

SDTM Validation

How can we do it right ?

Peter Van Reusel
Manager CRO Services
Business & Decision Life Sciences

Tel +32 2 774 11 00
Fax +32 2 774 11 99
Mobile +32 476 54 59 17
peter.vanreusel@businessdecision.com

Sint-Lambertusstraat 141 Rue Saint-
Lambert
1200 Brussels

www.businessdecision-lifesciences.com

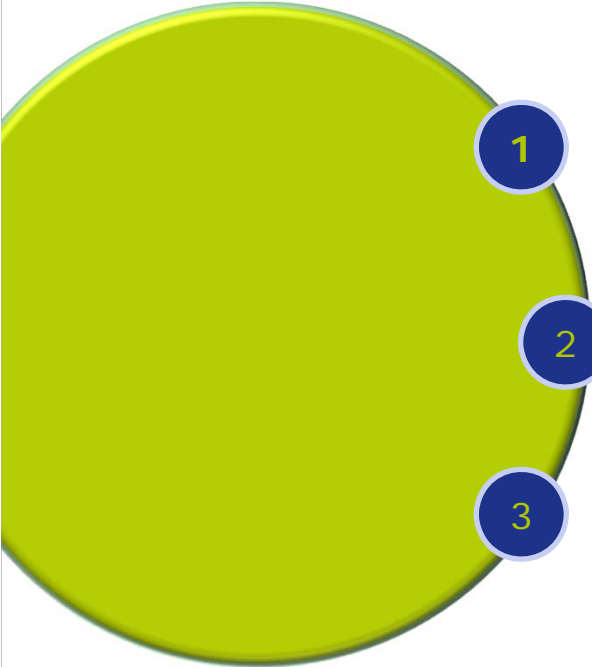


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Topics

- 
- 1 Current Situation
 - 2 Applied SDTM Compliance
 - 3 Summary

Topics

- 
- 1 **Current Situation**
 - 2 Applied SDTM Compliance
 - 3 Summary

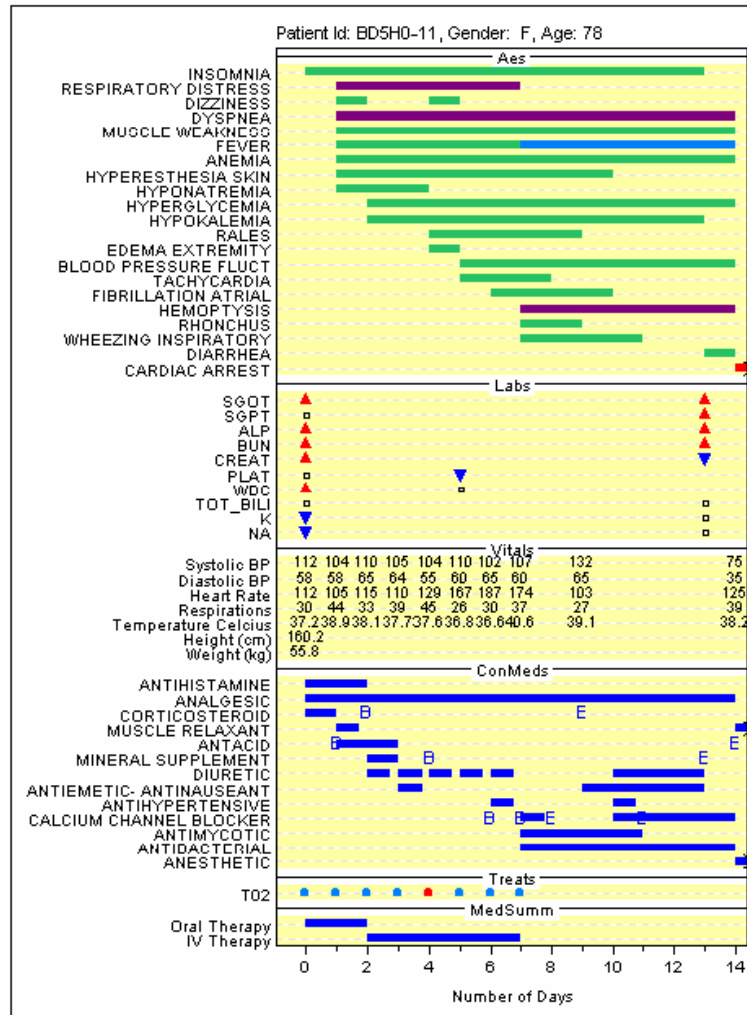
Submissions of NDAs to the FDA

- It is requested to submit clinical trial data (SDTM) & metadata (Define.xml) according to the CDISC standards
- Data standards allow the FDA to use standard tools
- CDISC SDTM = standard structure for study data tabulations

SDTM FDA Tools: Patient Profile Viewer

Subject BD5H0-11

Aes (Time Interval, by Intensity)	
█	Missing Value
█	Mild / Grade I
█	Moderate / Grade II
█	Severe / Grade III
█	Very severe / Grade IV
Labs (Time Point)	
▲	High
□	Normal
▼	Low
■	Missing Value
○	Missing Range Values
Vitals (Time Point)	
○	Normal
?	Missing Value
ConMeds (Time Interval)	
Treats (Time Point, by Dose Frequency)	
■	Missing Value
●	1
●	3
●	4
MedSumm (Time Interval)	
⊠	Missing End
⊞	Missing Begin



SDTM FDA Tools: Web SDM (1)

Web Submission Data Manager - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Address C:\Demo\Links AE2.htm

FDA AE Preferences Settings Feedback Exit Help

Home Select Browse Report Subject Lists Advanced Load&Check Run Queue

User: BATCHAPP Administrator [admin], Context: Pilot_1:Pilot_1

374 rows

STUDYID	USUBJID	AGE	SEX	RACE	TRTCD	TRTGRP	AETERM	AFACTSDY	AFACTEDY
STY1234A0001	STY1234A00016603	58	M	WHITE	1	STY1234A	GASTROENTERITIS- PROBABLY VIRAL	50	52
STY1234A0001	STY1234A00016603	58	M	WHITE	1	STY1234A	COMMON COLD SYMPTOMS	190	193
STY1234A0001	STY1234A00016604	62	M	WHITE	3	CONTROL C	ADHESIVE CAPSULITIS OF RIGHT SHOULDER	-3	7
STY1234A0001	STY1234A00016604	62	M	WHITE	3	CONTROL C	HYPERLIPIDEMIA	59	
STY1234A0001	STY1234A00016604	62	M	WHITE	3	CONTROL C	HEMORRHAGE AT DISC MARGIN OF BOTH EYES	106	

STUDYID	AESTDT	AENDT	ASEQ	ADECOD	AEBODSYS	AEDUR	AEDURU	AESEV	AESER
STY1234A0001	04-Dec-1997	06-Dec-1997	1	GASTROENTERITIS	DIGESTIVE SYSTEM	2	DAYS	SEVERE	Y
STY1234A0001	23-Apr-1998	26-Apr-1998	2	UPPER RESPIRATORY INFECTION	RESPIRATORY SYSTEM	3	DAYS	MILD	N
STY1234A0001	10-Oct-1997	20-Oct-1997	1	JOINT DISORDER	MUSCULO-SKELETAL SYSTEM	10	DAYS	MILD	N
STY1234A0001	11-Dec-1997		2	HYPERLIPEMIA	METABOLIC & NUTRITIONAL DISORDERS			MILD	N
STY1234A0001	17-Apr-1998		3	RETINAL HEMORRHAGE	SPECIAL SENSES			MODERATE	N

STUDYID	SAEDTH	SAELIFE	SAEDISAB	SAEHOSP	SAECAN	SAEOD	SAEONG	SAEDTH	AECTRT
STY1234A0001	N	N	N	Y	N	N	N	N	DOSE NOT CHANGED
STY1234A0001	N	N	N	N	N	N	N	N	DOSE NOT CHANGED
STY1234A0001	N	N	N	N	N	N	N	N	DOSE NOT CHANGED
STY1234A0001	N	N	N	N	N	N	N	N	DOSE NOT CHANGED
STY1234A0001	N	N	N	N	N	N	N	N	DOSE NOT CHANGED

SDTM FDA Tools: Web SDM (2)

Web Submission Data Manager - Microsoft Internet Explorer

Address: http://localhost:8080/BatchApp/ctShowCompositeTable.jsp?savedQueryID=107

FDA Display Report

User: BATCHAPP Administrator [admin]

Home Select Browse Report Subject Lists Advanced Load&Check Run Queue

Results Manage Results Reports Manage Reports Create Report

Report Results [Avg cholesterol for age groups by visit] 4 rows

Options Save Results Edit Definition Save Definition Graphs Download

AGE	Gender																								
	Males										Females														
	Visit Group										Visit Group														
	1, 2, 3, 4					4, 5, 6, 7, 8					1, 2, 3, 4					4, 5, 6, 7, 8									
	Tot. CHOL		LDL		HDL		Tot. CHOL		LDL		HDL		Tot. CHOL		LDL		HDL		Tot. CHOL		LDL		HDL		
	TC	TM	TC	TM	TC	TM	TC	TM	TC	TM	TC	TM	TC	TM	TC	TM	TC	TM	TC	TM	TC	TM	TC	TM	
20 - 40	5	5.79	5	2.71	5	0.77	6	4.97	6	1.91	6	0.74	2	6.06	2	3.16	2	1.15							
40 - 60	88	4.89	88	2.5	88	1.05	90	4.82	90	2.39	88	1	75	5.48	75	2.89	74	1.22	83	4.92	83	2.46	83	1.21	
60 - 80	99	4.94	99	2.61	99	1.05	113	4.73	113	2.48	113	1.02	58	5.31	58	2.78	58	1.33	62	5.27	62	2.57	60	1.27	
80 -	1	5.07	1	2.51	1	1.71																			

Audit Information
 Data Source: SDMSAMPJ
 Subject List: null
 Report: Avg cholesterol for age groups by visit
 User: BATCHAPP Administrator
 Date: 09/02/2003 18:28:53 EDT

Done Local Intranet

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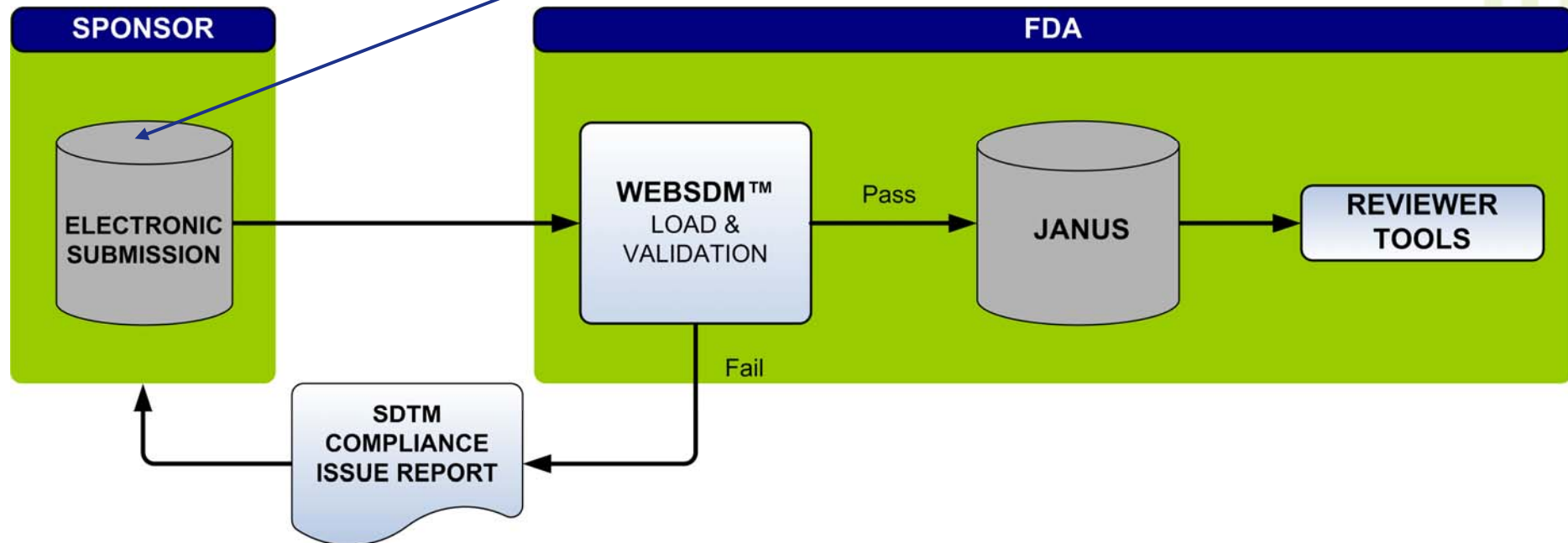
CDISC SDTM Conformance

- Follow **complete metadata structure**
- Follow **CDISC domain models**
- Include all **Required and Expected variables**
- Use CDISC-specified:
 - standard **domain names** and prefixes
 - standard **variable names**
 - **variable labels**
 - **data types** for all variables
 - **controlled terminology** and **format** guidelines
- Currently, adhere to the **SAS V5 XPT limitations**
- Ensure that each dataset includes a set of **keys**
- Ensure that each record in a dataset includes a **topic variable**
- Conform to all **business rules**

CDISC SDTM Submission Process

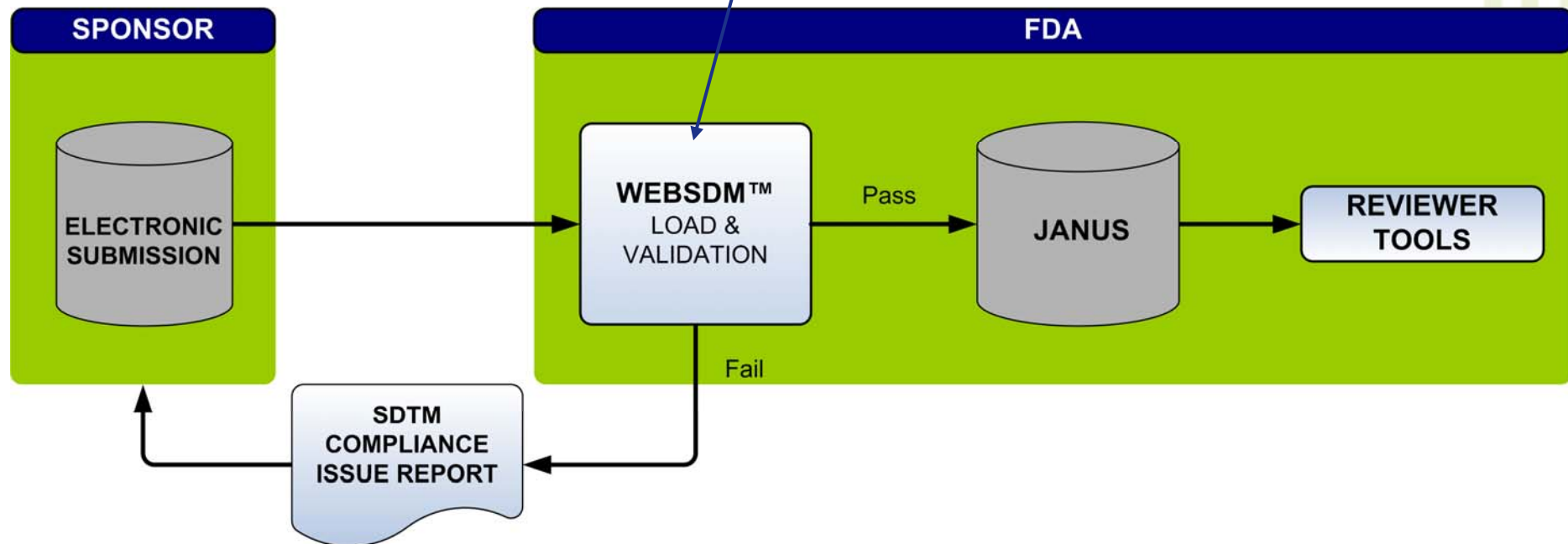
Data Tabulation Components:

- SDTM annotated CRFs
- SDTM datasets
- Define.xml metadata



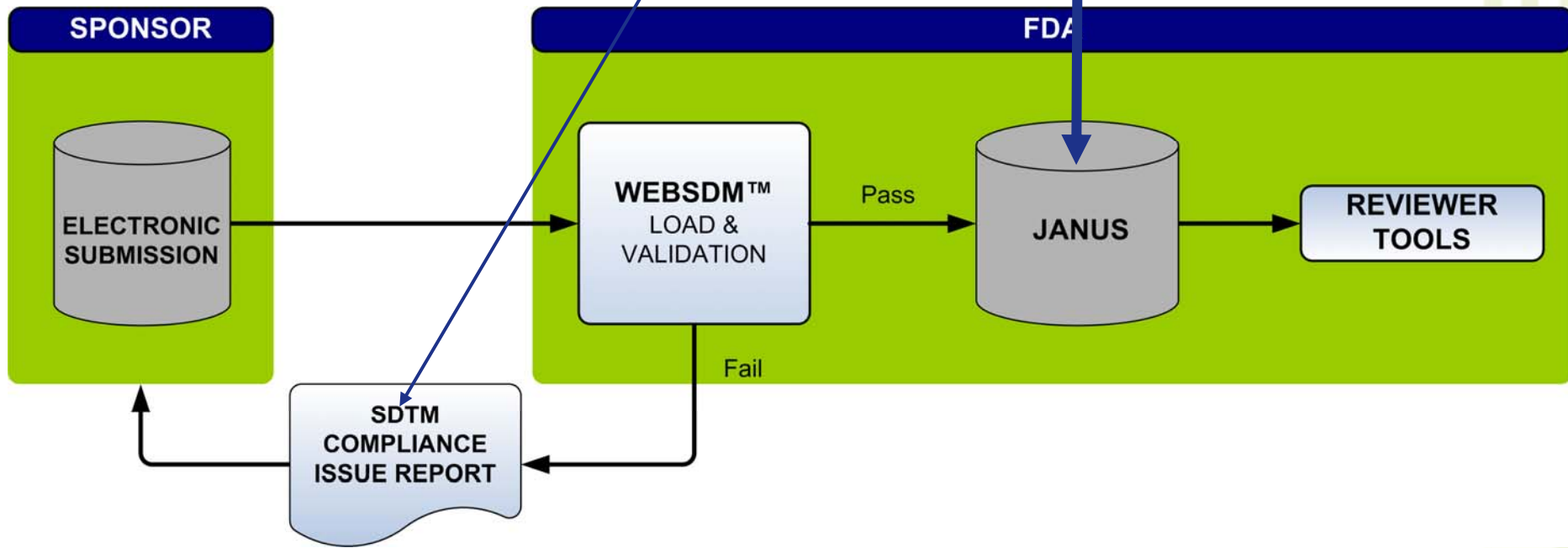
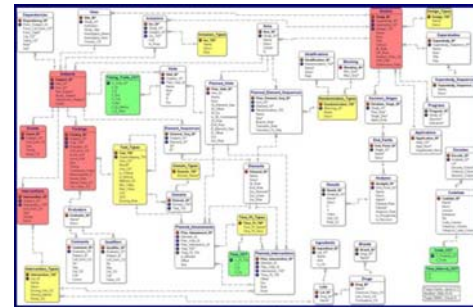
CDISC CRT Submission Process

WebSDM™ tool checks the CDISC SDTM data & metadata before loading it into the FDA's clinical data warehouse (Janus)

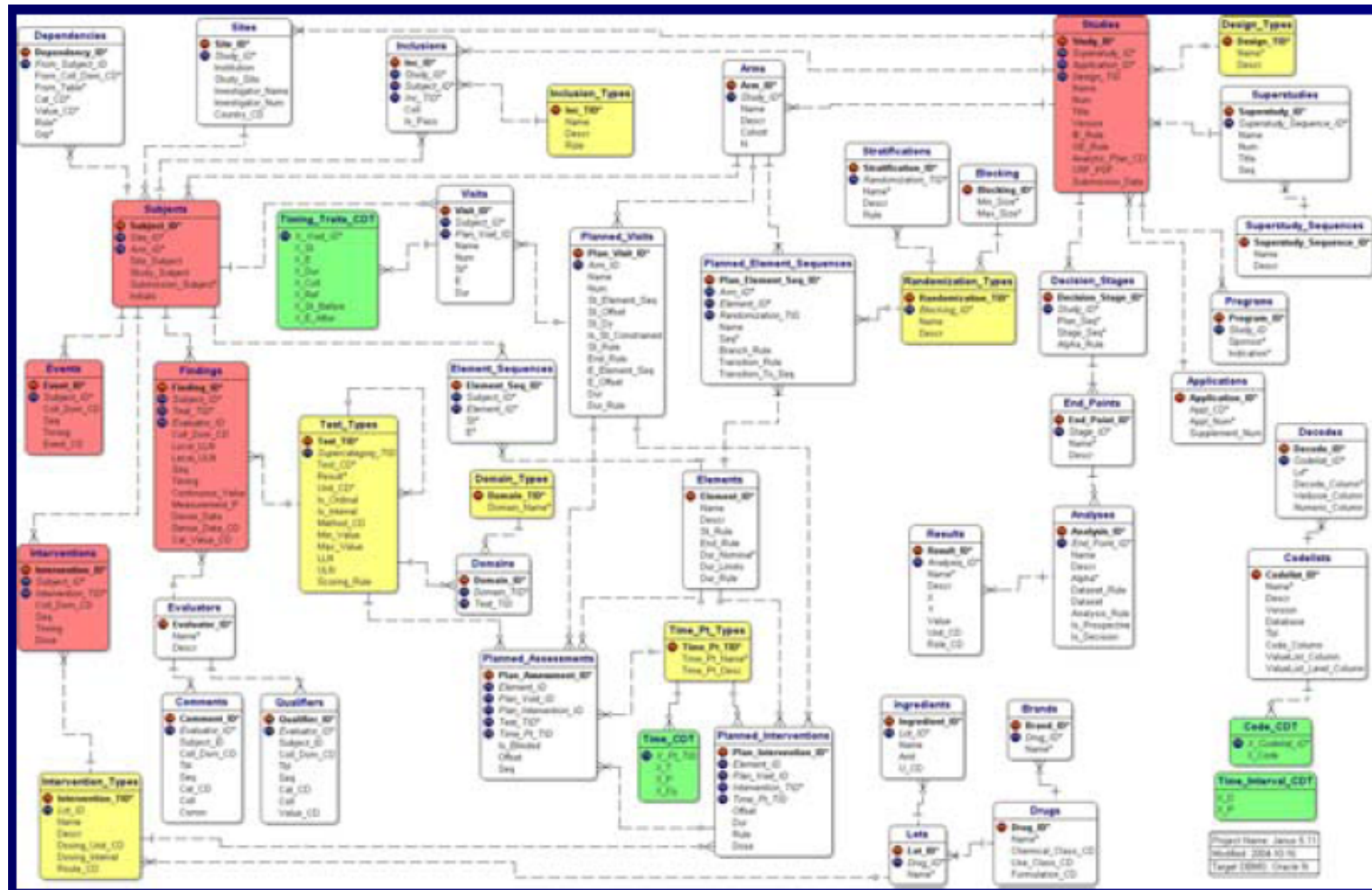


CDISC CRT Submission Process

CDISC SDTM compliance issues are reported to the sponsor



Janus



http://www.fda.gov/oc/datacouncil/janus_operational_pilot.html

WebSDM™ Load & Validation

WebSDM™ V2.6 Validation Checks:

- 108 Checks
- Severity definition: High – Medium – Low

<http://phaseforward.com/resource/whitepapers/Validation%20Checks%202.6/WebSDM%20V2.6%20Validation%20Checks%20FINAL.pdf>

SDTM Compliance Issues Report

- OBPS provides an SDTM issue list to the sponsor
- OBPS = Office of Business Process Support
- Loading issues can be caused by
 - Data & Metadata Inconsistency
 - Non conformity with:
 - » SDTM Model
 - » SDTM IG business rules
 - » Controlled Terminology

Topics

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SDTM Compliance Checks

We have created an expanded & enhanced list of checks

- 108 WebSDM™ checks
- Total check package:

	SDTM 3.1.1	SDTM 3.1.2
Data checks	135	214
Metadata checks	68	85
Mapping checks	55	55

SDTM compliance checks list is still growing

Categorization

- SDTM Compliance Checks Categories

- Data
- Metadata
- Mapping
- Class
- Domain
- Controlled Terminology
- Timing variables
- SDTM IG version
- Check version

CHECKID	SUB CHECKID	CHECK DESCRIPTION	ERROR MESSAGE	CATEGORIZING						SDTM IMPLEMENTATION GUIDE VERSION	CHECK VERSION	
				DATA	METADATA	MAPPING SHEET	CLASS	DOMAIN	CONTROLLED TERMINOLOGY			TIMING VARIABLES
0001		Check if all the date variables (--DTC, --STDTC, --ENDTC, RFSTDC, RFENDTC) have a ISO 8601 standard format.	DATE VARIABLE does not have a ISO 8601 format.	X			ALL	ALL	N	Y	3.1.1	0.1
0002		Check per LBTESTCD if the LBSTRESU is consistent within the trial.	The STANDARD UNIT is not consistent per LAB TEST or EXAMINATION.	X			FINDINGS	LB	N	N	3.1.1	0.1
0003	1	Check if AESER = "Y" that [AESCAN="Y" or AESCONG="Y" or AESDISAB="Y" or AESDTH="Y" or AESH0SP="Y" or AESJFE="Y" or AESME="Y" or AESOD="Y"] (Check only applies if serious criteria are completed).	The AE is serious, but none of the serious criteria is answered "Y".	X			EVENTS	AE	N	N	3.1.1	0.1
0003	2	Check if [AESCAN="Y" or AESCONG="Y" or AESDISAB="Y" or AESDTH="Y" or AESH0SP="Y" or AESJFE="Y" or AESME="Y" or AESOD="Y"] that AESER = "Y".	The AE is not serious, but one of the serious criteria is answered "Y".								3.1.1	0.1
		Check if --STRESC <> NULL	A STANDARD RESULT is									

How is the categorization used?

A subset of checks can be created :

**BY
DATA STANDARD
VERSION**

- SDTM IG 3.1.1
- SDTM IG 3.1.2
- Proprietary

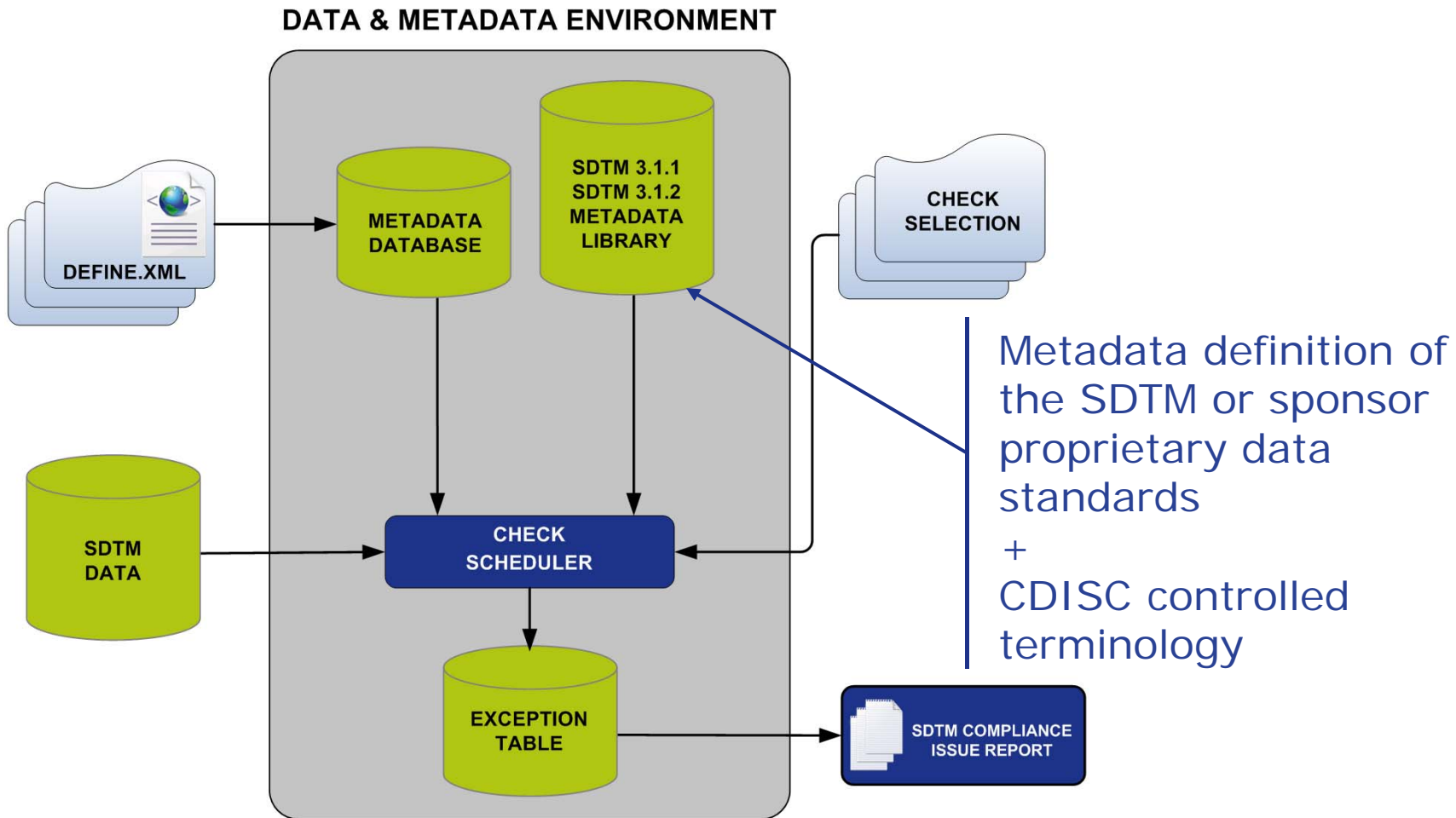
**BY
CHECK TYPE**

- All check types
- Data checks
- Metadata checks

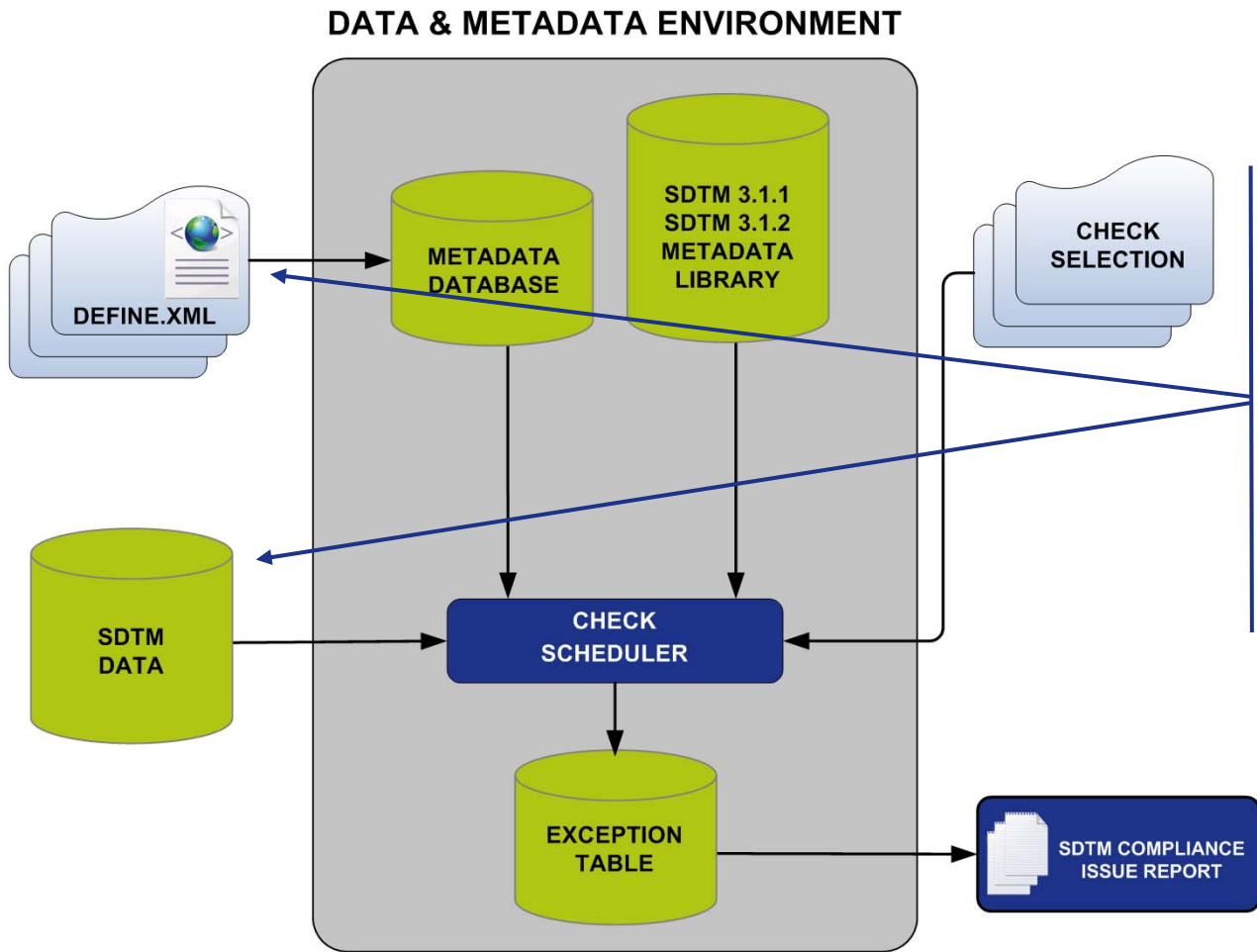
**BY
DOMAIN TYPE**

- All domains, one specific domain
- All Findings class domains
- All Interventions class domains
- All Events class domains
- All special purpose domains
- All Trial Design domains

Application Flowchart

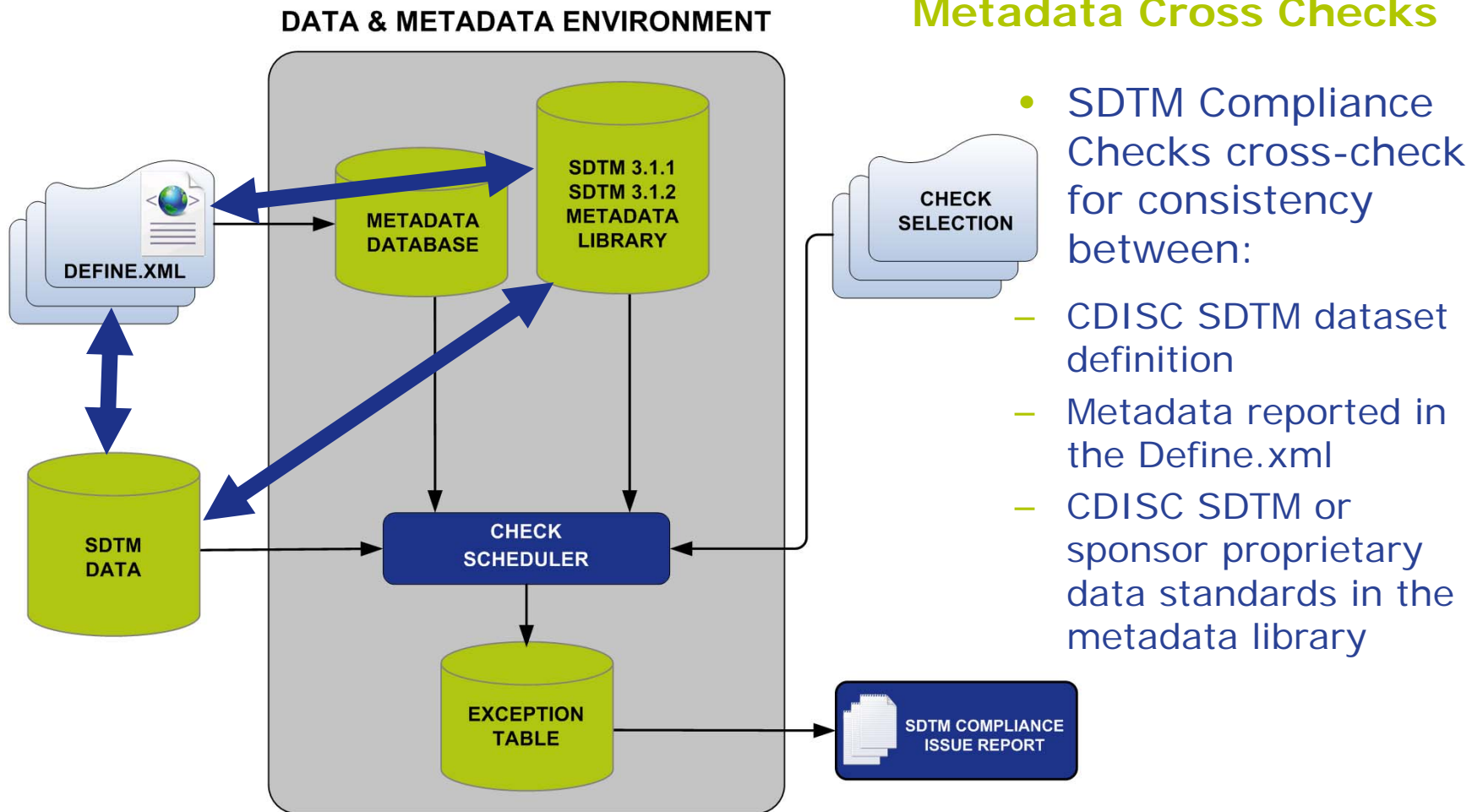


Application Flowchart

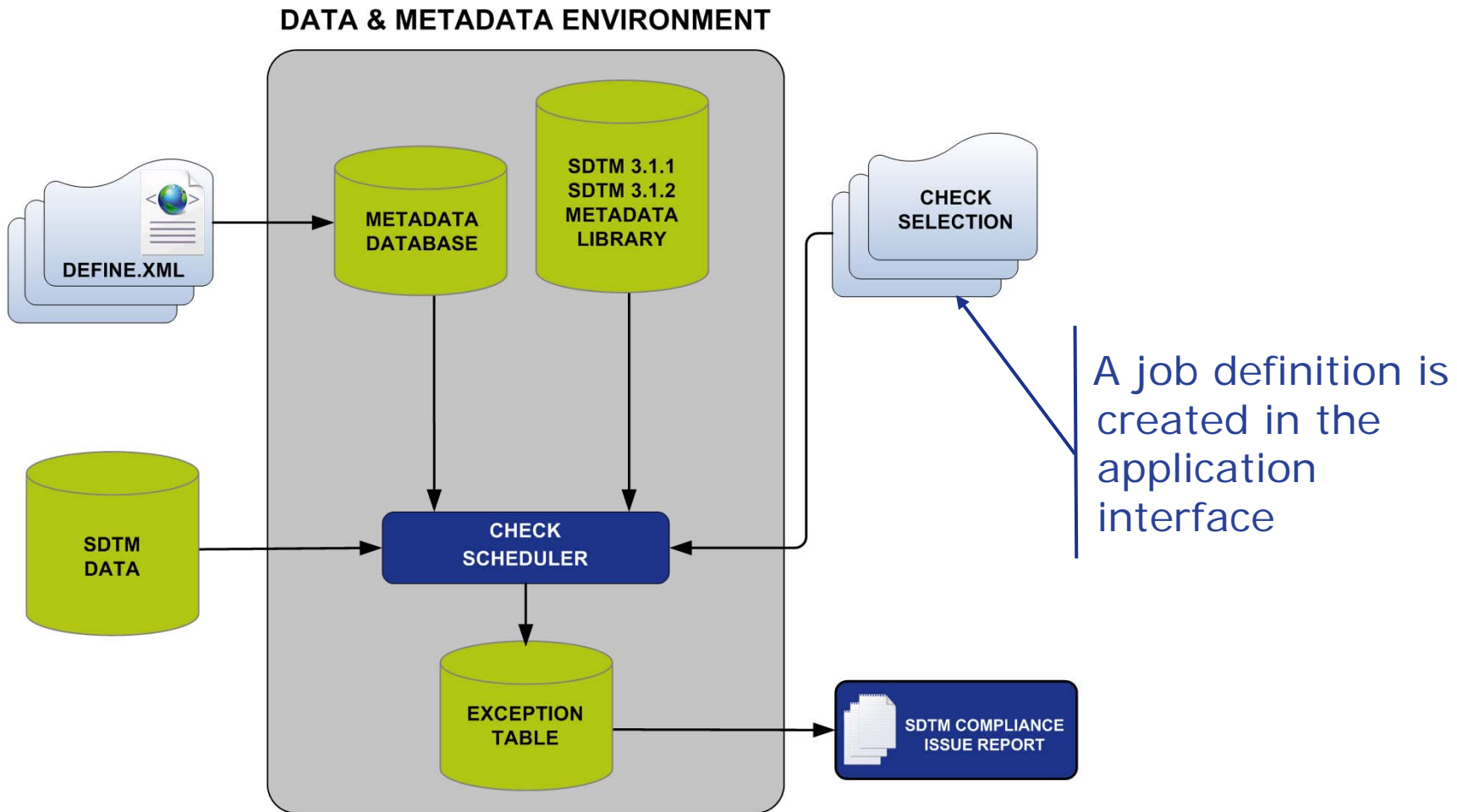


The SDTM compliance checks system reads the folder with the SDTM datasets & the define.xml metadata file

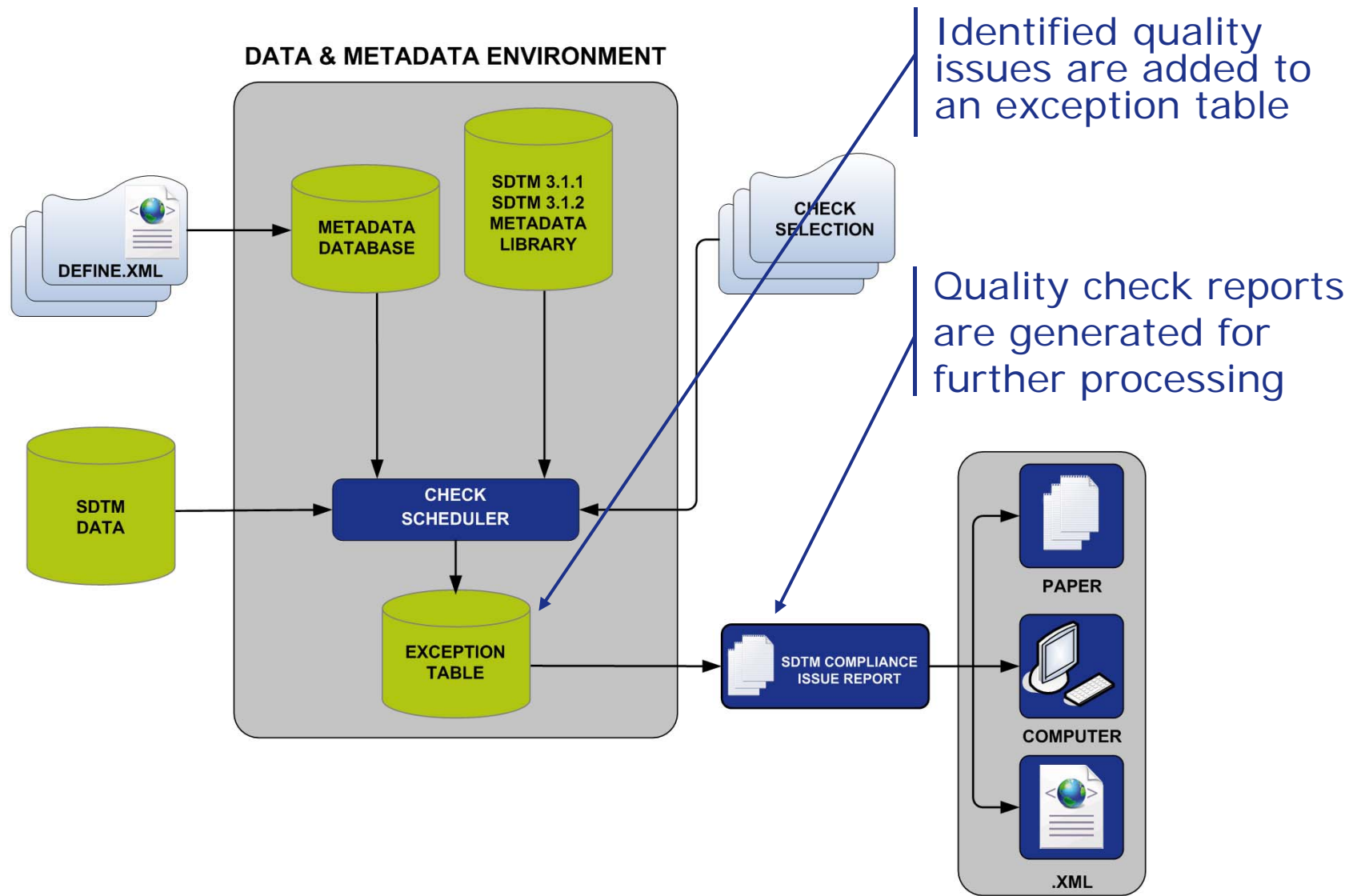
Application Flowchart



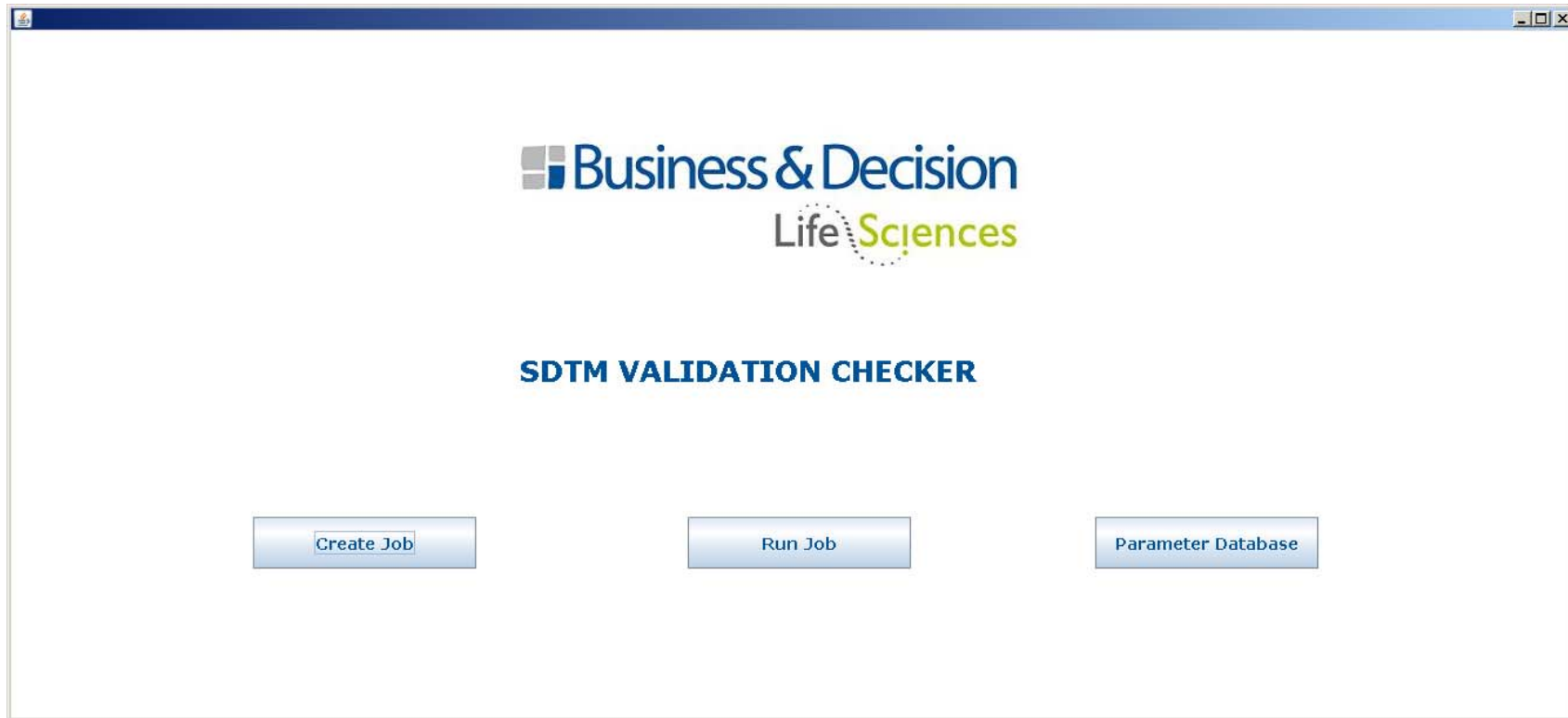
Application Flowchart



Application Flowchart



Application Interface



Application Interface

- Job Creation Screen
 - Check Selection :
 - Select Project and Study
 - Select Checks based on
 - Class – Events, Interventions, Findings, Trial Design, Special Purpose
 - Type – Data, Metadata, Programming
 - Individual
 - Select from dynamically created list of domains
 - Creates JobID
 - Check Description :
 - Detailed description of all checks
 - Possibility of adding/modifying check descriptions

Application Interface

- Check Selection :

Check Selection Form

Select the checks to run: **Check Description**

Choose Project: BBS Enter Job Description: Data Checks on Interventions **NEXT**

Choose StudyID: 1160-0007

Select All
 Data Checks
 Metadata Checks
 Mapping Checks
 Programming Checks

 Select All
 Events
 Interventions
 Findings
 Trial Design
 Special Purpose

 SDTM 3.1.1
 SDTM 3.1.2

CheckID	Select
Check001	<input checked="" type="checkbox"/>
Check002	<input type="checkbox"/>
Check003	<input type="checkbox"/>
Check004	<input type="checkbox"/>
Check005	<input checked="" type="checkbox"/>
Check006	<input checked="" type="checkbox"/>
Check007	<input type="checkbox"/>
Check008	<input type="checkbox"/>
Check009	<input type="checkbox"/>
Check010	<input type="checkbox"/>
Check011	<input type="checkbox"/>
Check012	<input checked="" type="checkbox"/>
Check013	<input checked="" type="checkbox"/>
Check014	<input checked="" type="checkbox"/>
Check015	<input type="checkbox"/>
Check016	<input type="checkbox"/>
Check017	<input type="checkbox"/>
Check018	<input type="checkbox"/>
Check019	<input type="checkbox"/>
Check020	<input type="checkbox"/>
Check021	<input type="checkbox"/>
Check022	<input type="checkbox"/>
Check023	<input type="checkbox"/>
Check024	<input type="checkbox"/>
Check025	<input type="checkbox"/>
Check026	<input checked="" type="checkbox"/>
Check027	<input checked="" type="checkbox"/>
Check028	<input checked="" type="checkbox"/>
Check029	<input checked="" type="checkbox"/>
Check030	<input checked="" type="checkbox"/>

Domains	Select
AS	<input type="checkbox"/>
CH	<input type="checkbox"/>
CO	<input type="checkbox"/>
DM	<input type="checkbox"/>
DS	<input type="checkbox"/>
EX	<input type="checkbox"/>
GW	<input type="checkbox"/>
IF	<input checked="" type="checkbox"/>
IS	<input type="checkbox"/>
LI	<input type="checkbox"/>
ML	<input type="checkbox"/>
PC	<input checked="" type="checkbox"/>
PP	<input type="checkbox"/>
RU	<input type="checkbox"/>
SUPAE	<input type="checkbox"/>
SUPCDM	<input type="checkbox"/>
SUPDM	<input type="checkbox"/>
SUPDMH	<input type="checkbox"/>
SUPPPC	<input type="checkbox"/>
SUPPPP	<input type="checkbox"/>

Application Interface

- Run Job Screen
 - Job List :
 - » Lists Job ID, Job description, Job owner, Job creation date
 - » Select the job to run
 - Job Description :
 - » Lists project and studyid for the selected job
 - » Lists checks to run for the selected job
 - » Lists domains on which selected checks run

Application Interface

- Job List

Job ID	Rep ID	Study ID	Job Owner	Job Description	Job Creation Date
1	855	1 65 0225	phorngs	25 Data & Metadata	2009-10-22 09:25
2	855	1 65 0224	phorngs	24 Data & Metadata without 10,16	2009-10-22 09:20
3	855	1 65 0225	phorngs	25 Data & Metadata without 10,16	2009-10-22 09:21
4	855	1 65 0224	indefonder	Final run	2009-10-22 09:43
5	855	1 65 0225	ocid	Final run	2009-10-22 09:34
6	855	1 65 0225	ocid	Final run 2	2009-10-22 09:43
7	855	1 65 0224	indefonder	24 Final run	2009-10-22 09:21
8	855	1 65 0225	indefonder	25 Final run	2009-10-22 09:24
9	855	1 65 0243	indefonder	43 Final run	2009-10-22 09:05
10	855	1 65 0243	dbasic	43 Metadata 42	2009-10-22 09:23
11	855	1 65 0225	indefonder	D-TS CHECKS	2009-10-22 09:43

Run

Business & Decision
Life Sciences

Application Interface

- Job Description

Job_ID	Rep_ID	Study_ID	List_Of_Checks	List_Of_Domains
5	065	1160-0020	Check0001	ALL
5	065	1160-0020	Check0002	ALL
5	065	1160-0020	Check0003	ALL
5	065	1160-0020	Check0004	ALL
5	065	1160-0020	Check0005	ALL
5	065	1160-0020	Check0006	ALL
5	065	1160-0020	Check0007	ALL
5	065	1160-0020	Check0008	ALL
5	065	1160-0020	Check0009	ALL
5	065	1160-0020	Check0010	ALL
5	065	1160-0020	Check0011	ALL
5	065	1160-0020	Check0012	ALL
5	065	1160-0020	Check0013	ALL
5	065	1160-0020	Check0014	ALL
5	065	1160-0020	Check0015	ALL
5	065	1160-0020	Check0016	ALL
5	065	1160-0020	Check0017	ALL
5	065	1160-0020	Check0018	ALL
5	065	1160-0020	Check0019	ALL
5	065	1160-0020	Check0020	ALL
5	065	1160-0020	Check0021	ALL
5	065	1160-0020	Check0022	ALL
5	065	1160-0020	Check0023	ALL
5	065	1160-0020	Check0024	ALL
5	065	1160-0020	Check0025	ALL
5	065	1160-0020	Check0026	ALL
5	065	1160-0020	Check0100	ALL
5	065	1160-0020	Check0101	ALL
5	065	1160-0020	Check0102	ALL
5	065	1160-0020	Check0103	ALL
5	065	1160-0020	Check0104	ALL
5	065	1160-0020	Check0105	ALL

Reporting Tool (1)

- 3 reports are created:
 - **Exception log**
 - Exception summary
 - Exception report
- > 50 exceptions per check per domain: only 3 exceptions are reported

CHECK_LIST	ERROR_LEVEL	COMPLETION_TIME
Check0001	The Check Completed Successfully	2009-01-27T9:55:00
Check0002	The Check Completed Successfully	2009-01-27T9:55:00
Check0003	The Check Completed Successfully	2009-01-27T9:55:00
Check0004	The Check Completed Successfully	2009-01-27T9:55:00
Check0005	The Check Completed Successfully	2009-01-27T9:55:00
Check0006	The Check Completed Successfully	2009-01-27T9:55:00
Check0007	The Check Completed Successfully	2009-01-27T9:55:00
Check0008	The Check Completed Successfully	2009-01-27T9:55:00
Check0009	The Check Completed Successfully	2009-01-27T9:55:00
Check0010	The Check Completed Successfully	2009-01-27T9:55:00
Check0011	The Check Completed Successfully	2009-01-27T9:55:00
Check0012	The Check Completed Successfully	2009-01-27T9:55:00
Check0013	The Check Completed Successfully	2009-01-27T9:55:00
Check0014	The Check Completed Successfully	2009-01-27T9:55:00
Check0015	The Check Completed Successfully	2009-01-27T9:56:00
Check0016	The Check Completed Successfully	2009-01-27T9:56:00
Check0017	The Check Completed Successfully	2009-01-27T9:56:00
Check0018	The Check Completed Successfully	2009-01-27T9:56:00
Check0019	The Check Completed Successfully	2009-01-27T9:56:00
Check0020	The Check Completed Successfully	2009-01-27T9:56:00

Reporting Tool (2)

- 3 reports are created:
 - Exception log
 - **Exception summary**
 - Exception report
- > 50 exceptions per check per domain: only 3 exceptions are reported

LIST OF CHECKS	DOMAIN	VARIABLE1	EXCEPTIONS COUNT	CHECK TYPE
Check0009	LB	LBORRES	73	DATA
Check0010	LB	LBORRESU	84	METADATA
Check0010	VS	VSORRESU	56	METADATA
Check0010	VS	VSSTRESU	56	METADATA
Check0015	CO	IDVAR	73	DATA
Check0100	IE	DOMAIN	1	DATA
Check0268	CM	COLUMN	1	METADATA
Check0271	VS	COMPALGO	5	METADATA

Reporting Tool (3)

- 3 reports are created:
 - Exception log
 - Exception summary
 - **Exception report**
- > 50 exceptions per check per domain: only 3 exceptions are reported

Reported Exception
Record Identifiers
Exception Attributes

CHECKID	ERRORMSG	STUDYID	DOMAIN	USUBJID	KEY1CD	KEY1	VAR1CD	VAR1	VAR2CD	VAR2
9	An ORIGINAL RESULT is completed but the STANDARD RESULT (CHARACTERISTIC) is missing.	1234-5678	LB	1234-5678-00002	LBSEQ	29	LBORRES	32,4	LBSTRESC	
9	An ORIGINAL RESULT is completed but the STANDARD RESULT (CHARACTERISTIC) is missing.	1234-5678	LB	1234-5678-00002	LBSEQ	13	LBORRES	19	LBSTRESC	
9	An ORIGINAL RESULT is completed but the STANDARD RESULT (CHARACTERISTIC) is missing.	1234-5678	LB	1234-5678-00001	LBSEQ	52	LBORRES	1,1	LBSTRESC	
9	TOO MANY FAILURES (73)									
10	The value cannot be found in the codelist attached to the variable.	1234-5678	LB	1234-5678-00016	LBSEQ	55	LBORRESU	10*6/uL		
10	The value cannot be found in the codelist attached to the variable.	1234-5678	LB	1234-5678-00027	LBSEQ	54	LBORRESU	10*6/uL		
10	The value cannot be found in the codelist attached to the variable.	1234-5678	LB	1234-5678-00008	LBSEQ	55	LBORRESU	10*6/uL		
10	TOO MANY FAILURES (84)									
10	The value cannot be found in the codelist attached to the variable.	1234-5678	VS	1234-5678-00024	VSSEQ	16	VSORRESU	kg		
10	The value cannot be found in the codelist attached to the variable.	1234-5678	VS	1234-5678-00020	VSSEQ	16	VSORRESU	kg		
10	The value cannot be found in the codelist attached to the variable.	1234-5678	VS	1234-5678-00012	VSSEQ	16	VSORRESU	kg		
10	TOO MANY FAILURES (56)									

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Summary

- SDTM compliance will help us adhere to the data standards
- SDTM Compliance Checks will facilitate loading into Janus
- Running these checks do not necessarily solve all findings but sponsor is prepared for FDA feedback
 - Consider documenting confirmed issues in FDA Reviewers' Guide
- FDA will not reject your submission!



LIFE SCIENCES

Thank you for your attention

Peter Van Reusel
Manager CRO Services
Business & Decision Life Sciences

Tel +32 2 774 11 00
Fax +32 2 774 11 99
Mobile +32 476 54 59 17
peter.vanreusel@businessdecision.com

Sint-Lambertusstraat 141 Rue Saint-
Lambert
1200 Brussels

www.businessdecision-lifesciences.com



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