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

Mark Lambrecht (SAS)

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The clinical trial challenges

With the growth of industry standards, the level of complexity increases.

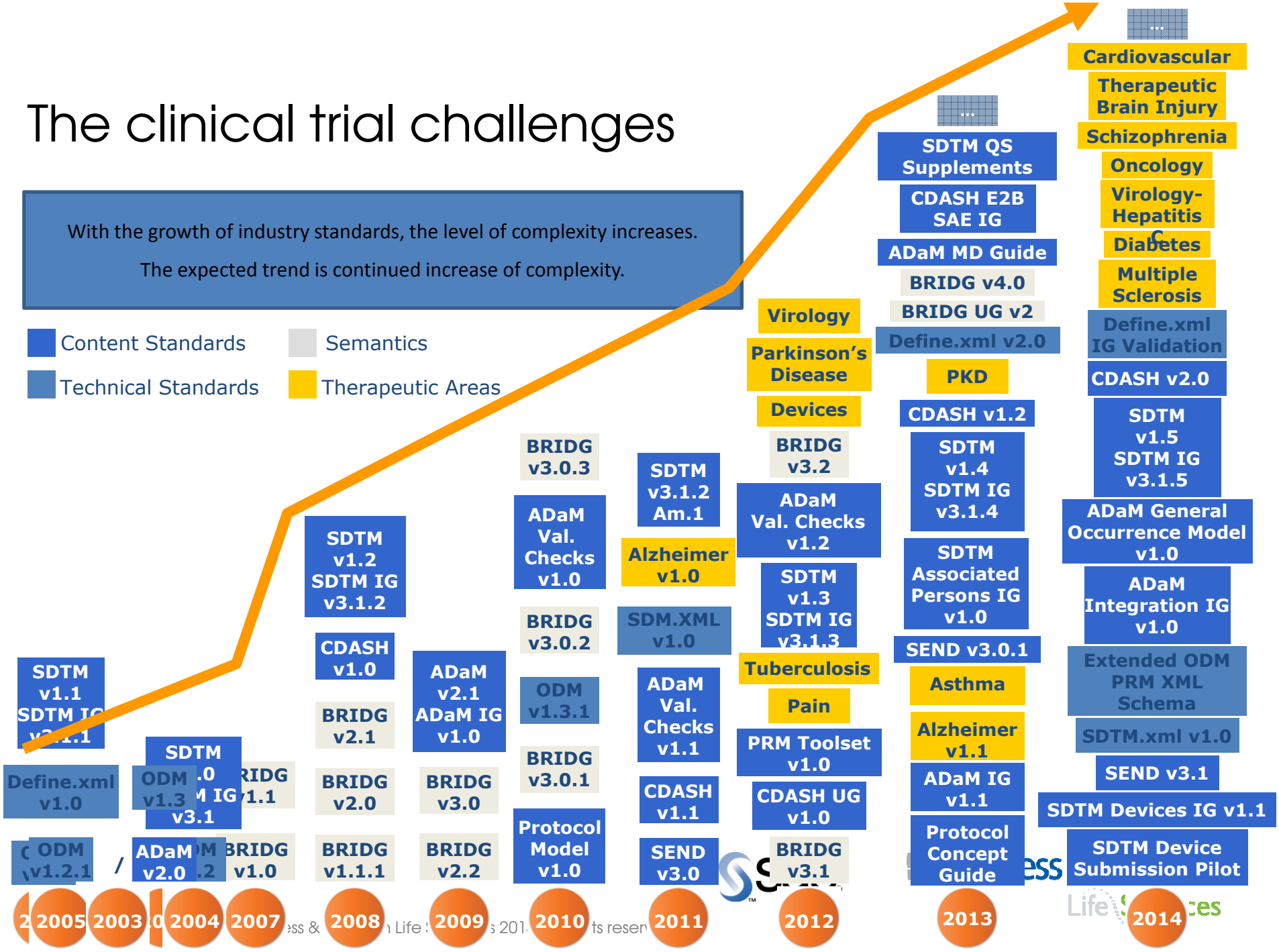
The expected trend is continued increase of complexity.

Content Standards

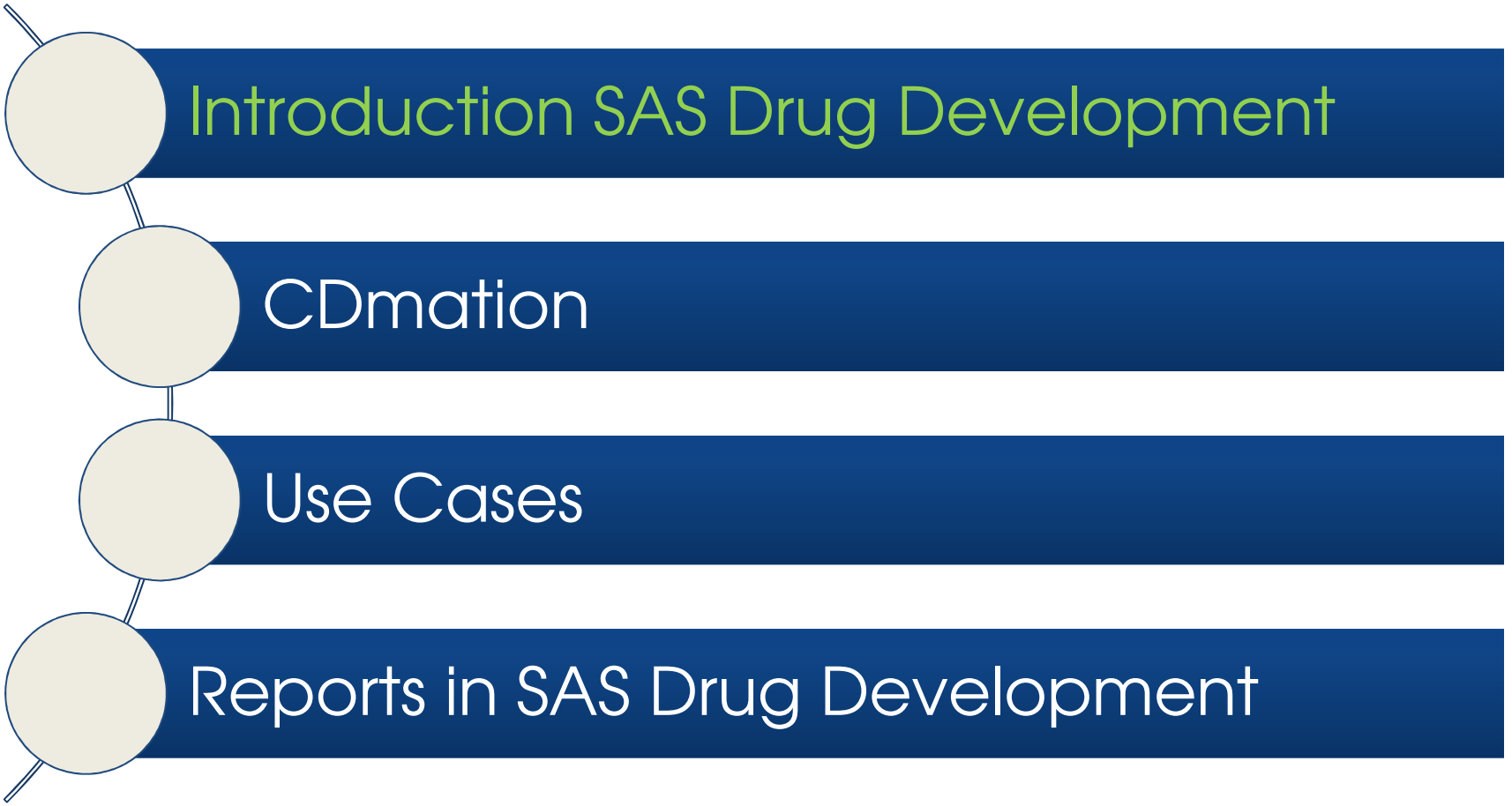
Technical Standards

Semantics

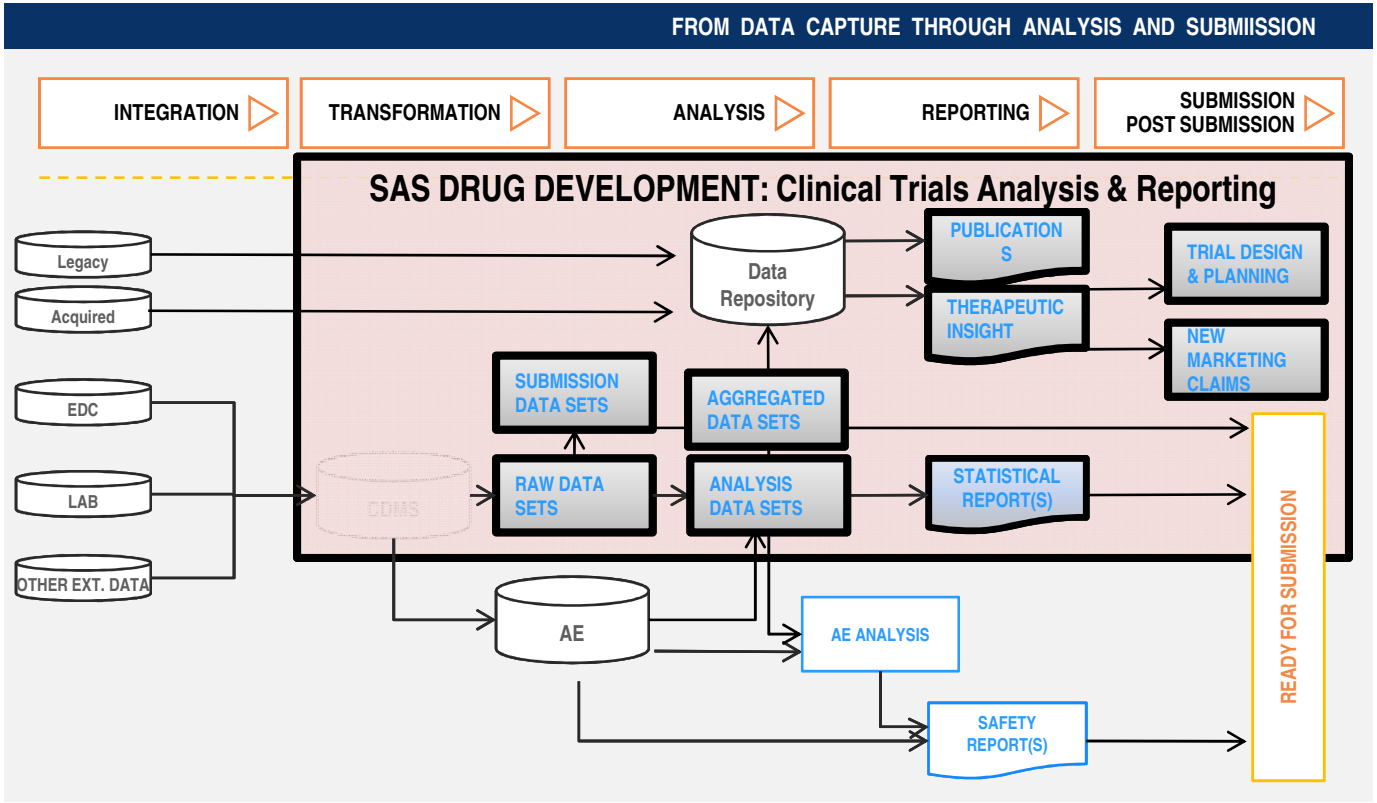
Therapeutic Areas



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

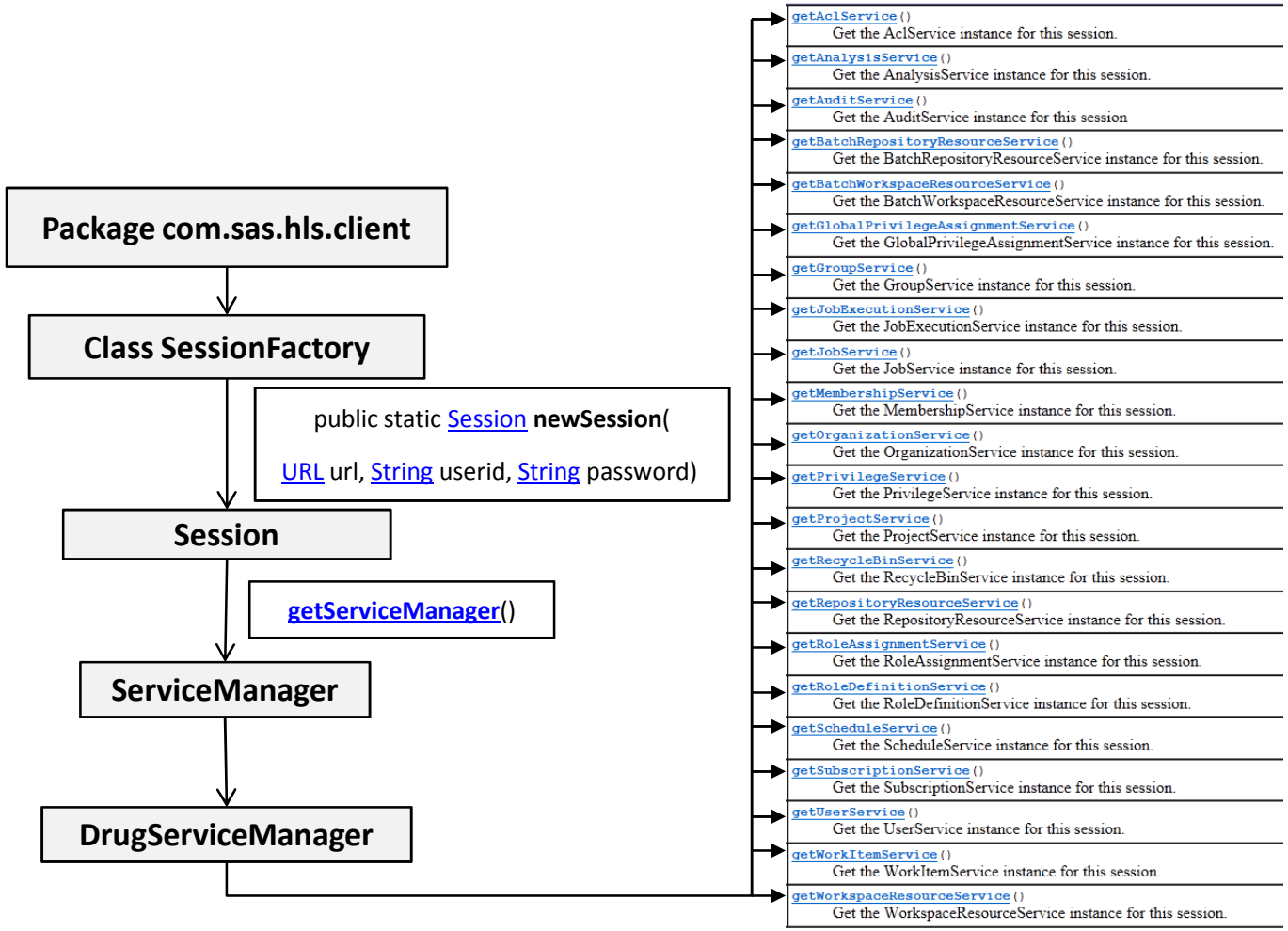
- Robust platform to cover other parts of clinical data management and statistics
- Need to store data
- Need to have several workflows
- Capability to execute SAS code
- Traceability, security and audit
- Reporting capabilities

But…

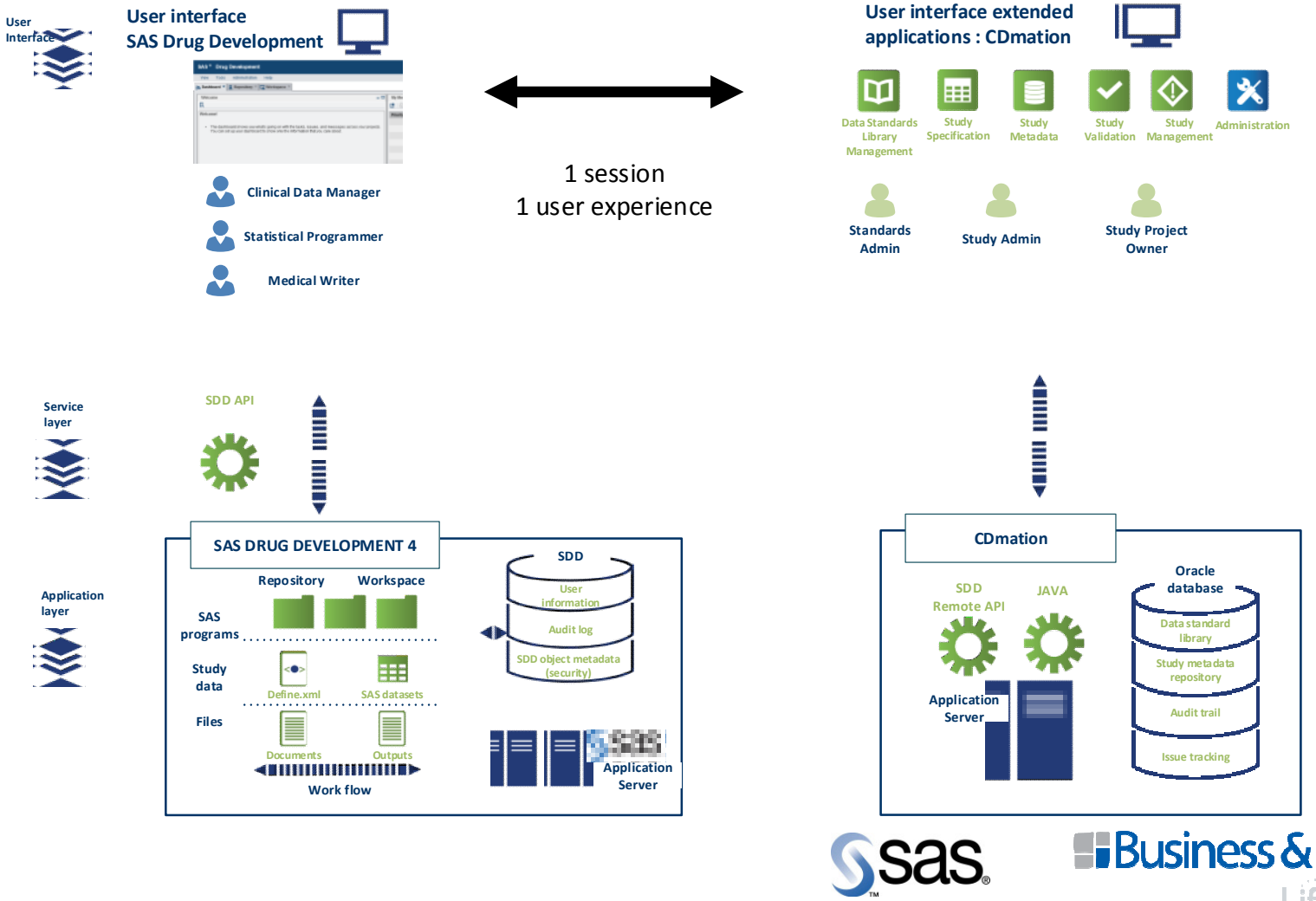
- *UI for granular data standards management*
- *Study specification process*
- *Study validation process*

Come to the rescue… Robust SDD Application Programming Interface

SDD 4.X JAVA API OVERVIEW



SDD = extensible and modular



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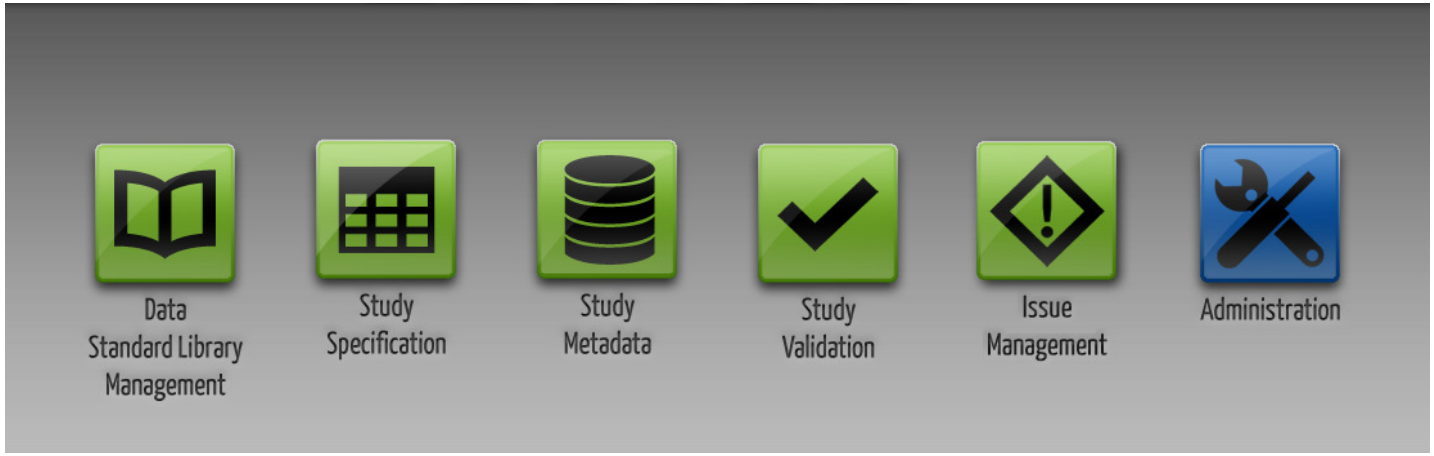
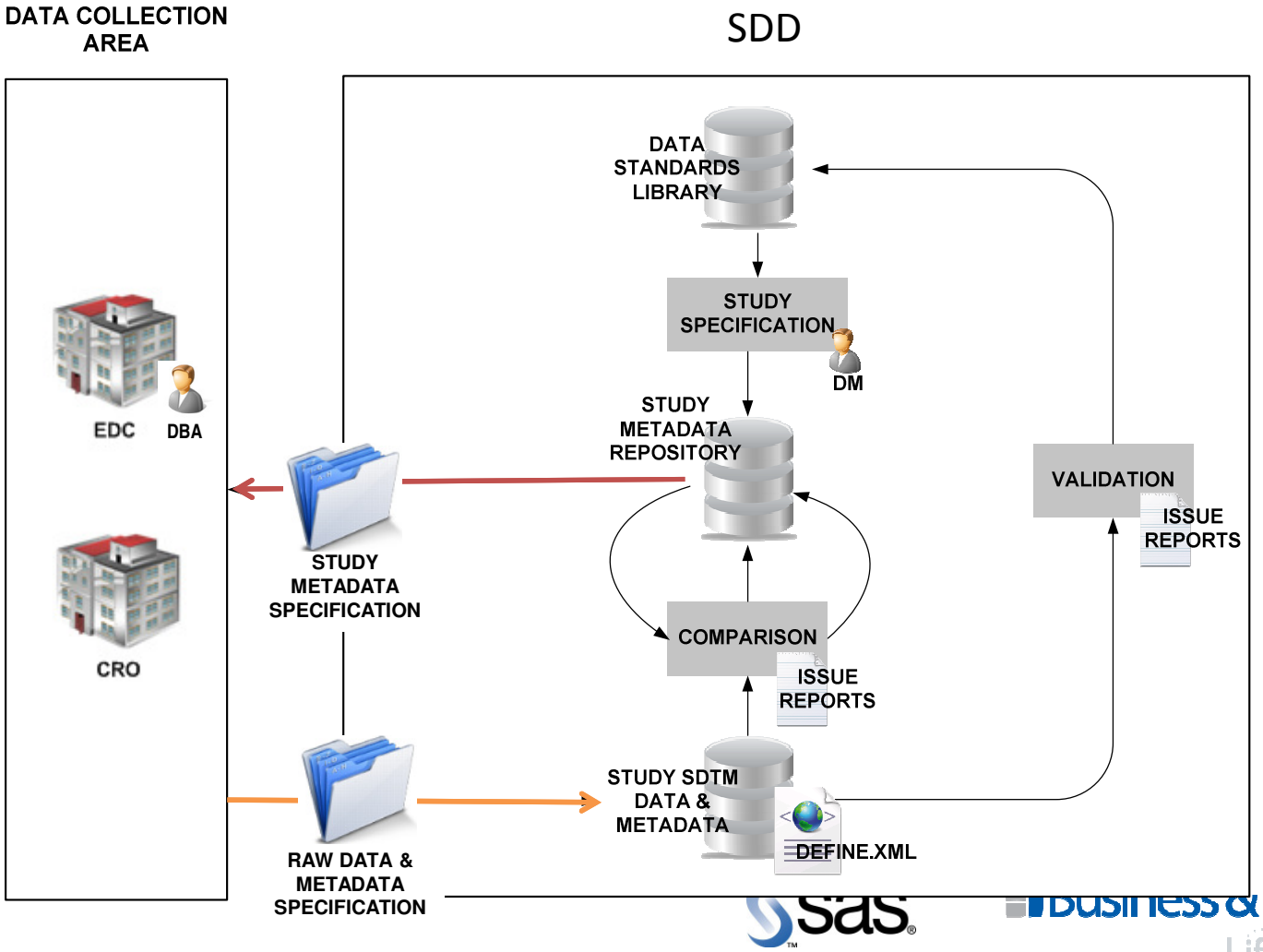
CDmation

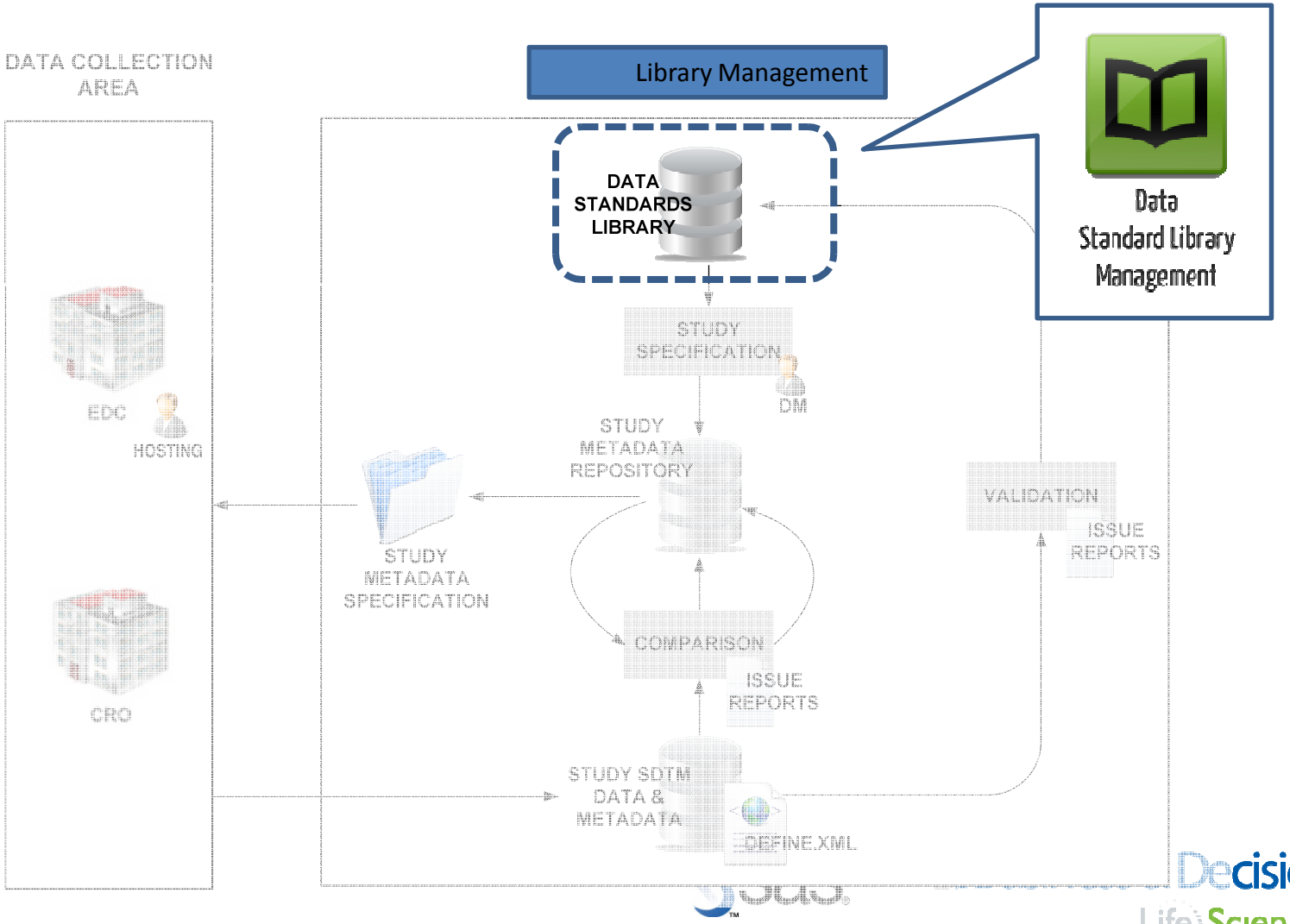
- **An integrated solution with six components**:



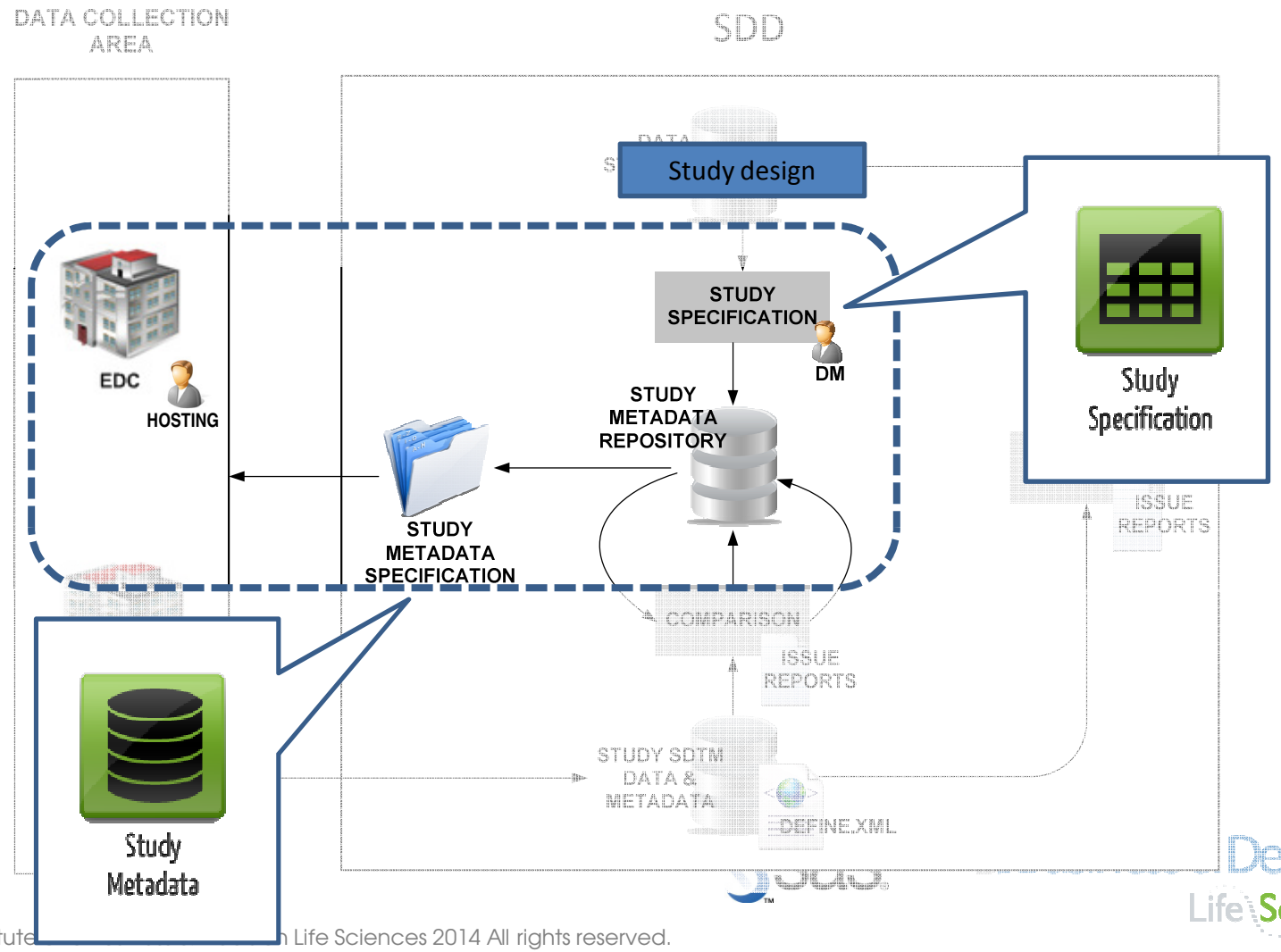
CDmation's playing field



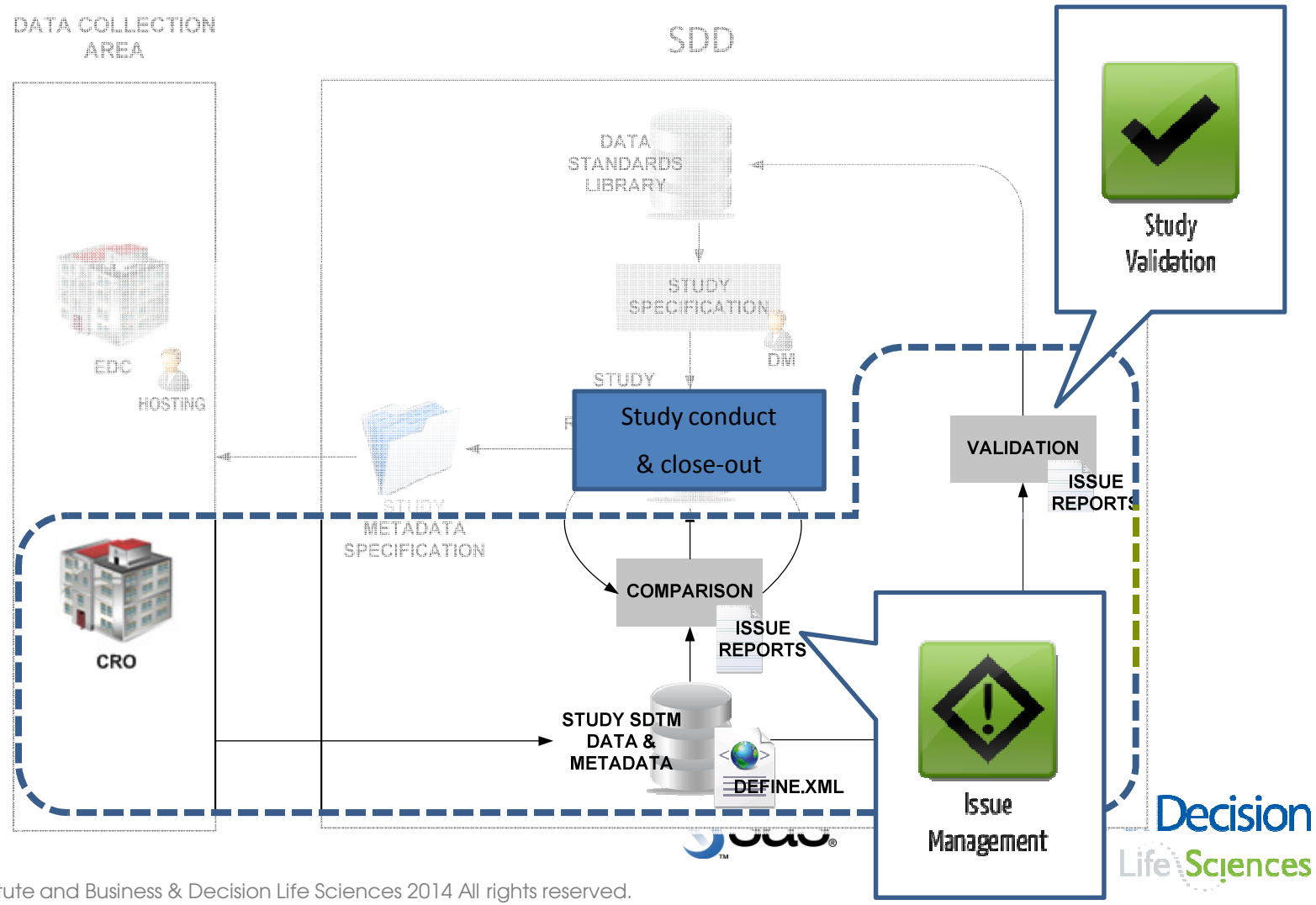
Functionalities



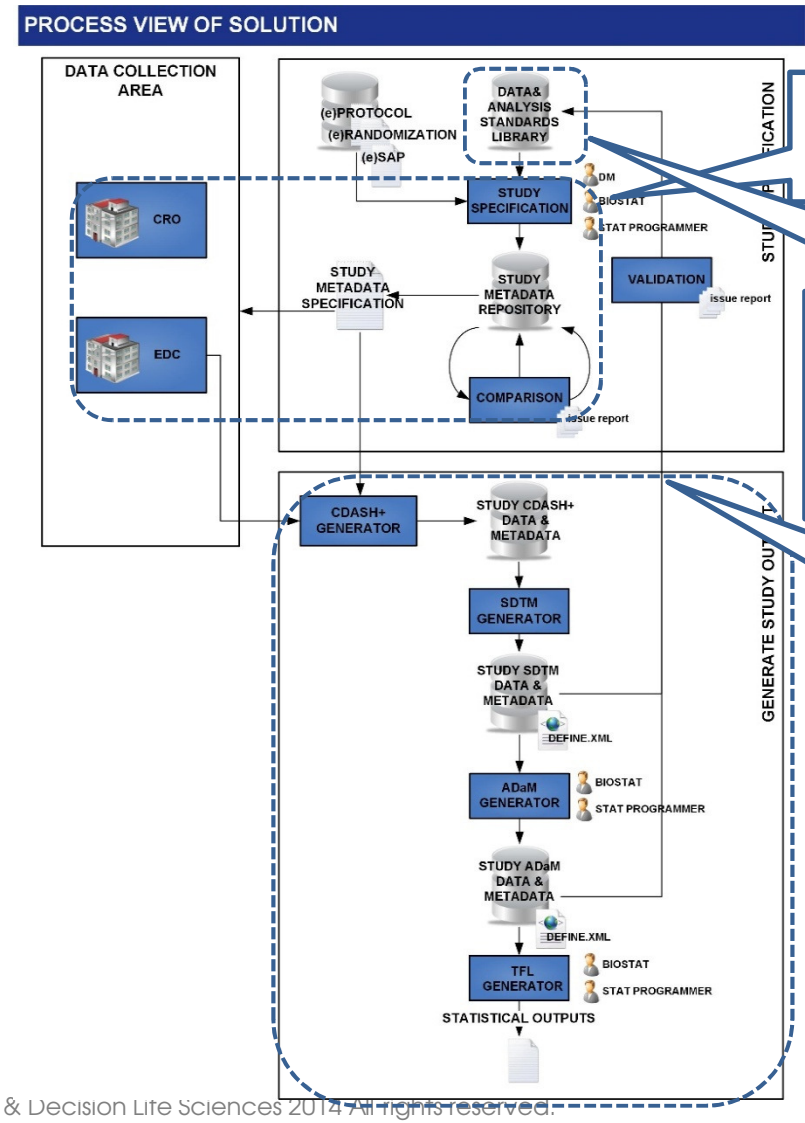
Functionalities



Functionalities



CDmation Roadmap



EDC Build

Extend library to include Analysis Standards

Generate Analysis

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Agenda

Use Case 1 – Study Specification

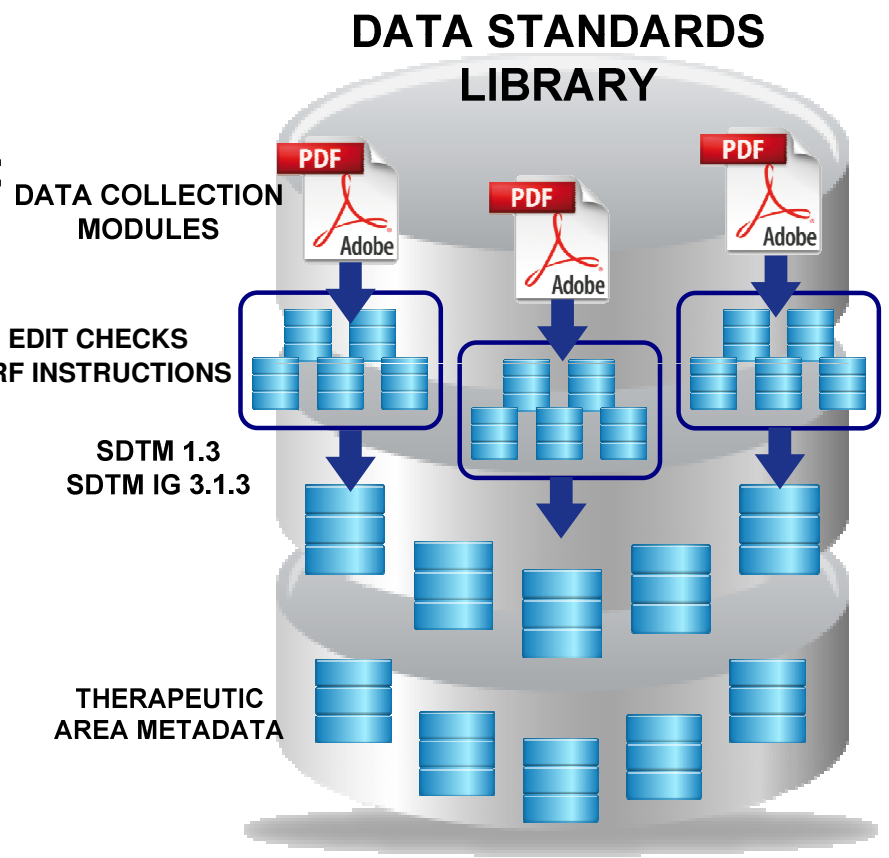
Study Specification and Metadata Repository

- 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

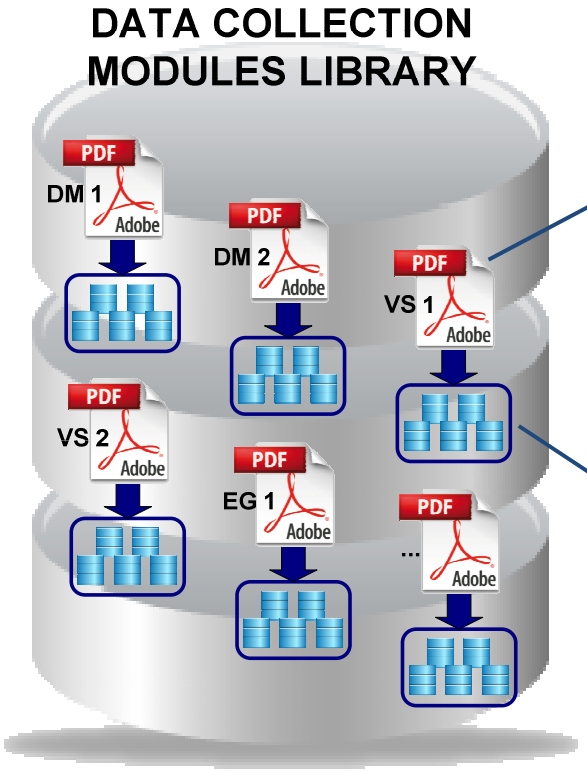
➢ **Ensures CDISC compliant study specifications for your CRO early in the process, maintains data consistency, facilitates submission activities and increases overall quality and reduces rework**

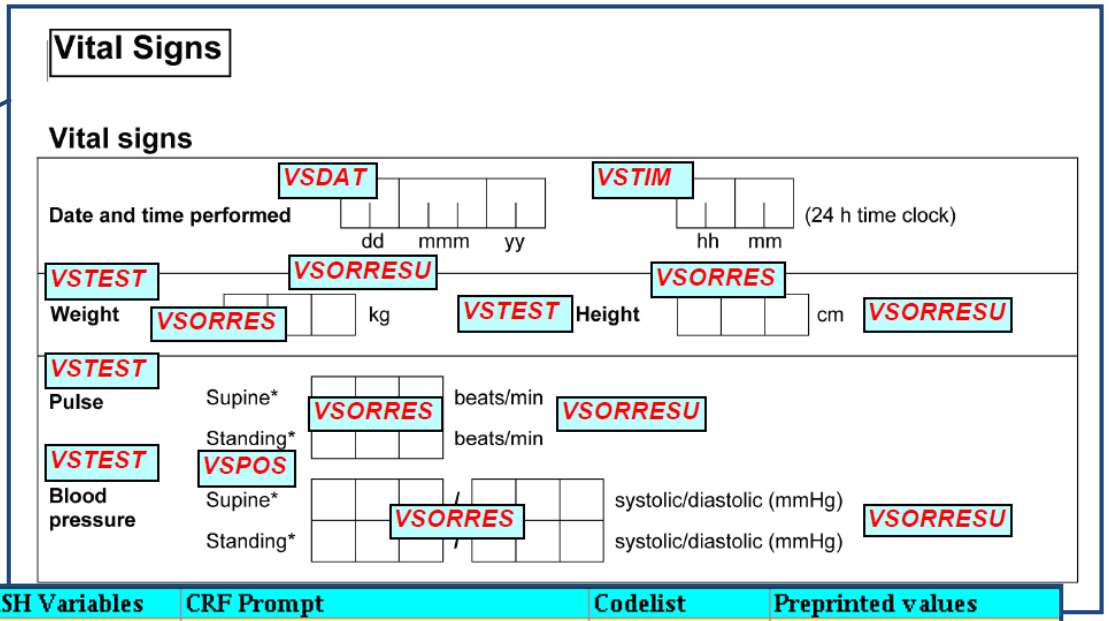
Data Standards Library

- 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

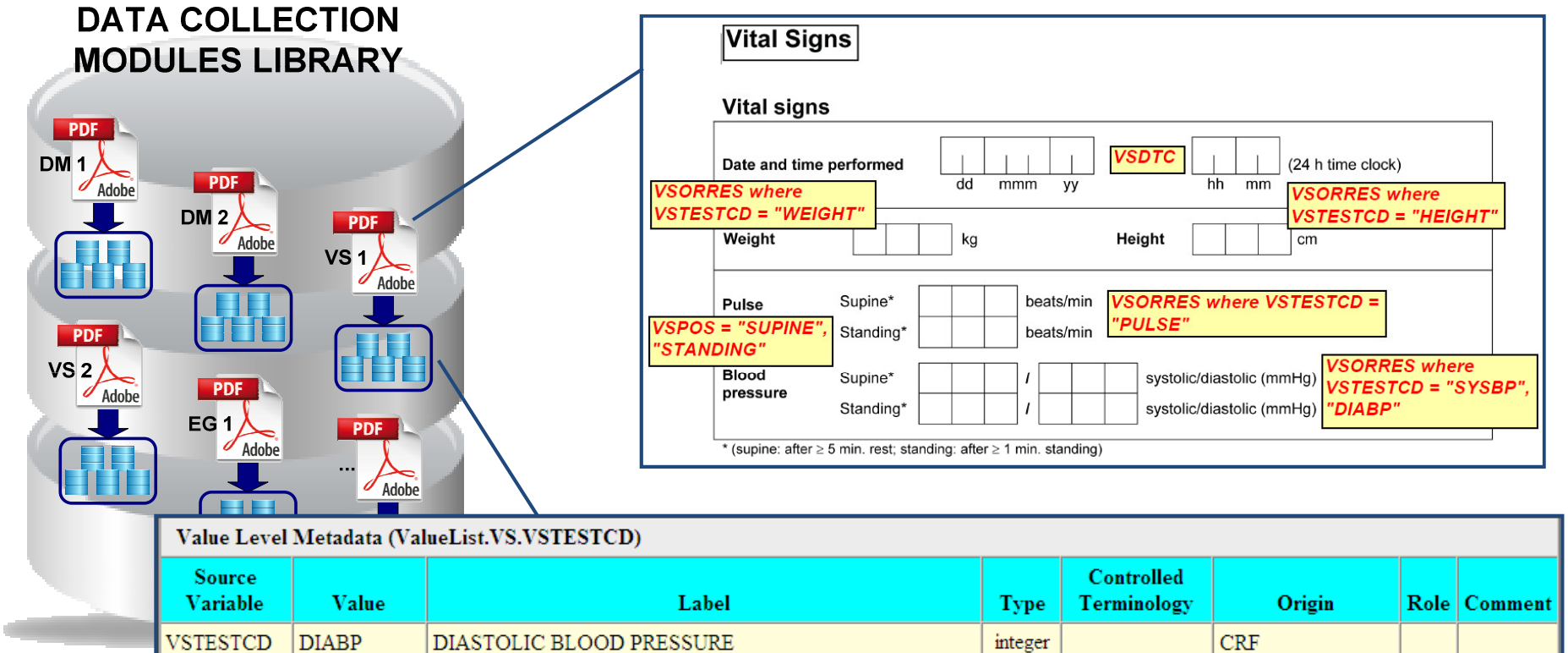




Collected CDASH Variables	CRF Prompt	Codelist	Preprinted values
VSDAT	Date		
VSTIM	Time		
VSPOS	Postion	POSITION	
VSTEST	*Test*	VLM VSTESTCD	Height
VSTEST	*Test*	VLM VSTESTCD	Weight
VSTEST	*Test*	VLM VSTESTCD	Pulse
VSTEST	*Test*	VLM VSTESTCD	Systolic Blood Pressure
VSTEST	*Test*	VLM VSTESTCD	Diastolic Blood Pressure
VSORRESU	*Unit*	VSRESU	cm
VSORRESU	*Unit*	VSRESU	kg
VSORRESU	*Unit*	VSRESU	beats/min
VSORRESU	*Unit*	VSRESU	mmHg

CRF template using CDASH annotations

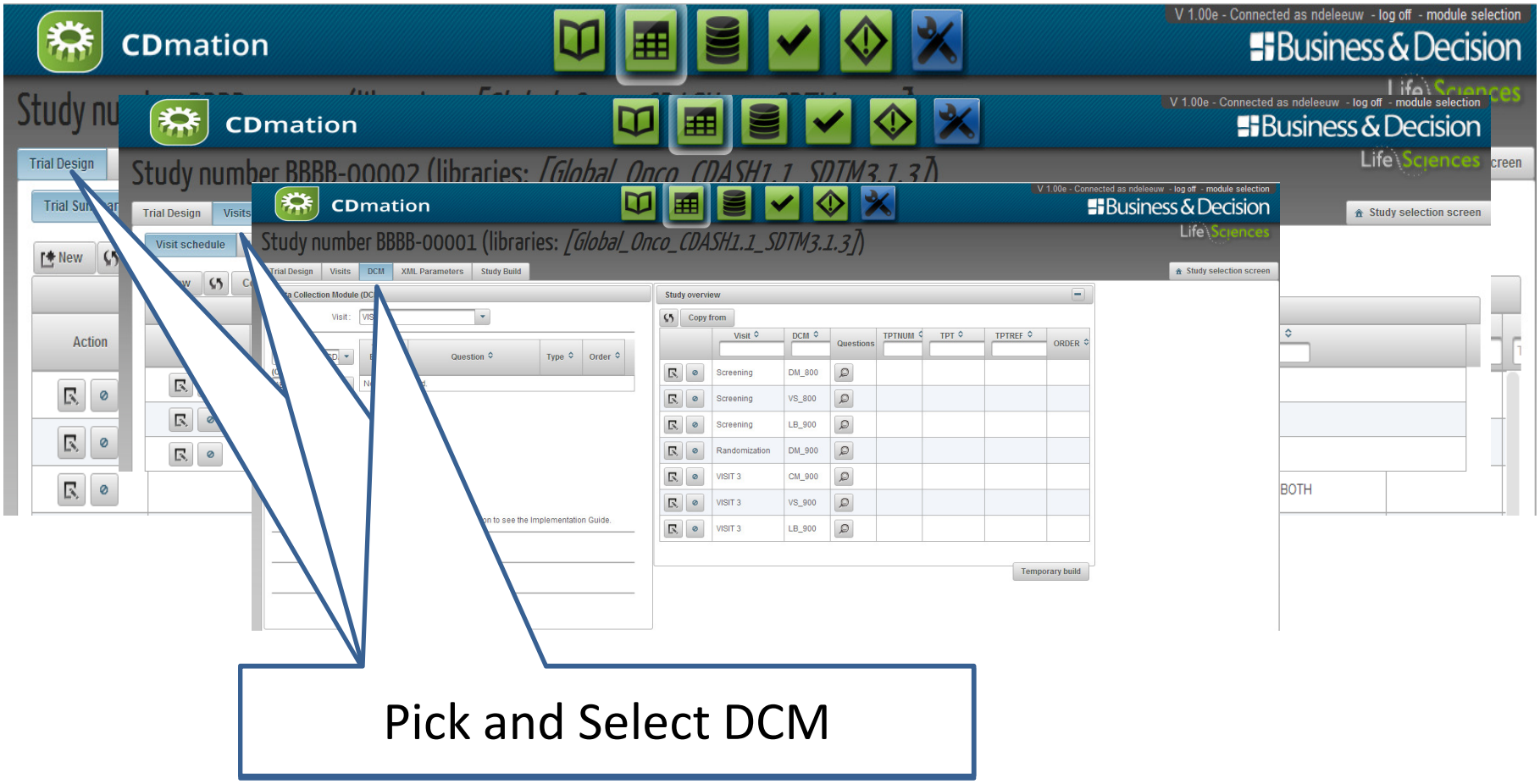
Data Collection Modules - SDTM



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



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 Abbre					
USUBJID	Unique Subjec					

Value Level Metadata (ValueList.VS.VSTESTCD)

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				
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	
M	
U	

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

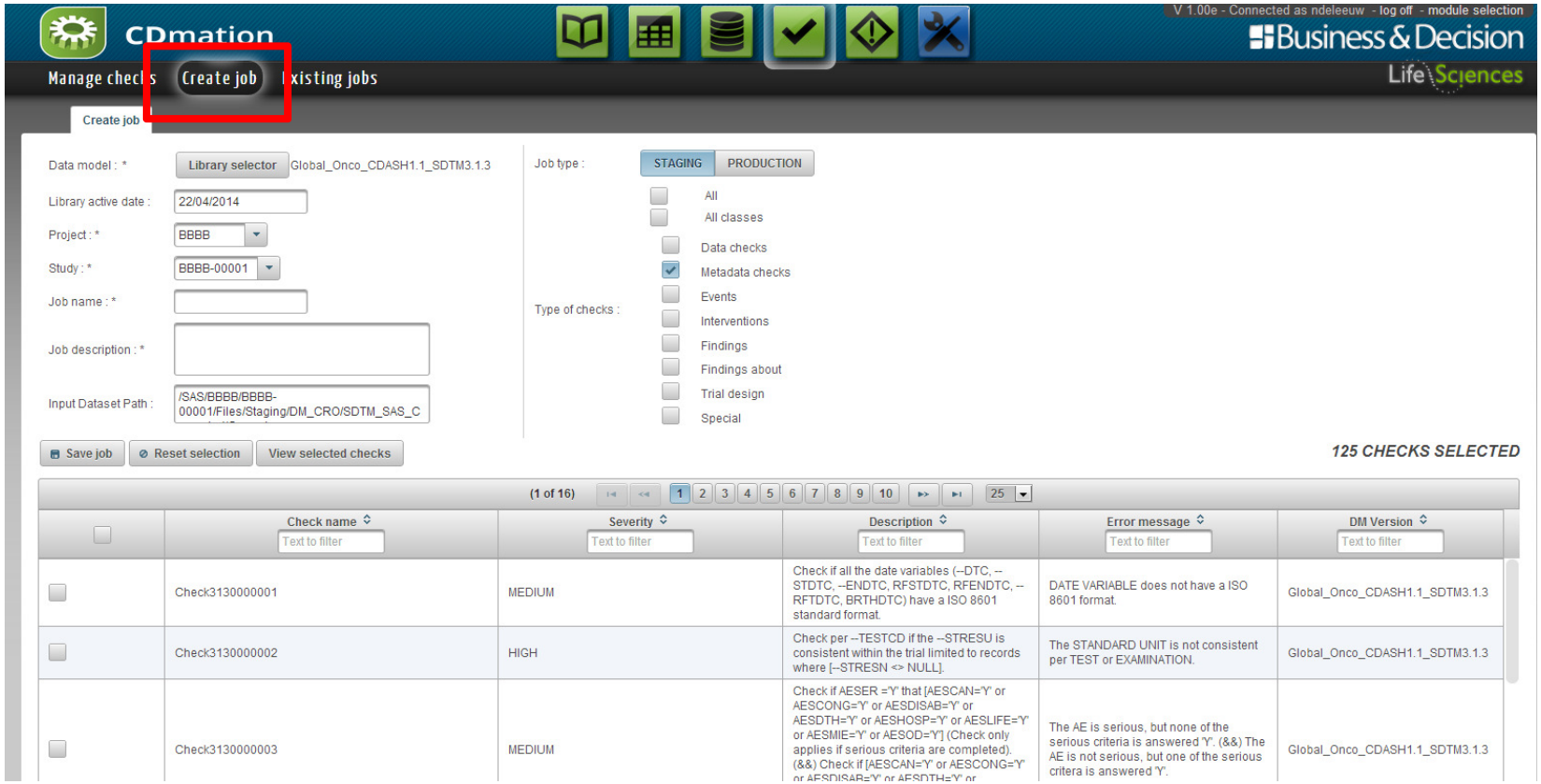
Use Case 2 – Study Validation

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



Run job => Review issues

DATA MODEL COMPLIANCE CHECKER

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	

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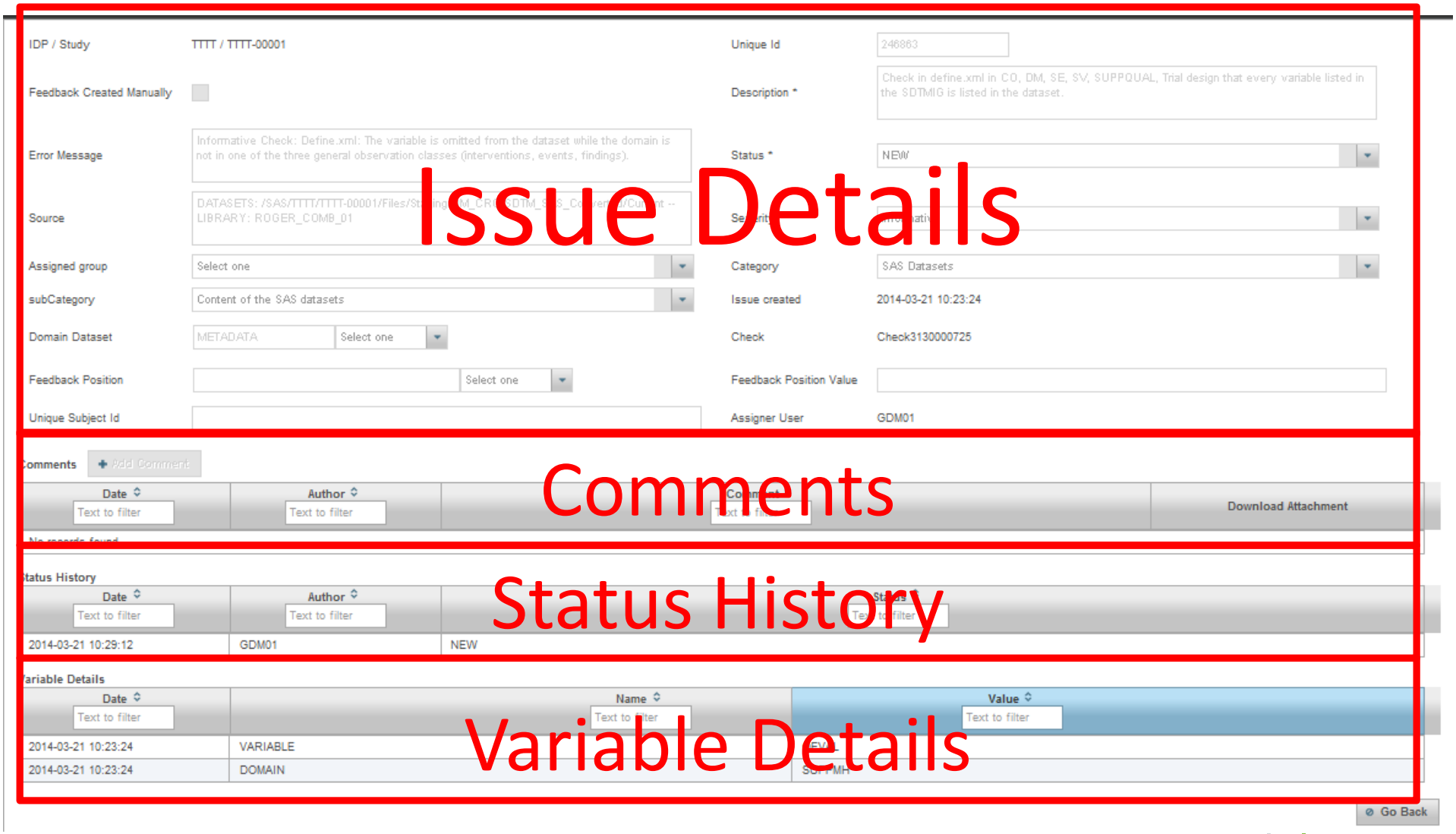
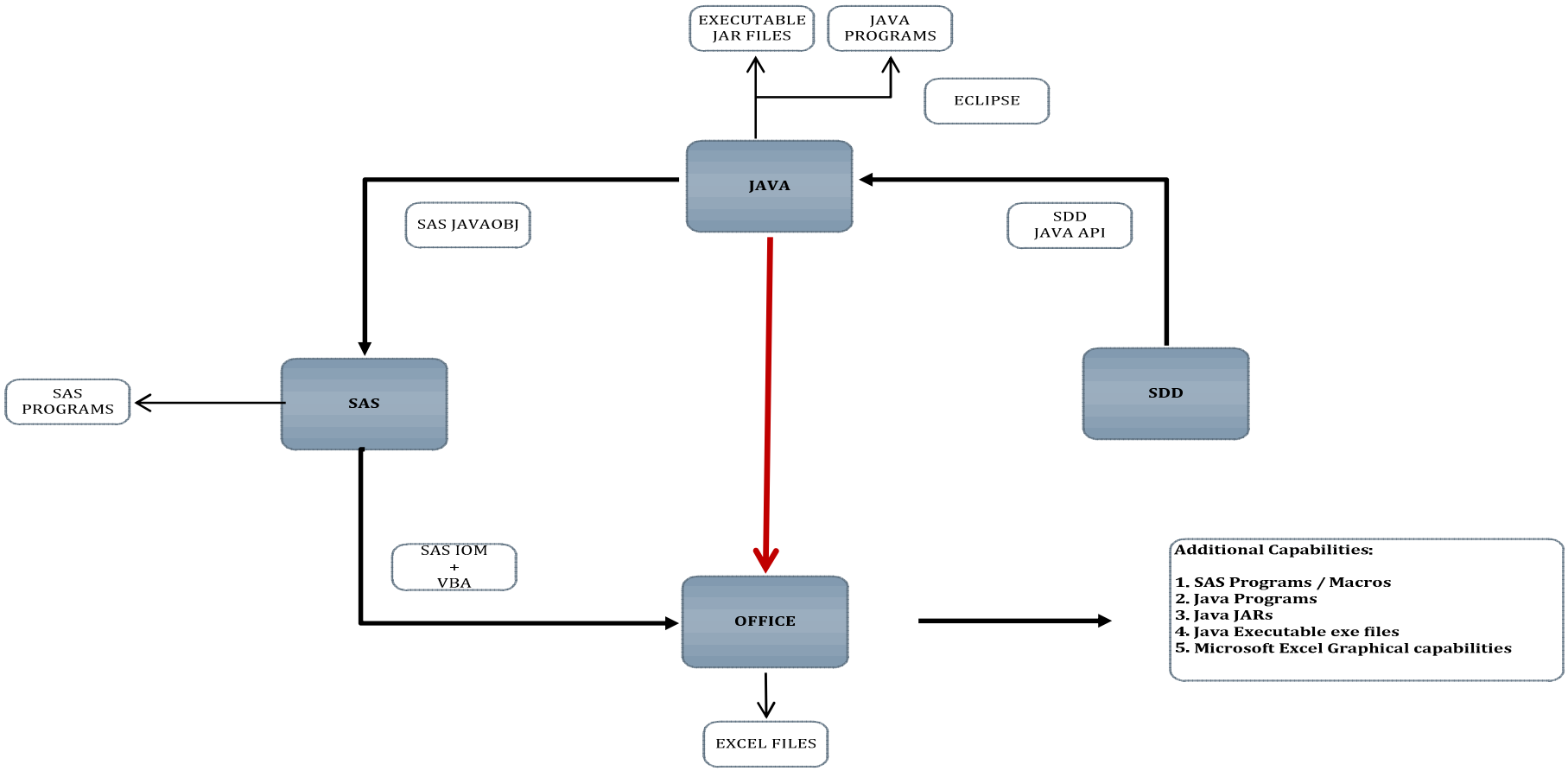
Manage Issues

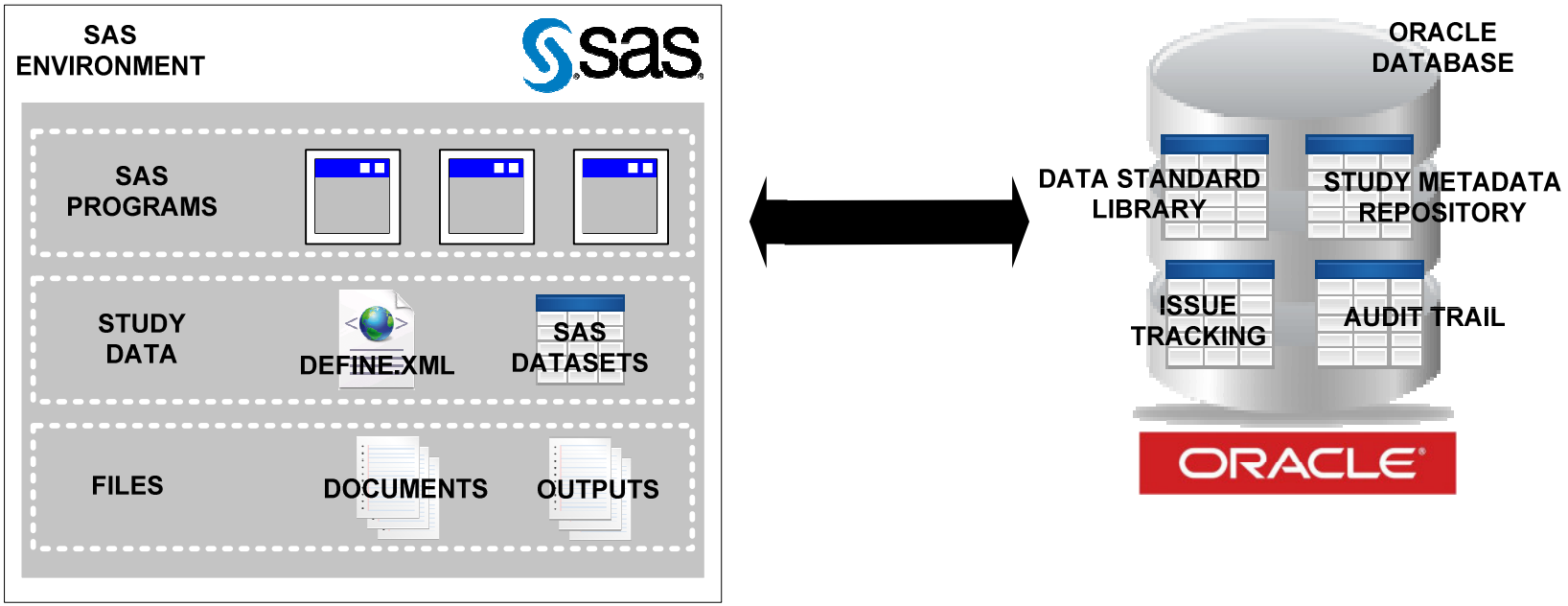


Agenda

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

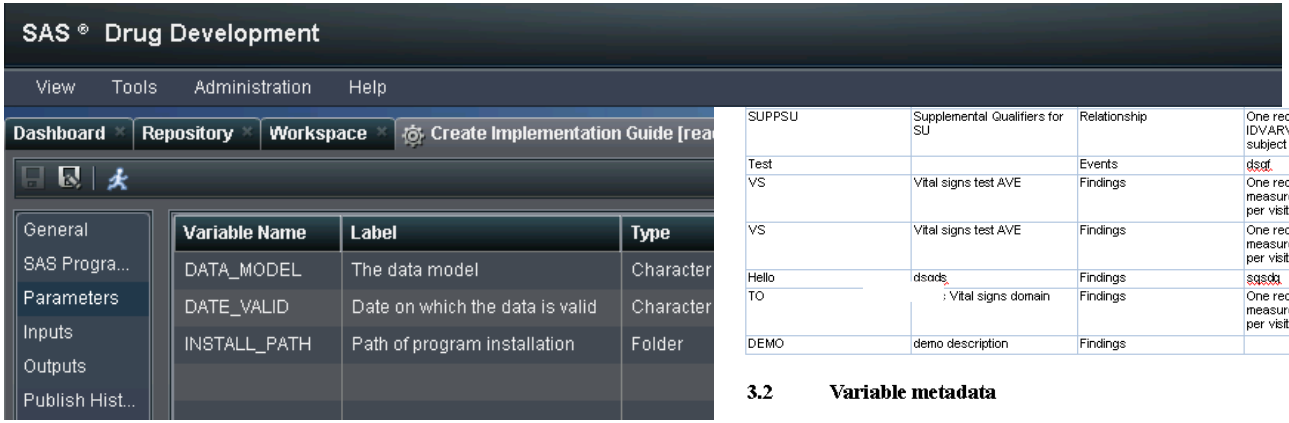
Reporting capability (1)

Data Standards Library Comparison

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



SUPPSU	Supplemental Qualifiers for SU	Relationship	One record per IDVAR, IDVARVAL, QNAM per subject	42	Tabulation
Test		Events	dsaf	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	dsads	Findings	sqsdq	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
Difference	DM	Demographic		X	
Ok	DS	Disposition	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

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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