

# On the submission's road with CDISC ADaM

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Paper RG04

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# Topics



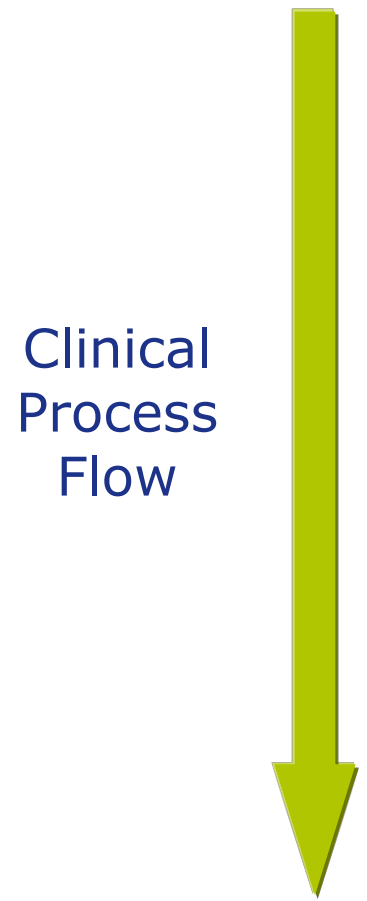
# Topics

- 
- 1 Introduction**
  - 2 Traceability Overview
  - 3 Traceability Checker System
  - 4 Reporting
  - 5 Conclusion

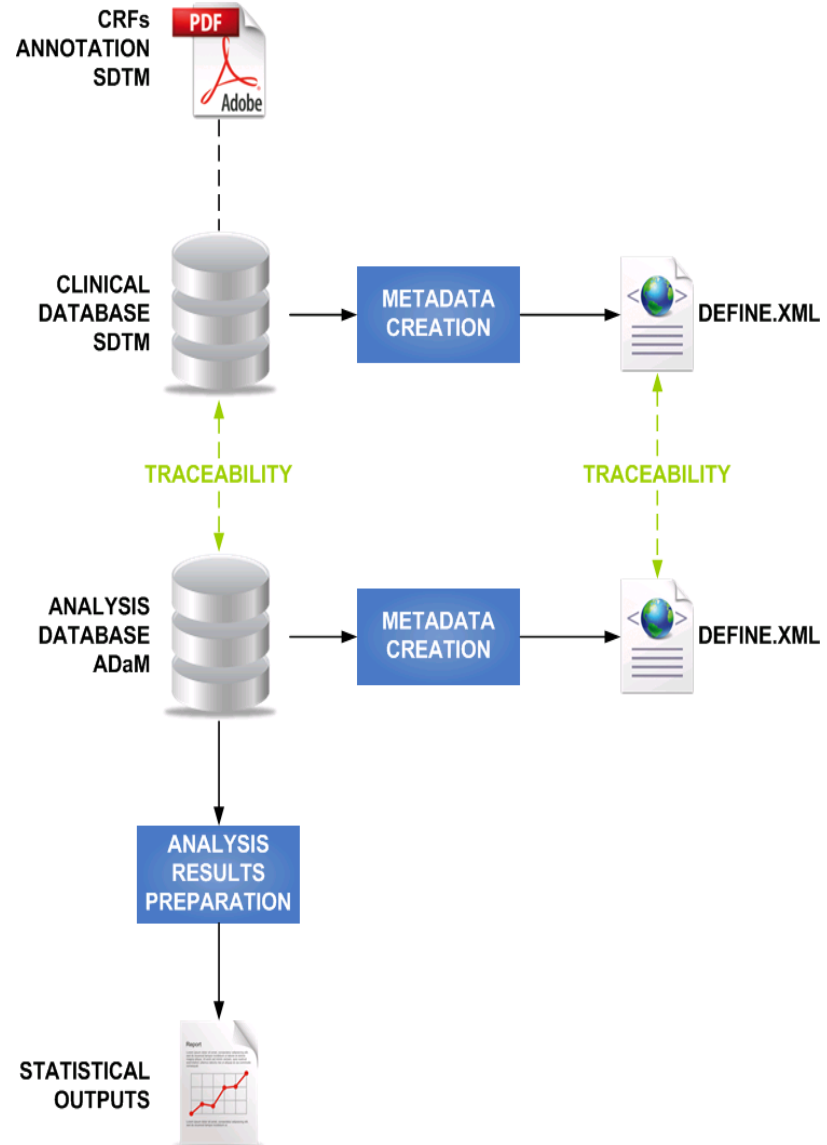
# ADaM Adoption by FDA

- ADaM is accepted by FDA since 2009
- Need for transparency of communication with and scientifically valid review by regulatory
- Fundamental Principles:
  - Analysis-ready
  - Traceability
- Data standards allow the FDA to use standard tools

# Clinical Data Flow



Clinical  
Process  
Flow



Review  
Process  
Flow

# Quality Control of Traceability

- Traceability is crucial for an efficient and productive review by the regulatory department
- A good and efficient quality control of the traceability between SDTM and ADaM can be challenging when not supported electronically
- Part of the quality control of traceability between SDTM and ADaM can be supported electronically

**Automation of the traceability quality control is the goal of the Traceability Checker System**

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**Facilitates clinical review process**

# Topics



# Traceability Overview

- Understanding relationship between the analysis results, the ADaM datasets, the SDTM datasets and the data collection process (i.e CDASH).
- Establishing the path between an element and its immediate predecessor
- Two levels:
  - Metadata traceability
    - Relationship between an analysis result and analysis dataset(s)
    - Relationship of the analysis variable to its source dataset(s) and variable(s)
  - Data point traceability
    - Predecessor record(s)



# The Way Back

Table 1 Demographic Data - Per-Protocol

	Treatment 1	Treatment 2
Baseline body mass index (BMI) [kg/m <sup>2</sup> ]		
N	167	167
Mean	29.08	29.04
SD	4.84	4.80
Min	20.3	16.0
Median	28.69	28.47
Max	40.1	41.2
Baseline BMI (categorical) [N (%)]		
<25 kg/m <sup>2</sup>	41 ( 24.6%)	71 ( 21.1%)
25-30 kg/m <sup>2</sup>	60 ( 35.9%)	130 ( 38.7%)
>=30 kg/m <sup>2</sup>	66 ( 39.5%)	135 ( 40.2%)

• Patient Demographics - Part I

Patient X5 Page 4 (Demo\_Vis for Visit 1a) Page 4 of 1.

Visit Date **11-Dec-2007** Blank  Comment

PATIENT DEMOGRAPHICS - Part I **DSCAT = "PROTOCOL MILESTONE"**

Informed consent was obtained on  **DSSTDTC**

Gender **SEX**  1 = male, 2 = female

Date of birth **BRTHDTC**  Age **AGE** years **AGEU**

(Age is automatically calculated when screen is saved and closed)

Height  cm

Weight  kg

Waist circumference  cm

**VSORRES / VSORRESU where VSTESTCD = "HEIGHT", "WEIGHT", "WAIST"**

	STUDYID	USUBID	SUBID	BMI	BMGR1	BMGRIN	BMGR2	BMGR2N
2	9999-0001	9999-0001-000001	000001	27.77777778	<30 kg/m <sup>2</sup>		1 25-<30 kg/m <sup>2</sup>	2
3	9999-0001	9999-0001-000002	000002	25.503615702	<30 kg/m <sup>2</sup>		1 25-<30 kg/m <sup>2</sup>	2
4	9999-0001	9999-0001-000003	000003	26.175194521	<30 kg/m <sup>2</sup>		1 25-<30 kg/m <sup>2</sup>	2
5	9999-0001	9999-0001-000004	000004	35.15625	>=30 kg/m <sup>2</sup>		2 >=30 kg/m <sup>2</sup>	3
6	9999-0001	9999-0001-000005	000005	30.96929131	>=30 kg/m <sup>2</sup>		2 >=30 kg/m <sup>2</sup>	3
7	9999-0001	9999-0001-000006	000006	33.897163916	>=30 kg/m <sup>2</sup>		2 >=30 kg/m <sup>2</sup>	3
8	9999-0001	9999-0001-000007	000007	25.82446281	<30 kg/m <sup>2</sup>		1 25-<30 kg/m <sup>2</sup>	2
9	9999-0001	9999-0001-000008	000008	30.103806228	>=30 kg/m <sup>2</sup>		2 >=30 kg/m <sup>2</sup>	3
10	9999-0001	9999-0001-000009	000009	32.280962683	>=30 kg/m <sup>2</sup>		2 >=30 kg/m <sup>2</sup>	3
11	9999-0001	9999-0001-000010	000010	28.876133787	<30 kg/m <sup>2</sup>		1 25-<30 kg/m <sup>2</sup>	2
12	9999-0001	9999-0001-000011	000011	29.372387383	<30 kg/m <sup>2</sup>		1 25-<30 kg/m <sup>2</sup>	2
13	9999-0001	9999-0001-000012	000012	26.714652608	<30 kg/m <sup>2</sup>		1 25-<30 kg/m <sup>2</sup>	2
14	9999-0001	9999-0001-000013	000013	32.718619868	>=30 kg/m <sup>2</sup>		2 >=30 kg/m <sup>2</sup>	3
15	9999-0001	9999-0001-000014	000014	28.719272183	<30 kg/m <sup>2</sup>		1 25-<30 kg/m <sup>2</sup>	2
16	9999-0001	9999-0001-000015	000015	32.270420377	>=30 kg/m <sup>2</sup>		2 >=30 kg/m <sup>2</sup>	3

Variable	Label	Type	Controlled Terminology	Origin	Role	Comment
STUDYID	Study Identifier	text		Protocol, CRF Page 1	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	text	DOMAIN	Assigned	IDENTIFIER	
USUBID	Unique Subject Identifier	text		Protocol	IDENTIFIER	The USUBID variable has a fixed format: 'XXXX-YYYY-ZZZZZ', where 'XXXX' indicates the 4-digit compound code, 'YYYY' the 4-digit study code and 'ZZZZZ' the 6-digit patient code
VSEQ	Sequence Number	integer		Derived	IDENTIFIER	Sequence number (automatically generated) to ensure uniqueness within a dataset for a subject
VSTESTCD	Vital Signs Test Short Name	text		Assigned	TOPIC	
VSTEST	Vital Signs Test Name	text		Derived	SYNONYM QUALIFIER	
VSPOS	Vital Signs Position of Subject	text	POSITION	CRF Page 13	RECORD QUALIFIER	
VSORRES	Result or Finding in Original Units	text		Derived, CRF Page 9, 13	RESULT QUALIFIER	
VSORRESU	Original Units	text	VSRESU	CRF Page 9, 13	VARIABLE QUALIFIER	
VSTRESC	Character Result Finding in Std Format	text		Derived	RESULT QUALIFIER	
VSTRESN	Numeric Result Finding in Standard Units	float	3.1	Derived	RESULT QUALIFIER	

Variable	Label	Type	Controlled Terms or Format	Computational Algorithms or Method	Origin	Role	Comment
STUDYID	Study Identifier	text			DM	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
USUBID	Unique Subject Identifier	text			DM	IDENTIFIER	The USUBID variable has a fixed format: 'XXXX-YYYY-ZZZZZ', where 'XXXX' indicates the 4-digit compound code, 'YYYY' the 4-digit study code and 'ZZZZZ' the 6-digit patient code
SUBID	Subject Identifier for the Study	text			DM	IDENTIFIER	
HEIGHT	Baseline Height (cm)	integer		ADSL_HEIGHT	Derived	ANALYSIS	
WEIGHT	Baseline Weight (kg)	integer		ADSL_WEIGHT	Derived	ANALYSIS	
BMI	Baseline BMI (kg/m <sup>2</sup> )	integer		ADSL_BMI	Derived	ANALYSIS	
BMGR1	Category 1 of Baseline BMI	text	BMGR1L	ADSL_BMGR1	Derived	ANALYSIS	
BMGRIN	Category 1 of Baseline BMI, (N)	integer	BMGR1N	ADSL_BMGR1N	Derived	ANALYSIS	
BMGR2	Category 2 of Baseline BMI	text	BMGR2L	ADSL_BMGR2	Derived	ANALYSIS	
BMGR2N	Category 2 of Baseline BMI, (N)	integer	BMGR2N	ADSL_BMGR2N	Derived	ANALYSIS	
BMGR3	Category 3 of Baseline BMI	text	BMGR3L	ADSL_BMGR3	Derived	ANALYSIS	
BMGR3N	Category 3 of Baseline BMI, (N)	integer	BMGR3N	ADSL_BMGR3N	Derived	ANALYSIS	

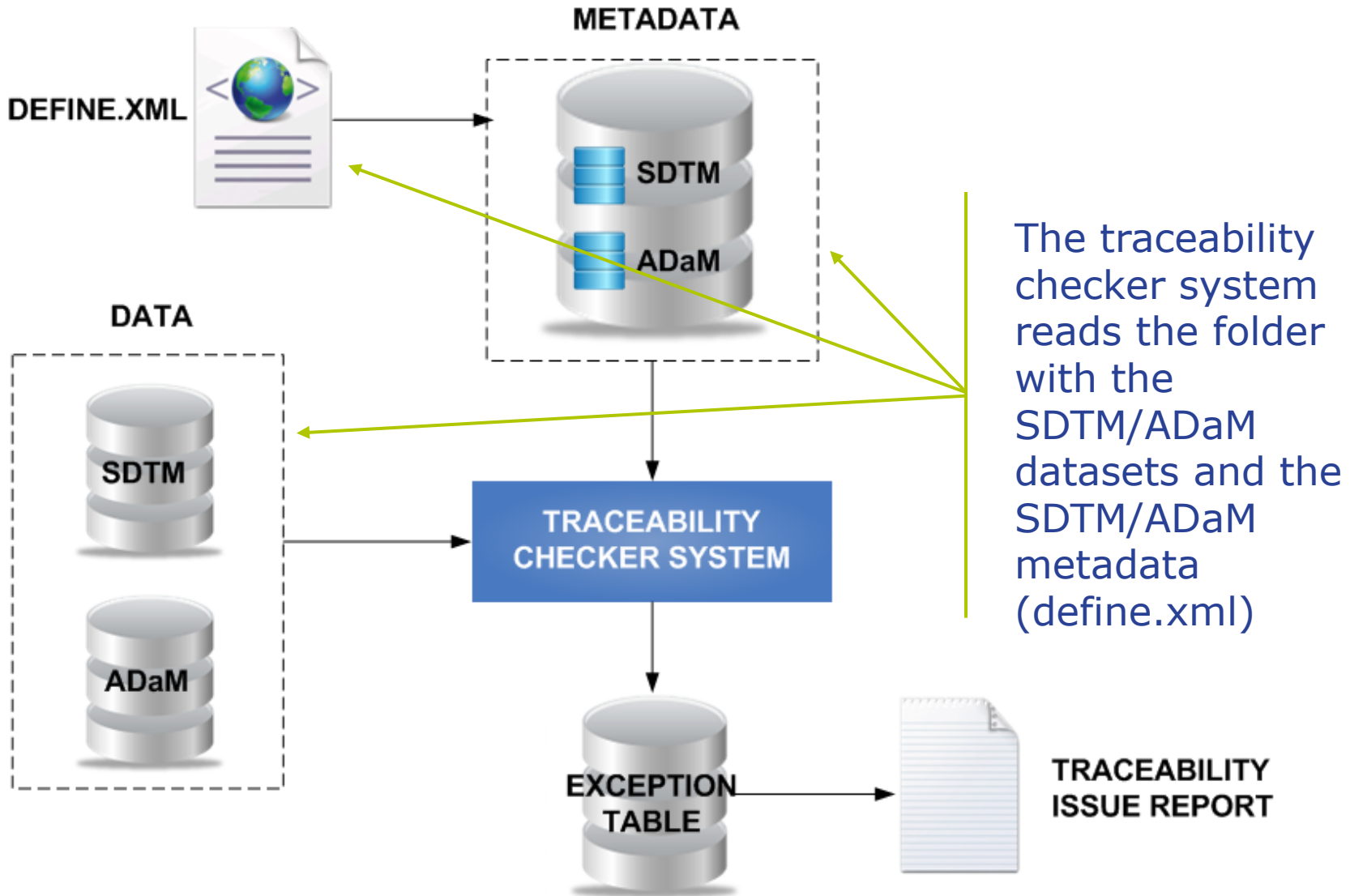
# Topics



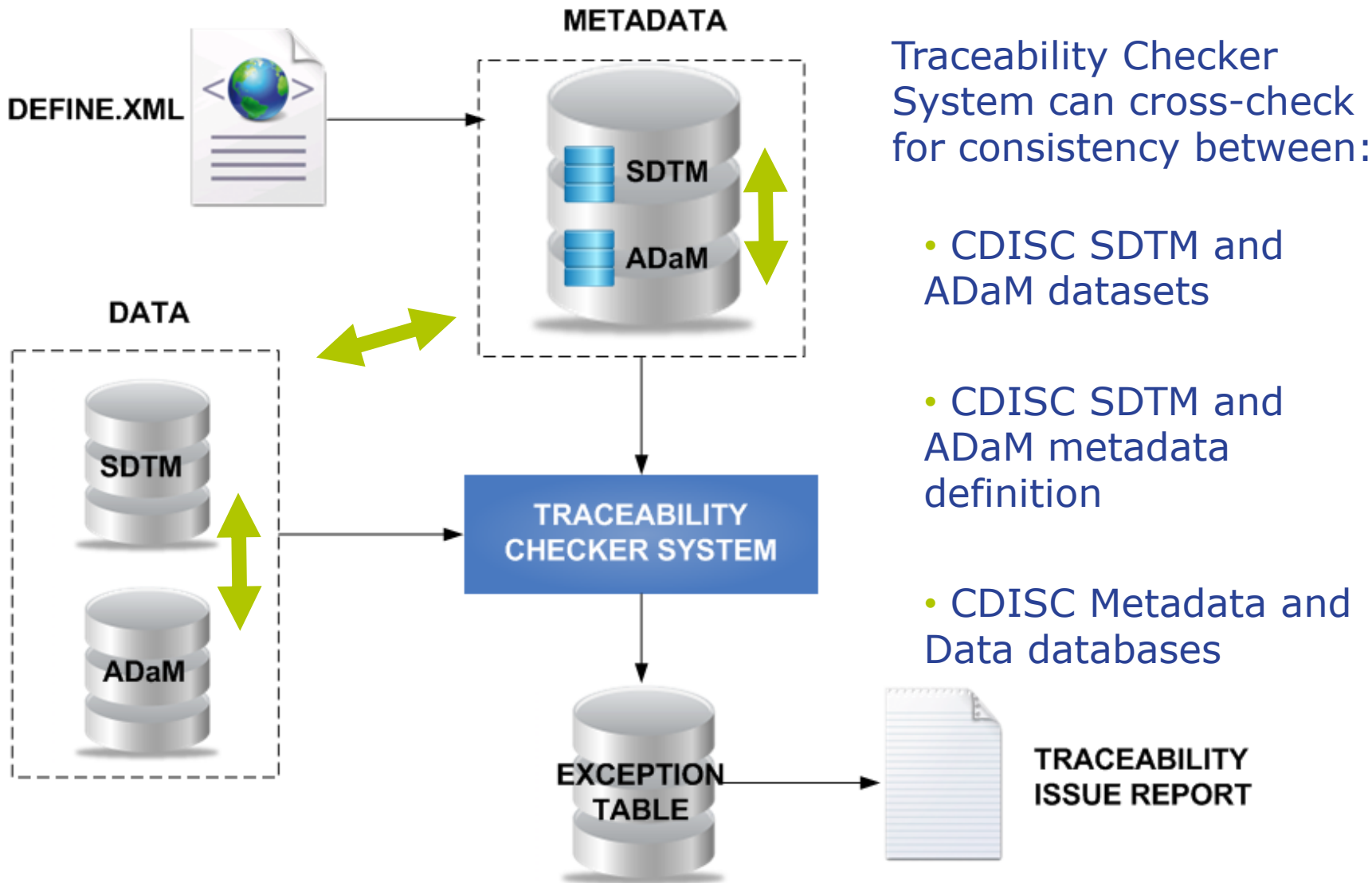
# Traceability Checker System

- Objective = Electronic support the quality control of traceability
- A controlled metadata environment is required for electronically checking the traceability
- Traceability check package:
  - Standard « ADaM vs SDTM » v1.2 checks (July 05, 2012)
  - Custom checks
- Traceability checks list is updated continuously

# Traceability Checker Flowchart (1)



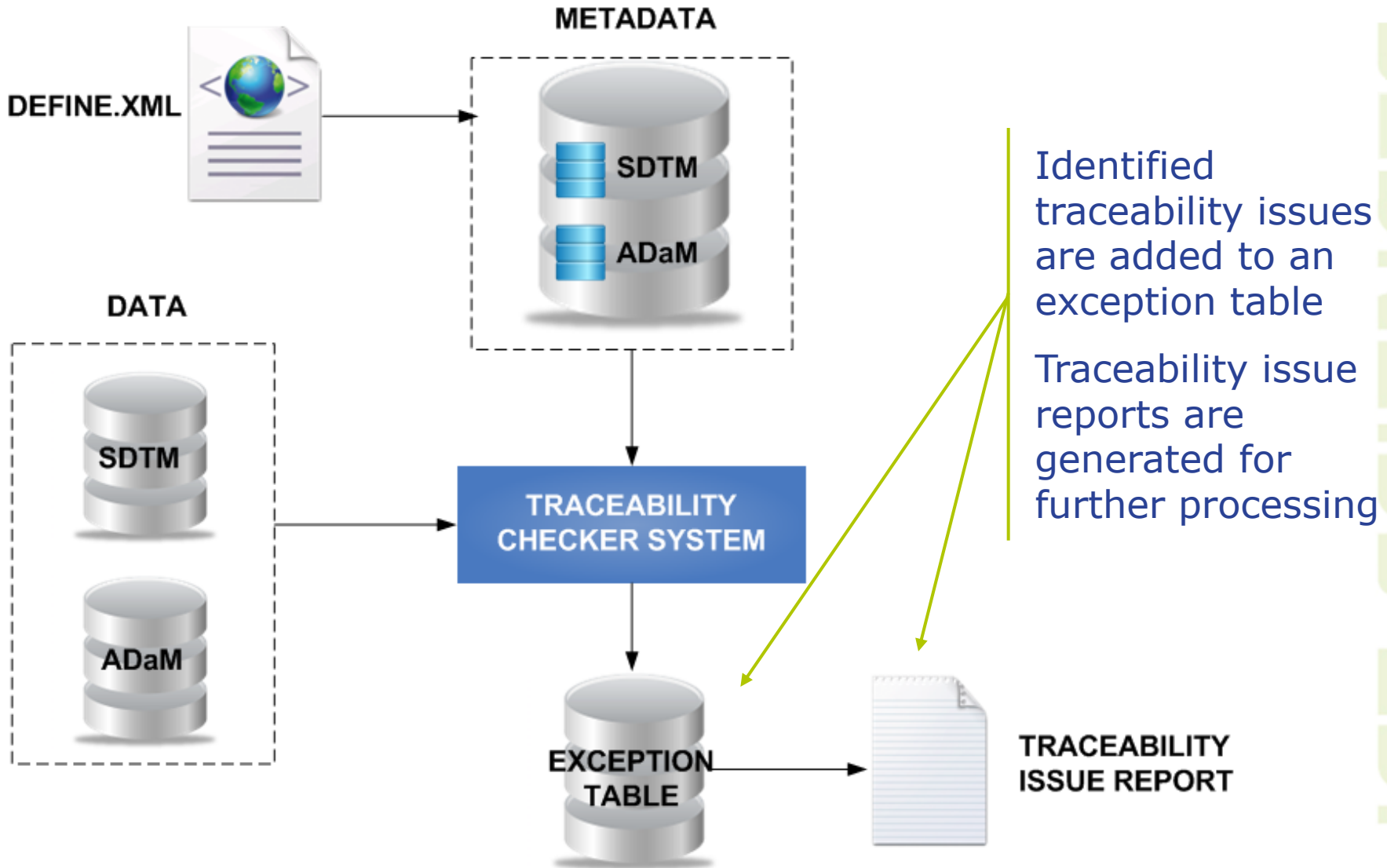
# Traceability Checker Flowchart (2)



Traceability Checker System can cross-check for consistency between:

- CDISC SDTM and ADaM datasets
- CDISC SDTM and ADaM metadata definition
- CDISC Metadata and Data databases

# Traceability Checker Flowchart (3)



# Topics



# Reporting (1)

- 3 reports are created:
  - **Exception Log**
  - Exception Metadata
  - Exception Data

STUDYID	CHECK_ID	ERROR_LEVEL	COMPLETION_TIME
STUDY 123	0101	The Check Completed Successfully	2013-09-05T10-35-50
STUDY 123	0102	The Check Completed Successfully	2013-09-05T10-35-53
STUDY 123	0103	The Check Completed Successfully	2013-09-05T10-35-58
STUDY 123	0104	The Check Completed Successfully	2013-09-05T10-36-35
STUDY 123	0105	The Check Completed Successfully	2013-09-05T10-36-58
STUDY 123	0201	The Check Completed Successfully	2013-09-05T10-37-12
STUDY 123	0202	The Check Completed Successfully	2013-09-05T10-37-20
STUDY 123	0203	The Check Completed Successfully	2013-09-05T10-37-32



# Reporting (2)

- 3 reports are created:
  - Exception Log
  - **Exception Metadata**
  - Exception Data

## Reported Exception

## Identifier

## Exception Attributes

CHECK_ID	ERROR_MESSAGE	STUDYID	DOMAIN	VAR1CD	VAR1	VAR2CD	VAR2
0101	A variable present in ADaM is indicated as a copy of a variable present in SDTM but the variables do not have identical metadata attributes	STUDY 123	DM	VARIABLE NAME	AGEU	LENGTH ADaM	10
0101	A variable present in ADaM is indicated as a copy of a variable present in SDTM but the variables do not have identical metadata attributes	STUDY 123	DM	VARIABLE NAME	COUNTRY	CT ADaM	COUNTRY
0101	A variable present in ADaM is indicated as a copy of a variable present in SDTM but the variables do not have identical metadata attributes	STUDY 123	MH	VARIABLE NAME	MHENDTC	LABEL ADaM	End Date of Medical History Event
0105	The variable referenced in the computational algorithm of the ADaM variable does not exist in SDTM or ADaM variable metadata	STUDY 123	FI	COMP. ALGORITHM	ADEFF.PARCAT1	VARIABLE NAME	FI.FICATCD
0105	The variable referenced in the computational algorithm of the ADaM variable does not exist in SDTM or ADaM variable metadata	STUDY 123	DM	COMP. ALGORITHM	ADSL.RACE0TH	VARIABLE NAME	DM.QNAM

# Reporting (3)

- 3 reports are created:
  - Exception Log
  - Exception Metadata
  - **Exception Data**

## Reported Exception

## Identifier

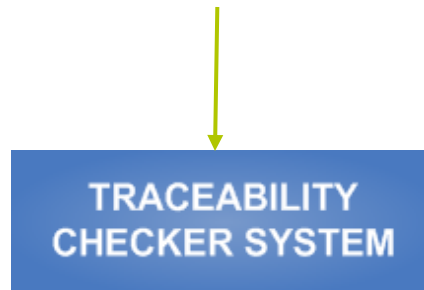
## Exception Attributes

CHECK ID	ERROR MESSAGE	STUDYID	DOMAIN	USUBJID	VAR1CD	VAR1	VAR2CD	VAR2
0201	A variable present in ADaM is indicated as a copy of a variable present in SDTM but the values are not identical	STUDY 123	ADAE	900006	VARIABLE ADAM VS SDTM	ADAE.AEOUT VS AE.AEOUT	VALUE	NOT RECOVERED
0201	A variable present in ADaM is indicated as a copy of a variable present in SDTM but the values are not identical	STUDY 123	ADCM	200004	VARIABLE ADAM VS SDTM	ADCM.CMSTDY VS CM.CMSTDY	VALUE	-1137
0201	A variable present in ADaM is indicated as a copy of a variable present in SDTM but the values are not identical	STUDY 123	ADAE	200001	VARIABLE ADAM VS SDTM	ADAE.AEACN VS AE.AEACN	VALUE	NA
0202	The values of USUBJID are not present in SDTM.DM	STUDY 123	ADSL	500003				
0202	The values of USUBJID are not present in SDTM.DM	STUDY 123	ADSL	500004				
0202	The values of USUBJID are not present in SDTM.DM	STUDY 123	ADSL	500005				

# Common Exception Examples (1)

- ADaM variable = ADSL.RACEOTH
- Derived variable with computational algorithm:

*Equals to **DM.QVAL** when **DM.QNAM**="RACEOTH"*

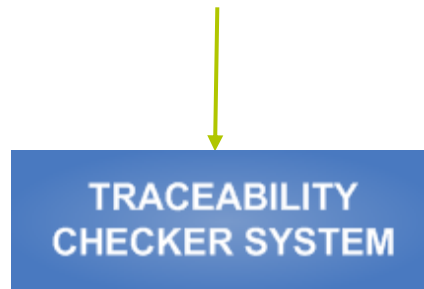


*Equals to **SUPPDM.QVAL** when **SUPPDM.QNAM**="RACEOTH"*

## Common Exception Examples (2)

- ADaM variable = ADSL.RACE
- Copied variable from DM.RACE with length = 100

ADSL.RACE length = **50**

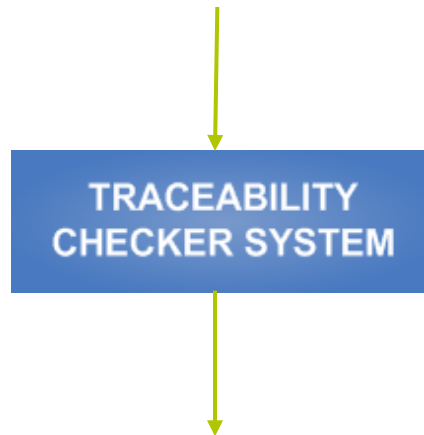


ADSL.RACE length = **100**

## Common Exception Examples (3)

- ADaM variable = ADSL.AGE
- Copied variable from DM.AGE

ADSL.AGE is indicating as a copy of DM.AGE



ADSL.AGE values  $\neq$  DM.AGE values

-> ADSL.AAGE variable to be added with corresponding computational algorithm for analysis transparency

# Topics



# Conclusion

- Traceability is one of the most difficult part in ADaM
- Traceability between CDISC SDTM and ADaM can be electronically tested before submitting to the regulatory department for review
- The system only needs datasets and corresponding metadata to work
- The system provides a user-friendly report which is used as basis for further processing
- Can be used for both ADaM conversion projects or usual derivation studies





**Thank you  
for your attention**

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