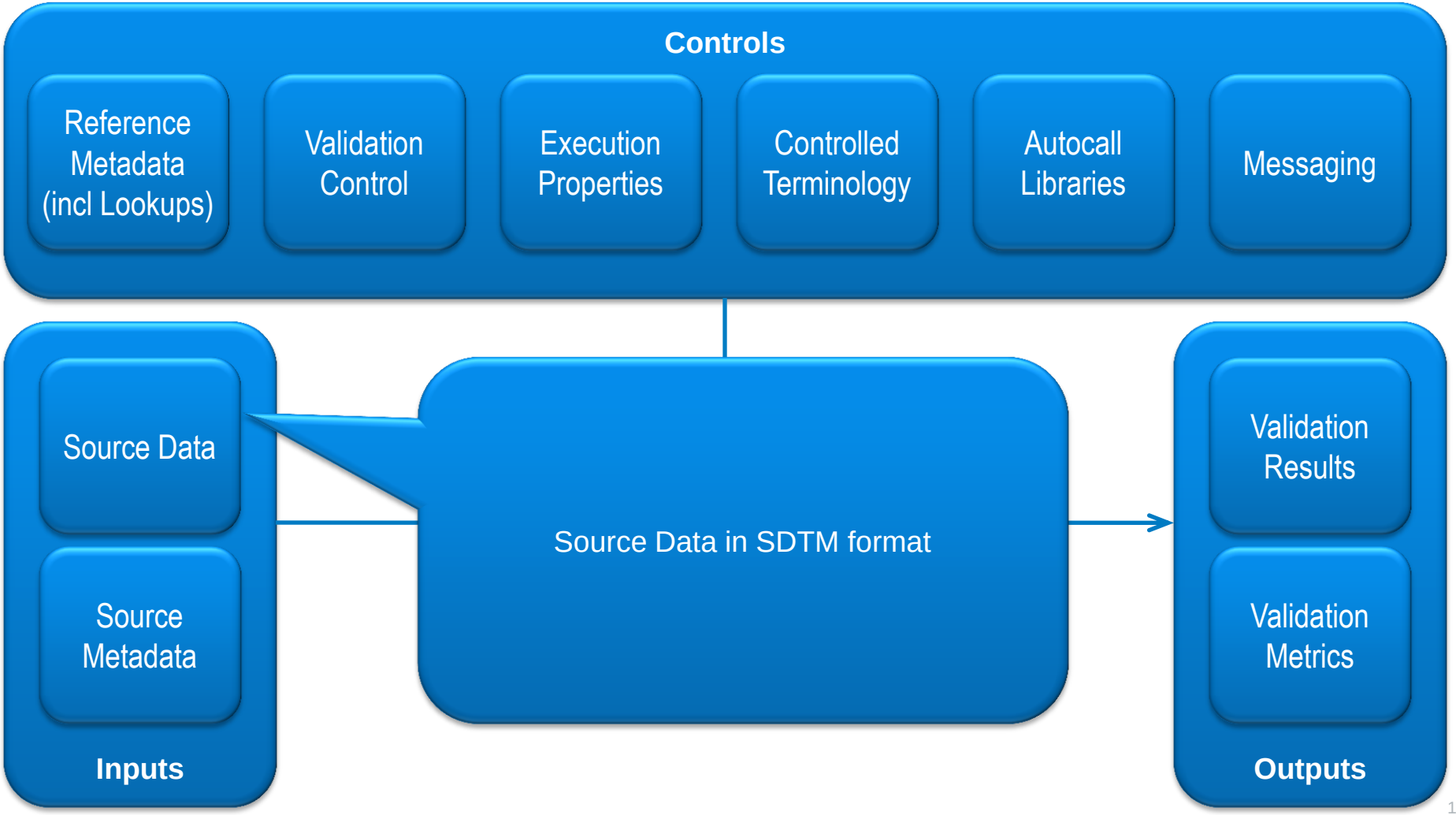

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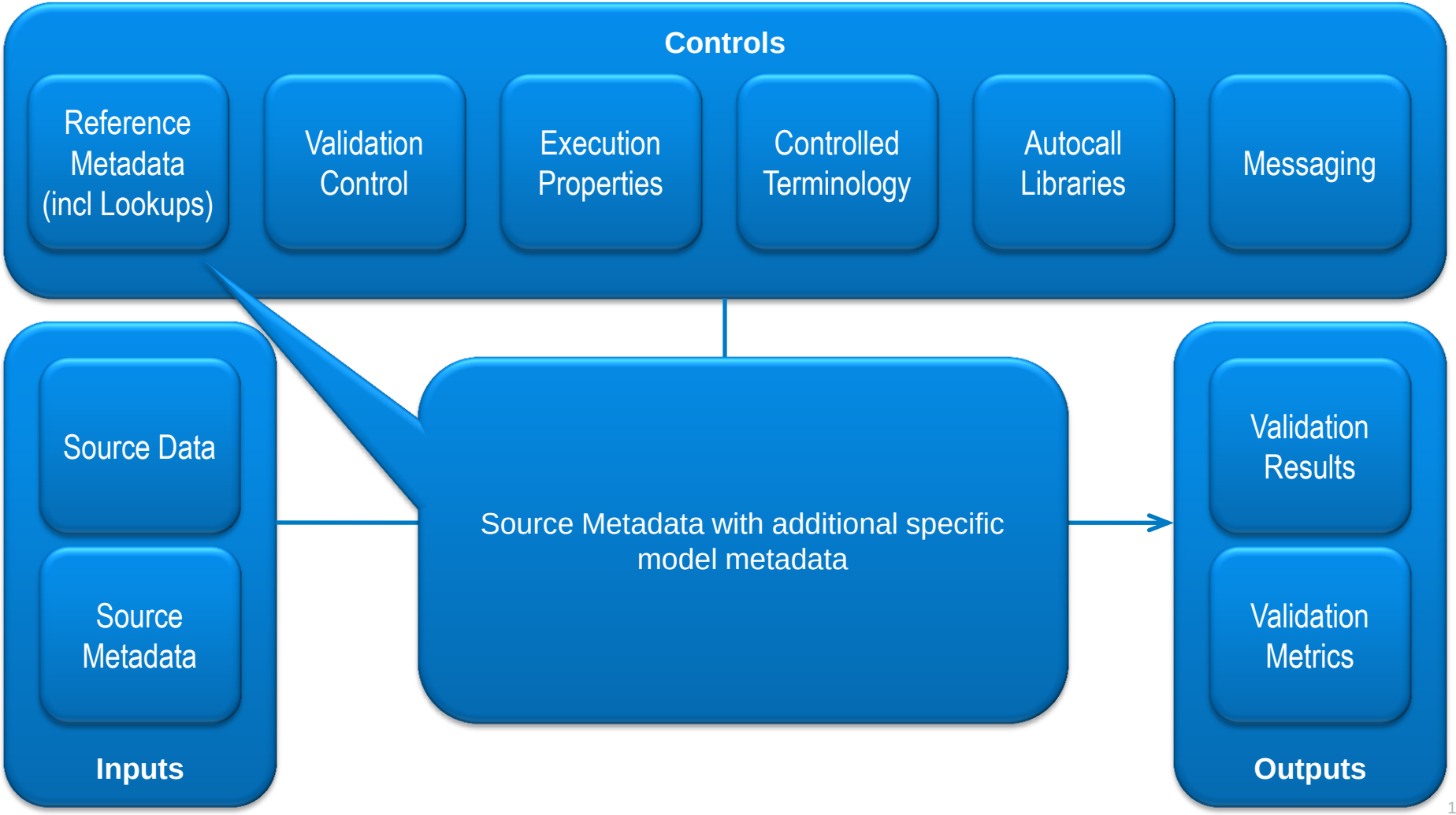

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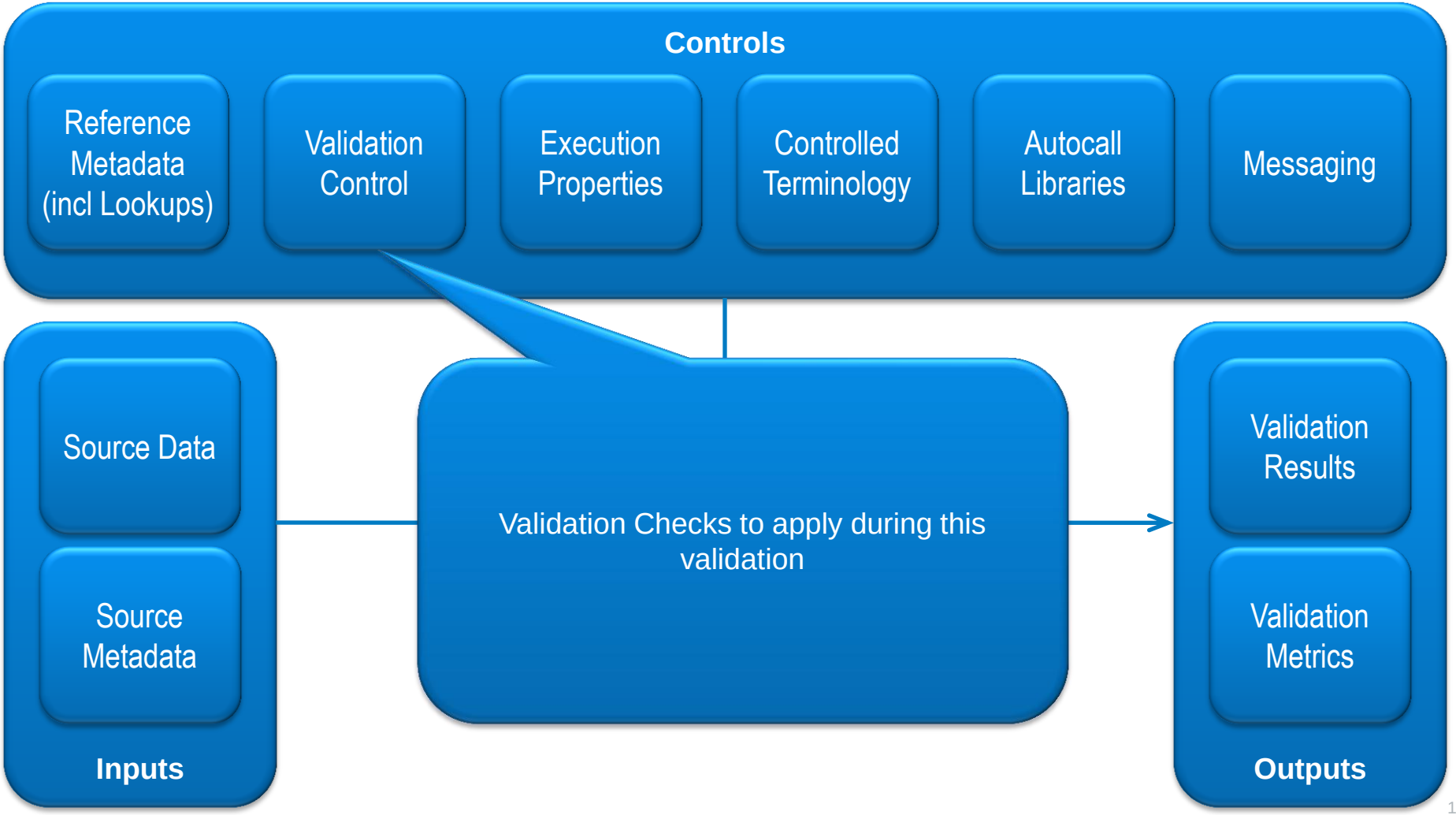

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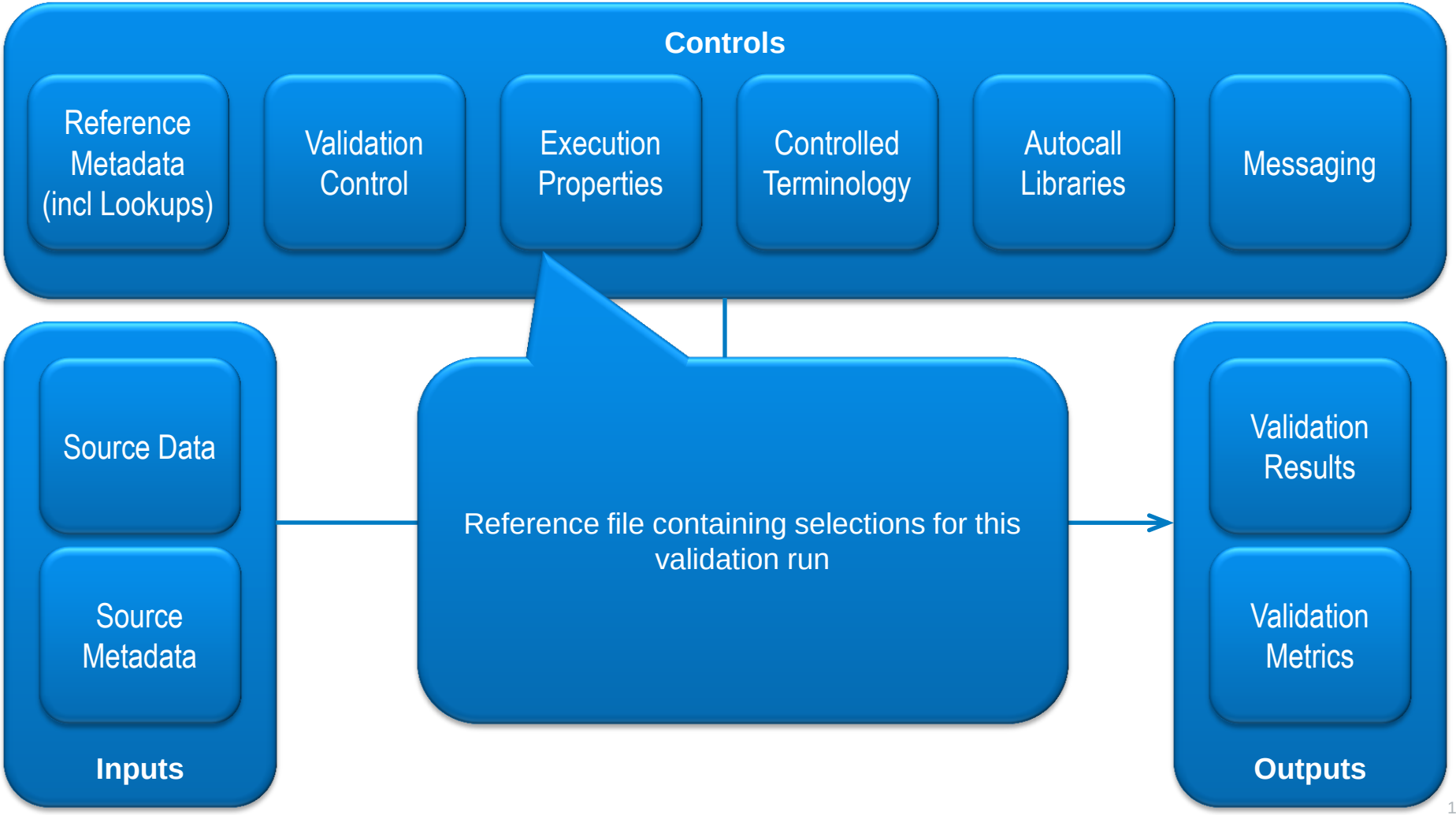

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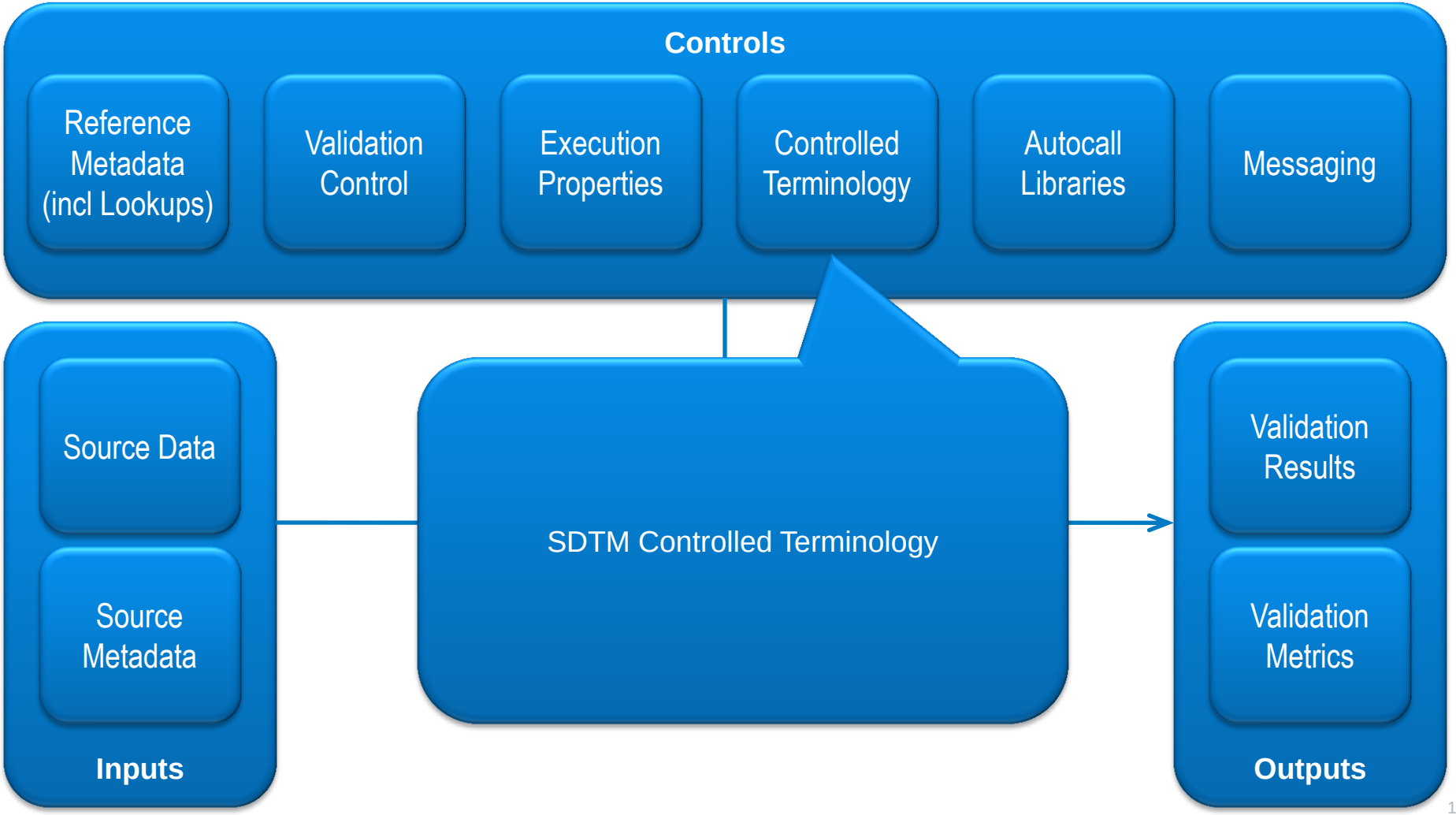

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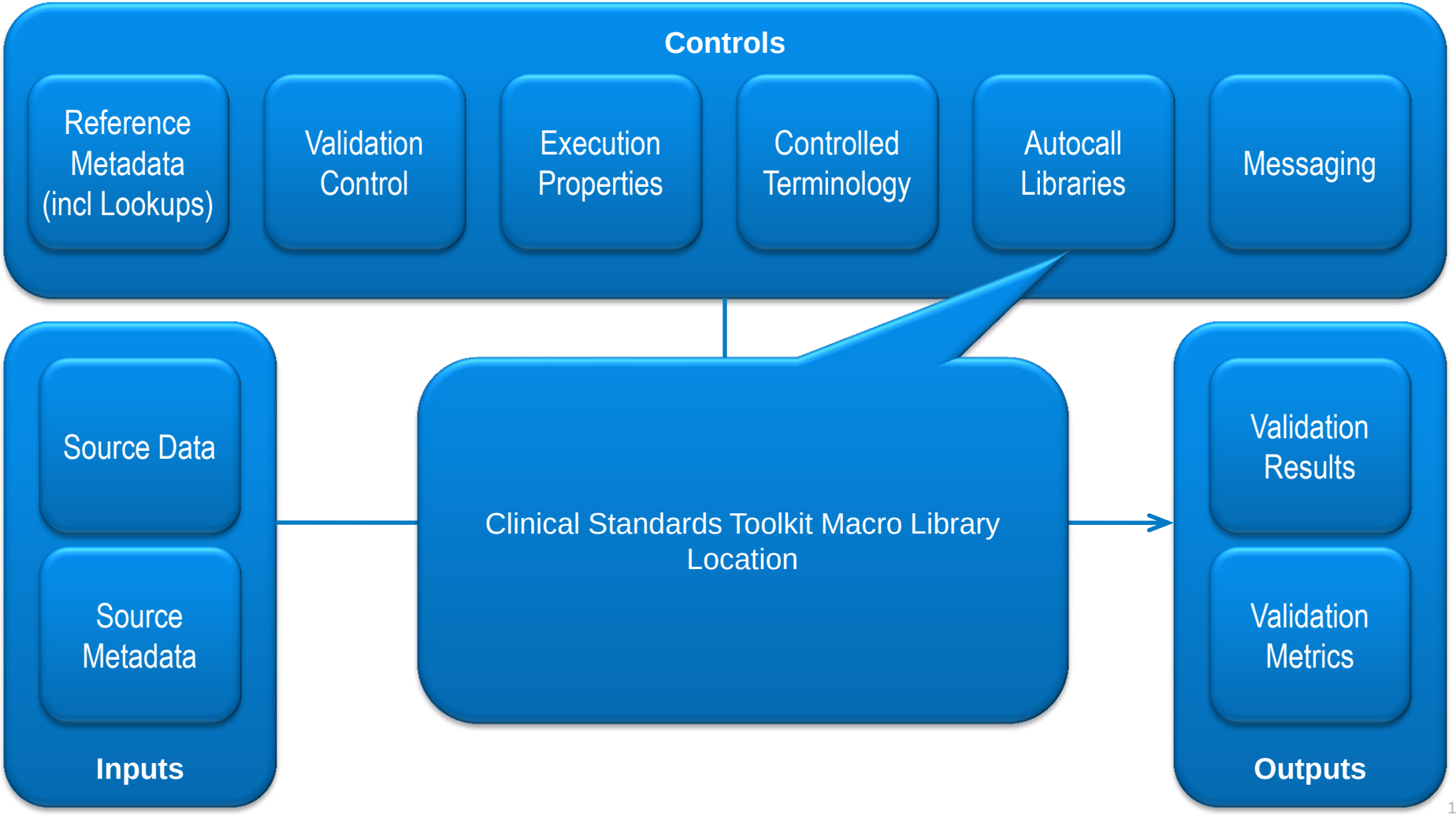

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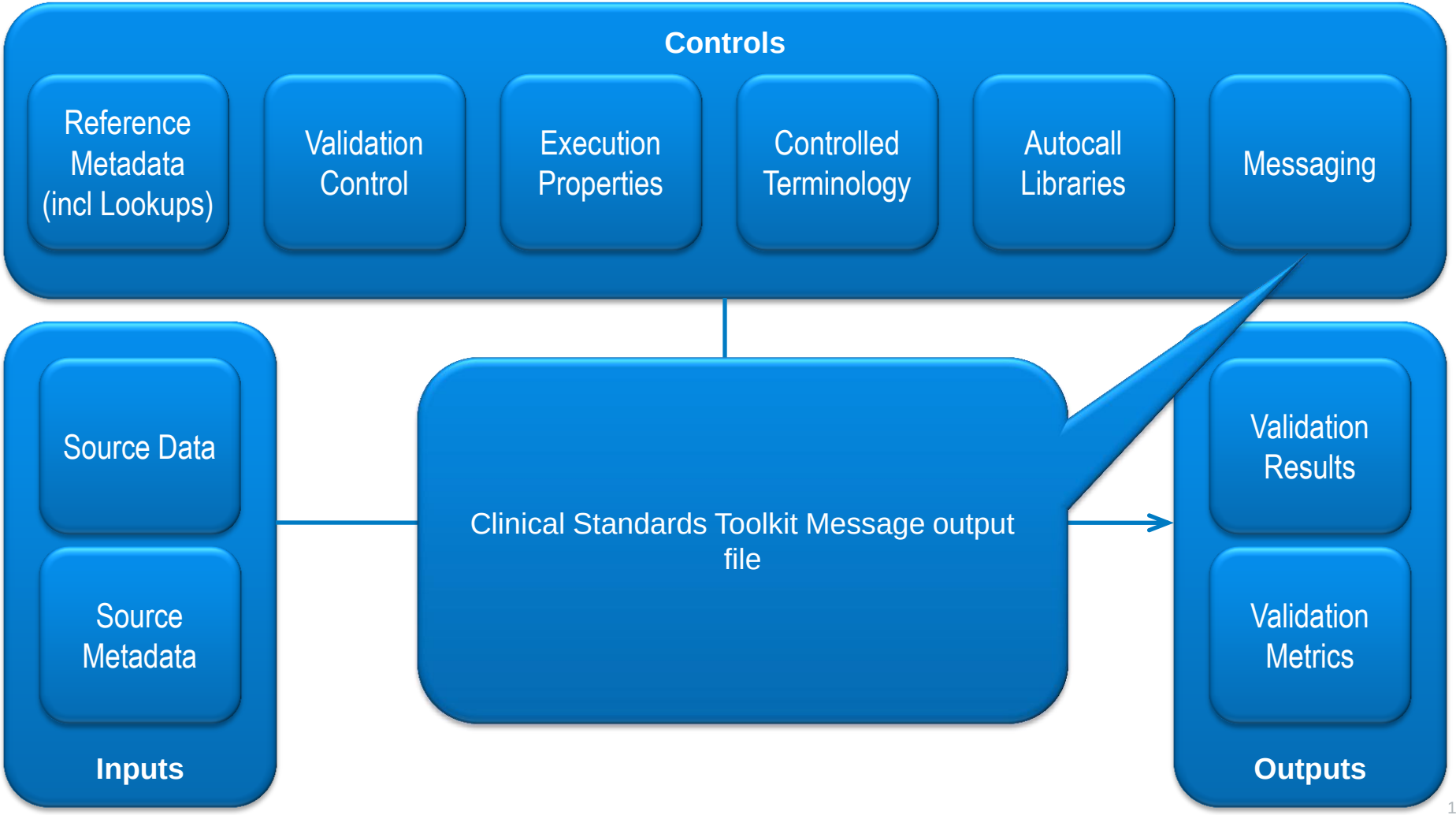

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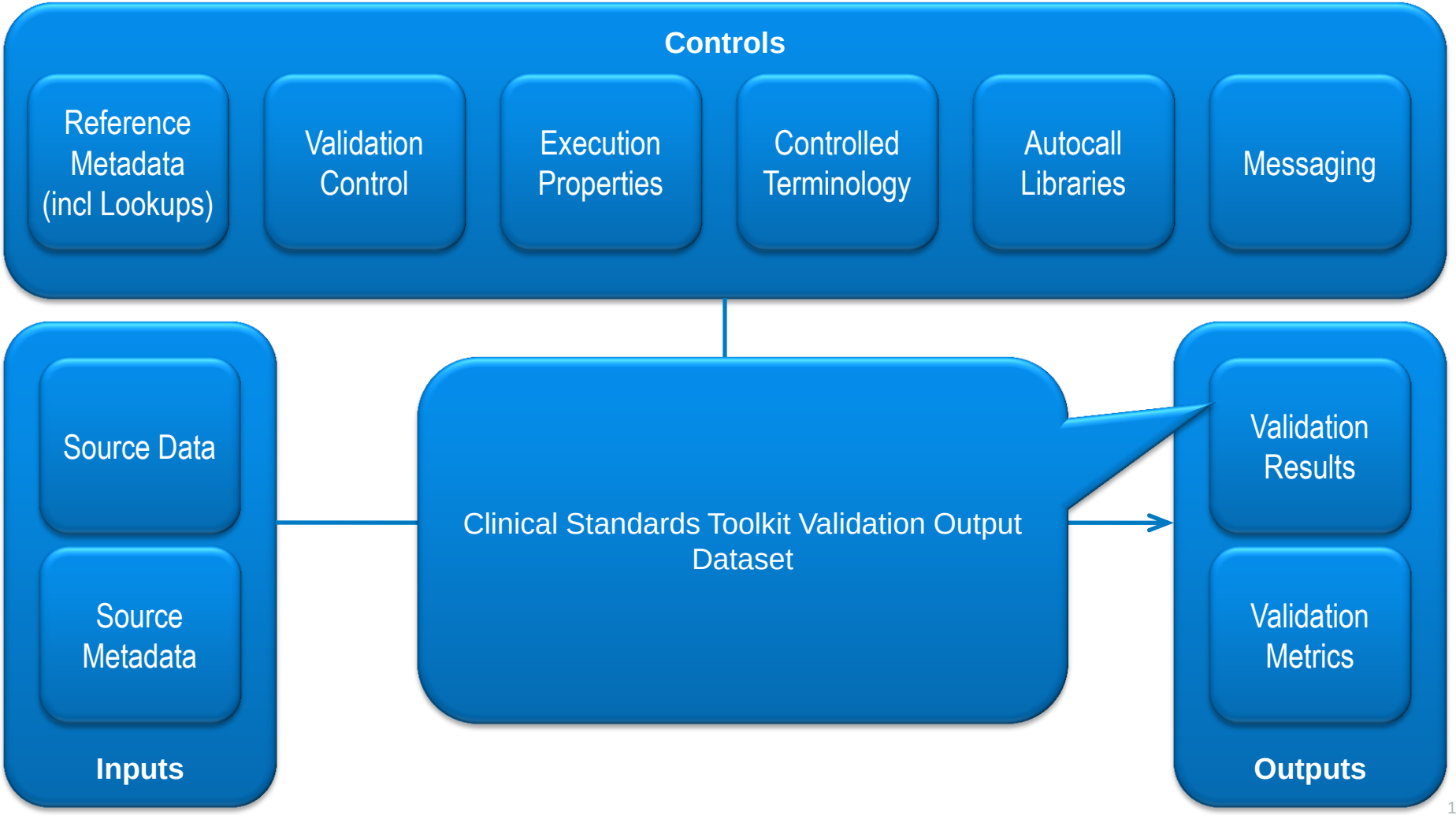

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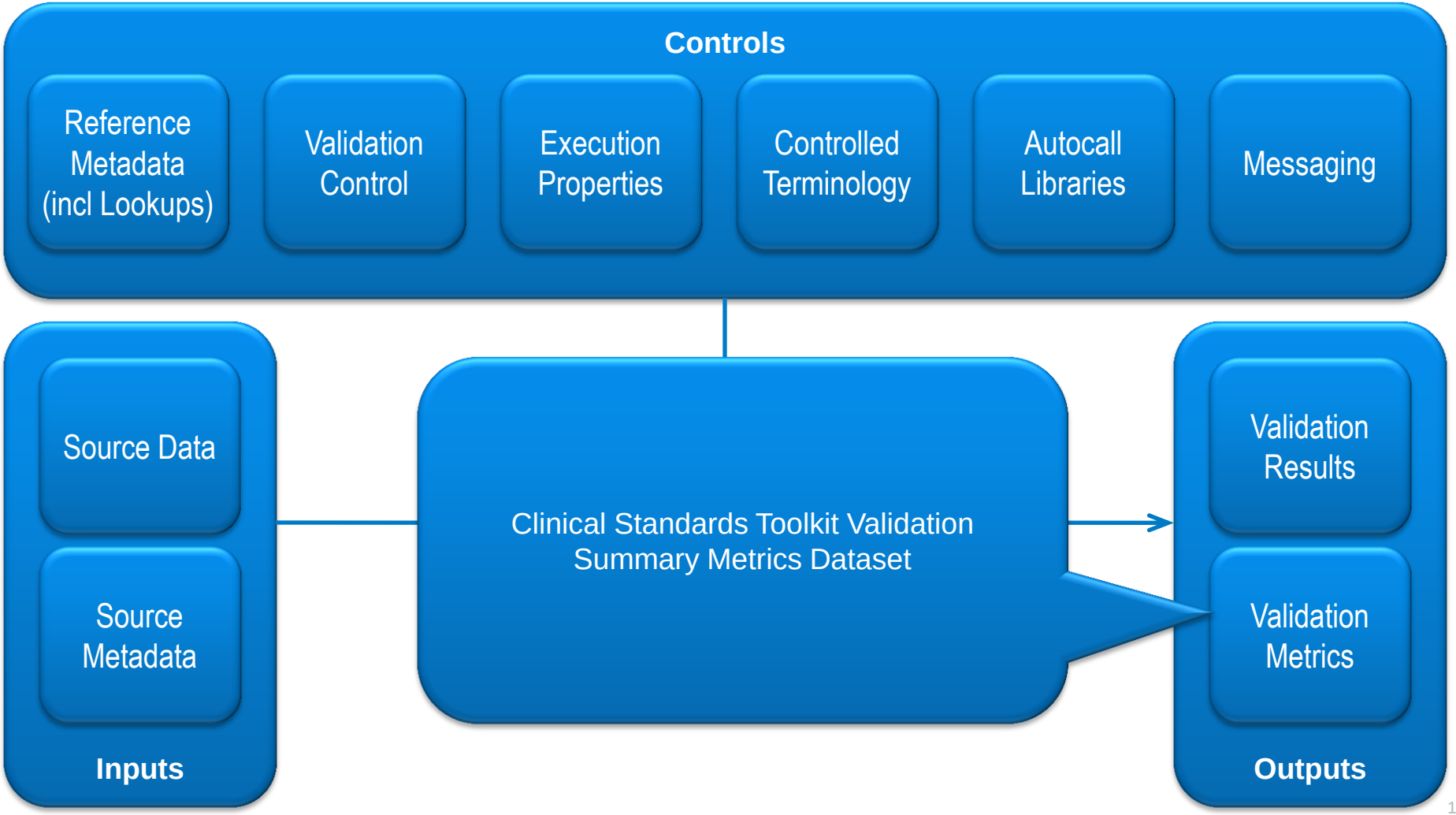

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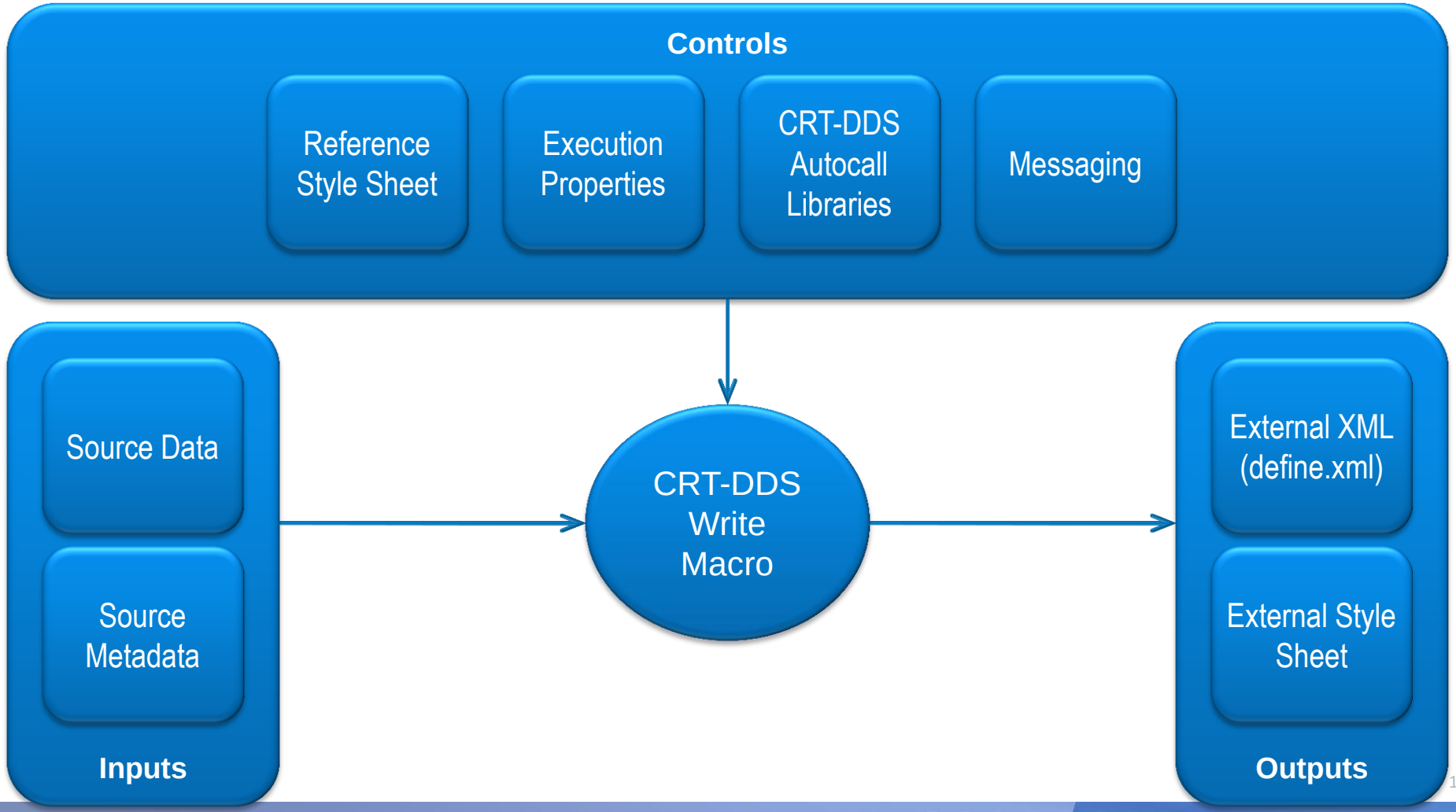

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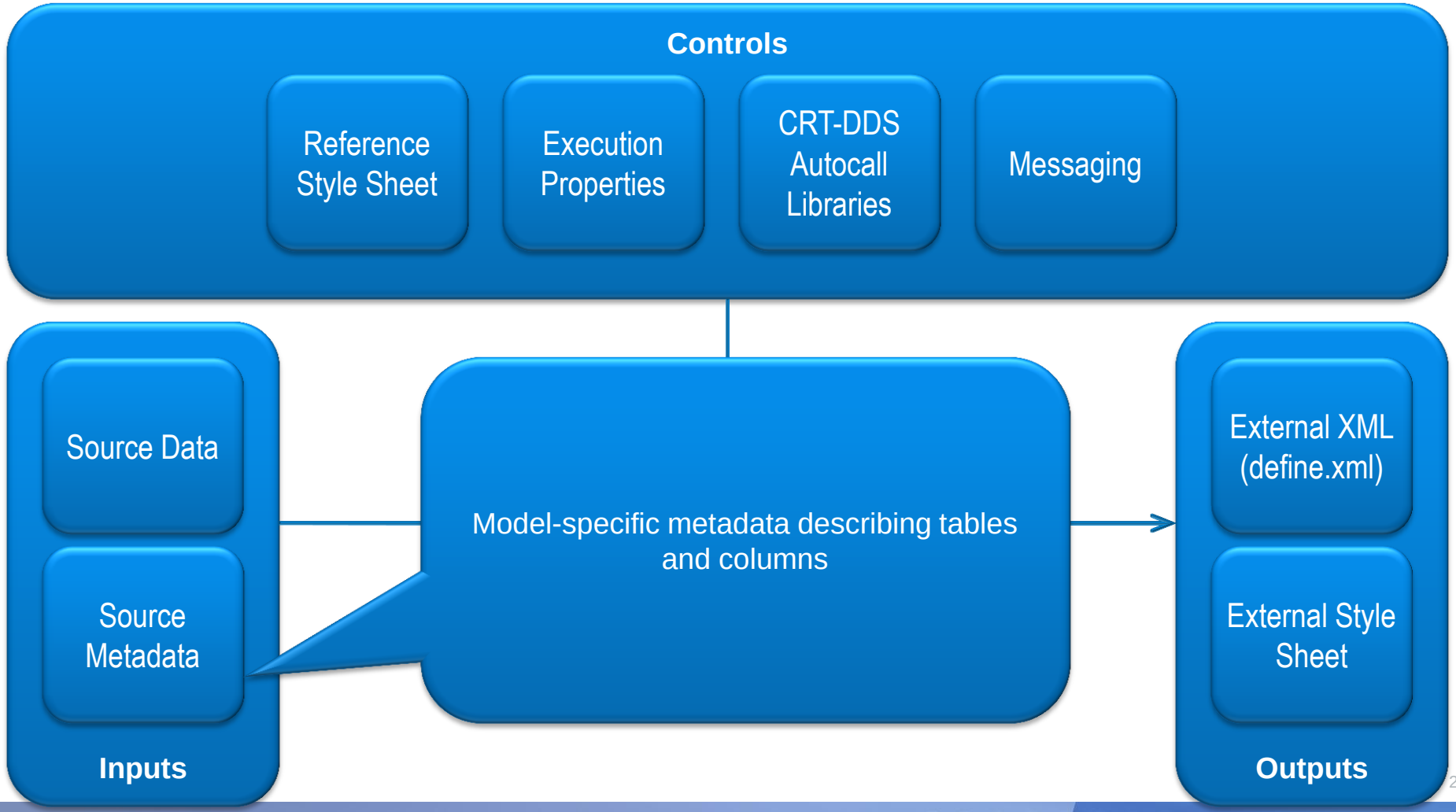

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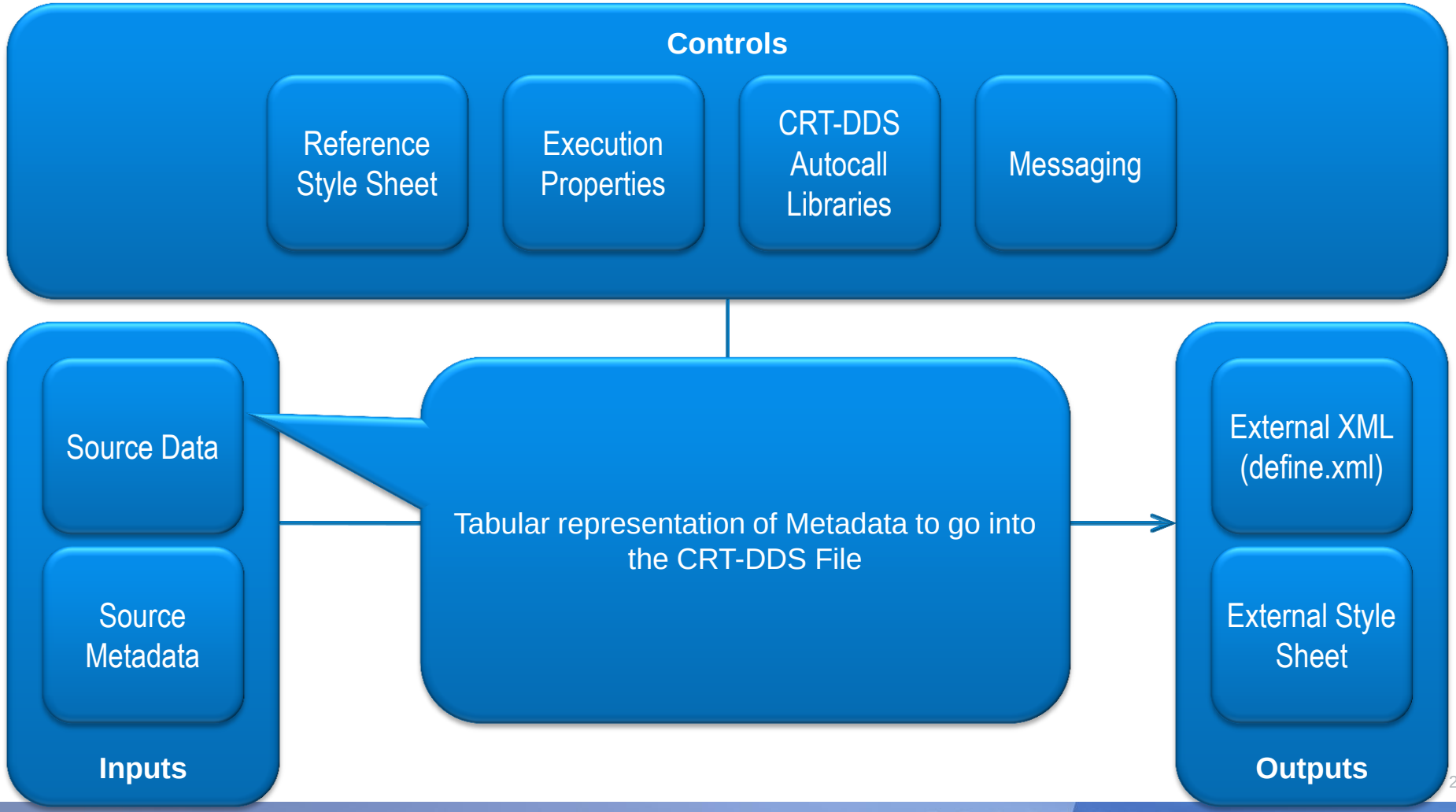

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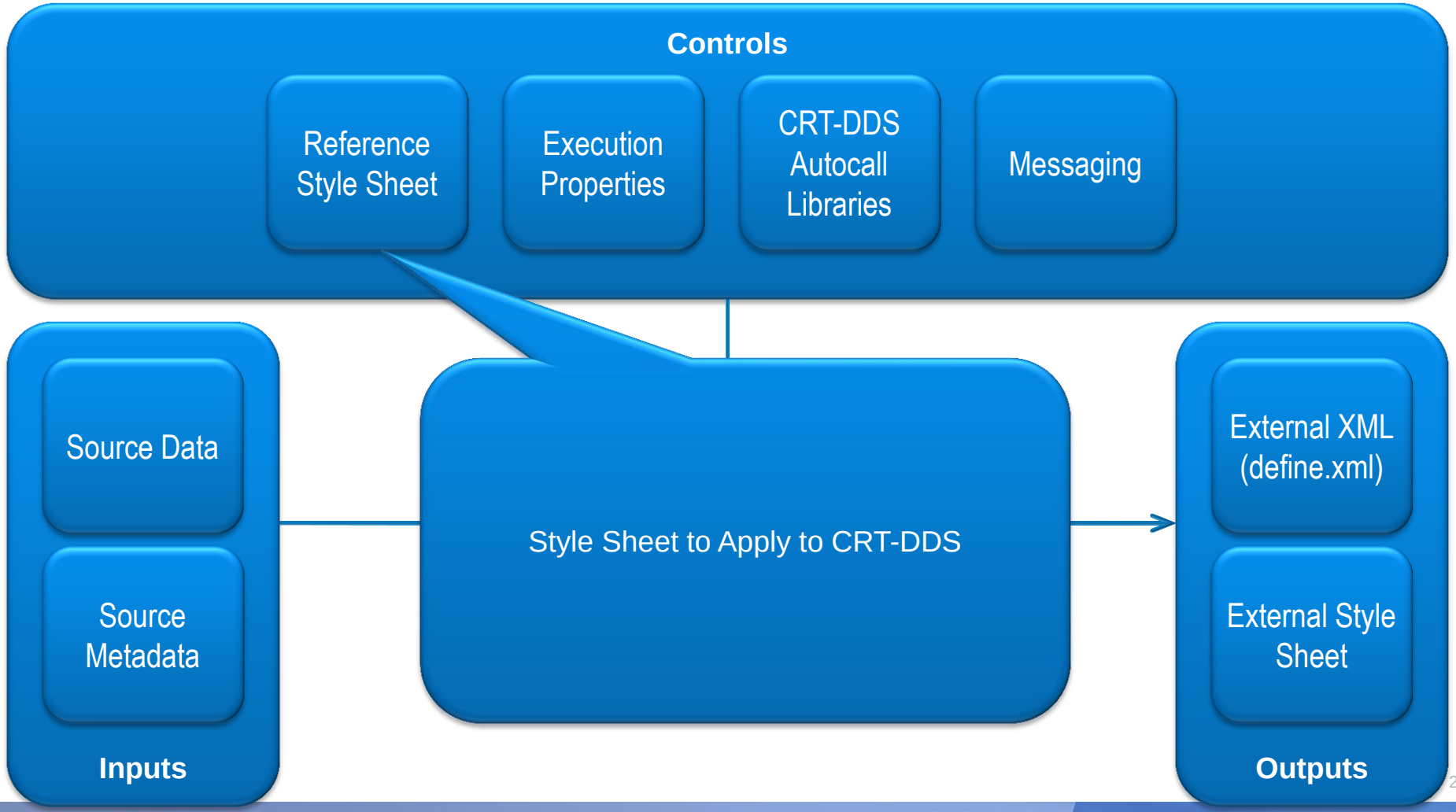

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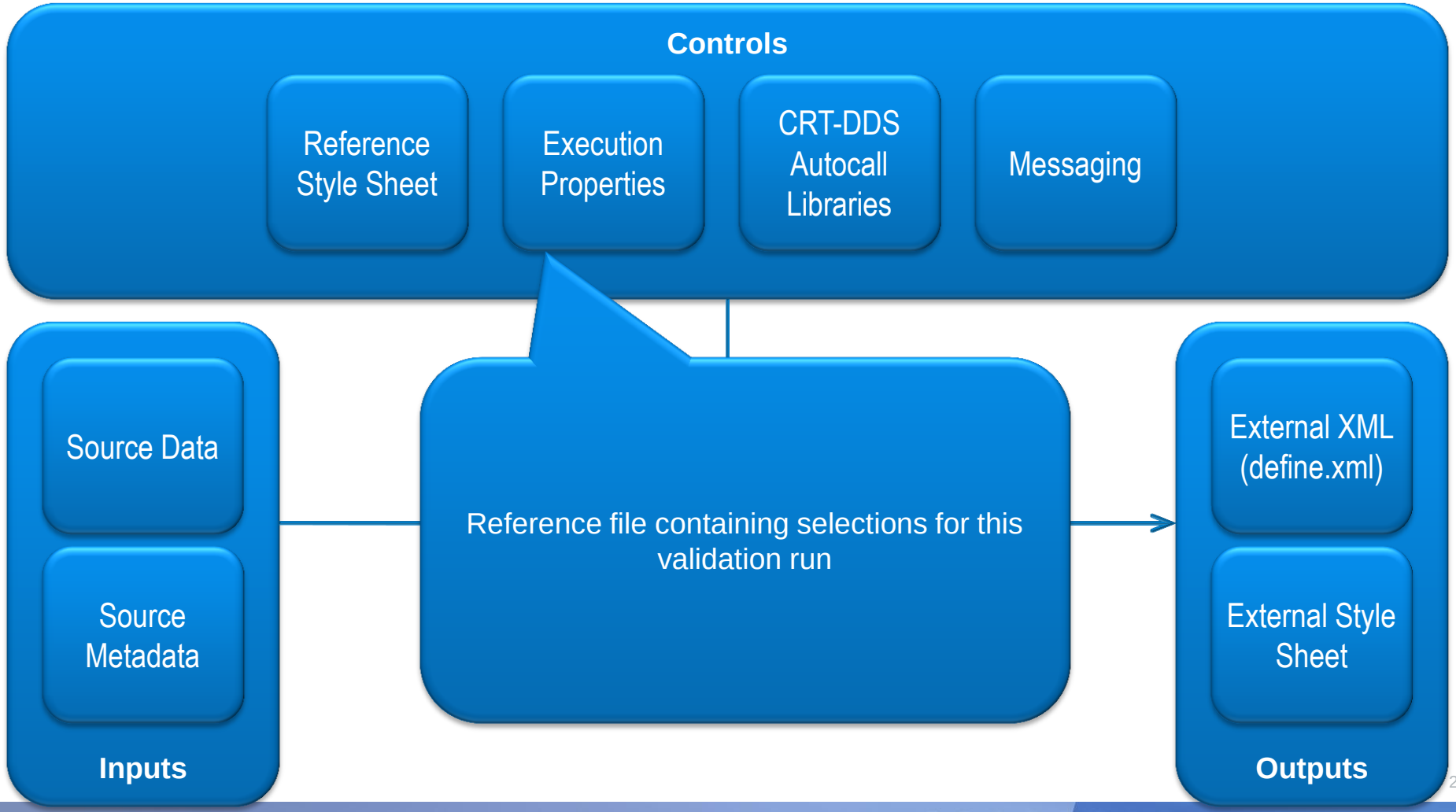

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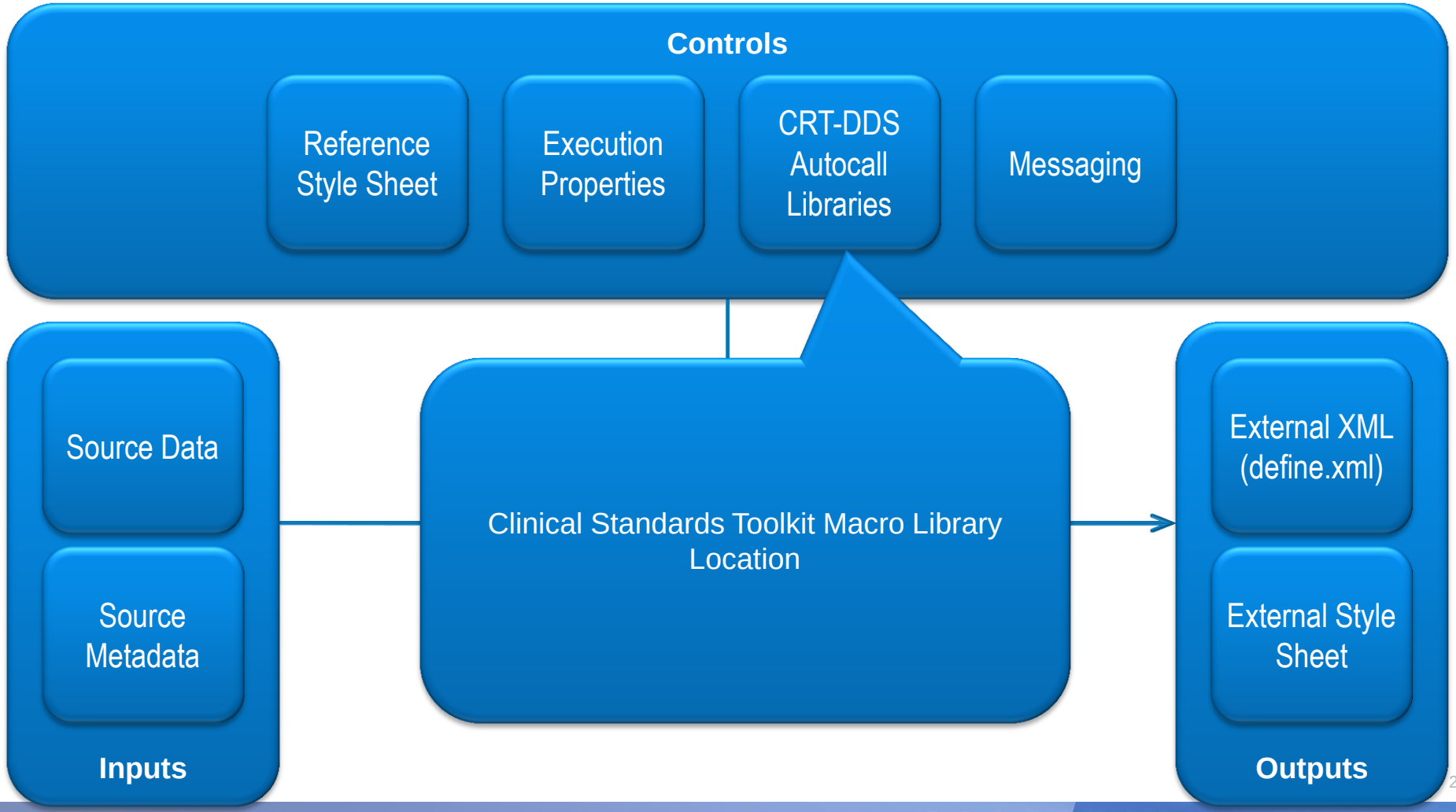

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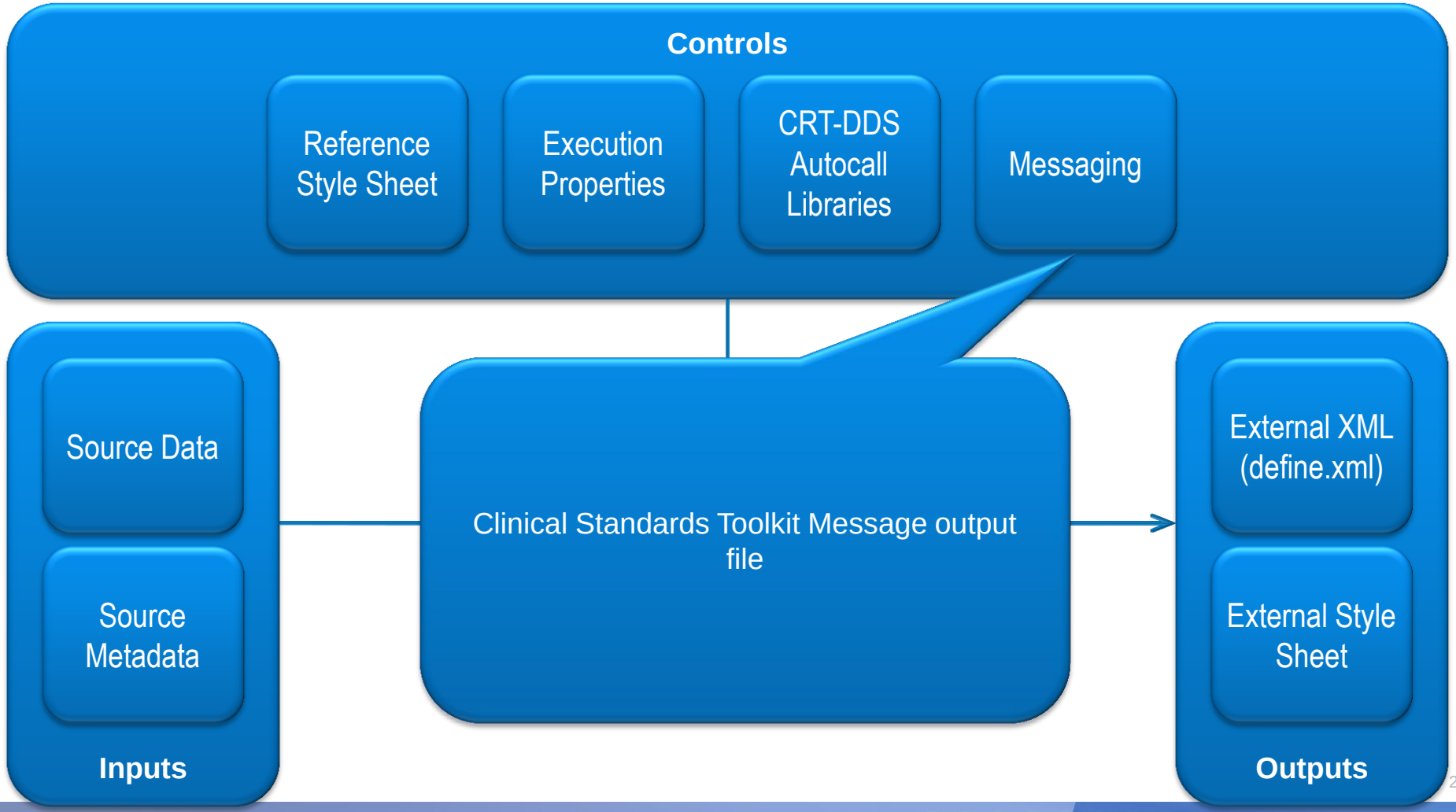

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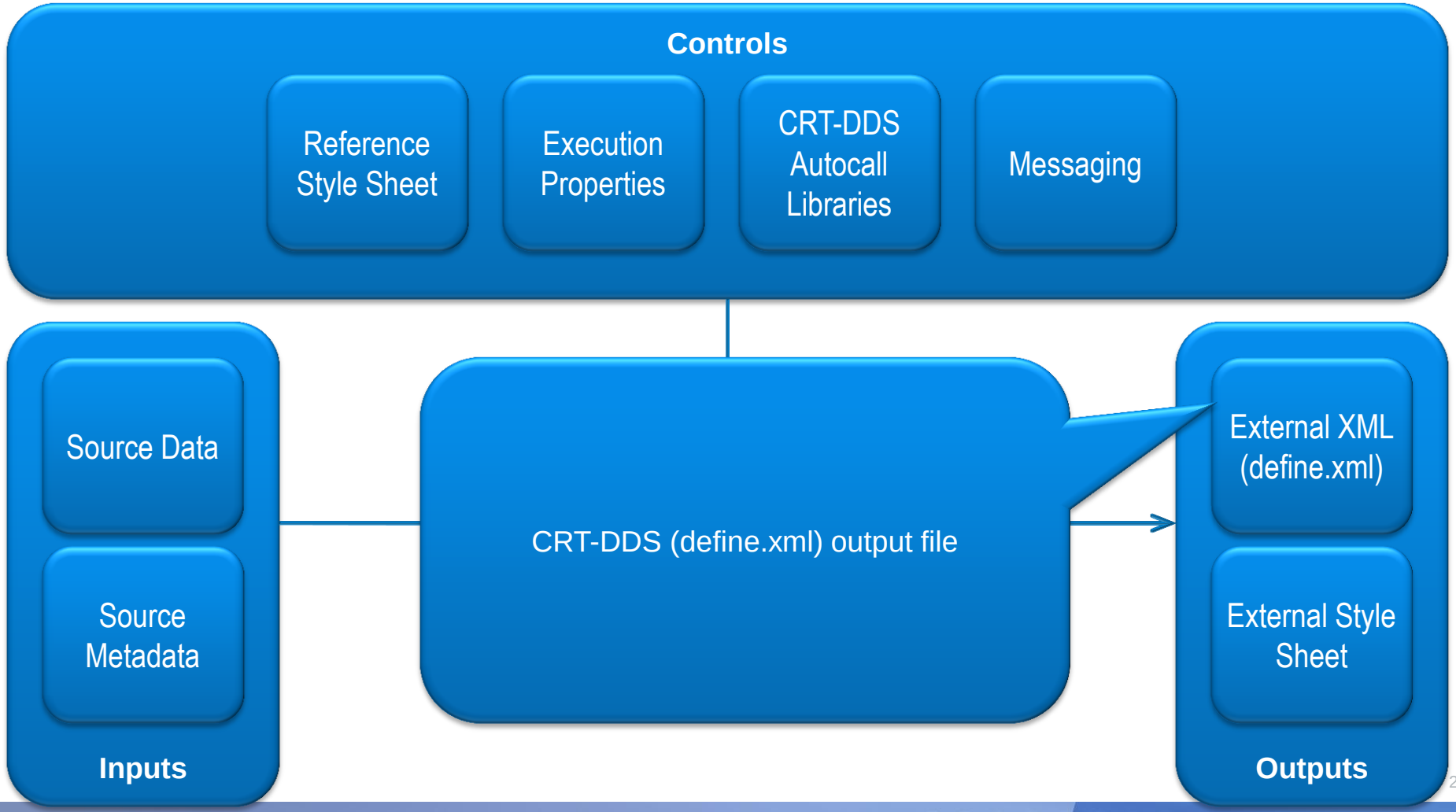

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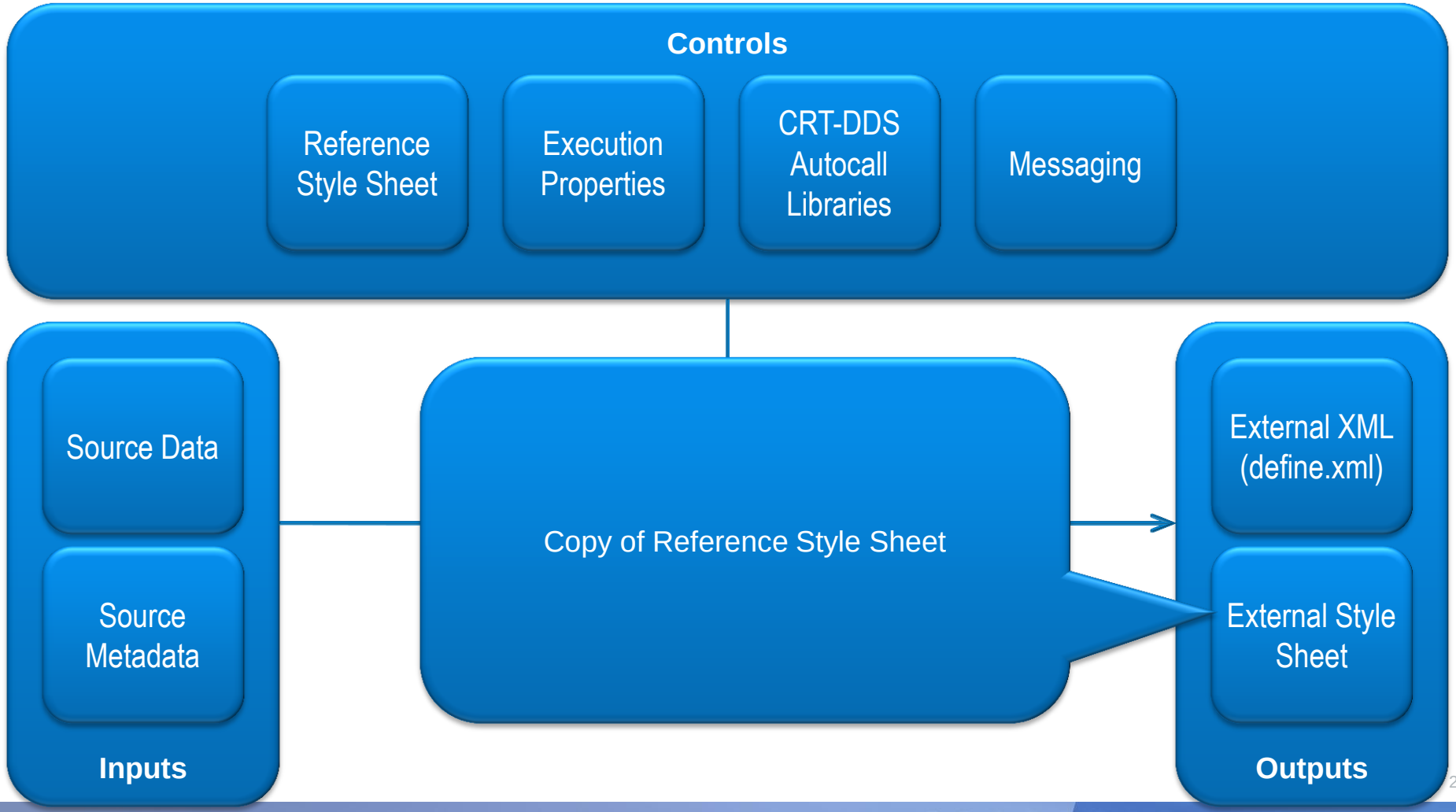

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How to get hold of the Clinical Standards Toolkit

- Needs to be licensed
- No additional cost
- Should get a Plan file for the install

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Supported Platforms

Windows

- 32-bit only
- SAS 9.1.3 or SAS 9.2

HP UX Itanium

- SAS 9.2

Solaris

- SAS 9.2

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Introduction to…

SAS Clinical Data Integration 2.2

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Desired Solutions Characteristics

- Support for CDISC standards
- Flexible implementation options
- Centralized management of integration
- Incorporates data quality management
- Easily extensible
- Support within analytical environment
- Leverage existing IT investments

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What is SAS Clinical Data Integration?

- SAS Clinical Data Integration is a **data transformation solution** designed to help companies organize, standardize and manage their **clinical research data** and **metadata**.
- The solution enables companies to:
  - **Integrate** data from disparate sources
  - **Standardize** their **in-process** data to industry models
  - **Migrate legacy** data to modern standard models
  - Leverage standardized data to **efficiently prepare data for analysis and submission** to regulatory authorities

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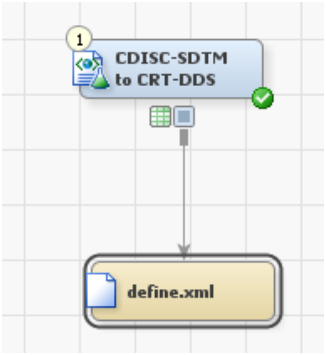
SAS *Clinical* Data Integration Capabilities



All the capabilities of SAS Data Integration, *plus*

- Pre-built support for CDISC models
  - SDTM
  - CRT-DDS (define.xml)
- Pre-built transformations for CDISC models
- Validation checks for incoming data
- Extensible to new or customized models

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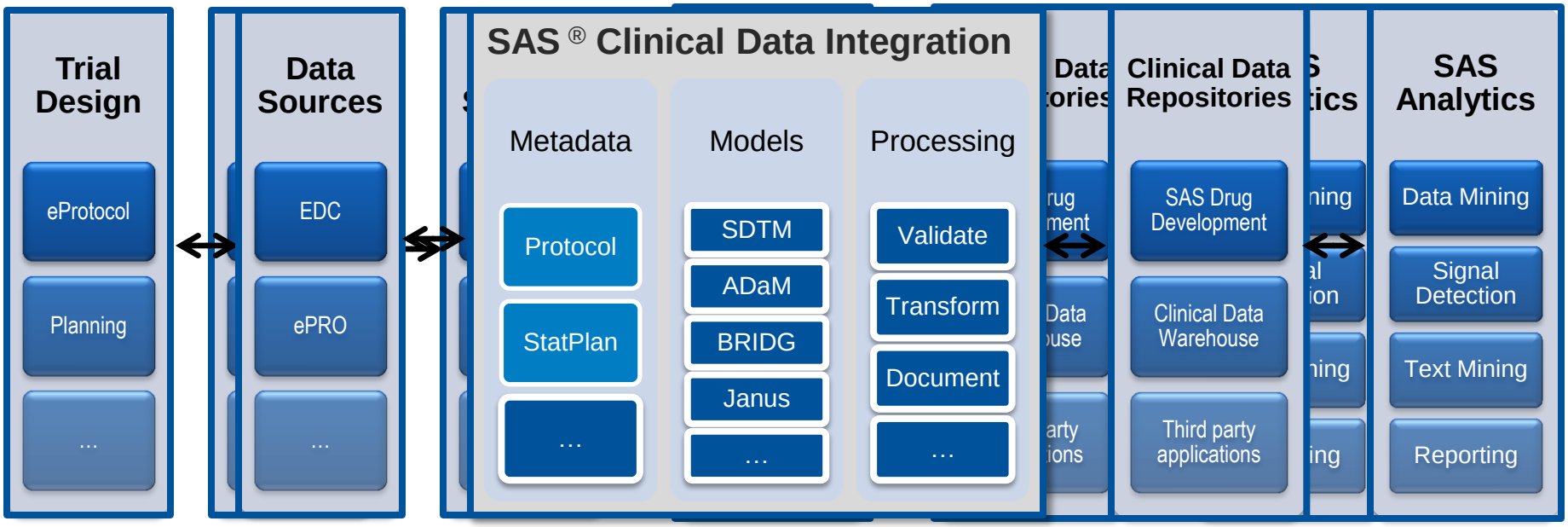
An Enterprise Solution – SAS Health and Life Sciences Framework



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Demonstration

SAS Clinical Data Integration 2.2

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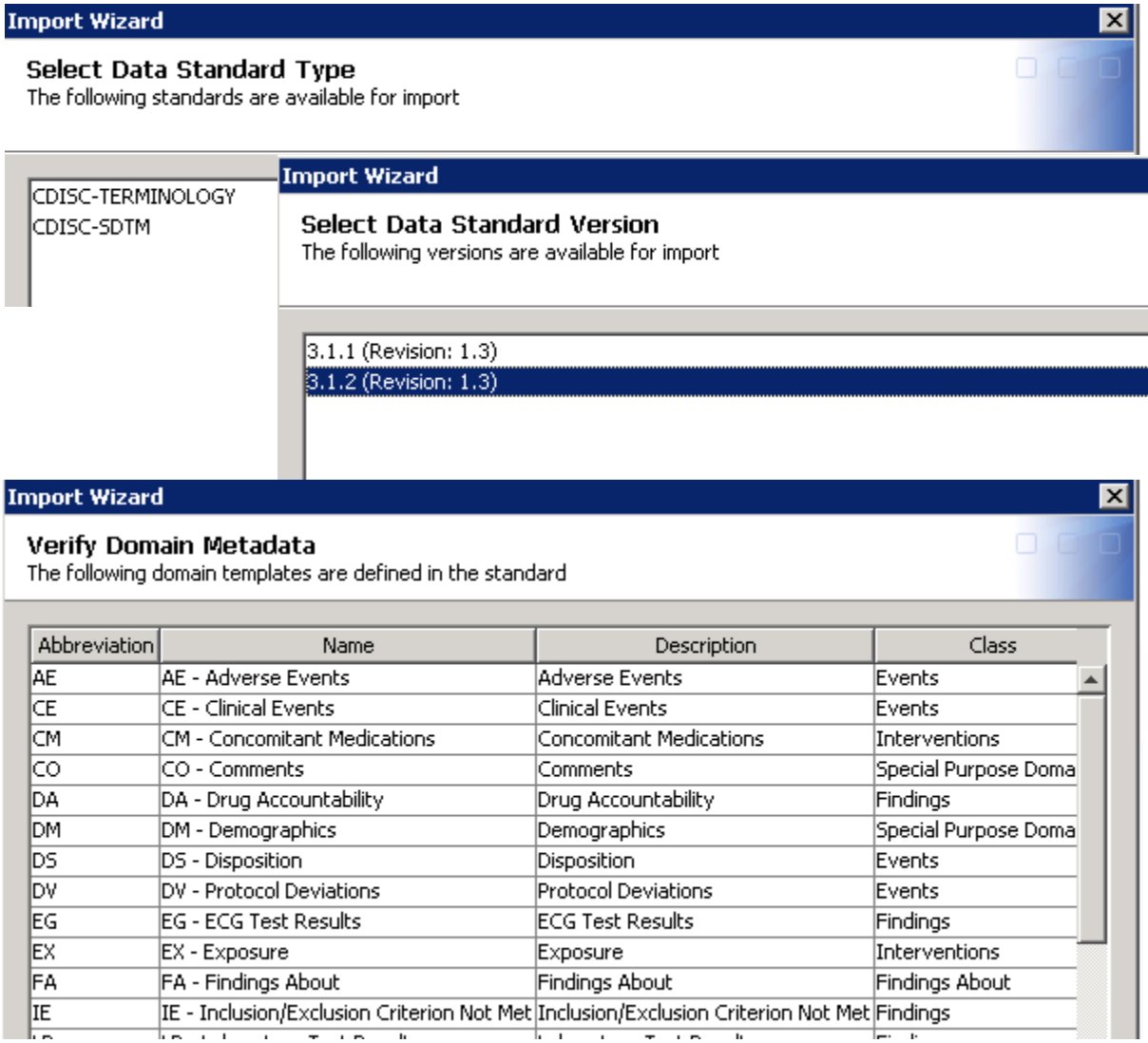
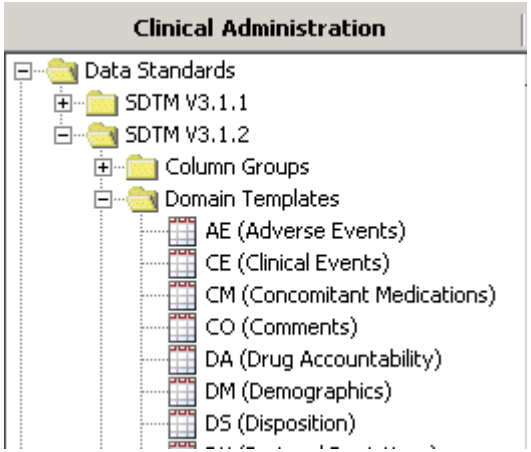
Administrate Your Standards





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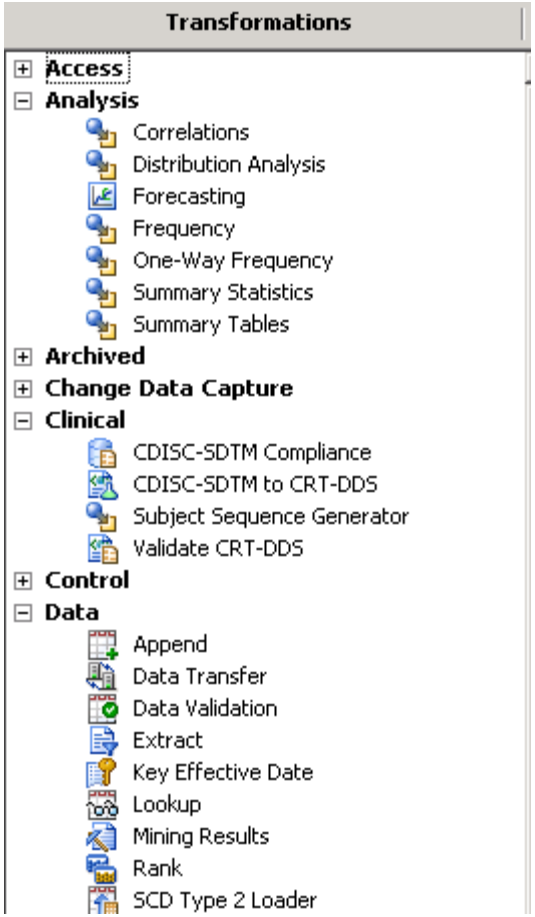
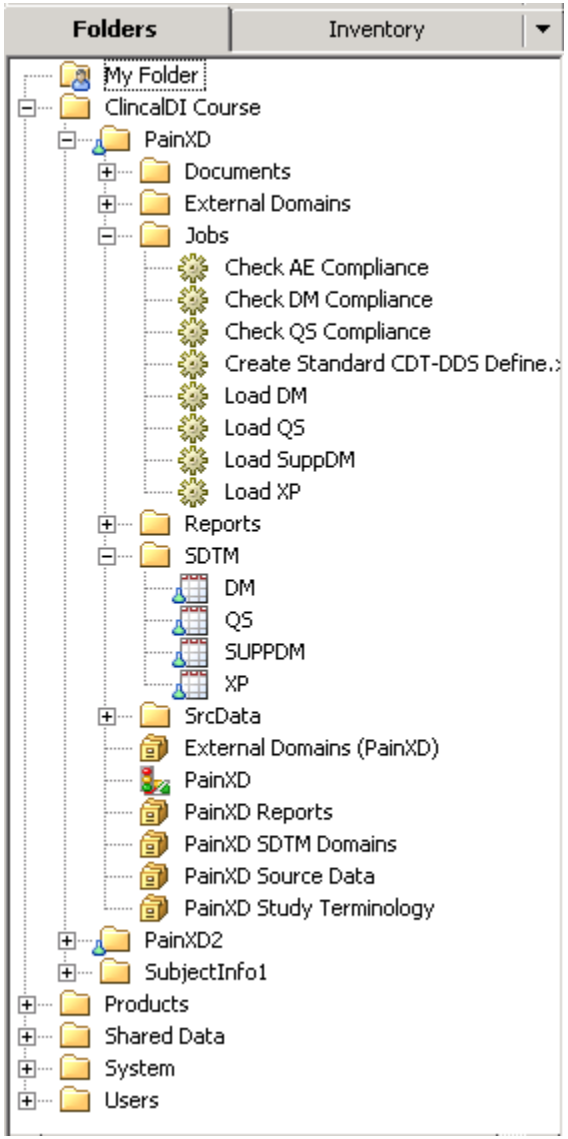
Transformation and Folders Tab





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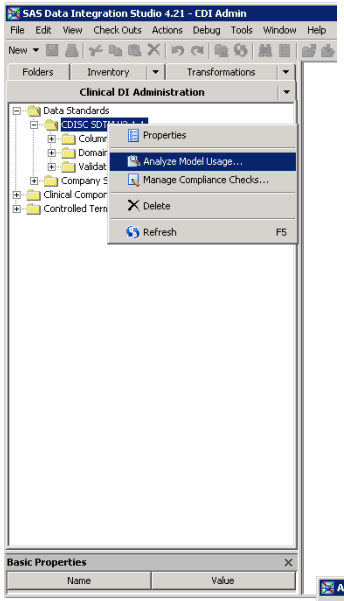
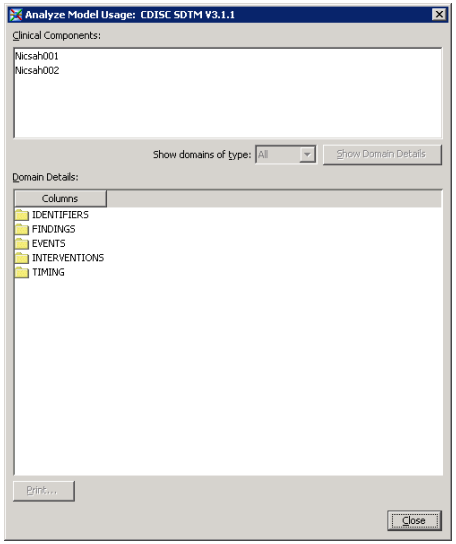
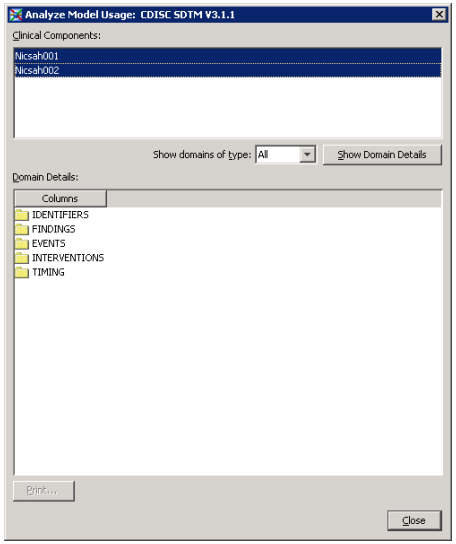
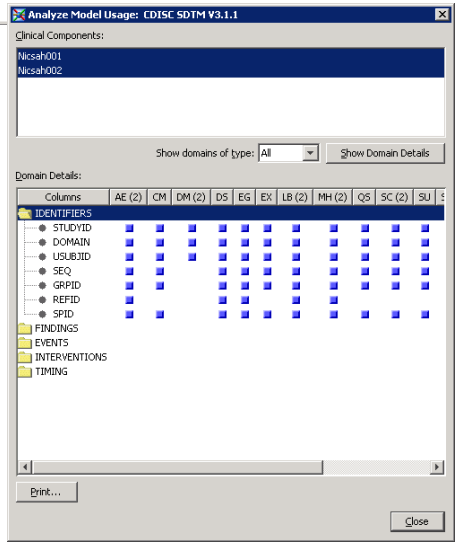
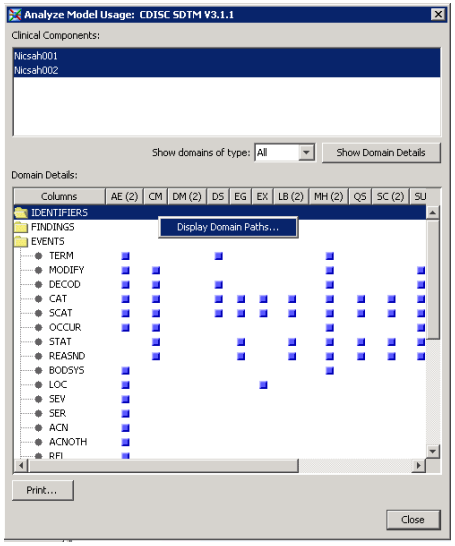
Analyze Model Usage











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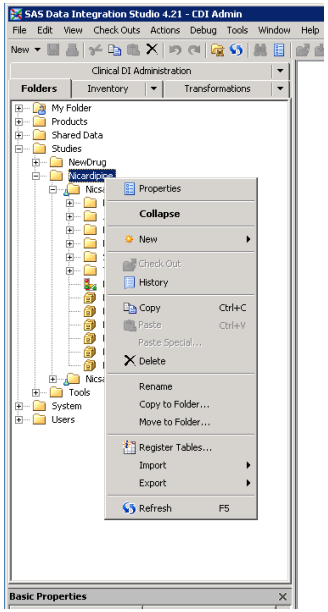
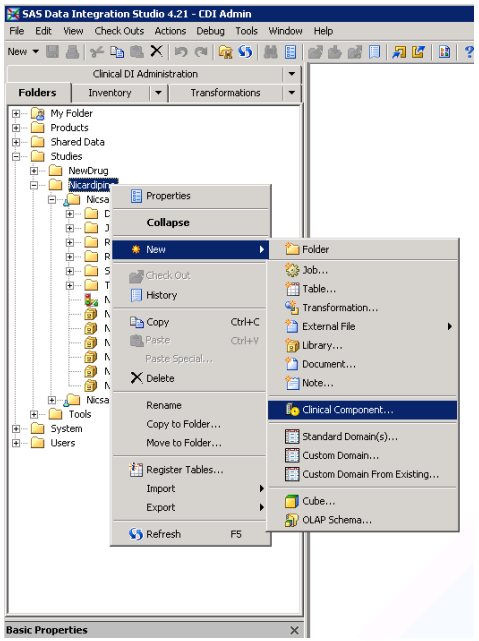
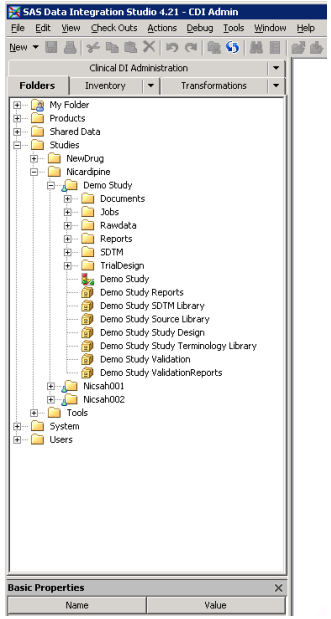
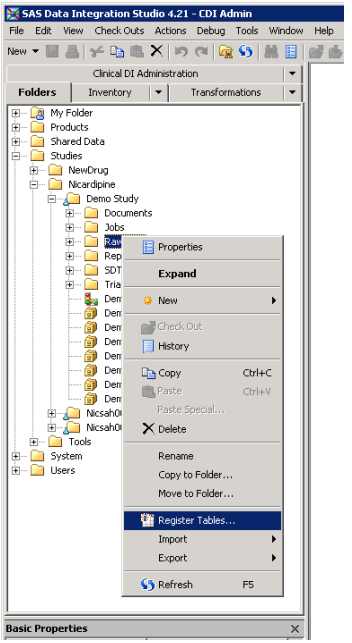
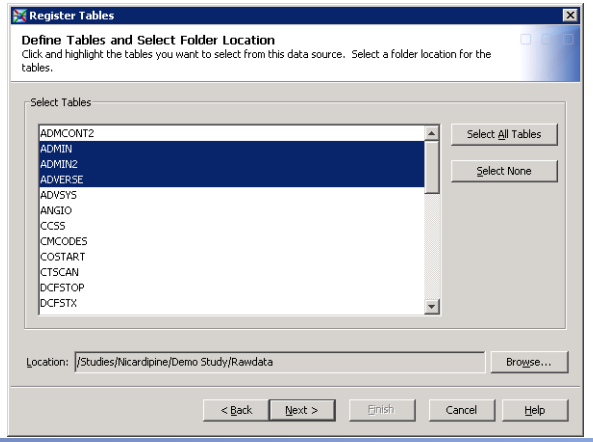
Define a Clinical Study and Register Tables

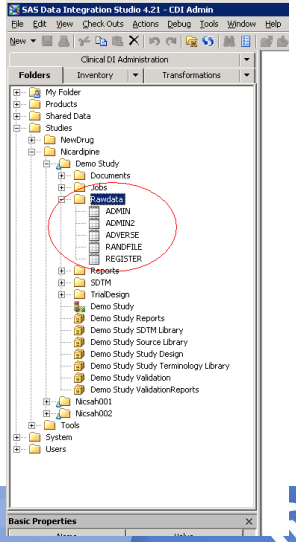












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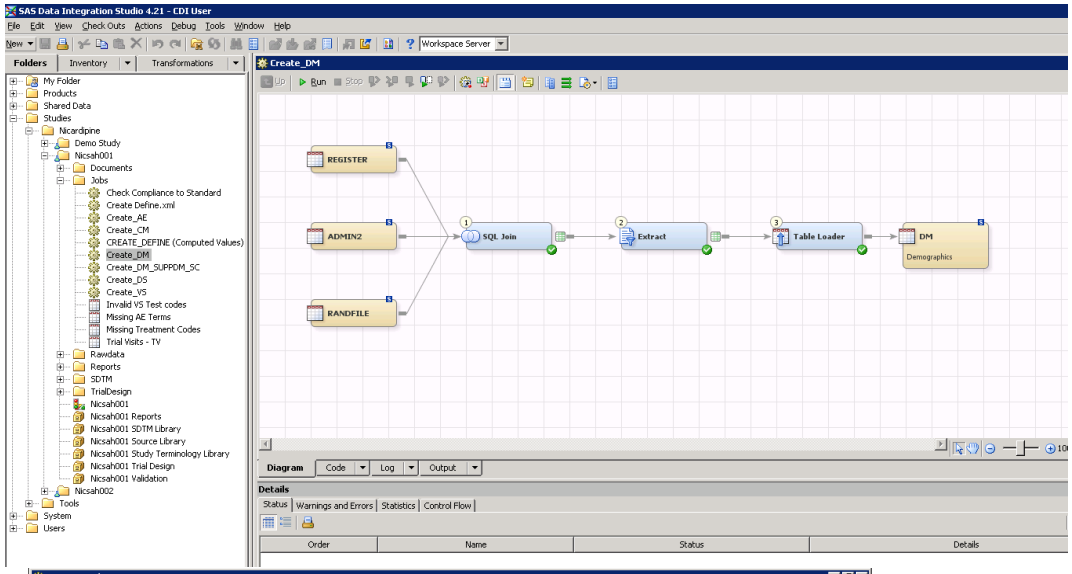
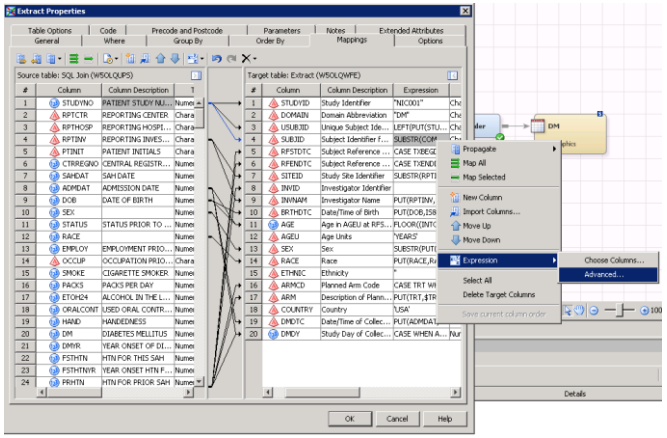
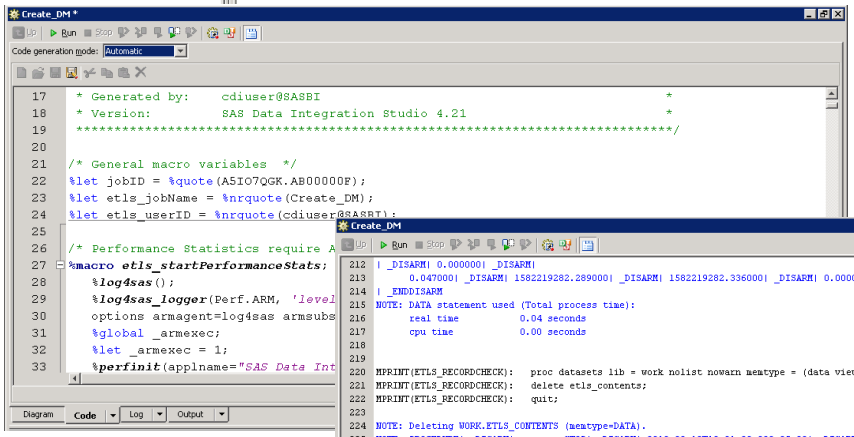
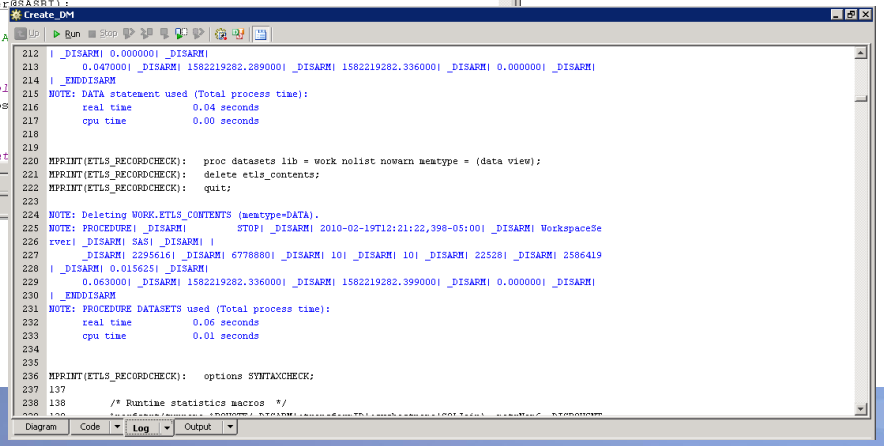
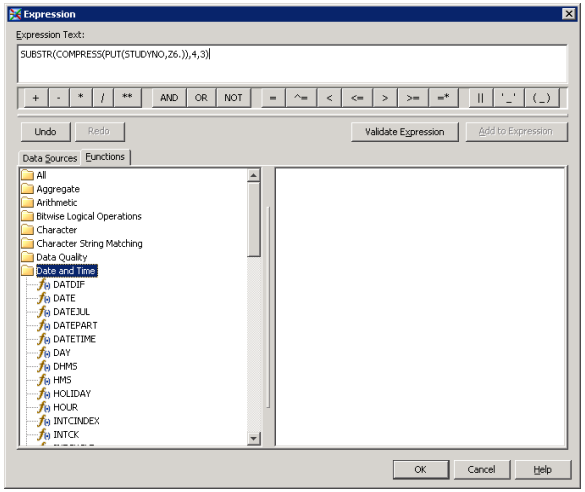
Create DM Jobs











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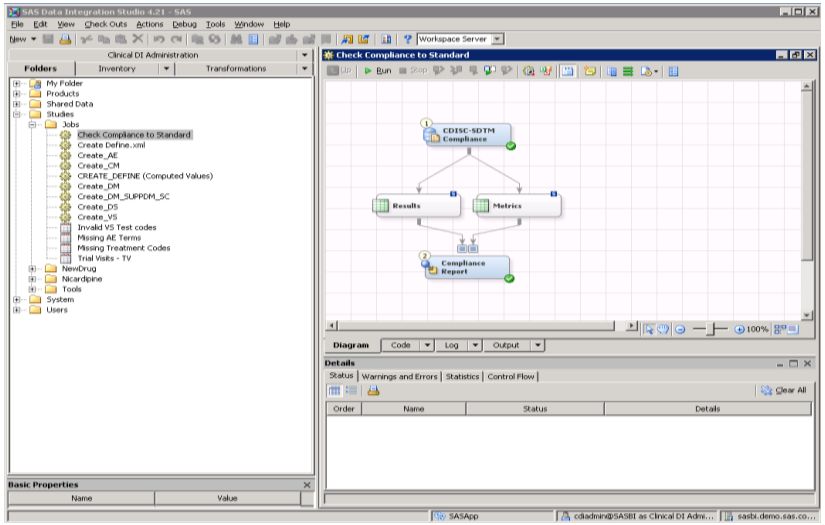
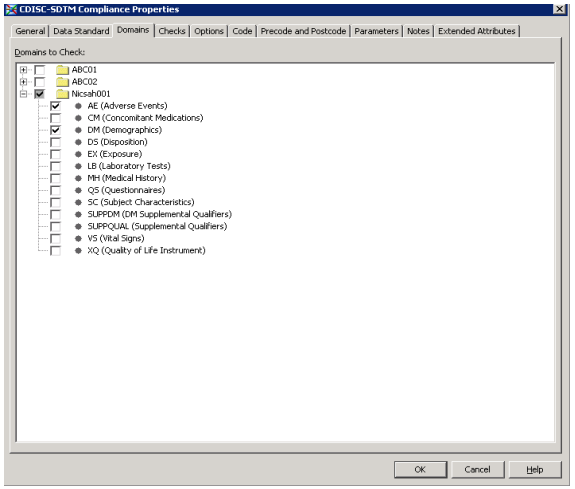
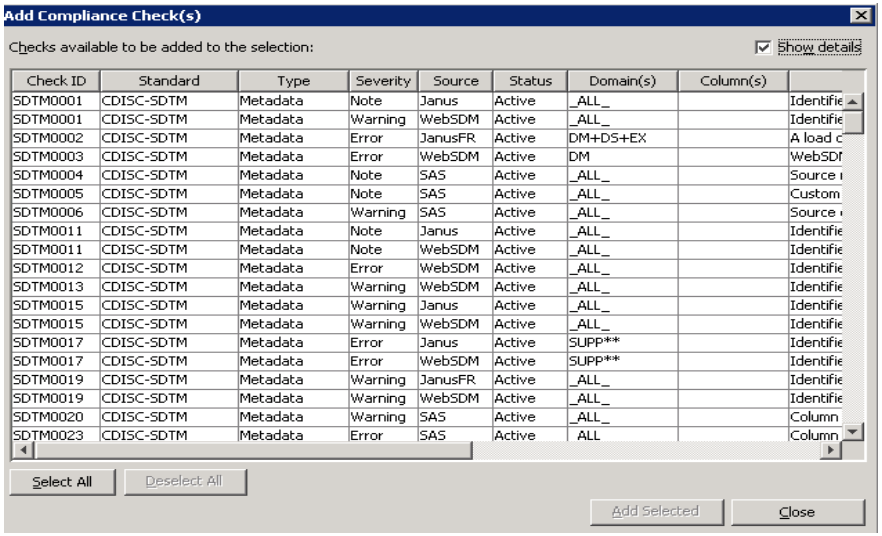
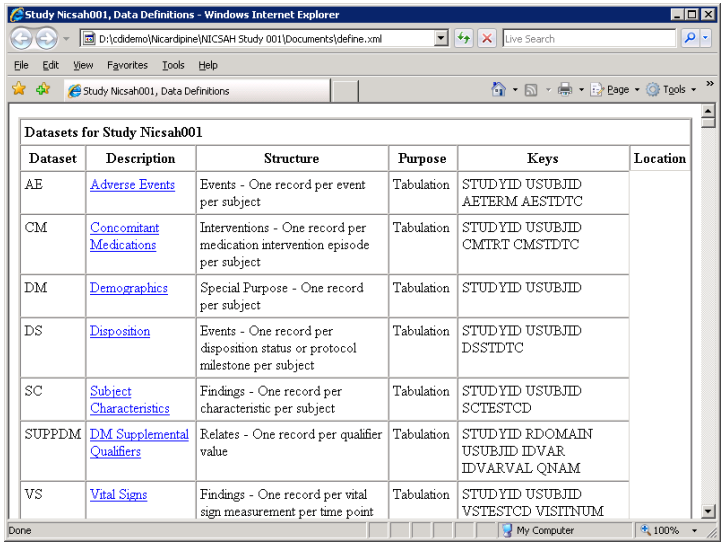
Perform Compliance Check and Report it









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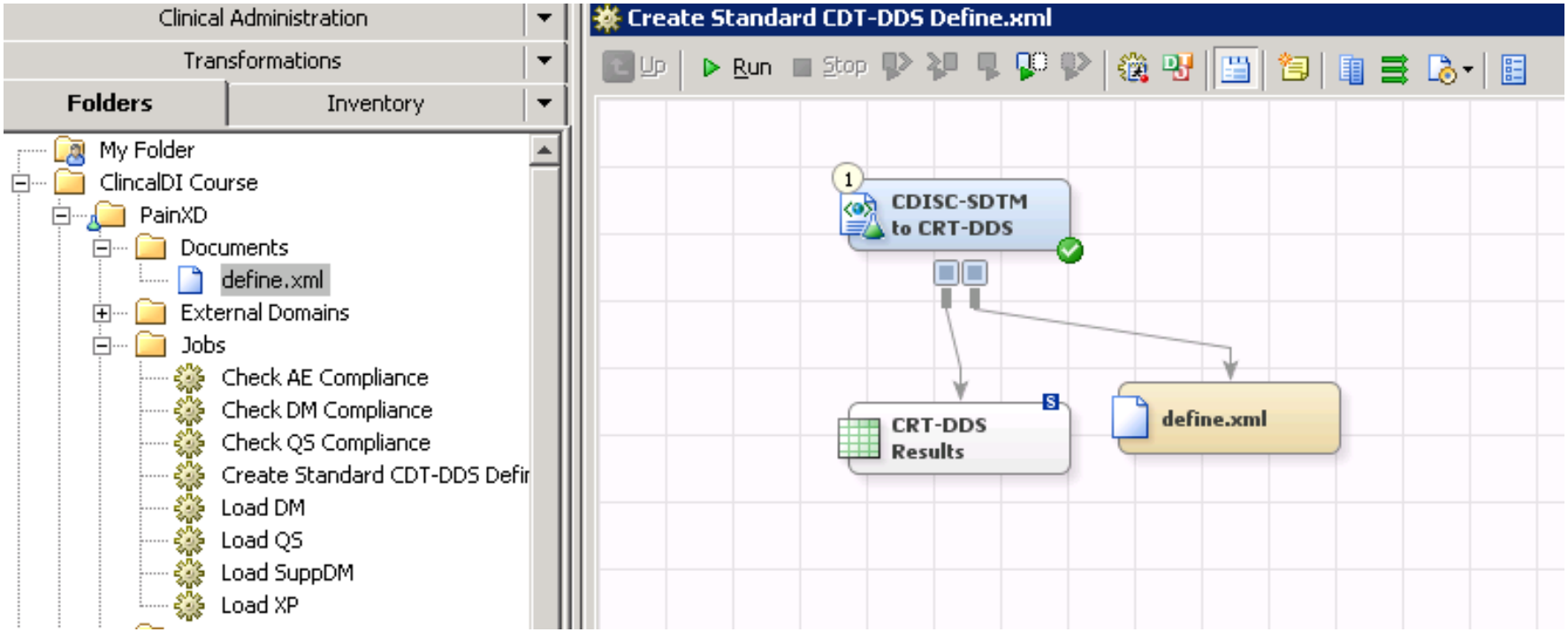
Create CRT-DDS / Define.xml



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Navigate in the Define.xml file

Datasets for Study PainXD

Dataset	Description	Structure	Purpose	Keys	Location
DM	Demographics	Special Purpose Domains - One record per subject	Tabulation	STUDYID USUBJID	
QS	Questionnaires	Findings - One record per questionnaire per question per time point per visit per subject	Tabulation	STUDYID USUBJID QSTESTCD QSCAT VISITNUM	
SUPPQUAL	DM Supplemental Qualifiers	Special Purpose Datasets - One record per IDVAR, IDVARVAL, and QNAM value per subject	Tabulation	STUDYID RDOMAIN USUBJID QNAM	
XP	Pain Diary	FINDINGS -	Tabulation	STUDYID USUBJID XPSEQ XPTESTCD XPDTC	

Go t

Dat

Demographics Dataset (DM)

Variable	Label	Type	Controlled Terms or Format	Origin	Role	Comment
STUDYID	Study Identifier	text			Identifier	
DOMAIN	Domain Abbreviation	text			Identifier	
USUBJID	Unique Subject Identifier	text				
SUBJID	Subject Identifier for the Study	text				
RFSTDTC	Subject Reference Start Date/Time	text				
RFENDTC	Subject Reference End Date/Time	text				
SITEID	Study Site Identifier	text				
INVID	Investigator Identifier	text				
INVNAM	Investigator Name	text				
BRTHDTC	Date/Time of Birth	text				
AGE	Age	float				
AGEU	Age Units	text	AGEU			
SEX	Sex	text	SEX			
RACE	Race	text	RACE		RecordQualifier	

RACE, Reference Name (RACE)	
AMERICAN INDIAN OR ALASKA NATIVE	AMERICAN INDIAN OR ALASKA NATIVE
ASIAN	ASIAN
BLACK OR AFRICAN AMERICAN	BLACK OR AFRICAN AMERICAN
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER
WHITE	WHITE

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Introduction to…

JMP Clinical

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Explore the Hidden Patterns in Clinical Trials Data with JMP Clinical

- JMP Clinical creates analytical reports on CDISC data
- SAS® Analytics running behind a JMP® user interface
- Interactive JMP® features for dynamics analysis
- An intuitive dashboard makes it easy to get started
- Examine patient profiles from many perspectives
- Apply trusted statistical methods with flexible options
- Use sophisticated pattern-discovery capabilities

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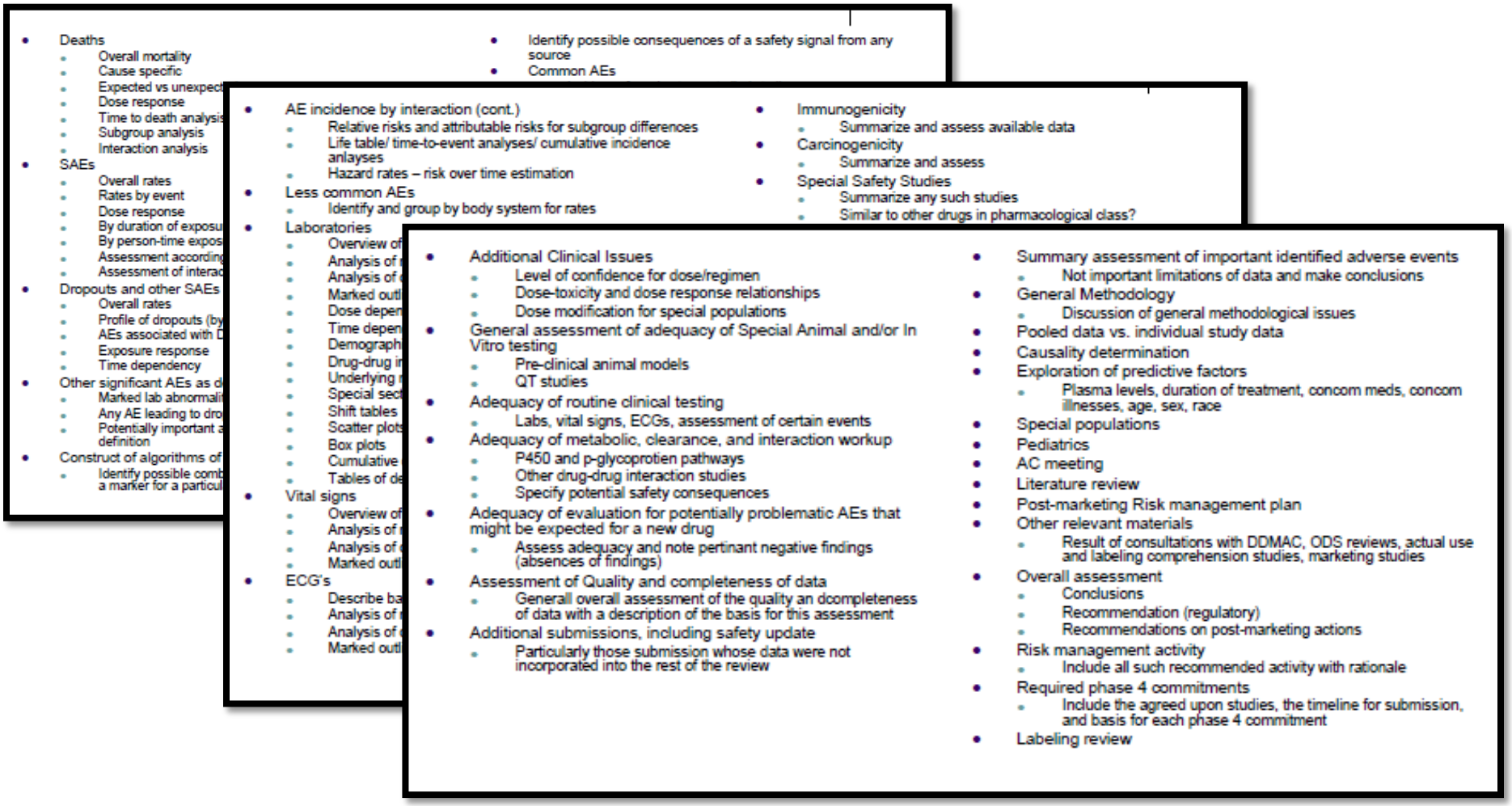
From the ICH E3 reviewer guidance, what types of reports the FDA looks at



- Deaths
  - Overall mortality
  - Cause specific
  - Expected vs unexpect
  - Dose response
  - Time to death analysis
  - Subgroup analysis
  - Interaction analysis
- SAEs
  - Overall rates
  - Rates by event
  - Dose response
  - By duration of exposu
  - By person-time expos
  - Assessment according
  - Assessment of interac
- Dropouts and other SAEs
  - Overall rates
  - Profile of dropouts (by
  - AEs associated with D
  - Exposure response
  - Time dependency
- Other significant AEs as d
  - Marked lab abnormali
  - Any AE leading to dro
  - Potentially important a definition
- Construct of algorithms of
  - Identify possible comb a marker for a particul
- Identify possible consequences of a safety signal from any source
- Common AEs
- AE incidence by interaction (cont.)
  - Relative risks and attributable risks for subgroup differences
  - Life table/ time-to-event analyses/ cumulative incidence anlayses
  - Hazard rates – risk over time estimation
- Less common AEs
  - Identify and group by body system for rates
- Laboratories
  - Overview of
  - Analysis of r
  - Analysis of c
  - Marked outl
  - Dose depen
  - Time depen
  - Demograph
  - Drug-drug ir
  - Underlying r
  - Special sect
  - Shift tables
  - Scatter plots
  - Box plots
  - Cumulative
  - Tables of de
- Vital signs
  - Overview of
  - Analysis of r
  - Analysis of c
  - Marked outl
- ECG's
  - Describe ba
  - Analysis of r
  - Analysis of c
  - Marked outl
- Immunogenicity
  - Summarize and assess available data
- Carcinogenicity
  - Summarize and assess
- Special Safety Studies
  - Summarize any such studies
  - Similar to other drugs in pharmacological class?
- Additional Clinical Issues
  - Level of confidence for dose/regimen
  - Dose-toxicity and dose response relationships
  - Dose modification for special populations
- General assessment of adequacy of Special Animal and/or In Vitro testing
  - Pre-clinical animal models
  - QT studies
- Adequacy of routine clinical testing
  - Labs, vital signs, ECGs, assessment of certain events
- Adequacy of metabolic, clearance, and interaction workup
  - P450 and p-glycoprotien pathways
  - Other drug-drug interaction studies
  - Specify potential safety consequences
- Adequacy of evaluation for potentially problematic AEs that might be expected for a new drug
  - Assess adequacy and note pertinant negative findings (absences of findings)
- Assessment of Quality and completeness of data
  - Generall overall assessment of the quality an dcompleteness of data with a description of the basis for this assessment
- Additional submissions, including safety update
  - Particularly those submission whose data were not incorporated into the rest of the review
- Summary assessment of important identified adverse events
  - Not important limitations of data and make conclusions
- General Methodology
  - Discussion of general methodological issues
- Pooled data vs. individual study data
- Causality determination
- Exploration of predictive factors
  - Plasma levels, duration of treatment, concom meds, concom illnesses, age, sex, race
- Special populations
- Pediatrics
- AC meeting
- Literature review
- Post-marketing Risk management plan
- Other relevant materials
  - Result of consultations with DDMAC, ODS reviews, actual use and labeling comprehension studies, marketing studies
- Overall assessment
  - Conclusions
  - Recommendation (regulatory)
  - Recommendations on post-marketing actions
- Risk management activity
  - Include all such recommended activity with rationale
- Required phase 4 commitments
  - Include the agreed upon studies, the timeline for submission, and basis for each phase 4 commitment
- Labeling review

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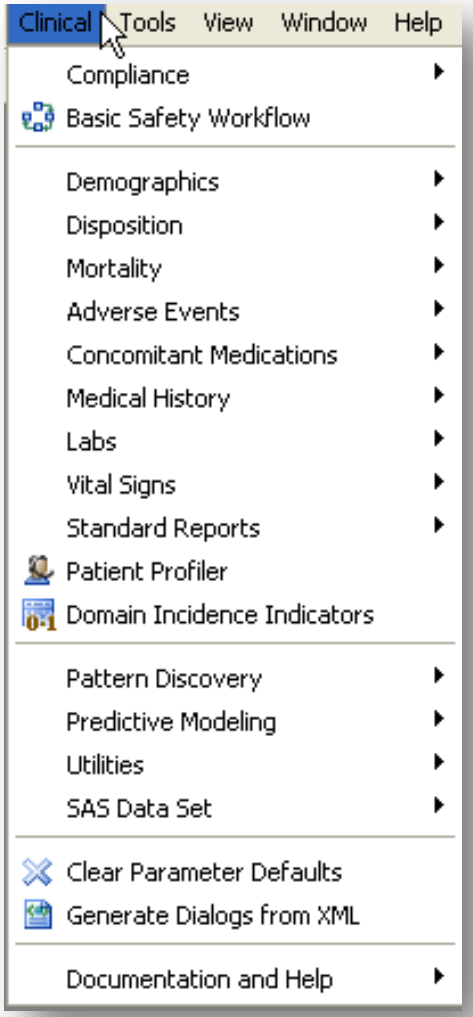
JMP Clinical Process Flow



The order of this menu is important. The order follows the order layout for the FDA reviewer guidance

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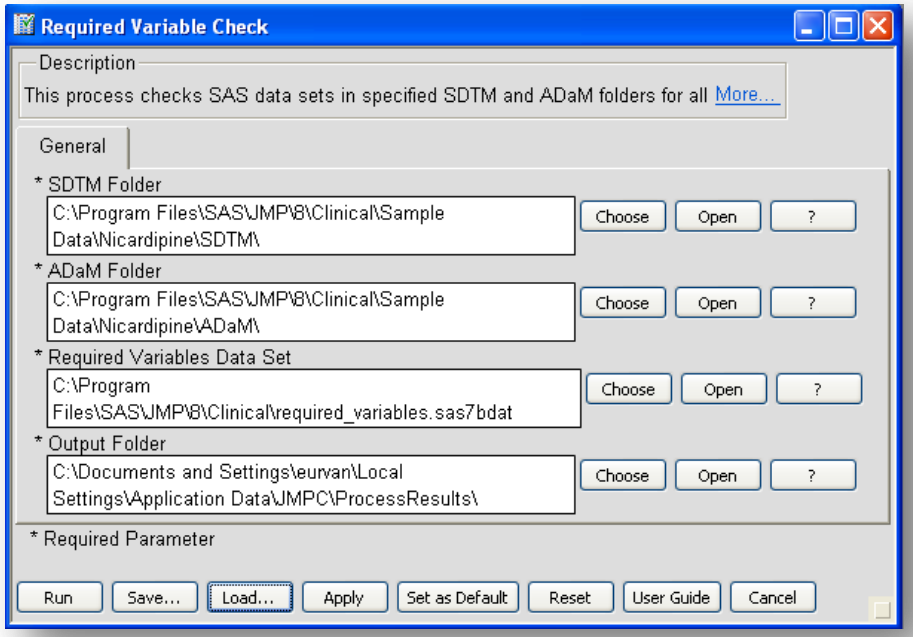
JMP Clinical Ease of Use



- *Dialogs are organised such as only the SDTM and ADaM folders needs to be defined*
- *Once an application has ran, the next dialogs will automatically populate the same settings (same folder definition)*
- *BENEFITS*
  - *Easy to use*
  - *Reduced learning curve*
  - *No programming requirements*

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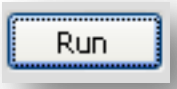
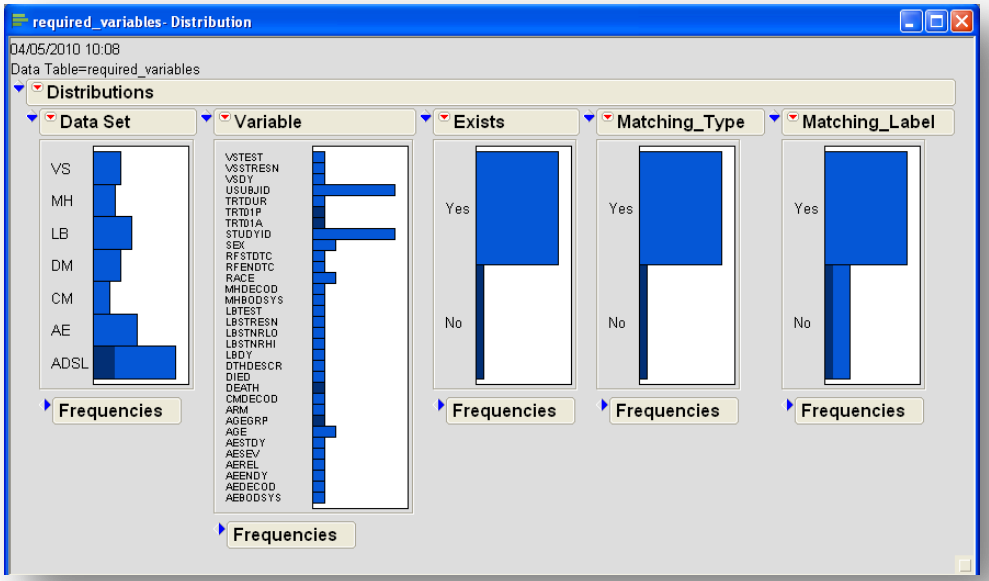
JMP Clinical Output Files



_processinfo.sas7bdat	17 KB	SAS Data Set
ProjectLog_Test.txt	1 KB	Text Document
required_variables.sas7bdat	17 KB	SAS Data Set
RequiredVariableCheck Script.jsl	1 KB	JMP Script
RequiredVariableCheck.log	14 KB	SAS.OutputLog.701
RequiredVariableCheck__required_variables.sas	3 KB	SAS System Program
sasclean.jsl	5 KB	JMP Script



- *SAS data sets*
- *ProcessInfo files to track what has been performed, when it has been performed, how much time this process ran*
- *SAS logs to track SAS runs*
- *SAS program with the settings of the application*
- *JSL scripts generating the dynamic and interactive graphics*
- *BENEFITS*
  - *All the SAS files that is needed for the submission*

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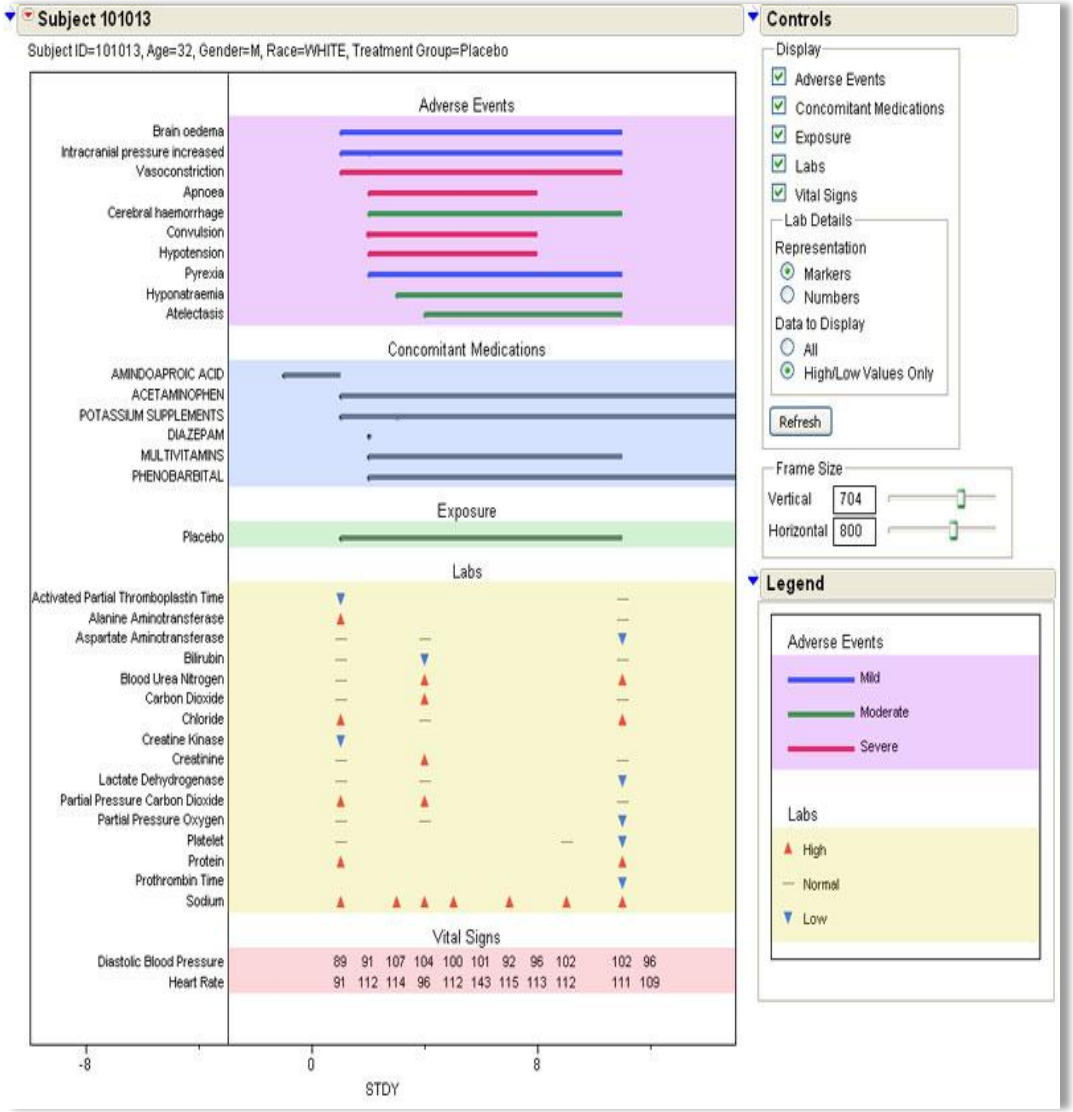
JMP Clinical Patient Profiles



- *Create interactive patient profiles instantly for any individual or group of subjects*
- *You can also select from patient details – adverse events, medical history, vital signs, etc. – to customize patient profiles*
- *BENEFITS*
  - *Easy to use*
  - *No programming requirements*
  - *Create customized patient profile templates to select display of relevant safety domains.*
  - *See the medical history for any subject*

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Demonstration

JMP Clinical 2.1

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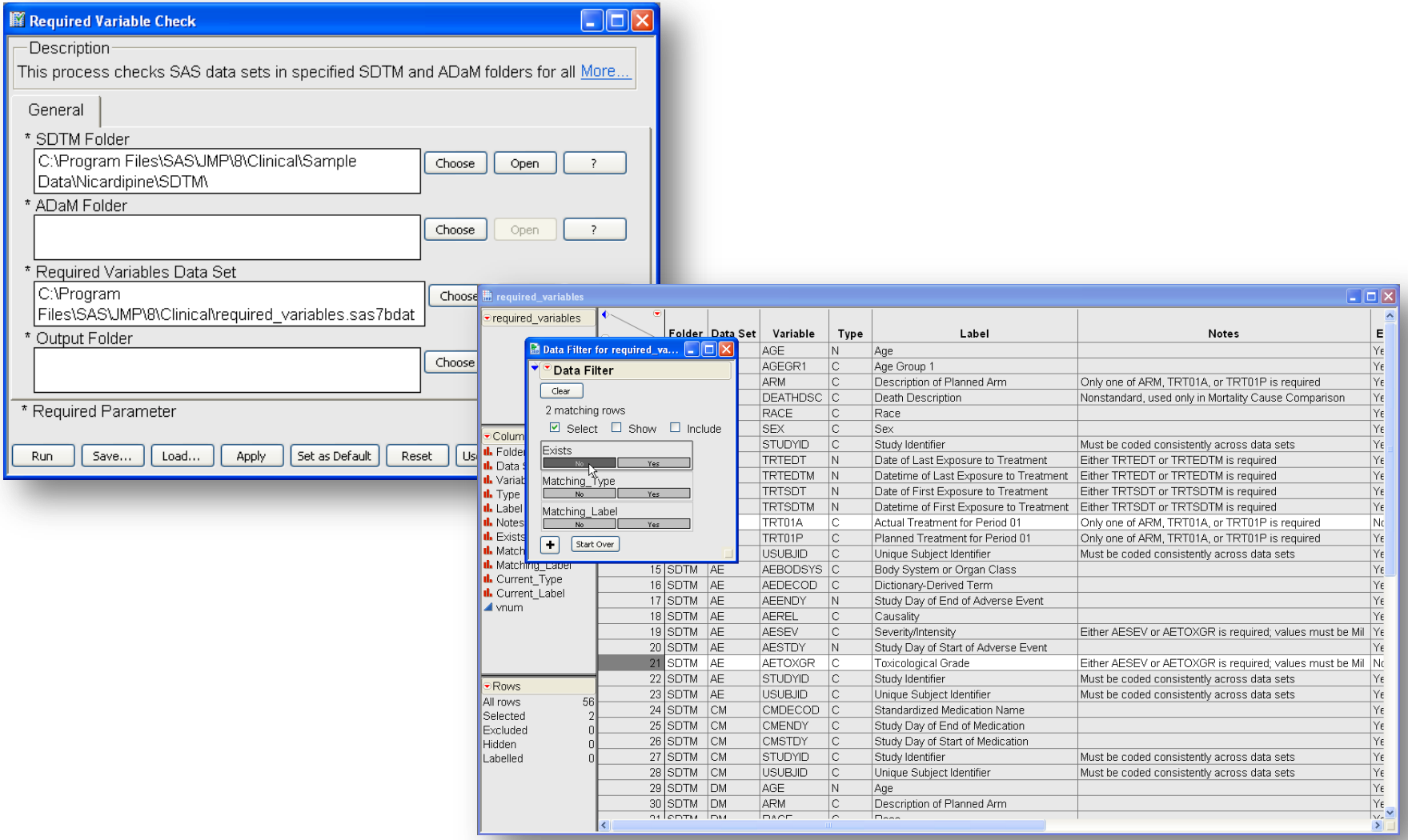
Verify CDISC Data Consistency



	Folder	Data Set	Variable	Type	Label	Notes
			AGE	N	Age	
			AGEGR1	C	Age Group 1	
			ARM	C	Description of Planned Arm	Only one of ARM, TRT01A, or TRT01P is required
			DEATHDSC	C	Death Description	Nonstandard, used only in Mortality Cause Comparison
			RACE	C	Race	
			SEX	C	Sex	
			STUDYID	C	Study Identifier	Must be coded consistently across data sets
			TRTEDT	N	Date of Last Exposure to Treatment	Either TRTEDT or TRTEDTM is required
			TRTEDTM	N	Datetime of Last Exposure to Treatment	Either TRTEDT or TRTEDTM is required
			TRTSDT	N	Date of First Exposure to Treatment	Either TRTSDT or TRTSDTM is required
			TRTSDTM	N	Datetime of First Exposure to Treatment	Either TRTSDT or TRTSDTM is required
			TRT01A	C	Actual Treatment for Period 01	Only one of ARM, TRT01A, or TRT01P is required
			TRT01P	C	Planned Treatment for Period 01	Only one of ARM, TRT01A, or TRT01P is required
			USUBJID	C	Unique Subject Identifier	Must be coded consistently across data sets
15	SDTM	AE	AEBODSYS	C	Body System or Organ Class	
16	SDTM	AE	AEDECOD	C	Dictionary-Derived Term	
17	SDTM	AE	AEENDY	N	Study Day of End of Adverse Event	
18	SDTM	AE	AEREL	C	Causality	
19	SDTM	AE	AESEV	C	Severity/Intensity	Either AESEV or AETOXGR is required; values must be Mil
20	SDTM	AE	AESTDY	N	Study Day of Start of Adverse Event	
21	SDTM	AE	AETOXGR	C	Toxicological Grade	Either AESEV or AETOXGR is required; values must be Mil
22	SDTM	AE	STUDYID	C	Study Identifier	Must be coded consistently across data sets
23	SDTM	AE	USUBJID	C	Unique Subject Identifier	Must be coded consistently across data sets
24	SDTM	CM	CMDECOD	C	Standardized Medication Name	
25	SDTM	CM	CMENDY	C	Study Day of End of Medication	
26	SDTM	CM	CMSTDY	C	Study Day of Start of Medication	
27	SDTM	CM	STUDYID	C	Study Identifier	Must be coded consistently across data sets
28	SDTM	CM	USUBJID	C	Unique Subject Identifier	Must be coded consistently across data sets
29	SDTM	DM	AGE	N	Age	
30	SDTM	DM	ARM	C	Description of Planned Arm	

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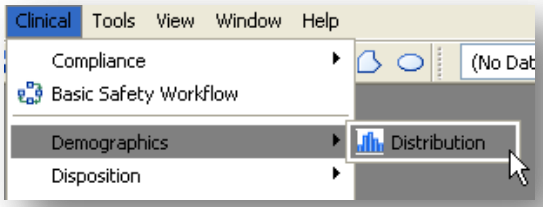
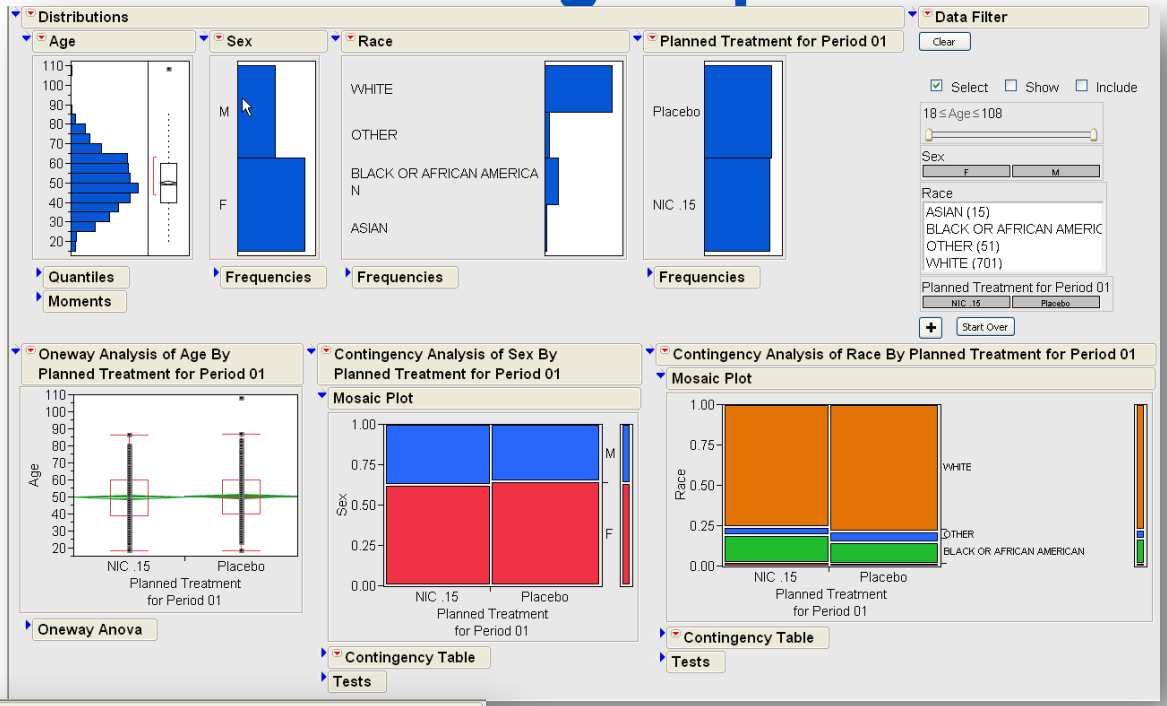
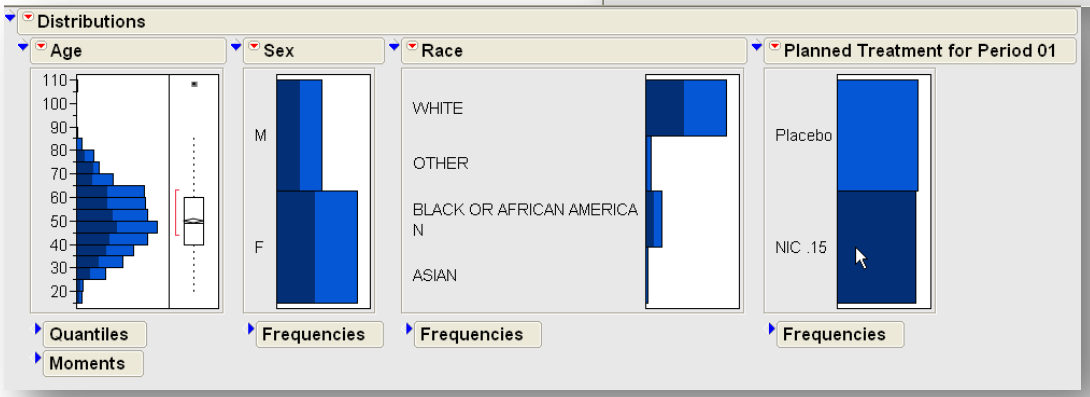
Relationships between demographic characteristics and treatment group







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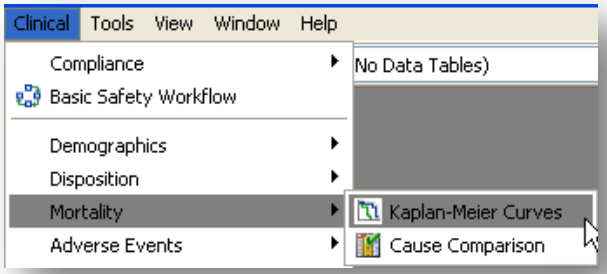
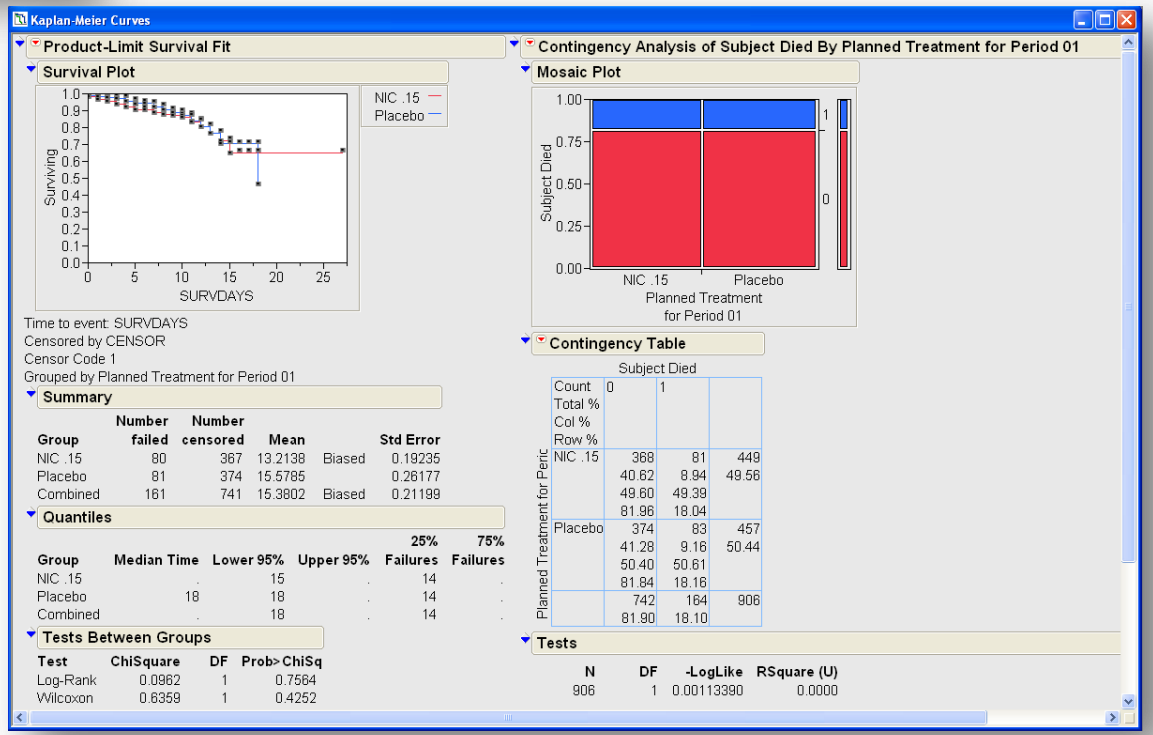
Visualize Relationships between Mortality Rate and treatment groups





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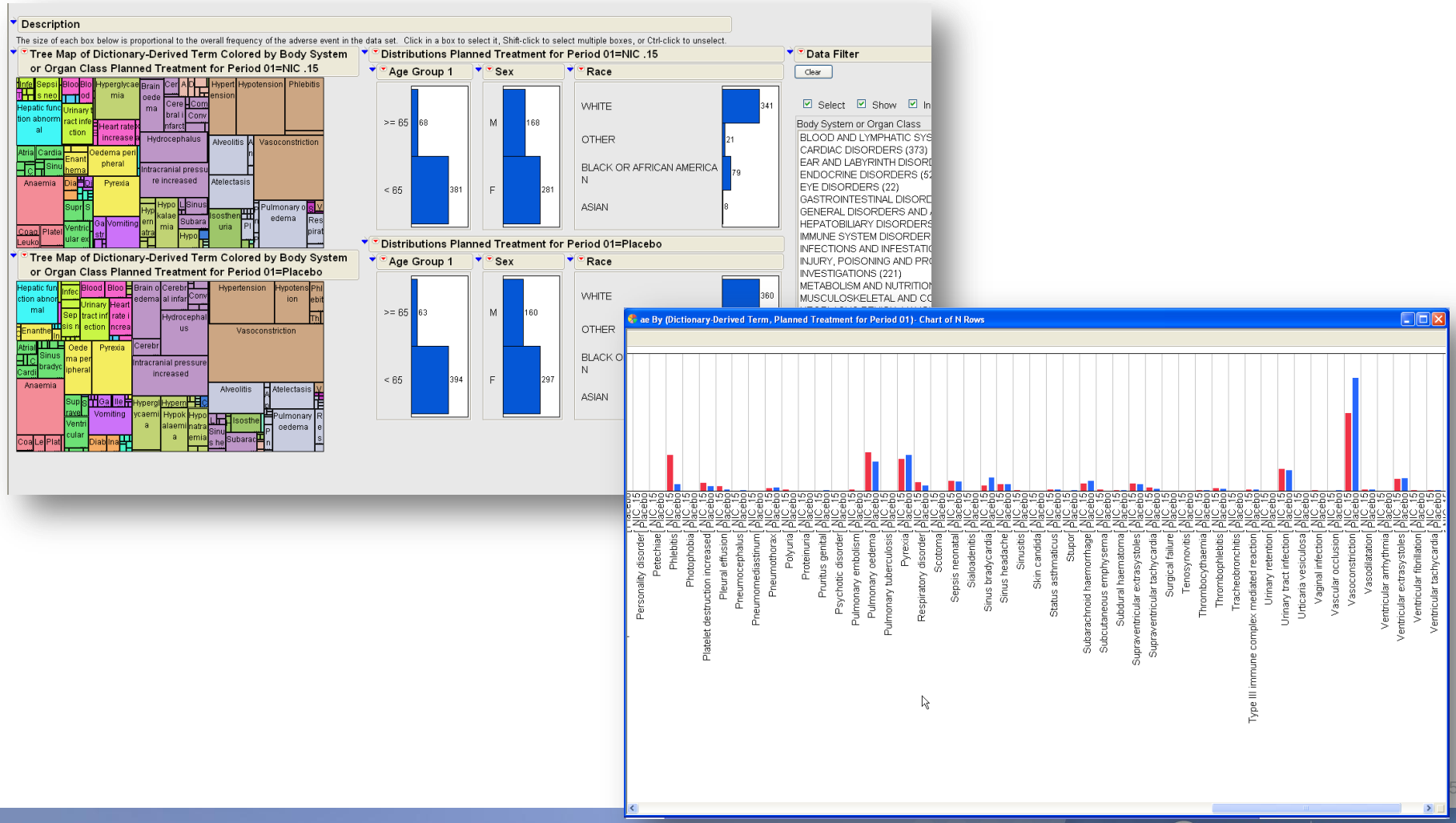
Visualize Frequency Rates of Adverse Events and Correlation with Demographic Characteristics



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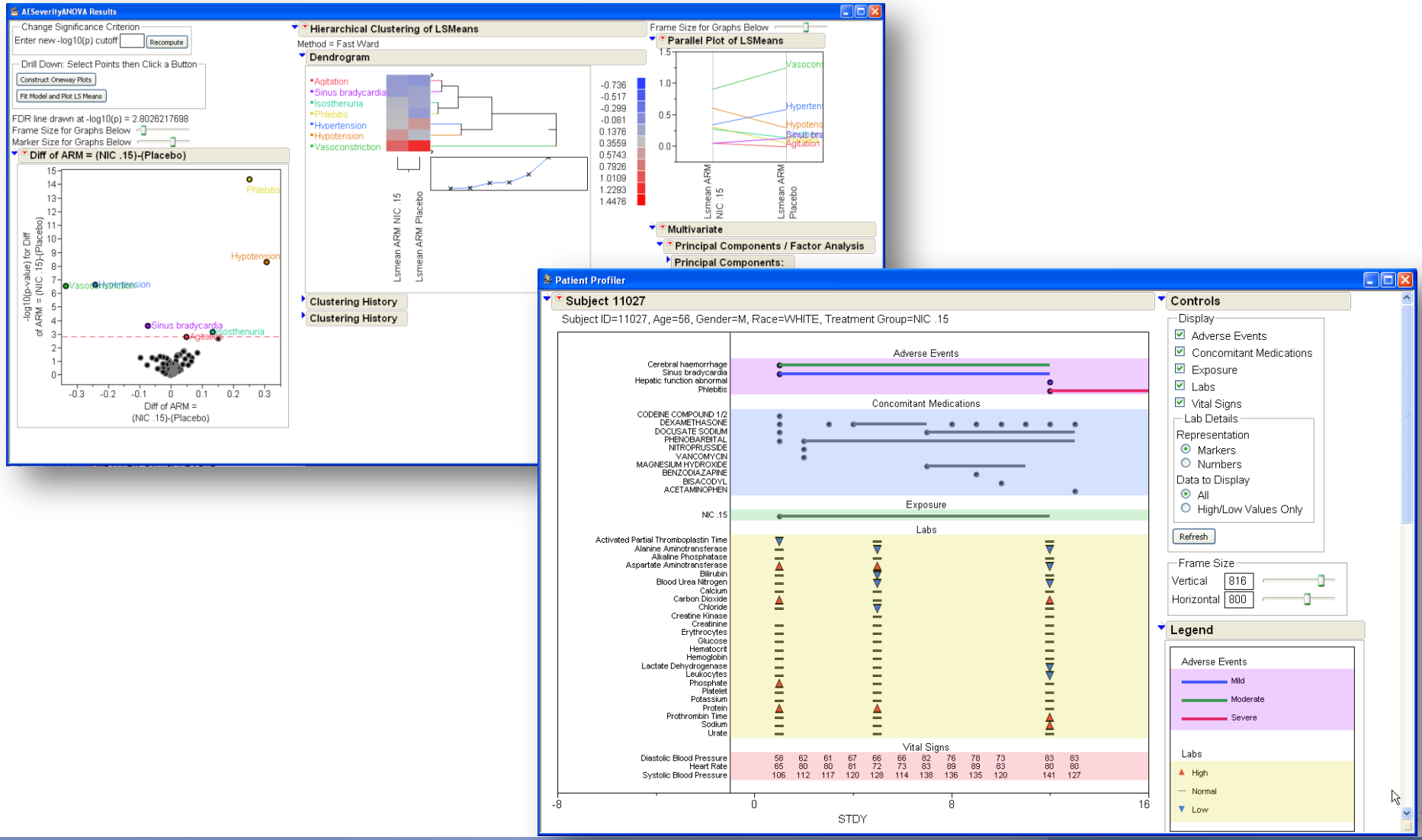
Visualise Adverse Events Mixed Model Analysis Reports linked to Patient Profiler



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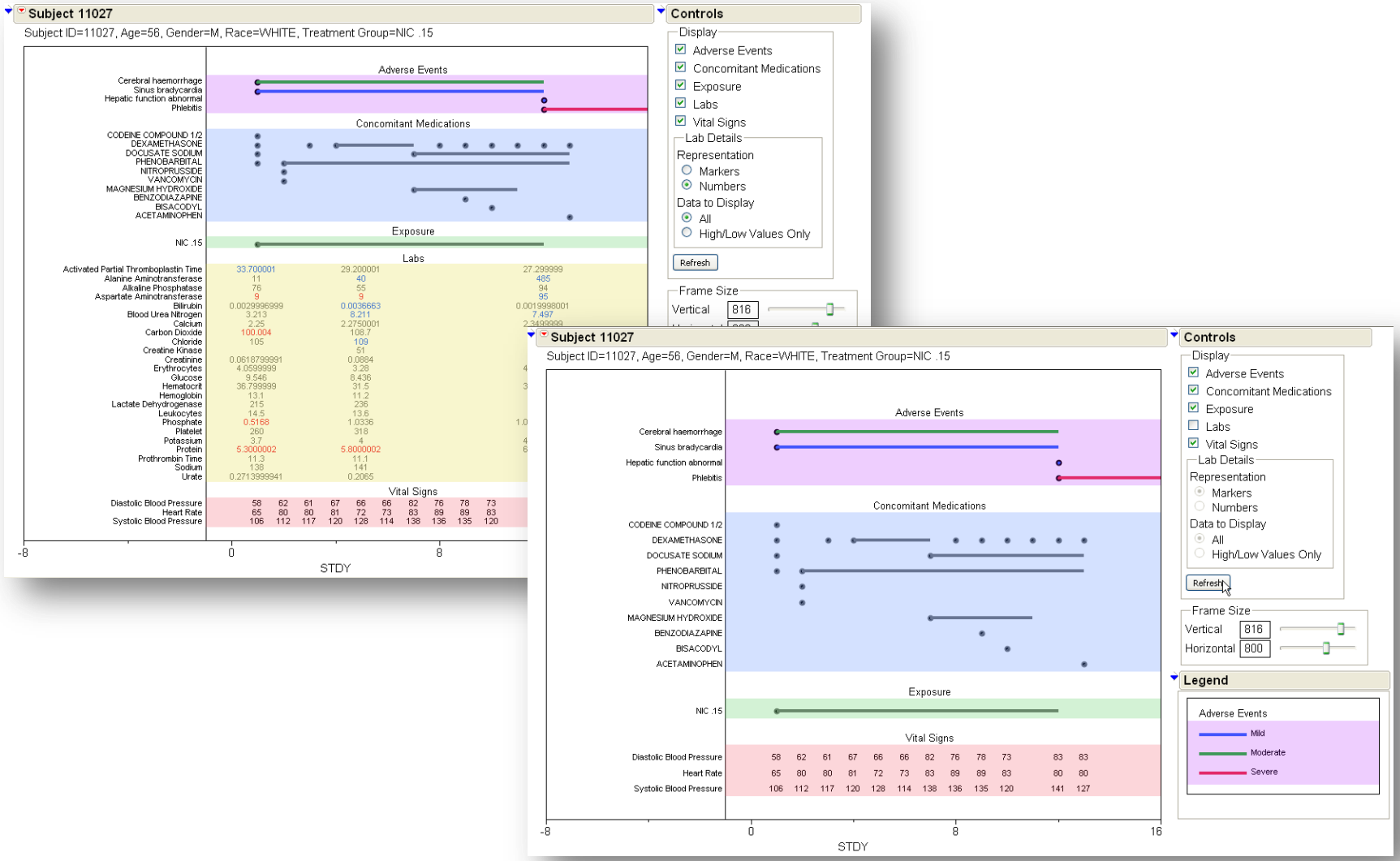
Patient Profiler



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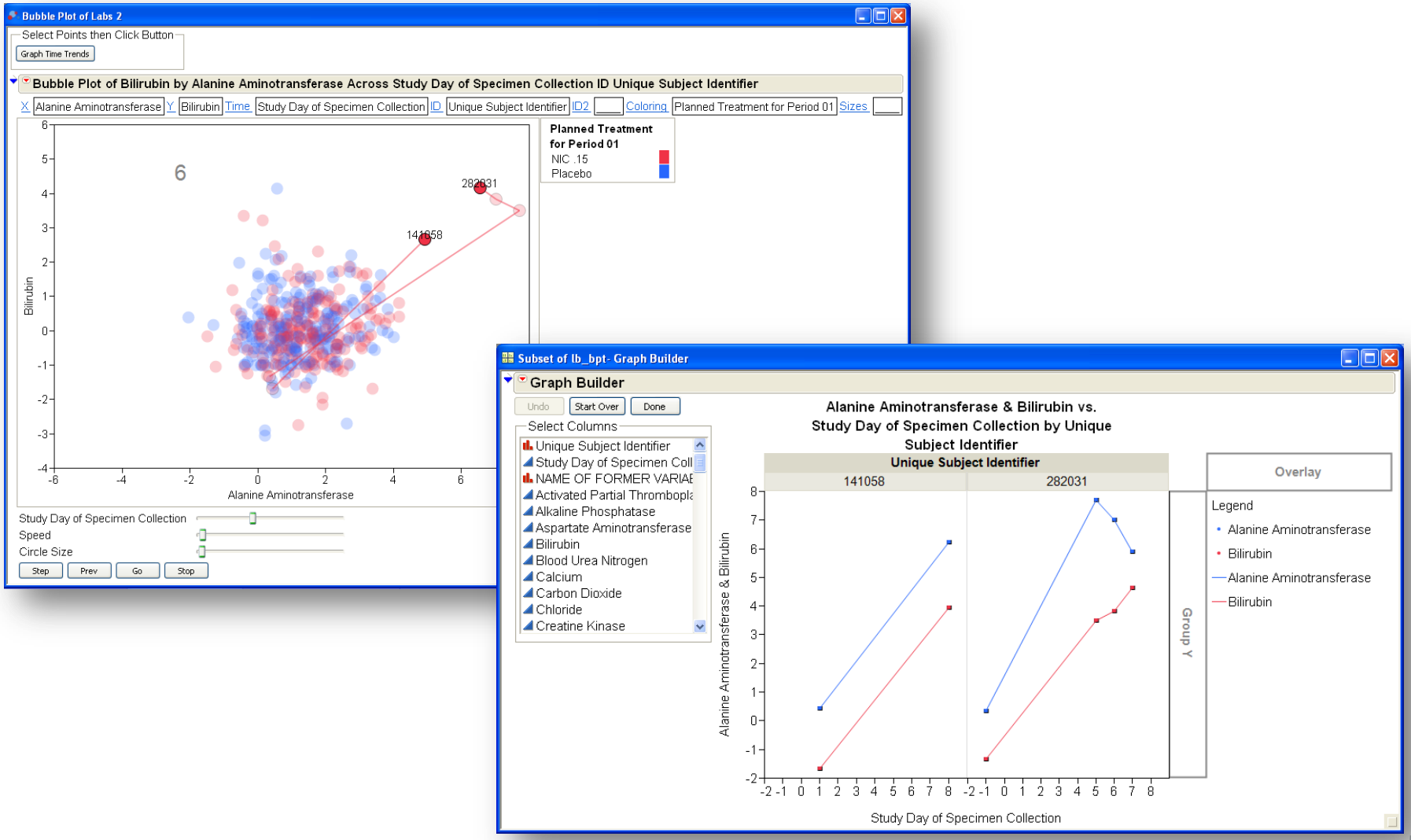
Monitor Animated Patients Laboratory Tests



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