

**SAS Drug Development in action:
efficient standards libraries and study management
modules together called CDmation.**

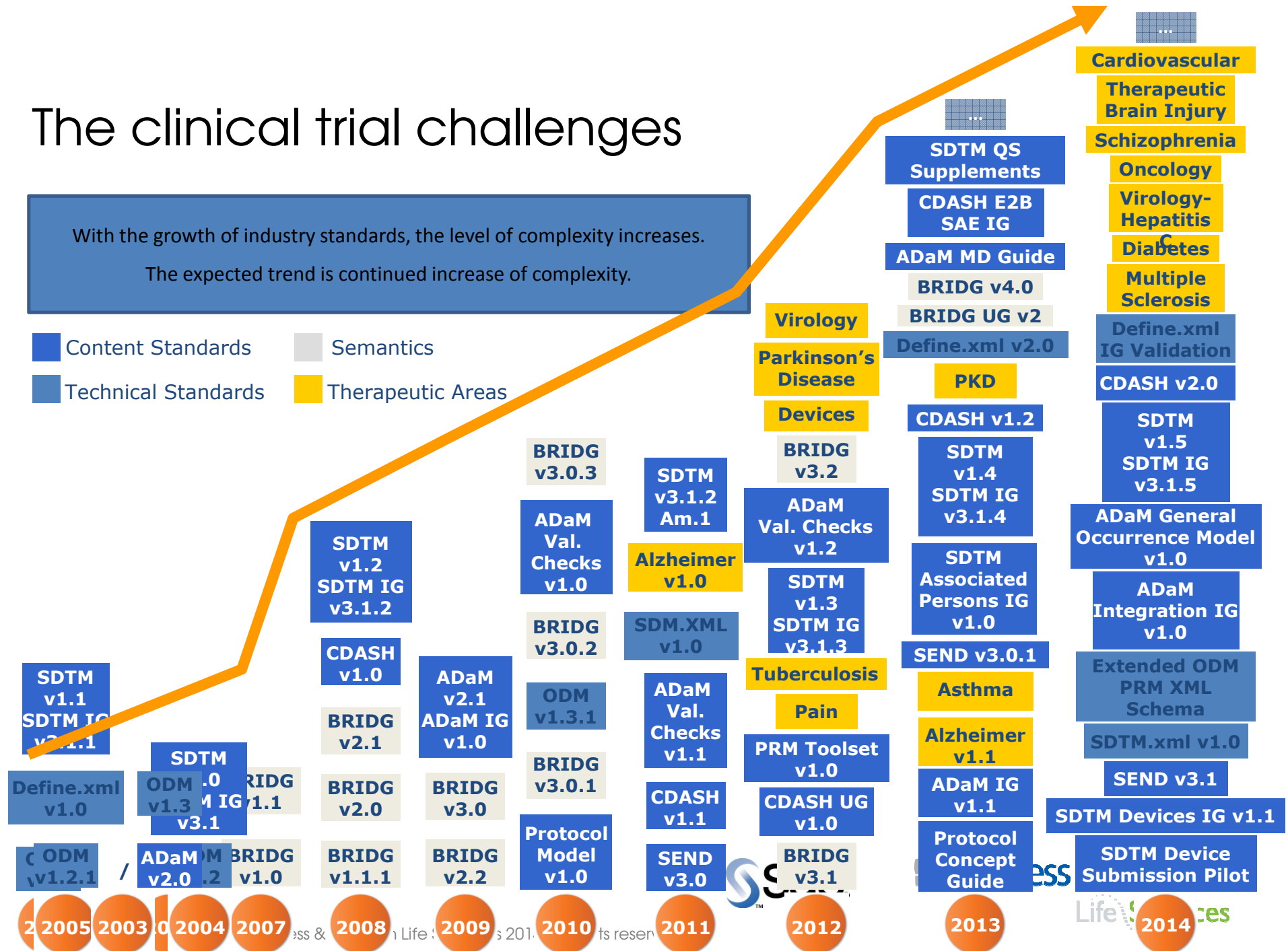
Mark Lambrecht (SAS)

Peter Van Reusel (Business & Decision Life Sciences)

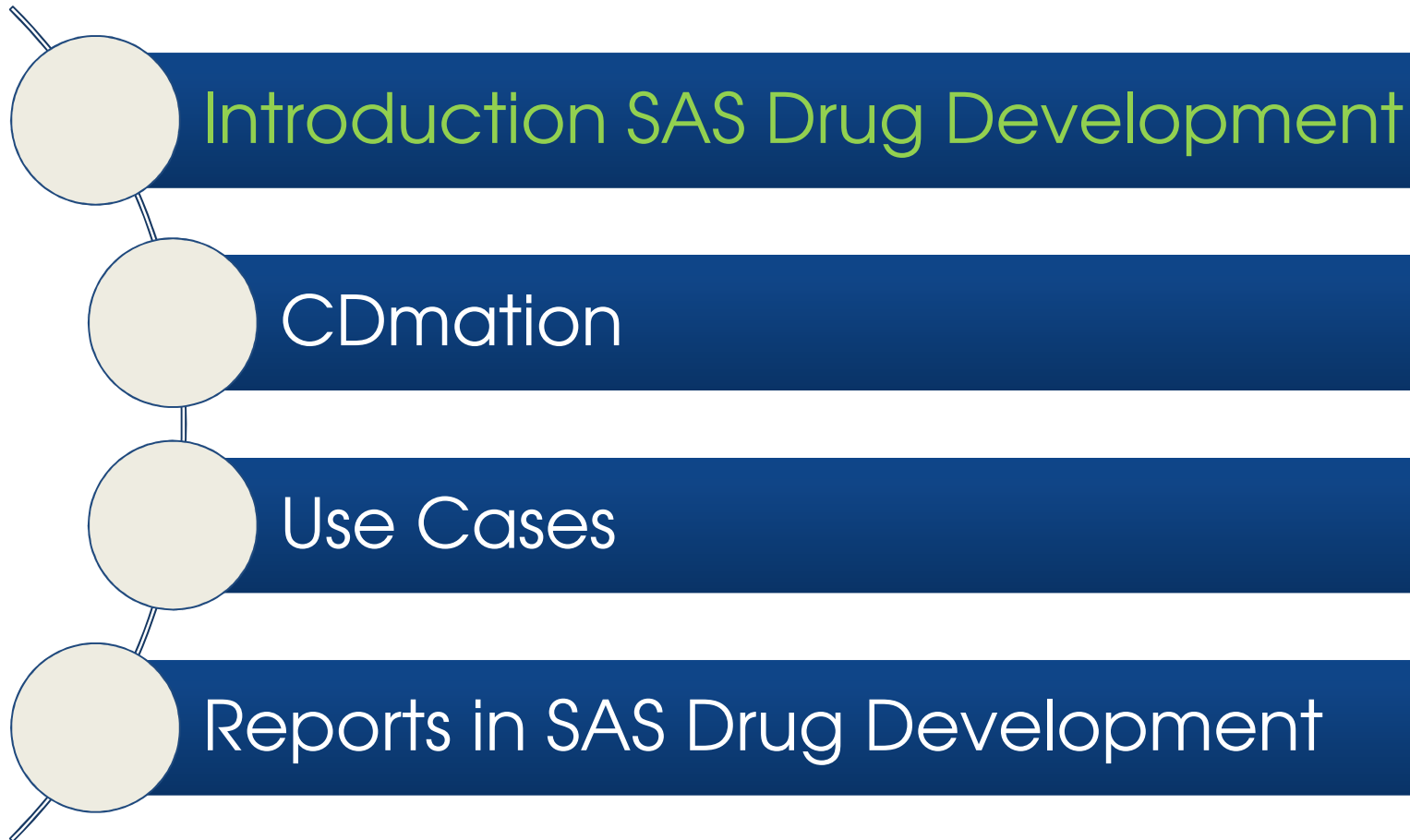


With the growth of industry standards, the level of complexity increases.
The expected trend is continued increase of complexity.

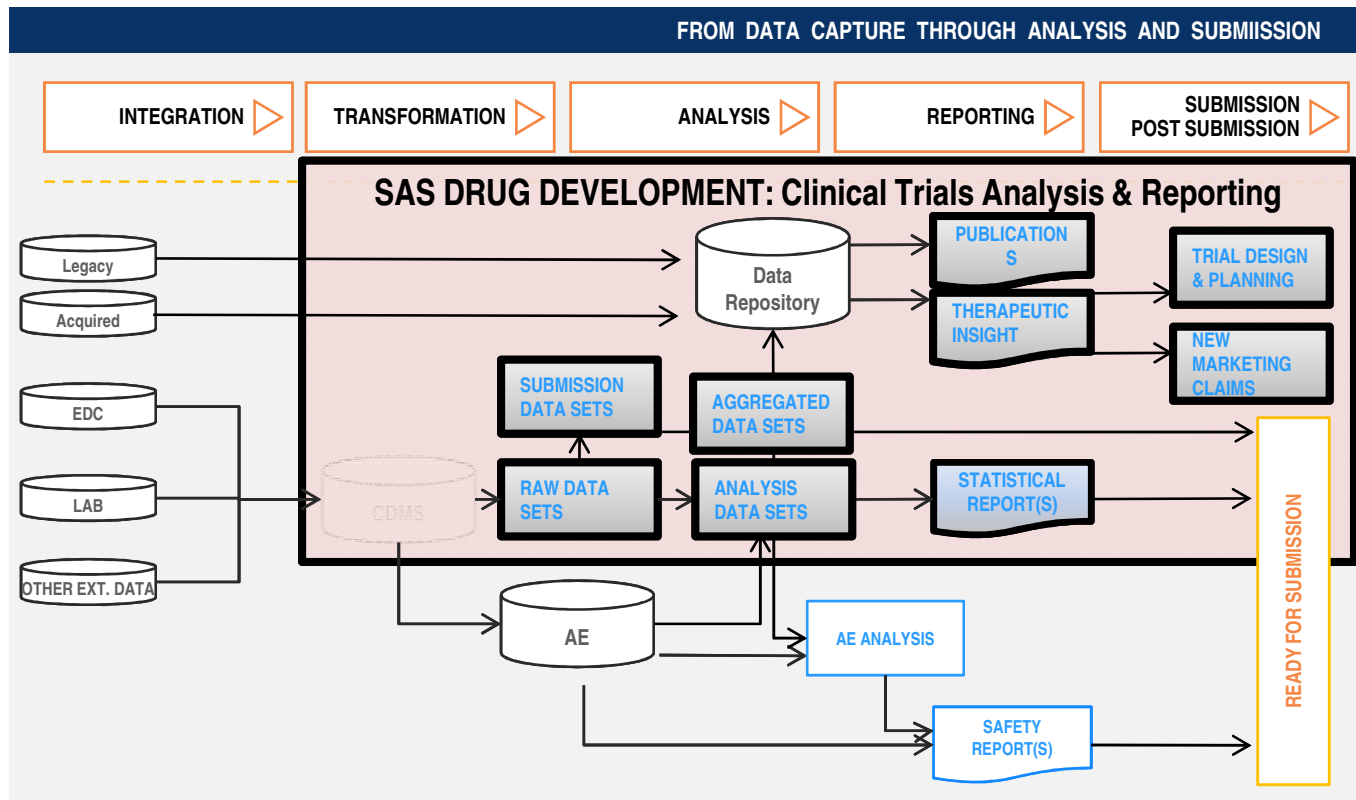
The expected trend is continued increase of complexity.



Agenda



Clinical Trials Process

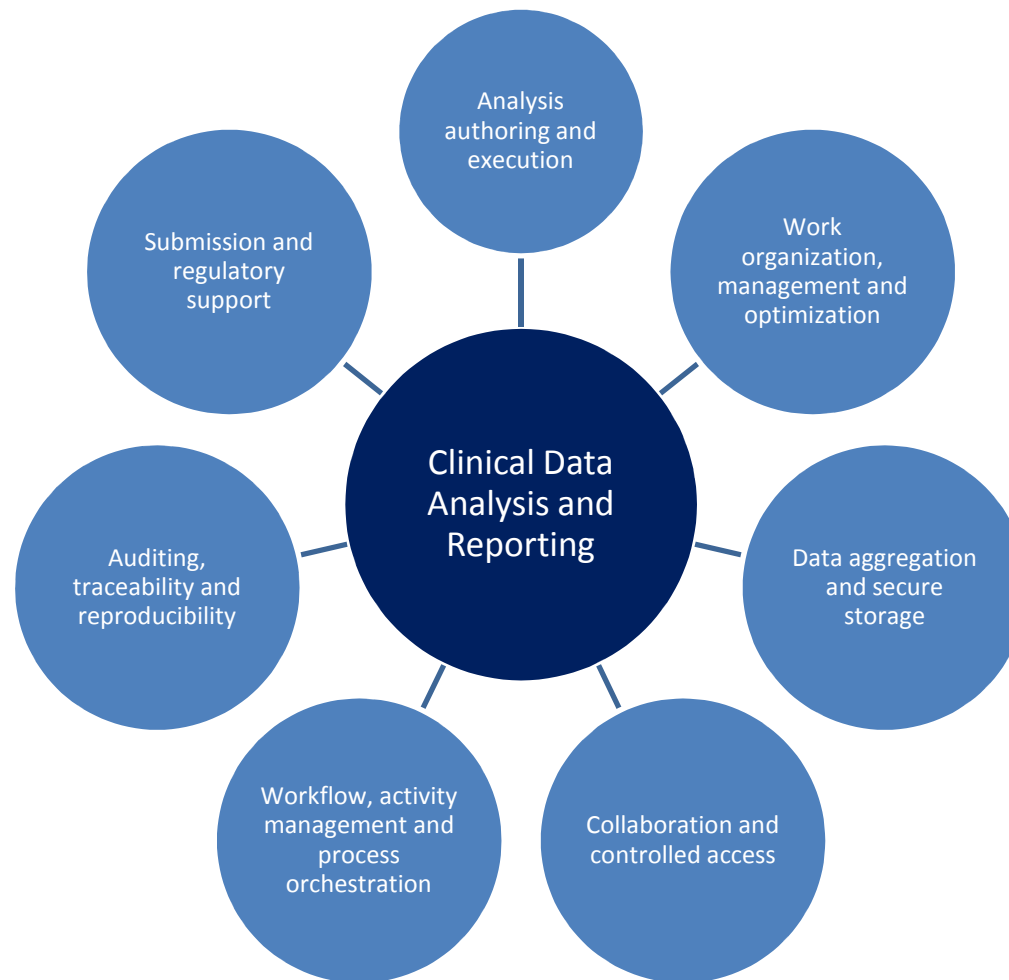


SAS and the Next Generation of Clinical Research

Collaboration and Access	Confidence and Control	Process Improvements	Advanced Analytics
• Access-anywhere web interface • User, team and role-based access • Messaging and alerts • Shared libraries	• Compliant, regulated environment • Activity traceability • Transparency • Reproducibility	• Workflow support and process orchestration • eProtocol, EDC and eSubmission integration • Automated work assignments and transitions	• Scientific analytics • Business analytics • Data exploration • Data visualization



Clinical Data Analysis and Reporting Business Needs



Needs for a metadata management solution versus SDD

OK

- Robust platform to cover other parts of clinical data management and statistics
- Need to store data
- Need to have several workflows
- Capability to execute SAS code
- Traceability, security and audit
- Reporting capabilities



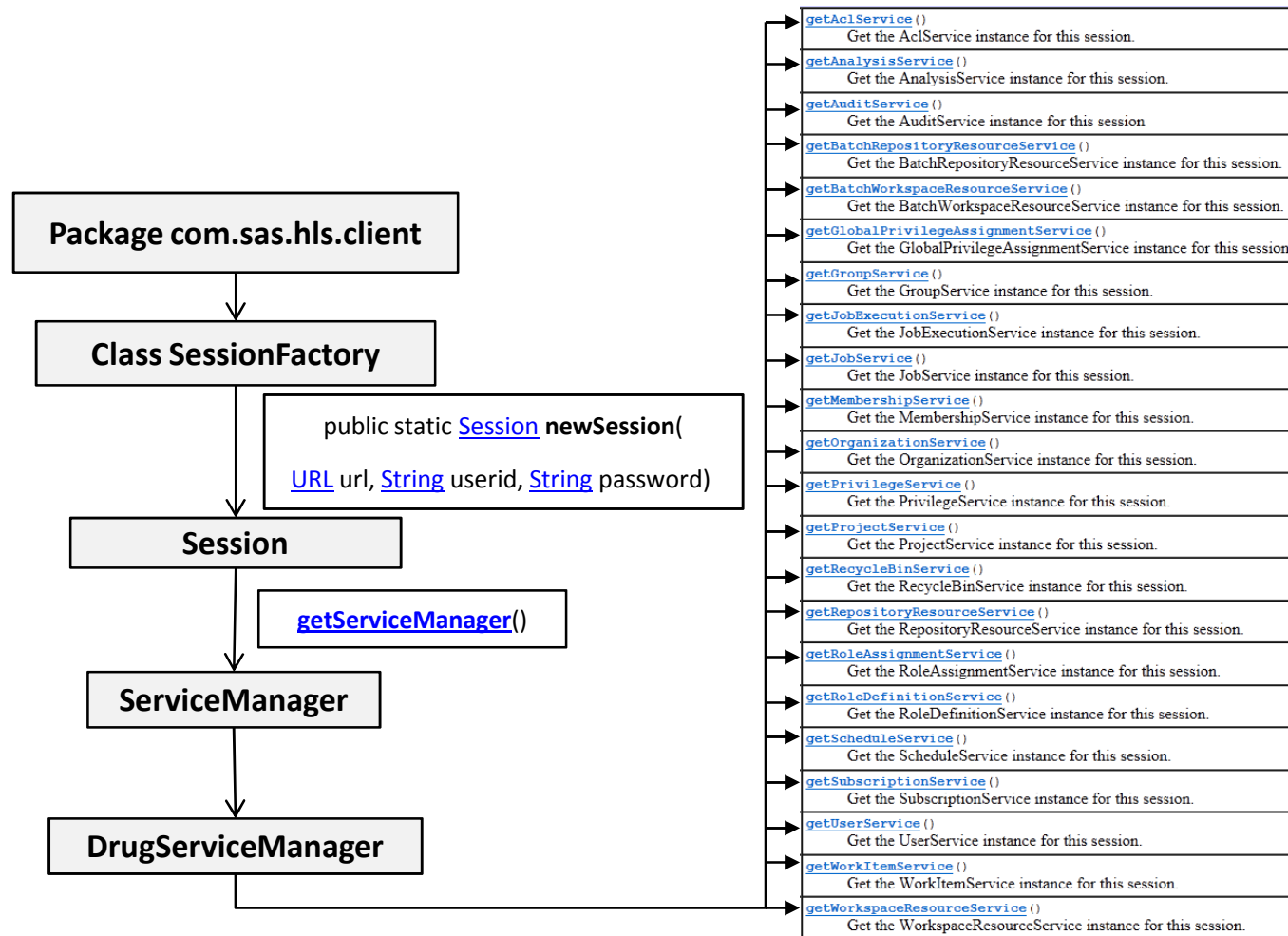
But...

- *UI for granular data standards management*
- *Study specification process*
- *Study validation process*

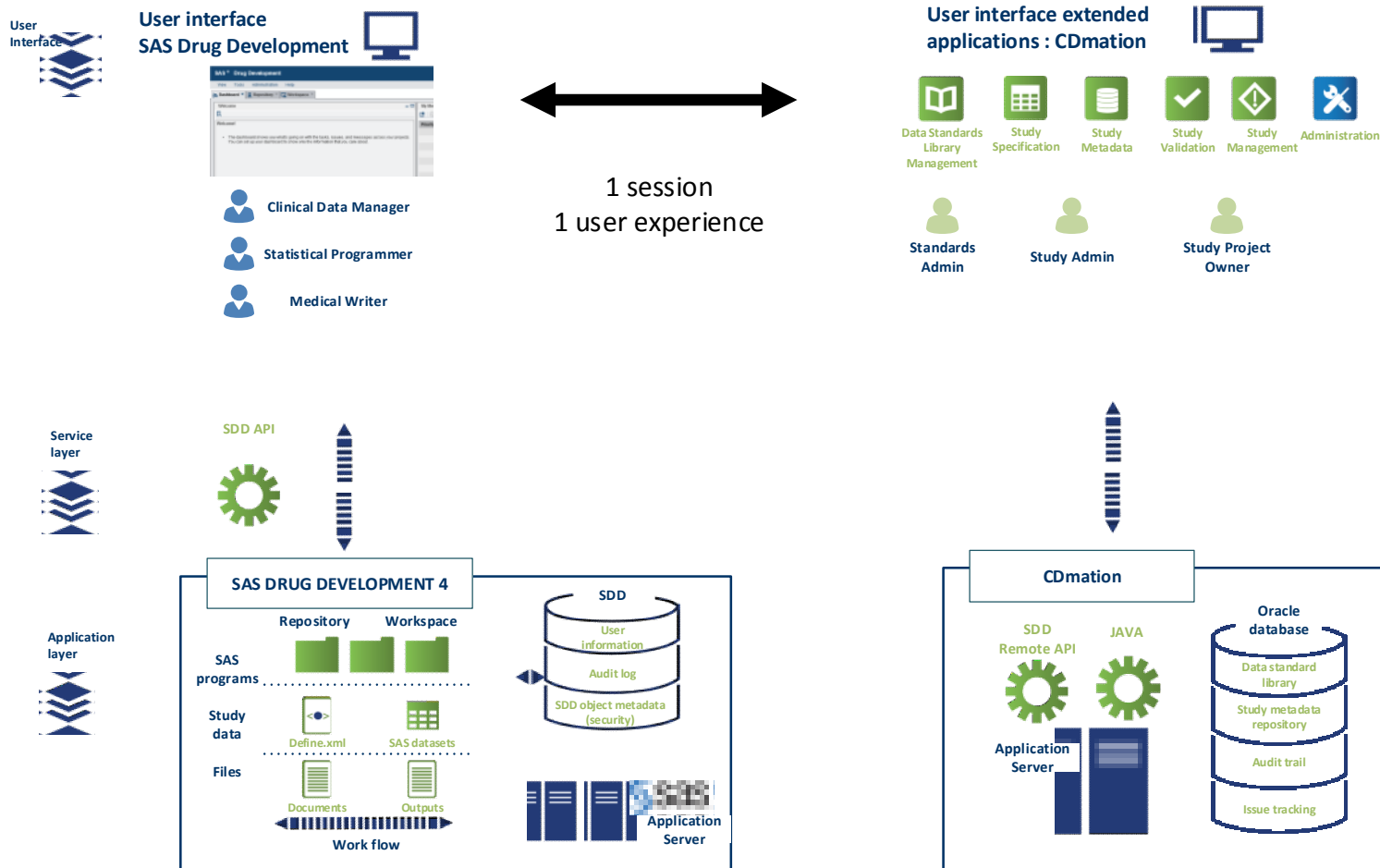


Come to the rescue... Robust SDD Application Programming Interface

SDD 4.X JAVA API OVERVIEW



SDD = extensible and modular

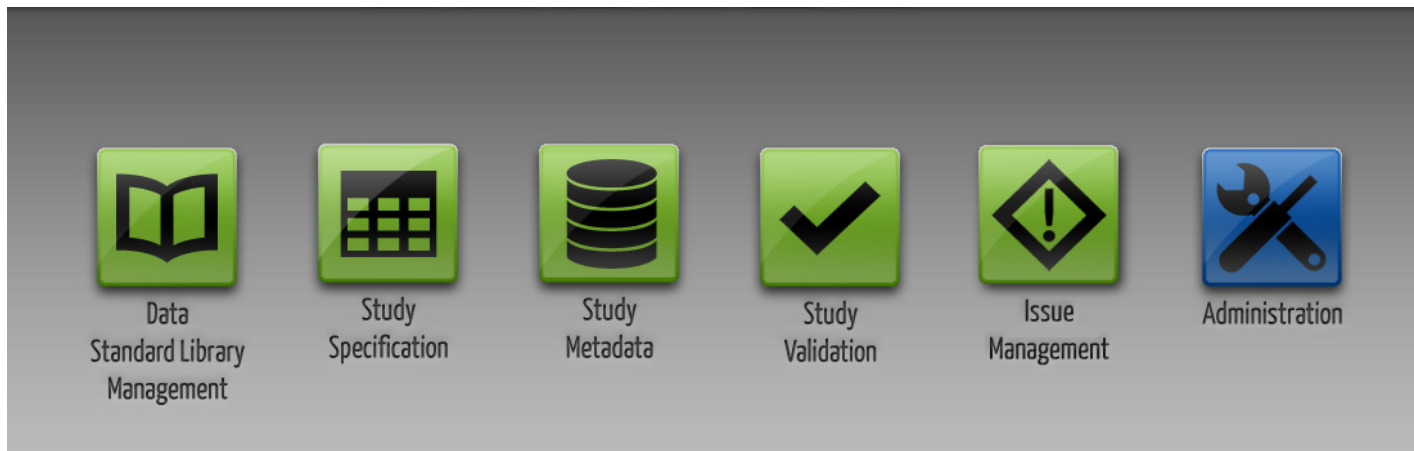


Agenda

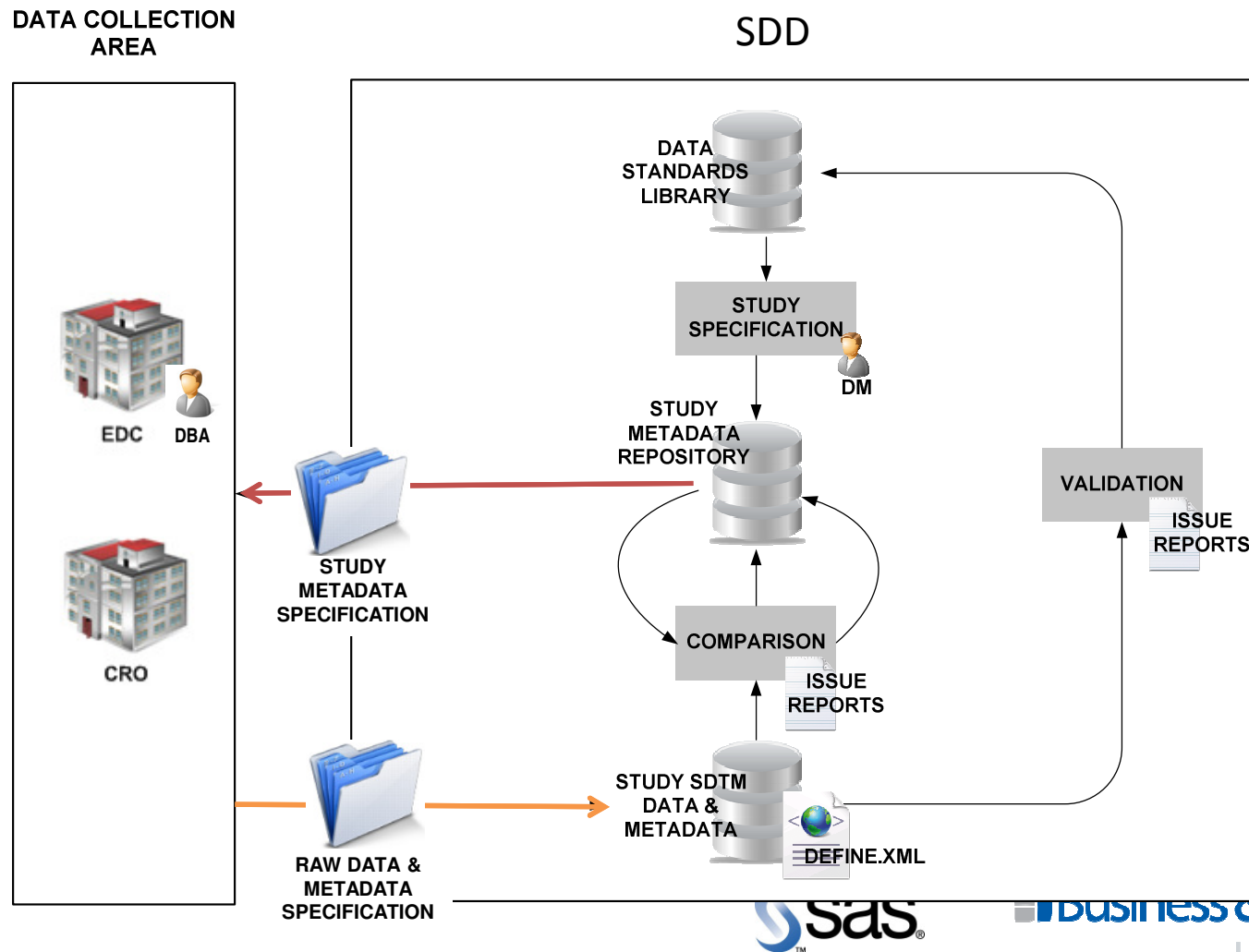


CDmation

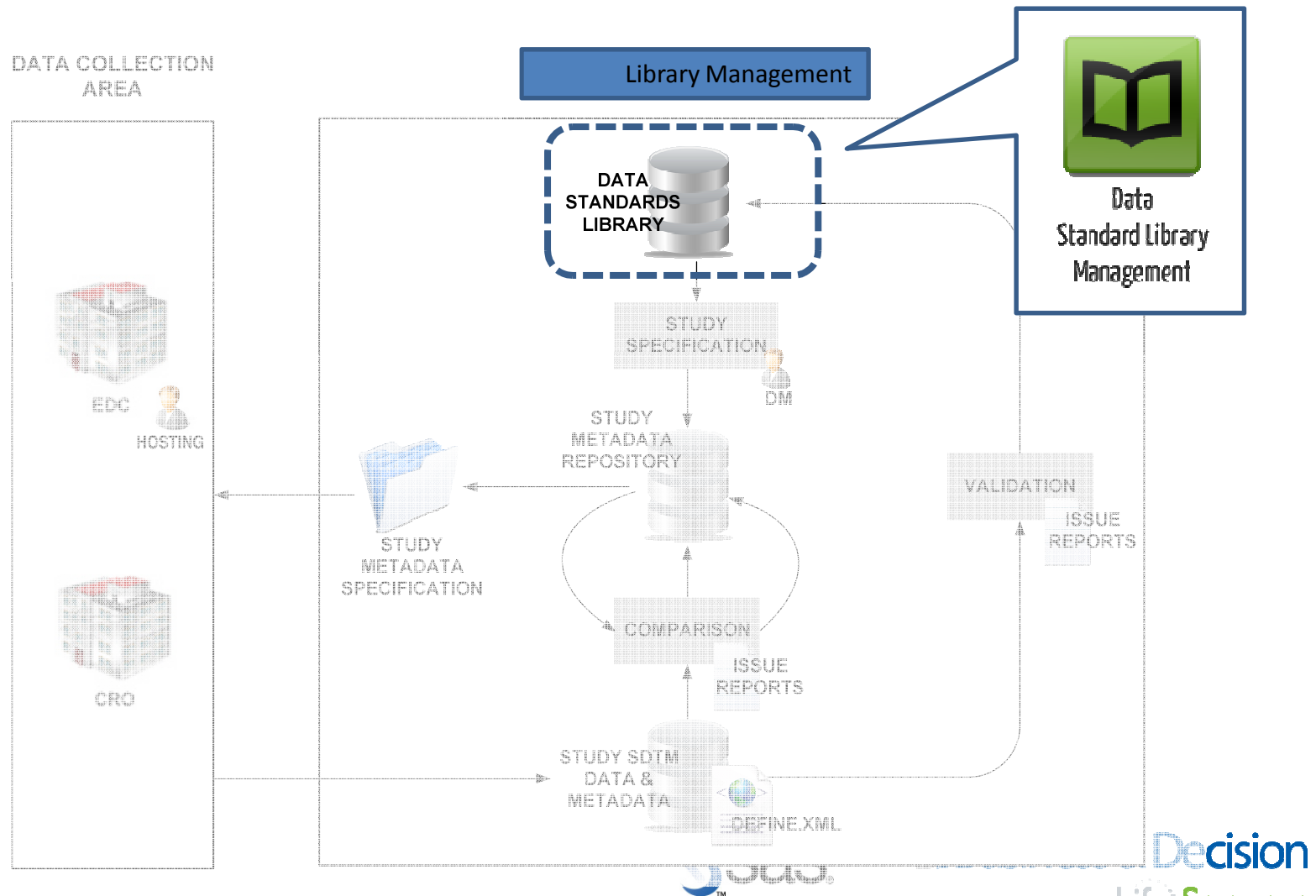
- An integrated solution with six components:



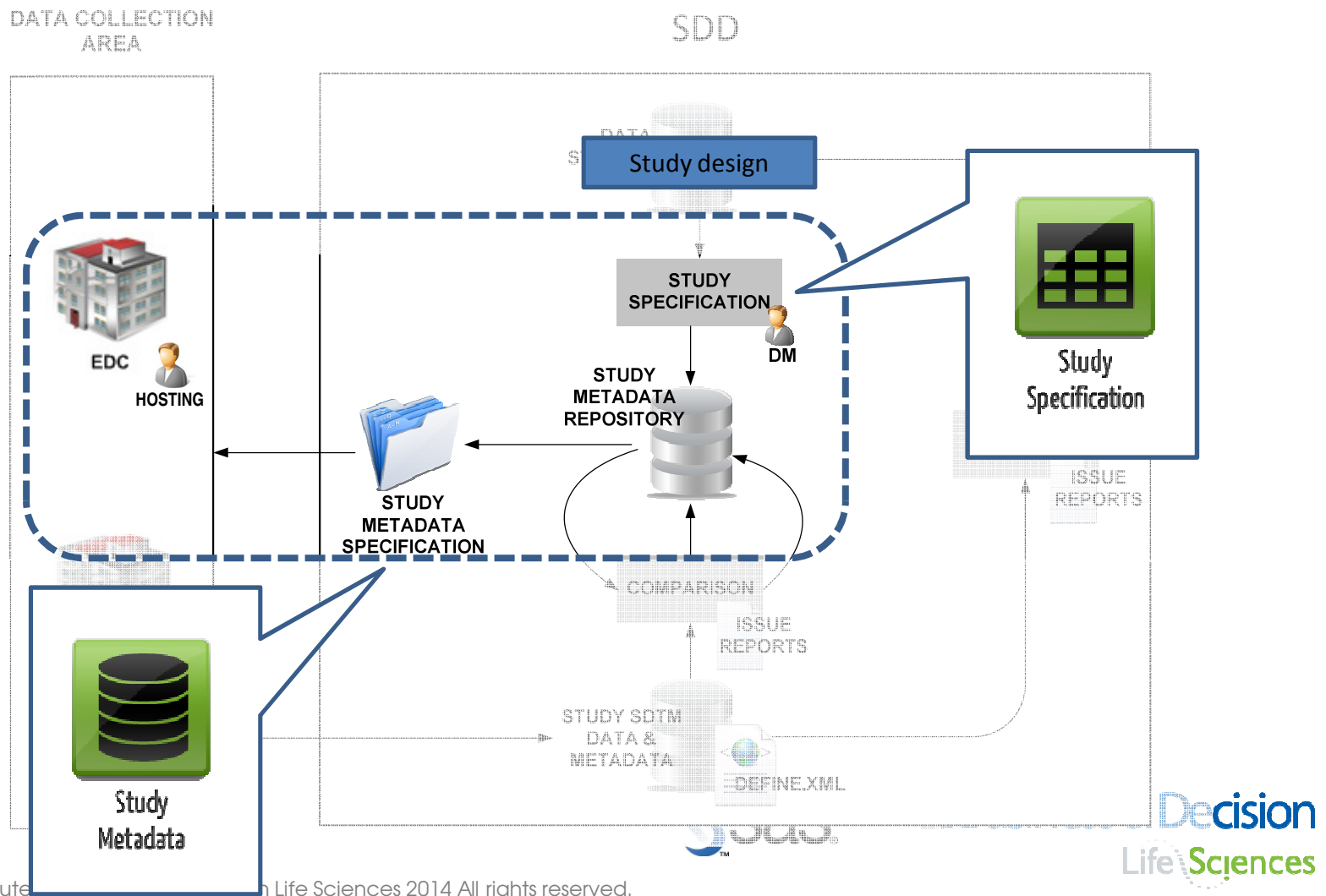
CDmation's playing field



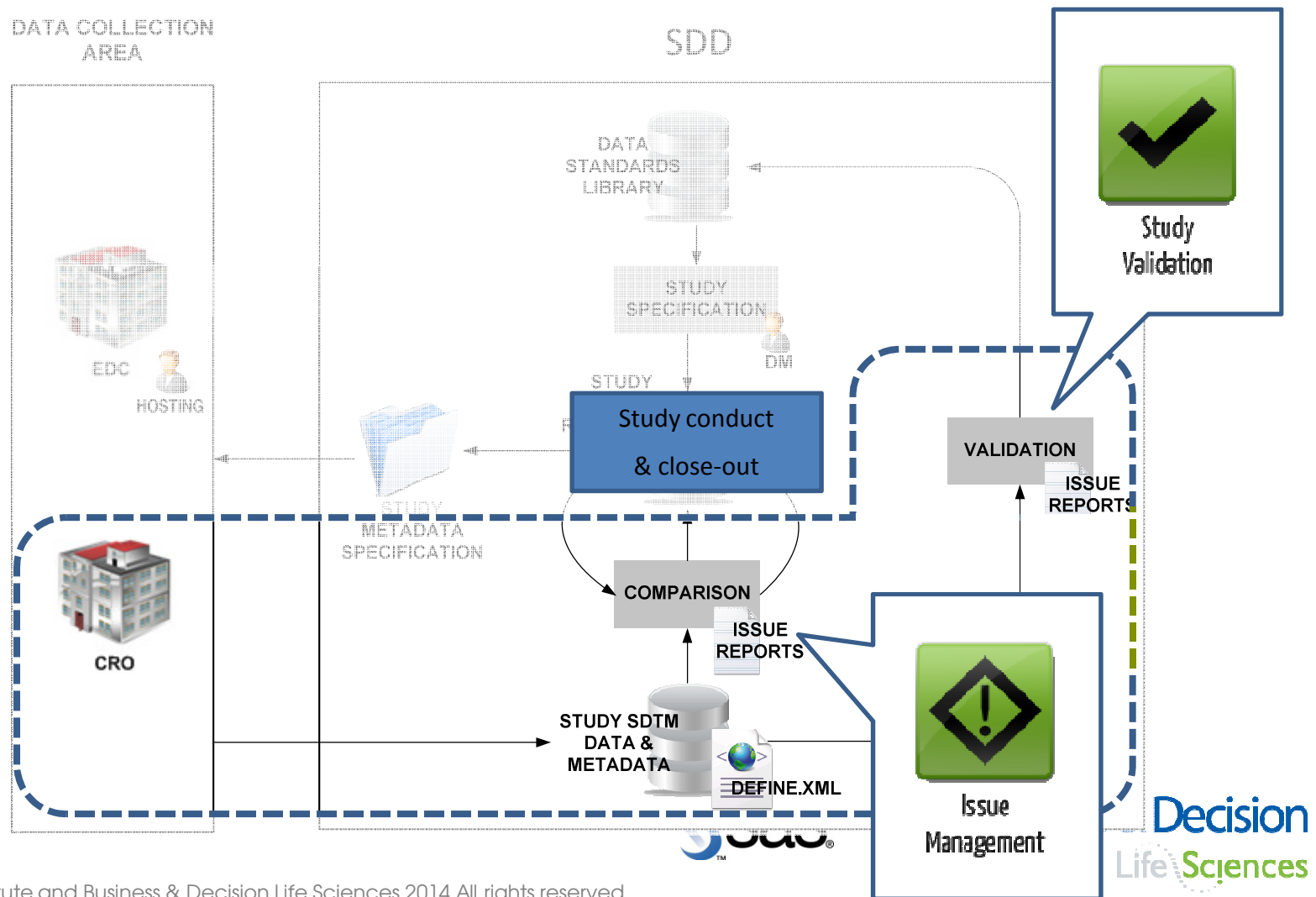
Functionalities



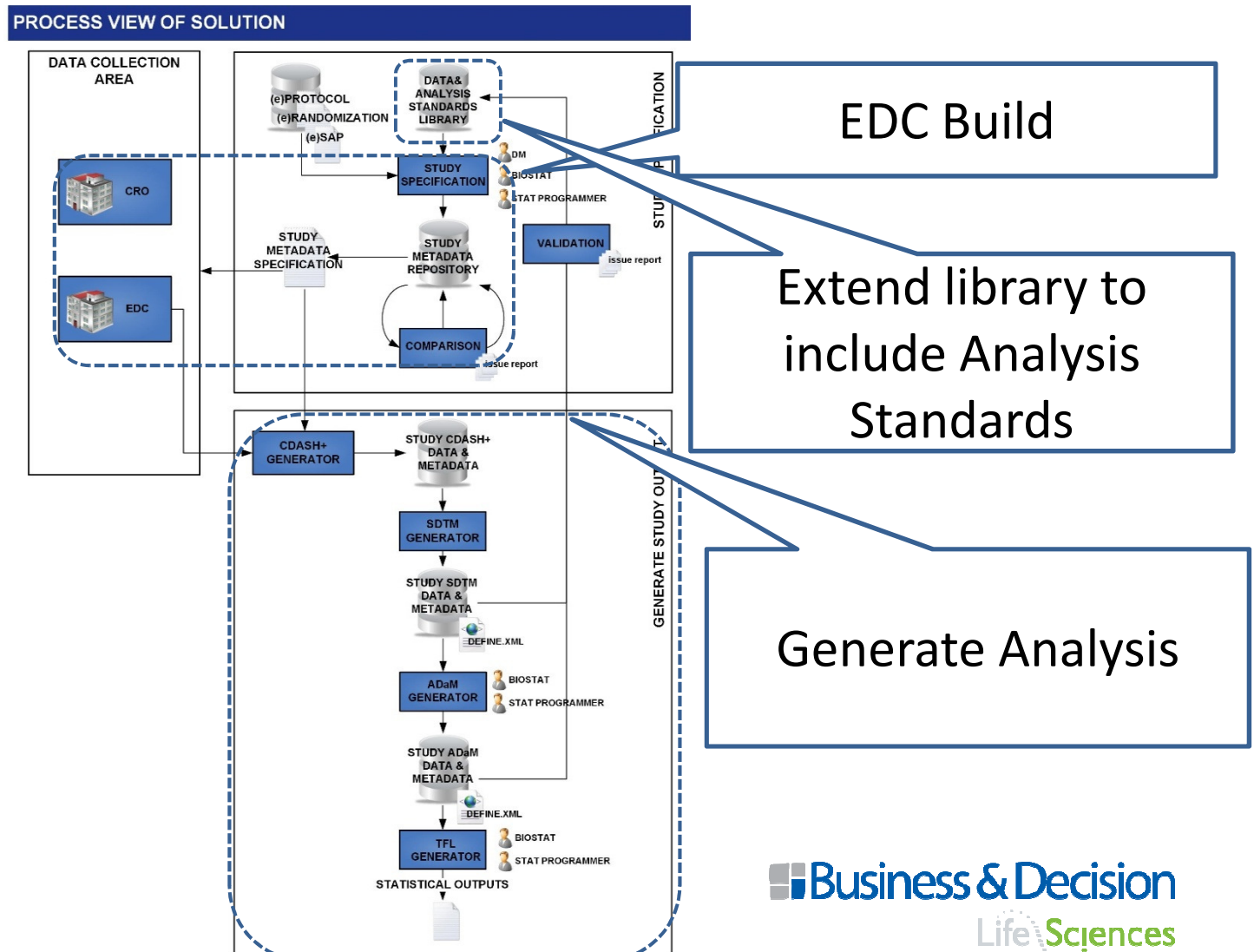
Functionalities



Functionalities



CDmation Roadmap



Agenda



Use Case 1 – Study Specification

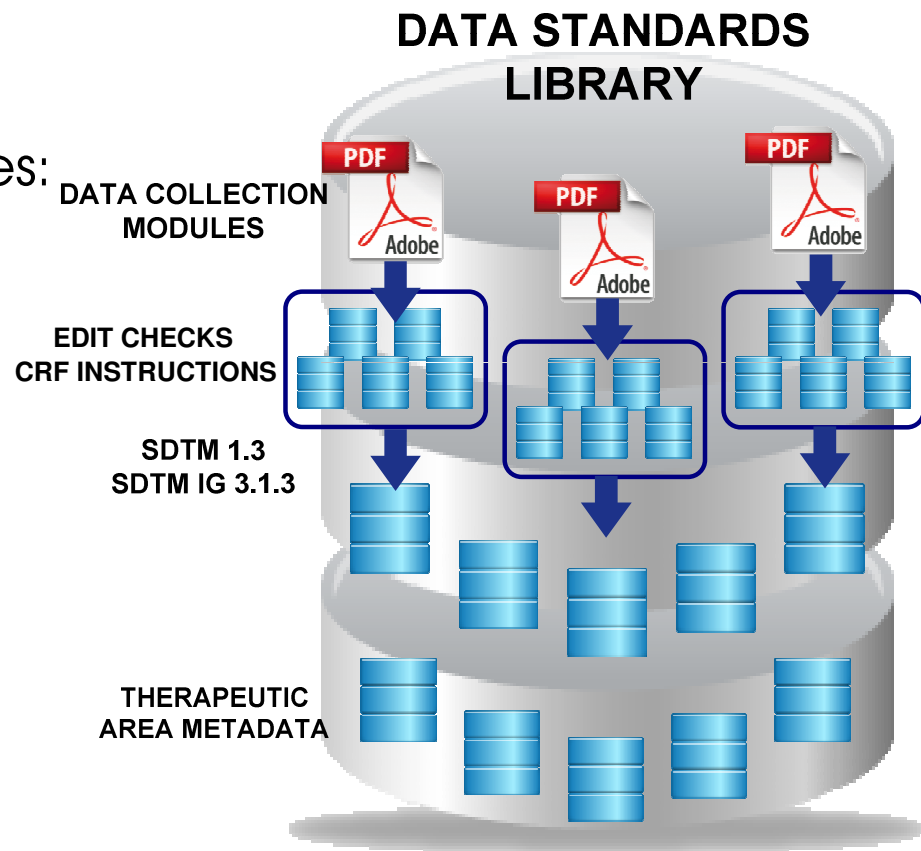
Study Specification and Metadata Repository

- Pick and Select study creation
 - Creation of Trial Design specifications
 - Defines all study specifications in a controlled manner
 - Allows generating a study metadata repository for comparison reporting within and across studies
 - Generates a define.xml upfront
- **Ensures CDISC compliant study specifications for your CRO early in the process, maintains data consistency, facilitates submission activities and increases overall quality and reduces rework**

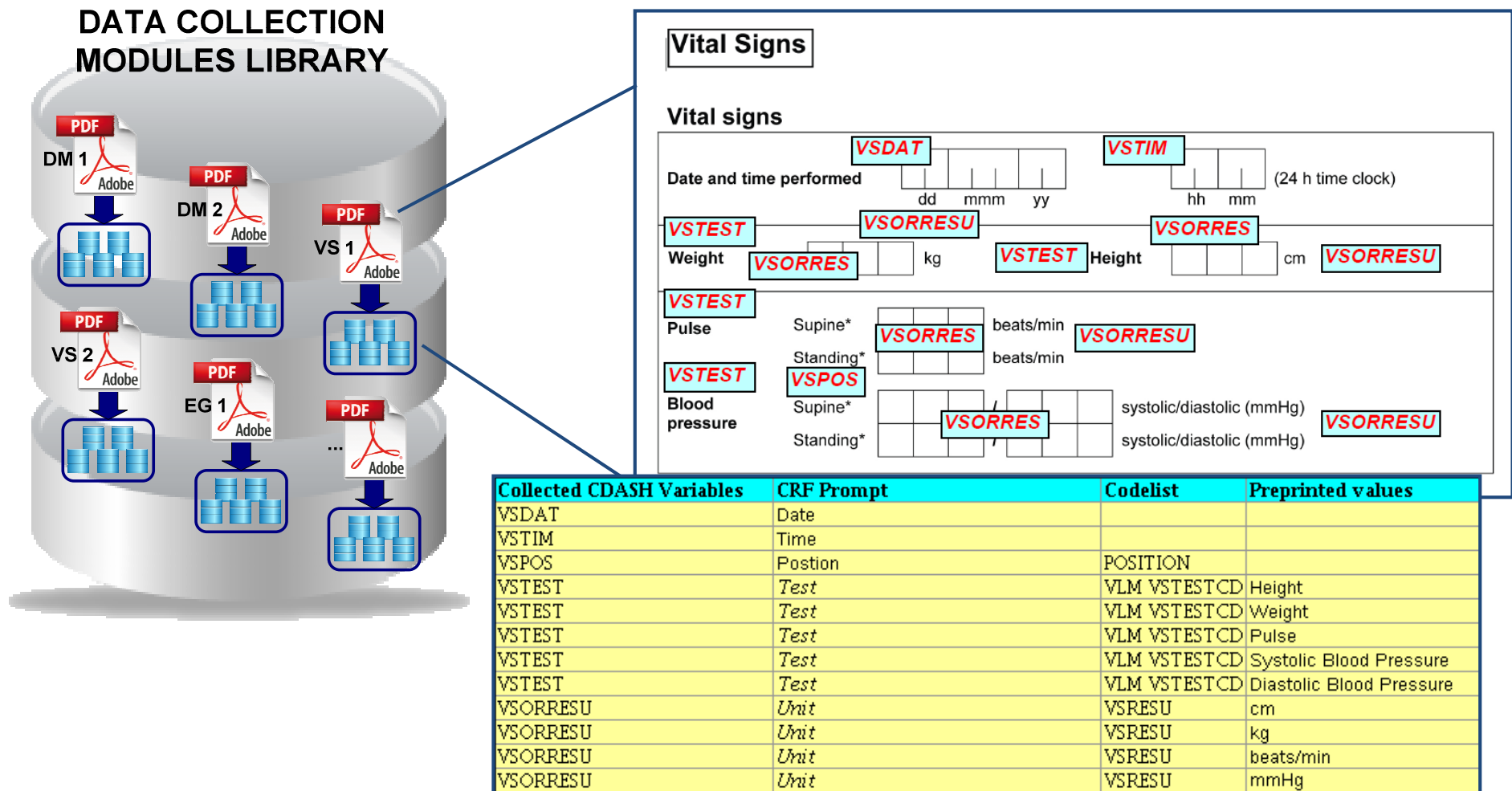


Data Standards Library

- The Data Standards Library contains :
 - Data Collection Modules:
 - using CDASH metadata
 - with clustered SDTM metadata
 - annotated for CDASH
 - annotated for SDTM
 - front end edit checks
 - CRF completion Instructions
 - Metadata Definitions :
 - SDTM Standards
 - Therapeutic Area Standards



Data Collection Modules - CDASH

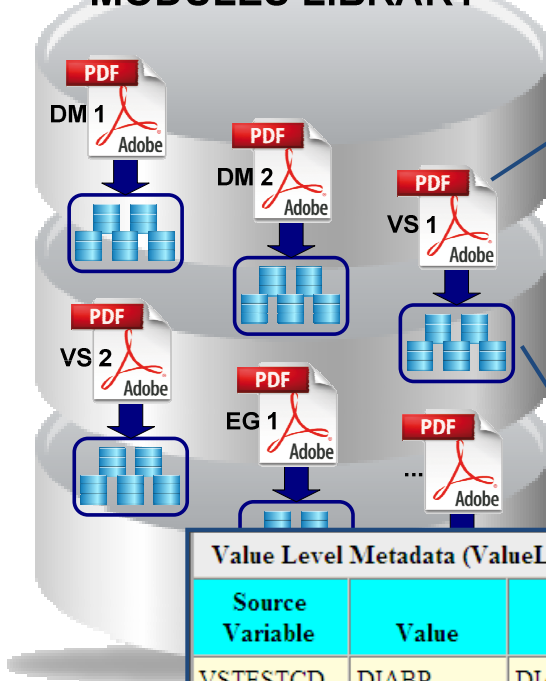


CRF template using CDASH annotations



Data Collection Modules - SDTM

DATA COLLECTION MODULES LIBRARY



Vital Signs

Vital signs

Date and time performed (24 h time clock)
dd mmm yy VSDTC hh mm

VSORRES where VSTESTCD = "WEIGHT"

Weight kg **VSORRES where VSTESTCD = "HEIGHT"**

Height cm

Pulse Supine* beats/min **VSORRES where VSTESTCD = "PULSE"**
Standing* beats/min

VSPOS = "SUPINE", "STANDING"

Blood pressure Supine* / systolic/diastolic (mmHg) **VSORRES where VSTESTCD = "SYSBP", "DIABP"**
Standing* / systolic/diastolic (mmHg)

* (supine: after ≥ 5 min. rest; standing: after ≥ 1 min. standing)

Value Level Metadata (ValueList.VS.VSTESTCD)

Source Variable	Value	Label	Type	Controlled Terminology	Origin	Role	Comment
VSTESTCD	DIABP	DIASTOLIC BLOOD PRESSURE	integer		CRF		
VSTESTCD	HEIGHT	HEIGHT	integer		CRF		
VSTESTCD	PULSE	PULSE RATE	integer		CRF		
VSTESTCD	SYSBP	SYSTOLIC BLOOD PRESSURE	integer		CRF		
VSTESTCD	WEIGHT	WEIGHT	integer		CRF		



Study Specification

The screenshot displays the CDmation software interface for study specification. The top navigation bar includes the CDmation logo, a series of icons (book, grid, database, checkmark, warning, wrench), and the Business & Decision Life Sciences logo. The main window shows a 'Study overview' table with columns for Visit, DCM, Questions, TPTNUM, TPT, TPTREF, and ORDER. The table lists various study events like Screening, Randomization, and VISIT 3, each associated with a specific DCM (e.g., DM_800, VS_800, LB_900, CM_900, VS_900, LB_900). A callout box with the text 'Pick and Select DCM' has three arrows pointing to the 'DCM' column in the table, the 'Visit' column, and the 'Questions' column.

Visit	DCM	Questions	TPTNUM	TPT	TPTREF	ORDER
Screening	DM_800					
Screening	VS_800					
Screening	LB_900					
Randomization	DM_900					
VISIT 3	CM_900					
VISIT 3	VS_900					
VISIT 3	LB_900					

Pick and Select DCM

Define.xml

Dataset	Description	Class	Structure	Purpose	Keys	Location				
CM	Concomitant Medications	Interventions	One record per recorded medication occurrence or constant-dosing interval per subject	Tabulation	STUDYID, USUBJID, CMTRT, CMSTDTC	Tabulations/cm.xpt				
EX	Exposure	Interventions	One record per constant dosing	Tabulation	STUDYID, USUBJID,	Tabulations/ex.xpt				
AE	Adverse Events									
		Variable	Label	Type	Controlled Terminology	Origin	Role	Comment		
		STUDYID	Study Identifier	text		Protocol, CRF	IDENTIFIER	The STUDYID variable has a fixed format: 'XXXX-YYYY', where 'XXXX' indicates the 4-digit compound code and the 'YYYY' the 4-digit study code		
		DOMAIN	Domain Abbreviation	Value Level Metadata (ValueList.VS.VSTESTCD)						
		USUBJID	Unique Subject Identifier	Source Variable	Value	Label	Type	Controlled Terminology	Origin	Comment
				VSTESTCD	BMI	BODY MASS INDEX	integer		Derived	See Computational Method: VS.BMI
				VSTESTCD	DIABP	DIASTOLIC BLOOD PRESSURE	integer		CRF	
				VSTESTCD	HEIGHT	HEIGHT	integer		CRF	
				VSTESTCD	PULSE					
				VSTESTCD	SYSBP					
				VSTESTCD	WEIGHT					
				POSITION, Reference Name (Codelist.POSITION)						
				Code Value			Code Text			
				STANDING			STANDING			
				SUPINE			SUPINE			
				SEX, Reference Name (Codelist.SEX)						
				Code Value			Code Text			
				F			Female			
				M			Male			
				U			Unknown			
				Computational Algorithms (VS.BMI)						
				Reference Name	Computation Method					
				VS.BMI	Equals to WEIGHT DIVIDED BY HEIGHT SQUARED					
				Computational Algorithms (VS.VSDY)						
				Reference Name	Computation Method					
				VS.VSDY	Equals to (VS.VSDTC - DM.RFSTDTC) + 1 IF VSDTC is on or after RFSTDTC Equals to (VS.VSDTC - DM.RFSTDTC) IF VSDTC precedes RFSTDTC					



Use Case 2 – Study Validation

Study Validation

- Comparison reports against specifications
 - Validation performed on structural and content level
 - Output in Excel spreadsheet, HTML and PDF report
 - Output also stored in the Feedback Tracker
- Ensures improved vendor communication, CDISC compliance and readiness, increases quality, reduces rework.



Select checks => Create Job

CDmation Business & Decision Life Sciences

Manage checks **Create job** Existing jobs

Create job

Data model : * Library selector Global_Onco_CDASH1.1_SDTM3.1.3

Library active date : 22/04/2014

Project : * BBBB

Study : * BBBB-00001

Job name : *

Job description : *

Input Dataset Path : /SAS/BBBB/BBBB-00001/Files/Staging/DM_CRO/SDTM_SAS_C

Job type : STAGING PRODUCTION

Type of checks :

- ☐ All
- ☐ All classes
- ☐ Data checks
- ☒ Metadata checks
- ☐ Events
- ☐ Interventions
- ☐ Findings
- ☐ Findings about
- ☐ Trial design
- ☐ Special

Save job Reset selection View selected checks

125 CHECKS SELECTED

	Check name	Severity	Description	Error message	DM Version
	Text to filter	Text to filter	Text to filter	Text to filter	Text to filter
☐	Check3130000001	MEDIUM	Check if all the date variables (--DTC, --STDTC, --ENDTC, RFSTDTC, RFENDTC, --RFTDTC, BRTHDTC) have a ISO 8601 standard format.	DATE VARIABLE does not have a ISO 8601 format.	Global_Onco_CDASH1.1_SDTM3.1.3
☐	Check3130000002	HIGH	Check per --TESTCD if the --STRESU is consistent within the trial limited to records where [--STRESN <> NULL].	The STANDARD UNIT is not consistent per TEST or EXAMINATION.	Global_Onco_CDASH1.1_SDTM3.1.3
☐	Check3130000003	MEDIUM	Check if AESER = "Y" that [AESCAN="Y" or AESCONG="Y" or AESDISAB="Y" or AESDTH="Y" or AESHOSP="Y" or AESLIFE="Y" or AESMIE="Y" or AESOD="Y"] (Check only applies if serious criteria are completed). (&&) Check if [AESCAN="Y" or AESCONG="Y" or AESDISAB="Y" or AESDTH="Y" or	The AE is serious, but none of the serious criteria is answered "Y". (&&) The AE is not serious, but one of the serious criteria is answered "Y".	Global_Onco_CDASH1.1_SDTM3.1.3



Run job => Review issues



Reported Exception Record Identifiers Exception Attributes

CHECKID	ERRORMSG	SEVERITY	STUDYID	DOMAIN	USUBJID	KEY1CD	KEY1	VAR1CD	VAR1	VAR2CD	VAR2
1002	The STANDARD UNIT is not consistent per TEST or EXAMINATION.	High	1000-0000	LB				LBTESTCD	LIPASE	LBSTRESU	%
1002	The STANDARD UNIT is not consistent per TEST or EXAMINATION.	High	1000-0000	LB				LBTESTCD	LIPASE	LBSTRESU	mmol/L
1002	The STANDARD UNIT is not consistent per TEST or EXAMINATION.	High	1000-0000	LB				LBTESTCD	ALKP	LBSTRESU	U
1002	The STANDARD UNIT is not consistent per TEST or EXAMINATION.	High	1000-0000	LB				LBTESTCD	ALKP	LBSTRESU	U/L
1002	The STANDARD UNIT is not consistent per TEST or EXAMINATION.	High	1000-0000	LB				LBTESTCD	LIPASE	LBSTRESU	IU/L
1005	START DATE/TIME OF OBSERVATION falls after the END DATE/TIME OF OBSERVATION.	High	1000-0000	AE	1000-0000-00019	AESEQ	1	AESTDTC	1998-12-01T17:00	AEENDTC	1998-12-01T16:30
1005	START DATE/TIME OF OBSERVATION falls after the END DATE/TIME OF OBSERVATION.	High	1000-0000	AE	1000-0000-00037	AESEQ	1	AESTDTC	1998-12-15T07:40	AEENDTC	1998-11-25T08:00
1005	START DATE/TIME OF OBSERVATION falls after the END DATE/TIME OF OBSERVATION.	High	1000-0000	SE	1000-0000-00004	SESEQ	2	SESTDTC	1998-11-17T08:06:00	SEENDTC	1998-11-17T07:07:00
1005	START DATE/TIME OF OBSERVATION falls after the END DATE/TIME OF OBSERVATION.	High	1000-0000	SE	1000-0000-00009	SESEQ	2	SESTDTC	1998-11-24T08:00:00	SEENDTC	1997-11-24T08:01:00
1005	START DATE/TIME OF OBSERVATION falls after the END DATE/TIME OF OBSERVATION.	High	1000-0000	SV	1000-0000-00022			SVSTDTC	1998-12-03	SVENDTC	1998-12-02
1005	START DATE/TIME OF OBSERVATION falls after the END DATE/TIME OF OBSERVATION.	High	1000-0000	SV	1000-0000-00010			SVSTDTC	1998-11-24	SVENDTC	1998-11-22
1005	START DATE/TIME OF OBSERVATION falls after the END DATE/TIME OF OBSERVATION.	High	1000-0000	SV	1000-0000-00014			SVSTDTC	1998-11-16	SVENDTC	1998-10-16
1005	START DATE/TIME OF OBSERVATION falls after the END DATE/TIME OF OBSERVATION.	High	1000-0000	SV	1000-0000-00035			SVSTDTC	1998-12-17	SVENDTC	1997-12-17
1007	The LENGTH of the --TEST variable is more than 40 characters.	High	1000-0000	LB	1000-0000-00001	LBSEQ	35	LBTEST	ERY. MEAN CORPUSCULAR HB CONCENTRATION MEAS	LENGTH	43
1007	The LENGTH of the --TEST variable is more than 40 characters.	High	1000-0000	LB	1000-0000-00030	LBSEQ	54	LBTEST	PARTIAL THROMBOPLASTINE TIME MEASUREMENTS	LENGTH	41
1008	The --TESTCD starts with a number.	High	1000-0000	LB	1000-0000-00001	LBSEQ	3	LBTESTCD	2AMYL		
1009	An ORIGINAL RESULT is completed but the STANDARD RESULT (CHARACTERISTIC) is missing.	High	1000-0000	IE	1000-0000-00006	IESEQ	1	IEORRES	N	IESTRESC	
1009	An ORIGINAL RESULT is completed but the STANDARD RESULT (CHARACTERISTIC) is missing.	High	1000-0000	SC	1000-0000-00031	SCSEQ	1	SCORRES	R-K	SCSTRESC	
1009	An ORIGINAL RESULT is completed but the STANDARD RESULT (CHARACTERISTIC) is missing.	High	1000-0000	SC	1000-0000-00014	SCSEQ	1	SCORRES	W-B	SCSTRESC	
1009	An ORIGINAL RESULT is completed but the STANDARD RESULT (CHARACTERISTIC) is missing.	High	1000-0000	SC	1000-0000-00022	SCSEQ	1	SCORRES	M-U	SCSTRESC	



Manage Issues

IDP / StudyTTTT / TTTT-00001

Unique Id246863

Feedback Created Manually☐

Description *

Check in define.xml in CO, DM, SE, SV, SUPPQUAL, Trial design that every variable listed in the SDTMIG is listed in the dataset.

Error Message

Informative Check: Define.xml: The variable is omitted from the dataset while the domain is not in one of the three general observation classes (interventions, events, findings).

Status *NEW

Source

DATASETS: /SAS/TTTT/TTTT-00001/Files/Study/MCR/SAS_Coverage/Content -- LIBRARY: ROGER_COMB_01

SeverityIntermediate

Assigned groupSelect one

CategorySAS Datasets

subCategoryContent of the SAS datasets

Issue created2014-03-21 10:23:24

Domain DatasetMETADATASelect one

CheckCheck3130000725

Feedback PositionSelect one

Feedback Position Value

Unique Subject Id

Assigner UserGDM01

Comments

+ Add Comment

Date	Author	Comments	Download Attachment
Text to filter	Text to filter	Text to filter	

No records found

Status History

Date	Author	Status
Text to filter	Text to filter	Text to filter
2014-03-21 10:29:12	GDM01	NEW

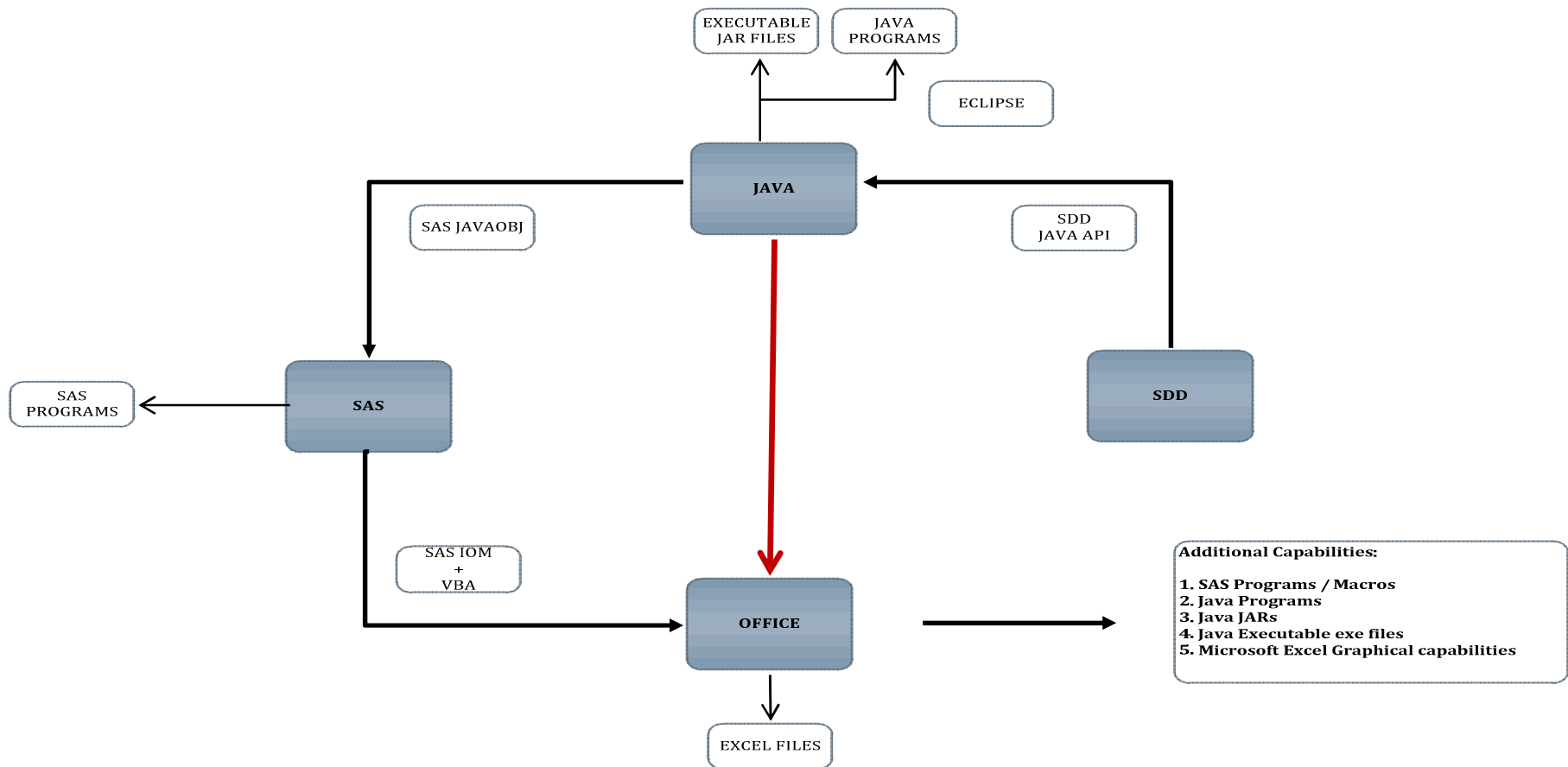
Variable Details

Date	Name	Value
Text to filter	Text to filter	Text to filter
2014-03-21 10:23:24	VARIABLE	SEV
2014-03-21 10:23:24	DOMAIN	SDTMIG

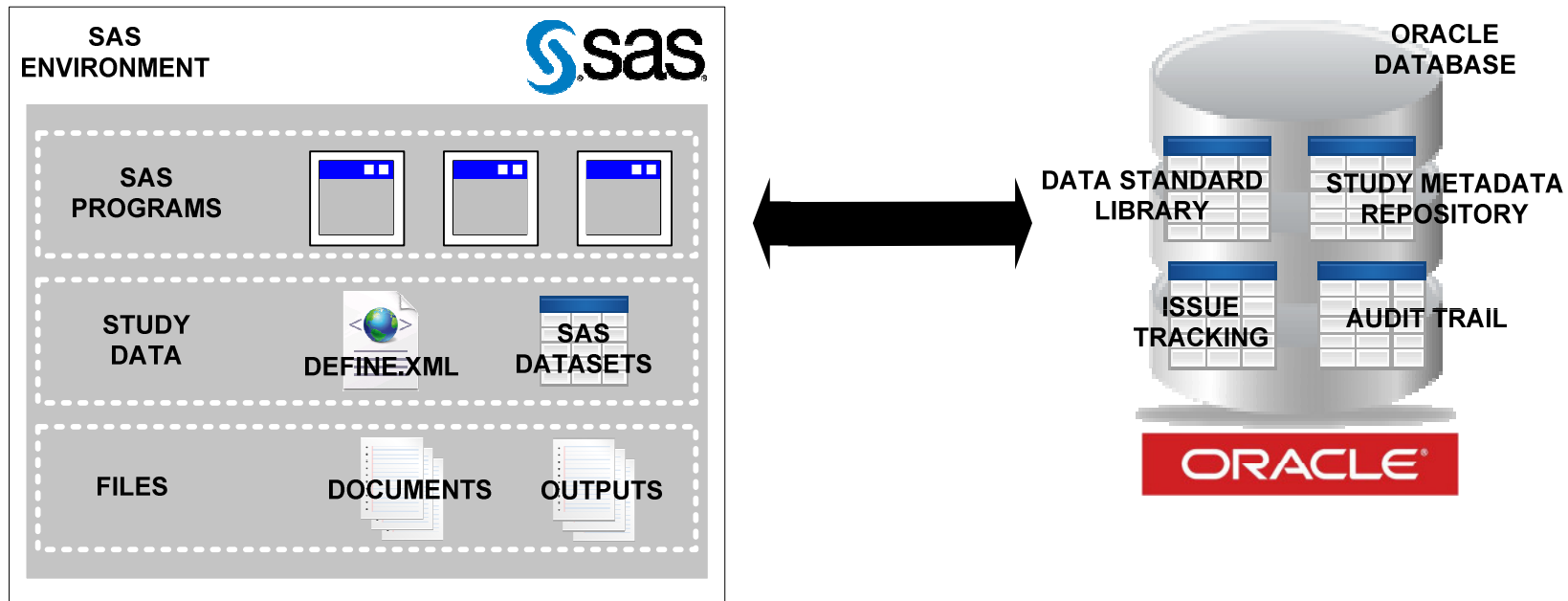
Agenda



REPORTING possibilities



Reporting capability



Data Standards Library Comparison
Implementation Guides
Completion Guides
Trial summary-based search reports
Metrics reports

Study metadata comparison across study versions
Study metadata comparison across projects
Define.xml
Export of trial design datasets
Study metadata-based search reports



Reporting capability (1)

Data Standards Library Comparison

SAS® Drug Development

ViewToolsAdministrationHelp

Log Off

DashboardRepositoryWorkspaceCompareOracle (1.0) [read-o...

GeneralSAS ProgramsParametersInputsOutputsPublish History

Variable Name	Label
START_PATH	Path of the programs
REPORTPATH	Path of the report
VERSION1	Date of version one
VERSION2	Date of version two
SOURCEWORD1	Name of source one
SOURCEWORD2	Name of source two
METADATA_LEVEL	Metadata Level (DOMAIN,VARIABLE,CODELIST,DC)
LIBRARY_NAME	Name of the library

CHECK	NAME	DESCRIPTION	DATASET	v22MAY2013	v30MAY2013
Ok	AE_101	testing AE 101d	DEMO	X	X
Ok	AE_900	AE_900	AE	X	X
Ok	AIMSV76_QS_001		QS	X	X
Ok	AVETST2	Field that can be used to describe the DCM content	CM	X	X
Ok	CM_900	CM_900	CM	X	X
Ok	CO_900	CO_900	CO	X	X
Ok	DM_900	DM_900	DM	X	X
Error	DS_900	DS_900	DS	X	
Error	DS_900	DS_900_A	DS		X
Error	DS_901	DS_901	DS	X	
Error	DS_901	DS_901_B	DS		X
Ok	EX_900	EX_900	EX	X	X
Ok	LB_900	LB_900	LB	X	X
Ok	LB_901	LB_901	LB	X	X
Ok	MH_900	MH_900	MH	X	X
Ok	MH_901	MH_901	MH	X	X
Ok	PR_807	PR_807	PR	X	X
Ok	PR_900	PR_900	PR	X	X
Ok	SU_900	SU_900	SU	X	X
Ok	SV_800	SV_800	SV	X	X
Ok	SV_900	SV_900	SV	X	X
Ok	SV_901	SV_901	SV	X	X
Ok	TEST_001	Description test 001	DM	X	X



Reporting capability (2)

Implementation Guides

SAS® Drug Development

View Tools Administration Help

Dashboard Repository Workspace Create Implementation Guide [read]

General

SAS Progra...

Parameters

Inputs

Outputs

Publish Hist...

Variable Name	Label	Type
DATA_MODEL	The data model	Character
DATE_VALID	Date on which the data is valid	Character
INSTALL_PATH	Path of program installation	Folder

SUPPSU	Supplemental Qualifiers for SU	Relationship	One record per IDVAR, IDVARVAL, QNAM per subject	42	Tabulation
Test		Events	dsdt	50	Tabulation
VS	Vital signs test AVE	Findings	One record per vital sign measurement per time point per visit per subject	70	Tabulation
VS	Vital signs test AVE	Findings	One record per vital sign measurement per time point per visit per subject	70	Tabulation
Hello	dsods	Findings	sqdsdt	80	Tabulation
TO	: Vital signs domain	Findings	One record per vital sign measurement per time point per visit per subject	99	Tabulation
DEMO	demo description	Findings		123	Tabulation

3.2 Variable metadata

This section describes for all variables the following

- ☐ Variable name
- ☐ Variable label
- ☐ Variable type (numeric or character) and length
- ☐ Controlled terminology used
- ☐ Origin (unique origin or combination of the following: CRF, eDT, derived, assigned and protocol)
- ☐ Role (identifier, topic, timing, grouping qualifier, result qualifier, synonym qualifier, record qualifier or variable qualifier)
- ☐ Core (required= req, expected= exp, permissible= perm)
- ☐ Comment (relevant information that further clarifies the variable)

11

Special purpose domains

DATASET	NAME	LABEL	LENGTH	ABBREVIATION	NAME	NAME	NAME	NAME
AE	STUDYID	Study Identifier	40	Req	Identifier	text		
AE	STUDYID	Study Identifier	40	Req	Identifier	text		
AE	STUDYID	Study Identifier	40	Req	Identifier	text		
AE	STUDYID	Study Identifier	40	Req	Identifier	text		



Reporting capability (3)

Study Metadata Comparison

- 2 different statuses:
 - Ok** : no metadata conflict
 - Difference** : difference in metadata value between studies

Status	Dataset	Label	A1000_0000	A1000_0001	A1000_0002
Ok	AE	Adverse Events	X	X	X

Status	Reference	Computational algorithm	A1000_0000	A1000_0001	A1000_0002
Difference	DM.AGE	Equal to (DS.DSSTDTC-DM.BRTHDTC)/365.25 where DSTERM = 'INFORMED CONSENT OBTAINED'		X	
Difference	DM.AGE	Equals to (DS.DSSTDTC-DM.BRTHDTC)/365.25 where DSTERM = 'INFORMED CONSENT OBTAINED'	X		X
Difference	DM	Demographic		X	
Ok	DS	Disposition	X	X	X



SAS Drug Development – integration with CDMation

- SAS Drug Development = open extensible platform
- Integration
 1. User access and security model
 - Re-use system metadata, login session of SDD
 - Integrated user experience (including single sign-on)
 - Integrated user roles & privileges
 2. Audit trail and permission reports
 - Access from SDD-executed SAS code to all metadata from SDD and CDMation (audit trail, permissions)
 3. Metadata validation flow across all parts
 - Jobs (SAS programs) running in controlled execution environment with complete access to CDMation standards and study metadata
 - One integrated repository for jobs, documents and other output





Thank you

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