



END TO END SDTM AUTOMATION

A METADATA CENTRIC APPROACH

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PhUSE US Connect 2019, February 25th

WHEN YOU NEED TO BE SURE

SGS

- Introduction
- MDR – metadata repository
- MDR driven tools
 - Annotation Tool
 - SDTM Mapping Tool
 - Metadata Center
 - YADLi
- Conclusion

- **Introduction**
- MDR – metadata repository
- MDR driven tools
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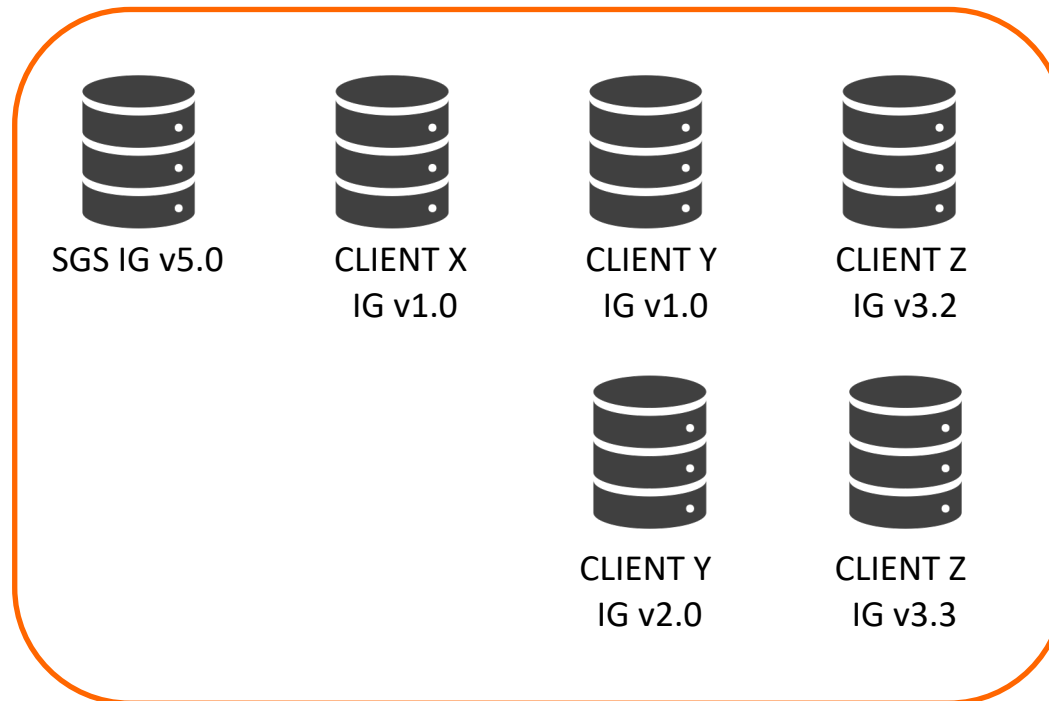
- What is the key to creating clinical databases that are compliant with CDISC SDTM standards?
 - Metadata driven approach
 - Seamless integration of processes and people



- Introduction
- **MDR – metadata repository**
- MDR driven tools
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- Master source of metadata containing multiple metadata libraries.

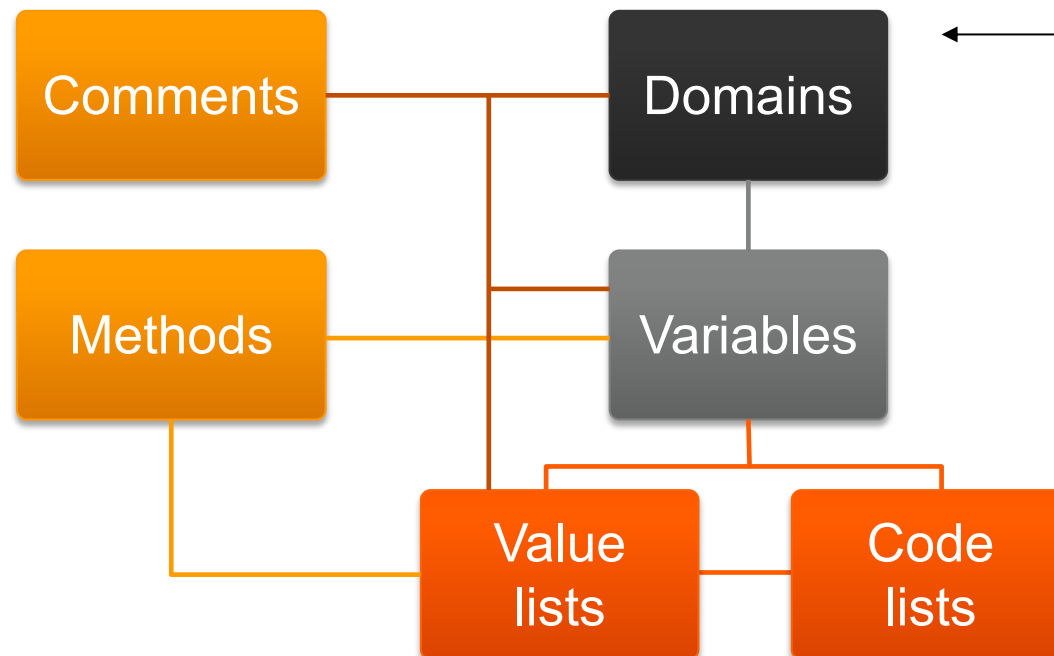
MDR



- Structure based on the Define-XML model
- Contains all available domains, variables, valuelists, codelists, comments and computational methods



SGS IG v5.0



■ 3 types of MDR libraries



SGS IG v5.0

- Maintained by SGS



CLIENT X
IG v1.0

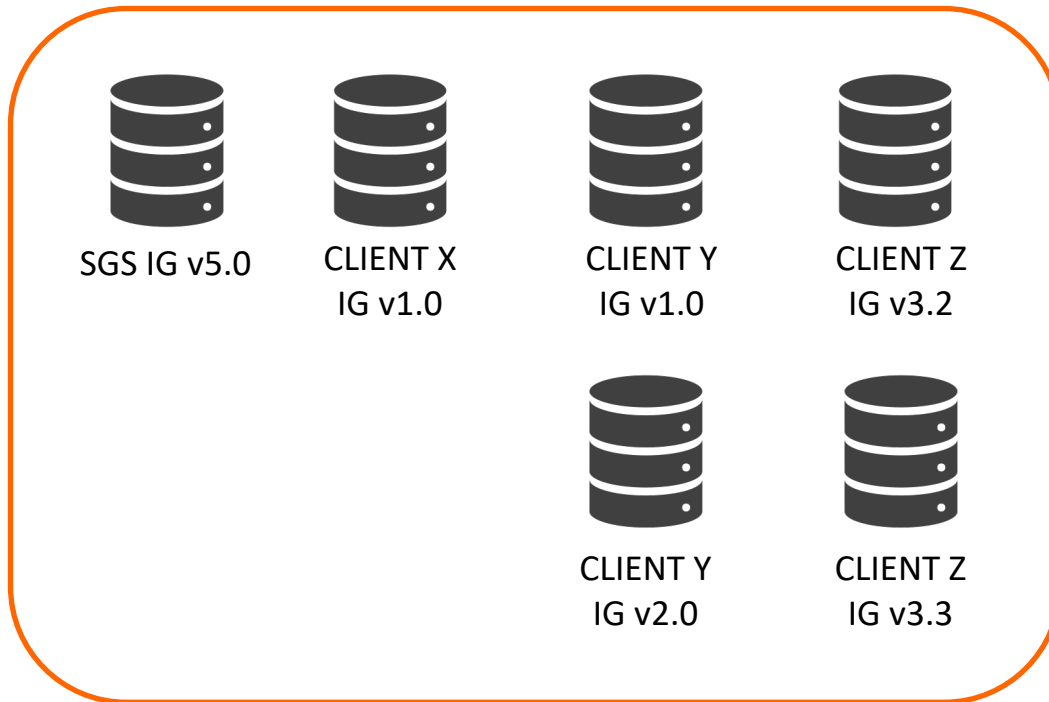
- Dictated by the client
- Maintained together with the client



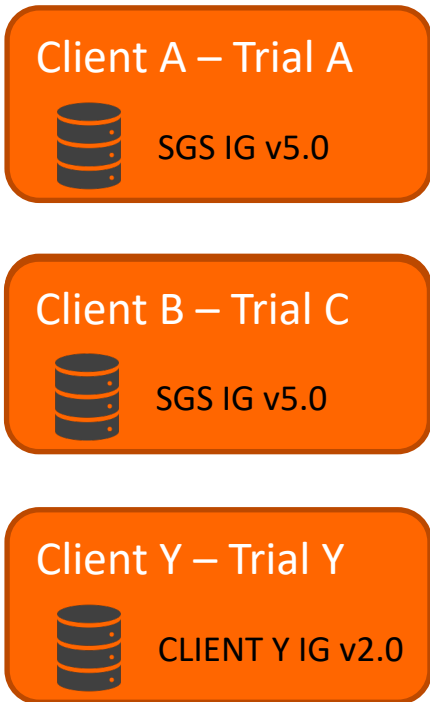
CLIE
IG · CLIENT Z
IG v4.0

- Maintained by the Client
- Implemented by SGS

MDR

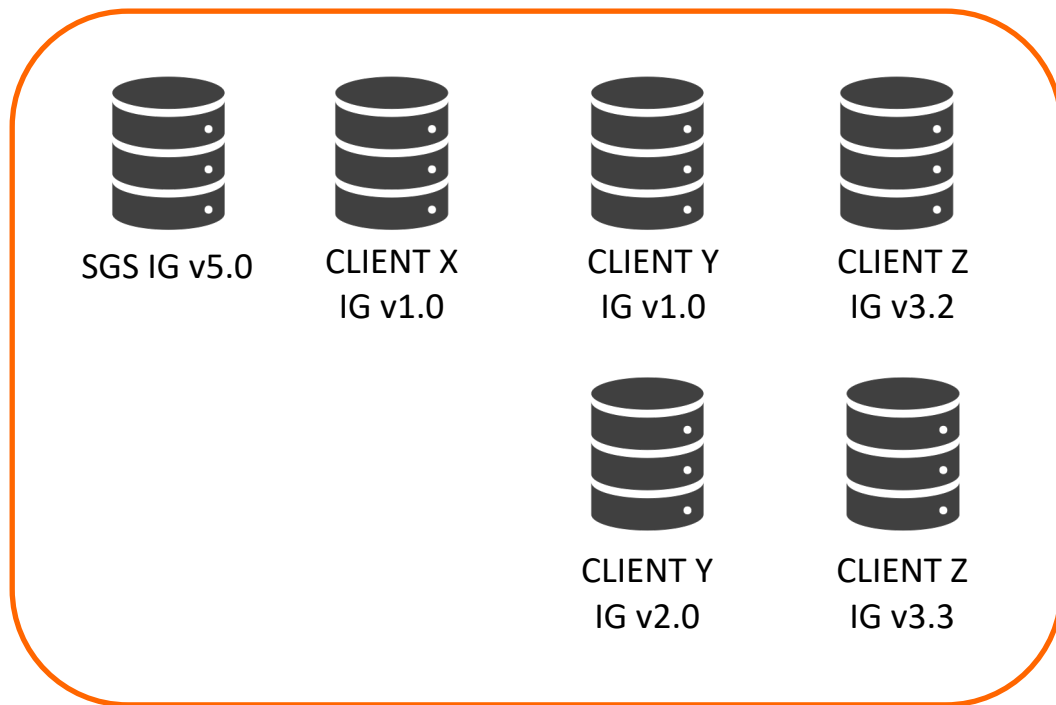


Trials



- Introduction
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- **MDR driven tools**
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 - SDTM Mapping Tool
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- Conclusion

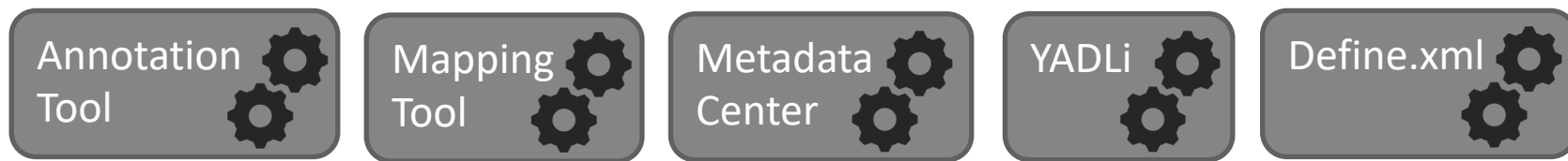
MDR



Trials



MDR Driven Tools



- Introduction
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 - **Annotation Tool**
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- How we used to annotate a CRF

[DS - Disposition]

Trial A: Demographic Data and Informed Consent Recording (DM) [frmDM]

Demographics [sctDM]

1.* ✓	Date of birth	[dtmBRTH] Req v / Req v / Req v BRTHDTC
2.* ✓	Subject signed informed consent on DSCAT = PROTOCOL MILESTONE	[dtmIFC] Req v / Req v / Req v DSSTDTC
3.*	Age	[numAGE] N3 (years) AGE AGEU

■ Font: Courier vs Arial

*[DS - Disposition]***Trial A: Demographic Data and Informed Consent Recording (DM) [frmDM]****Demographics [sctDM]**

1.* ✓	Date of birth	[dtmBRTH] Req ▾ / Req ▾ / Req ▾	BRTHDTC
2.* ✓	Subject signed informed consent on DSCAT = PROTOCOL MILESTONE	[dtmIFC] Req ▾ / Req ▾ / Req ▾	DSSTDTC
3.*	Age	[numAGE] N3 (years) AGE	AGEU

■ Size: 11 vs 18



[DS - Disposition]

Trial A: Demographic Data and Informed Consent Recording (DM) [frmDM]

Demographics [sctDM]

1.* ✓	Date of birth	[dtmBRTH] Req ▾ / Req ▾ / Req ▾	BRTHDTC
2.* ✓	Subject signed informed consent on DSCAT = PROTOCOL MILESTONE	[dtmIFC] Req ▾ / Req ▾ / Req ▾	DSSTDTC
3.*	Age	[numAGE] N3 (years)	AGE AGEU

■ Color



[DS - Disposition]

Trial A: Demographic Data and Informed Consent Recording (DM) [frmDM]

Demographics [sctDM]

1.* ✓	Date of birth	[dtmBRTH] Req ▾ / Req ▾ / Req ▾	BRTHDTC
2.* ✓	Subject signed informed consent on DSCAT = PROTOCOL MILESTONE	[dtmIFC] Req ▾ / Req ▾ / Req ▾	DSSTDTC
3.*	Age	[numAGE] N3 (years) AGE	AGEU

■ Domain missing



[DS - Disposition]

Trial A: Demographic Data and Informed Consent Recording (DM) [frmDM]

Demographics [sctDM]

1.* ✓	Date of birth	[dtmBRTH] Req v / Req v / Req v BRTHDTC
2.* ✓	Subject signed informed consent on DSCAT = PROTOCOL MILESTONE	[dtmIFC] Req v / Req v / Req v DSSTDTC
3.*	Age	[numAGE] N3 (years) AGE AGEU

■ Annotation properties



[DS - Disposition]

Trial A: Demographic Data and Informed Consent Reco

Demographics [sctDM]

1.* ✓	Date of birth	[dtmBRTH] Req ▾ / Req ▾ / Req
2.* ✓	Subject signed informed consent on DSCAT = PROTOCOL MILESTONE	[dtmIFC] Req ▾ / Req ▾ / Req
3.*	Age	[numAGE] N3 (years) AGE

T DM ▾

Page 2 20/01/2019 18:32:06

DSSTDTC

T DM ▾

Page 2 20/01/2019 18:32:44

DSCAT = PROTOCOL MILESTONE

T DS ▾

Page 2 20/01/2019 18:37:31

AGE

T DS ▾

Page 2 20/01/2019 18:37:41

AGEU

T SUPPQS ▾

Page 2 20/01/2019 18:46:26

BRTHDTC

■ Domain colors



[DS - Disposition]

Trial A: Demographic Data and Informed Consent Recording (DM) [frmDM]

Demographics [sctDM]

1.* ✓	Date of birth	[dtmBRTH] Req v / Req v / Req v	BRTHDTC
2.* ✓	Subject signed informed consent on DSCAT = PROTOCOL MILESTONE	[dtmIFC] Req v / Req v / Req v	DSSTDTC
3.*	Age	[numAGE] N3 (years) AGE	AGEU



[DM - Demographics]

[DS - Disposition]

Trial A: Demographic Data and Informed Consent Rec

Demographics [sctDM]

1.* ✓	Date of birth	[dtmBRTH] Req ▾ / Req ▾ /
2.* ✓	Subject signed informed consent on DSCAT = PROTOCOL MILESTONE	[dtmIFC] Req ▾ / Req ▾ /
3.*	Age	[numAGE] N3 (years) AGE

T DM ▾ Page 1 Indeterminate [DM - Demographics]
T DS ▾ Page 1 Indeterminate [DS - Disposition]
T DS ▾ Page 1 20/01/2019 17:20:58 DSCAT = PROTOCOL MILESTONE
T DM ▾ Page 1 20/01/2019 17:21:16 AGE
T DM ▾ Page 1 20/01/2019 17:21:20 AGEU
T DM ▾ Page 1 20/01/2019 17:21:58 BRTHDTC

[DS - Disposition]

Trial A: Demographic Data and Informed Consent Rec

Demographics [sctDM]

1.* ✓	Date of birth	[dtmBRTH] Req ▾ / Req ▾ / Re
2.* ✓	Subject signed informed consent on DSCAT = PROTOCOL MILESTONE	[dtmIFC] Req ▾ / Req ▾ / Req ▾
3.*	Age	[numAGE] N3 (years) AGE AGEU

DSSTDTC

AGEU



- Driven by the MDR
- Guide the user in generating annotations
- Provide automatic layout consistency
- Provide automatic adherence to client specifications
- The more the tool is used, the smarter it gets

- Annotation type
 - Annotation templates
 - Guide the user
 - Configurable per MDR

	Annottype	Textfont	Objecttype	Fillcolor	Annotcolor	Annotformat	Fontweight	Fonttype	Textsize	Border
	VARIABLE	Arial	FreeText	-	#0000FF	#VARNAME#	bold	italic	11	0
	SUPP	Arial	FreeText	-	#FF0000	SUPP#DOMAIN#.QVAL when QNAM = #QNAM#	bold	italic	11	0
	TESTCD	Arial	FreeText	-	#0000FF	#DOMAIN#ORRES when #DOMAIN#TESTCD = #FINDING#	bold	italic	11	0
	NOT_SUBMITTED	Arial	FreeText	-	#0000FF	[Not submitted]	bold	italic	11	0

- Annotation type demo
 - Weight of a subject
 - TESTCD



Weight [Weight]	[numWEIGHT] 0 < xxxxxx.	☐ kg [b] ☐ lbs
--------------------	----------------------------	--

-  Add Annotation
-  Add Page Comment
-  Page status >
-  Keyboard Navigation >
-  Skip Page for annotation
-  Use Page for annotation
-  Delete page annotations
-  Load drag and drop



ADD ANNOTATION

Annotation type



Domain

Subject

Author

Finding

Other value

Label

Search

Search annex

ADD ANNOTATION

Annotation type

Domain

Subject

Finding

Other value

Label

Search

VARIABLE.....#VARNAME#

CONSTANT.....#VARNAME# = #CONSTANTVALUE#

CONSTANT2.....#CONSTANTVALUE#

TESTCD.....#DOMAIN#ORRES when #DOMAIN#TESTCD = #FINDING#

TESTCD2.....#DOMAIN#STRESC when #DOMAIN#TESTCD = #FINDING# AND #DOMAIN#DRVFL = Y

TESTCD3.....#VARNAME# = #FREETEXT# when #DOMAIN#TESTCD = #FINDING#

TESTCD4.....#DOMAIN#STAT = NOT DONE when #DOMAIN#TESTCD=#FINDING#

SUPP.....SUPP#DOMAIN#.QVAL when QNAM = #QNAM#

SUPP2.....SUPP#DOMAIN#.QVAL when QNAM = #QNAM# and IDVAR = #VARNAME#

SUPP3.....SUPP#DOMAIN#.QVAL = #FREETEXT# when QNAM = #QNAM# and IDVAR = #VARNAME#

SUPP4.....#QNAM# in SUPP#DOMAIN#

COVAL.....CO.COVAL when IDVAR = #VARNAME#

RELREC.....Linked to related #FREETEXT# record via RELREC

FREETEXT.....#FREETEXT#

NOTE.....#FREETEXT#

NOT_SUBMITTED..[Not submitted]

REFERENCE.....For Annotations see CRF page #PAGENUMBER#

ANNOTVERSION...#FREETEXT#

CRFVERSION.....CRF version: #CRFVERSION#

DOMAIN.....[#DOMAIN# - #DSLABEL#]

ADD ANNOTATION

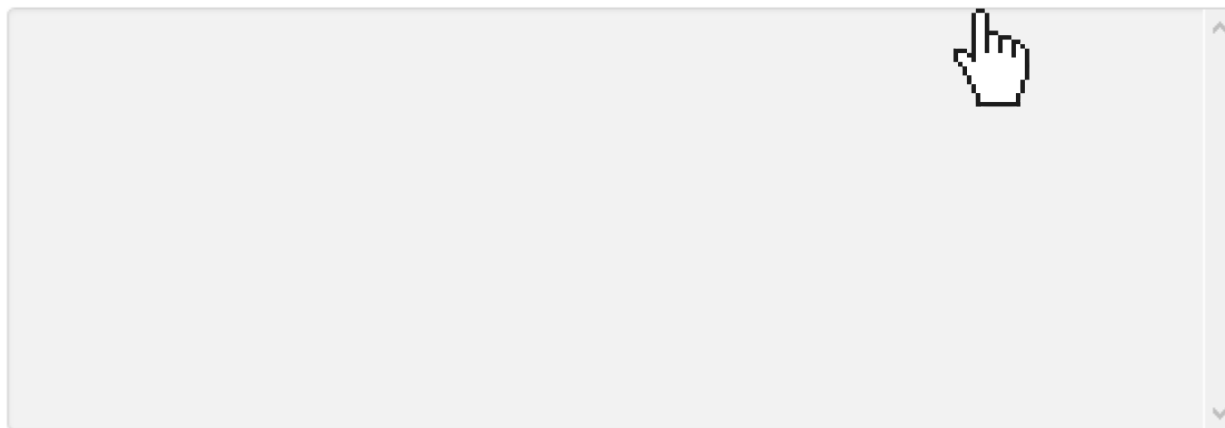
Annotation type ?

Domain

Subject

Author

Finding



Other value

Label

Search

Search annex

ADD ANNOTATION

Annotation type TESTCD.....#DOMAIN#ORRES when #DOMAIN#TESTCD = #FINDING# ?

Domain VOID,...

Subject PC.....Pharmacokinetic Concentrations

PD.....Pharmacodynamics

Finding PE.....Physical Examination

PP.....Pharmacokinetic Parameters

QS.....Questionnaires

RE.....Respiratory System Findings

RP.....Reproductive System Findings

RS.....Disease Response

SC.....Subject Characteristics

SR.....Skin Response

SS.....Subject Status

Other value TR.....Tumor Results

TU.....Tumor Identification

Label VS.....Vital Signs

X0.....Conversion data

X1.....Administrative data

Search XA.....Administrative Data

Z1.....Linking Verification

ADD ANNOTATION

Annotation type ?

Domain VOID,...

Subject **VS** Author **VS**

Finding

- ABSKNF.....Abdominal Skinfold Thickness
- ADOXY.....Oxygen Saturation on Room Air
- ADOXYSAT.....Adequate Oxygen Saturation on Room Air
- ATOXYREM.....Remove Oxygen Supplementation Attempts
- BMI.....Body Mass Index
- BMR.....Basal Metabolic Rate
- BODLNGTH.....Body Length
- BODYFAT.....Adipose Tissue; Body Fat; Fat Tissue
- BODYFATM.....Body Fat Measurement
- BSA.....Body Surface Area
- DIABP.....Diastolic Blood Pressure
- ENRGEXP.....Energy Expenditure
- EWEIGHT.....Estimated Weight
- FARMCIR.....Forearm Circumference
- FRMSIZE.....Body Frame Size

Other value

Label

Search Search annex

ADD ANNOTATION

Annotation type TESTCD.....#DOMAIN#ORRES when #DOMAIN#TESTCD = #FINDING#

Domain VS.....Vital Signs

Subject VS Author VS

Finding

- PULSE.....Pulse Rate
- PULSE.....Pulse Rate
- PULSEPR.....Pulse Pressure
- RESP.....Respiratory Rate
- SAD.....Sagittal Abdominal Diameter
- SSSKNF.....Subscapular Skinfold Thickness
- SYSBP.....Systolic Blood Pressure
- TBW.....Total Body Water
- TEMP.....Temperature
- TRSKNF.....Triceps Skinfold Thickness
- TRYO2REM.....3 Attempts To Remove O2 Supplementation
- VSALL.....All Tests
- WAISTHIP.....Waist to Hip Ratio
- WEIGHT.....Weight**
- WSTCIR.....Waist Circumference

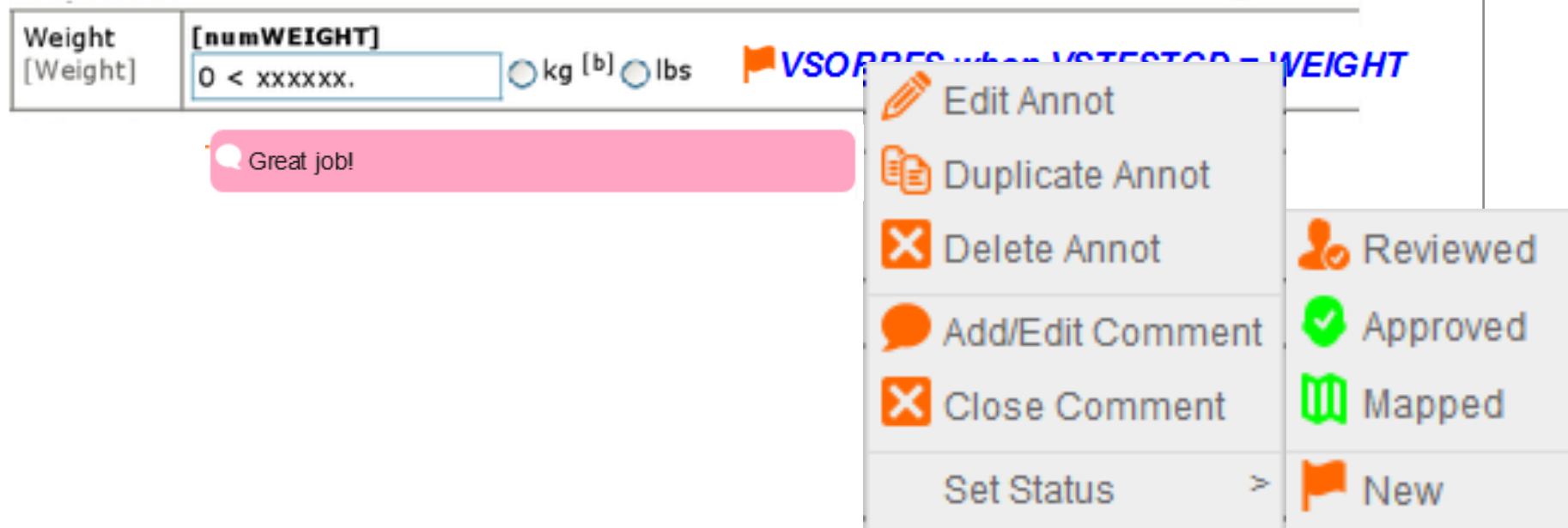
Other value

Label

Search

Search annex

- Tracking review process
 - Statuses
 - Multiple users at the same time



The screenshot displays the SGS Annotation Tool interface. At the top, there is a form for entering weight data. The form includes a label "Weight [Weight]", a text input field containing "[numWEIGHT]" and "0 < xxxxxx.", and two radio buttons for units: "kg [b]" and "lbs". To the right of the form, there is a blue flag icon and the text "VSORRES" and "VSTESTOR - WEIGHT". Below the form, there is a pink comment bubble that says "Great job!". A context menu is open over the form, listing several actions: "Edit Annot", "Duplicate Annot", "Delete Annot", "Add/Edit Comment", "Close Comment", and "Set Status". To the right of the context menu, there is a vertical list of status options: "Reviewed", "Approved", "Mapped", and "New".

Weight	[numWEIGHT]	kg [b]	lbs
[Weight]	0 < xxxxxx.	☐	☐

Great job!

- Edit Annot
- Duplicate Annot
- Delete Annot
- Add/Edit Comment
- Close Comment
- Set Status >

- Reviewed
- Approved
- Mapped
- New

■ Advantages

- More accurate and better quality aCRF
- Annotations stored/available in database
 - Use in other processes: SDTM mapping, define.xml
- Maintenance of MDR
 - Request for new values in valuelist/codelist (MDR)
- Future proof: Plug & play MDR

- Challenges
 - Screen vs exported PDF file
- Opportunities
 - Further automatisation: auto copy annotations from the library or previously annotated CRF's

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- Transform EDC source data to SDTM
- Guide the programmer in performing the mapping
- High flexibility
- High quality CDISC SDTM datasets

EDC (eCRF/eSource)



ORACLE[®]
HEALTH SCIENCES

InForm



ClinSpark[®]



Pre-Conversion



Convert the EDC (eCRF/eSource) structures to our general Mapping tool structure



Mapping Tool



Transform the converted EDC (eCRF/eSource) data to SDTM datasets



SDTM datasets



- To learn more about our pre-conversion
Pieter Blomme: paper DH03

Tuesday, February 26th

Time	Harbor B
12:00-12:30	DH03 From Source Data to SDTM: Enabling a Semi-automated Conversion <i>SGS Life Sciences</i>



SDTM MAPPING TOOL



Annot tool

[HOME](#)[CRF](#)[REPORTS](#)[LIBRARIES \(1142\)](#)

044. ----- Demographics 1.....|.....43|.....16|.....



[DM - Demographics]

Demographics 1

	Date of birth	DM1.DOB T	BRTHDTC
	Sex at birth	DM1.SEX	☐ Male ☐ Female SEX
	Race	DM1.RACE	☐ Not allowed to ask as per local regulations ☐ Please specify: RACE = NOT ALLOWED TO ASK AS PER LOCAL REGULATIONS
	Specify race:	DM1.RACES	RACE
	Ethnicity	DM1.ETHN	☐ Not allowed to ask per local regulations ☐ Hispanic or Latino ☐ Not Hispanic or Latino ETHNIC = NOT ALLOWED TO ASK AS PER LOCAL REGULATIONS ETHNIC

- All input fields, radio buttons and checkboxes presented like a pivot table

File Edit Search Filter Window Help									
Mapping	Visitmap	Repeatingvisits	Patient	PreProcess	PostProcess	AfterConversion	DBMF	Data	Errorlog
FORMREFNAME	CCCONTROLREFNAME	FINDING	DOMAIN	TARGET	PARAM1	PARAM2	P1	P2	
DM1	ETHN_DEC	N	DM	ETHNIC					
DM1	DOBDT	N	DM	BRTHDTC					
DM1	SEX	N	DM	SEX					
DM1	RACE	N	DM	RACE					

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- Automate setup of trial specific metadata
- Start: copy the complete MDR library
programmer will make the metadata trial specific

Domains

MDR

PR	DA	PP
SU	DD	PC
CE	EG	QS
DV	IS	SC
HO	MS	RS
MH	MI	TR

Trial

DM	EX	VS
SE	AE	TA
CO	DS	TE
SV	EG	TV
CM	IE	TI
EC	LB	TS

- Automate setup of trial specific metadata
- Start: copy the complete MDR library
programmer will make the metadata trial specific

Variables

MDR - DS

DSGRPID	DSREFID
DSSPID	DSSCAT
EPOCH	DSDTC

Trial

STUDYID	DOMAIN
USUBJID	DSSEQ
DSTERM	DSDECOD
DSCAT	DSSTDTC
DSSTDY	

- Automate setup of trial specific metadata
- Start: copy the complete MDR library
programmer will make the metadata trial specific

DATASET	DESCRIPTION	CLASS	STRUCTURE	PURPOSE	KEYS
TA	Trial Arms	Trial Design	One record per planned Element per Arm	Tabulation	STUDYID
DM	Demographics	Special-Purpose	One record per subject	Tabulation	STUDYID
CM	Concomitant/Prior Medications	Interventions	One record per recorded intervention occurrence or const.	Tabulation	STUDYID
EX	Exposure	Interventions	One record per protocol-specified study treatment, const.	Tabulation	STUDYID
AE	Adverse Events	Events	One record per adverse event per subject	Tabulation	STUDYID
DS	Disposition	Events	One record per disposition status or protocol milestone p.	Tabulation	STUDYID
EG	ECG Test Results	Findings	One record per ECG observation per time point per visit p.	Tabulation	STUDYID
LB	Laboratory Test Results	Findings	One record per lab test per time point per visit per subject	Tabulation	STUDYID
VS	Vital Signs	Findings	One record per vital sign measurement per time point pe.	Tabulation	STUDYID
RELREC	Related Records	Relationship	One record per related record, group of records or dataset	Tabulation	STUDYID
SUPPEX	Supplemental Qualifiers for EX	Relationship	One record per IDVAR, IDVARVAL and QNAM per subject	Tabulation	STUDYID
SUPPLB	Supplemental Qualifiers for LB	Relationship	One record per IDVAR, IDVARVAL and QNAM per subject	Tabulation	STUDYID
SUPPVS	Supplemental Qualifiers for VS	Relationship	One record per IDVAR, IDVARVAL and QNAM per subject	Tabulation	STUDYID

■ Automation

- Use the information collected via other in-house developed applications
- Annotation tool
 - SGSSTATE flag
 - ORIGIN
 - CRF pages
- SDTM mapping tool
 - Calculate the maximum length of the variables in the SDTM datasets

- Metadata checks
 - Addition to Pinnacle21 validation
 - Validate metadata integrity and compliance with the specific MDR library
- Audit trail
 - Record every manipulation of metadata on trial level
 - What was manipulated + Old value
 - Person performed the manipulation
 - When it was manipulated
 - Produce reports
 - All manipulations performed from a specific date
 - Retrieve metadata as it was on a specific date

■ Opportunities

- Past: creation of metadata late in the process of creating SDTM datasets
- Now: move the creation of the metadata to the front of the process
 - Pave the path for future tasks
 - Discuss and agree upon metadata with the client upfront
 - In line with define.xml purpose

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■ YADLi = **Y**et **A**nother **D**ata **L**oader **i**mproved

- Load any kind of source data
- Perform data manipulations

Vendor data

TXT, CSV, SAS7BDAT,
XPT, XLSX,...



SDTM datasets

Load the mapped YADLi data
into the SDTM database



YADLi

Load file in
database

Keep log: who
loaded
what data
when

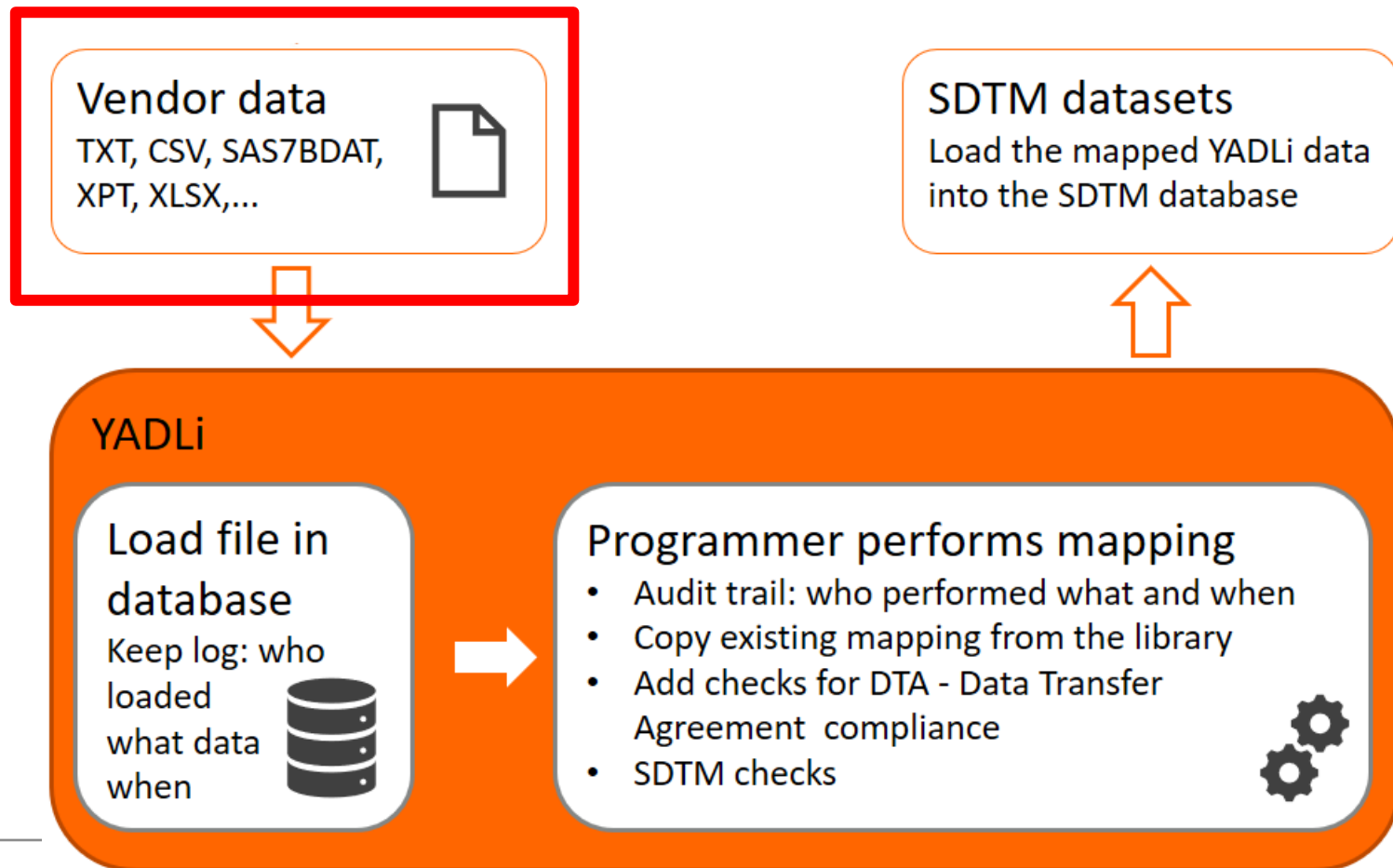


Programmer performs mapping

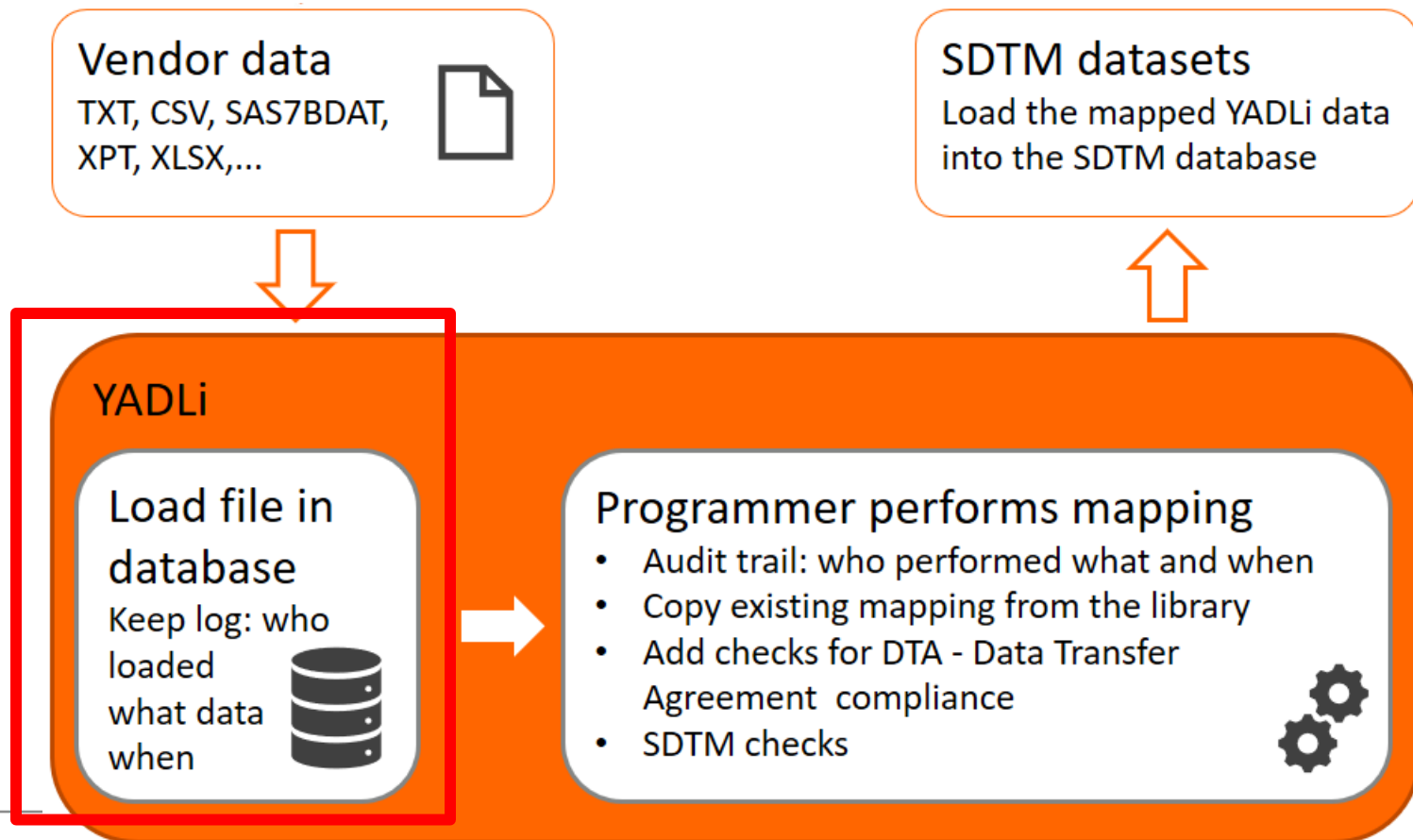
- Audit trail: who performed what and when
- Copy existing mapping from the library
- Add checks for DTA - Data Transfer Agreement compliance
- SDTM checks



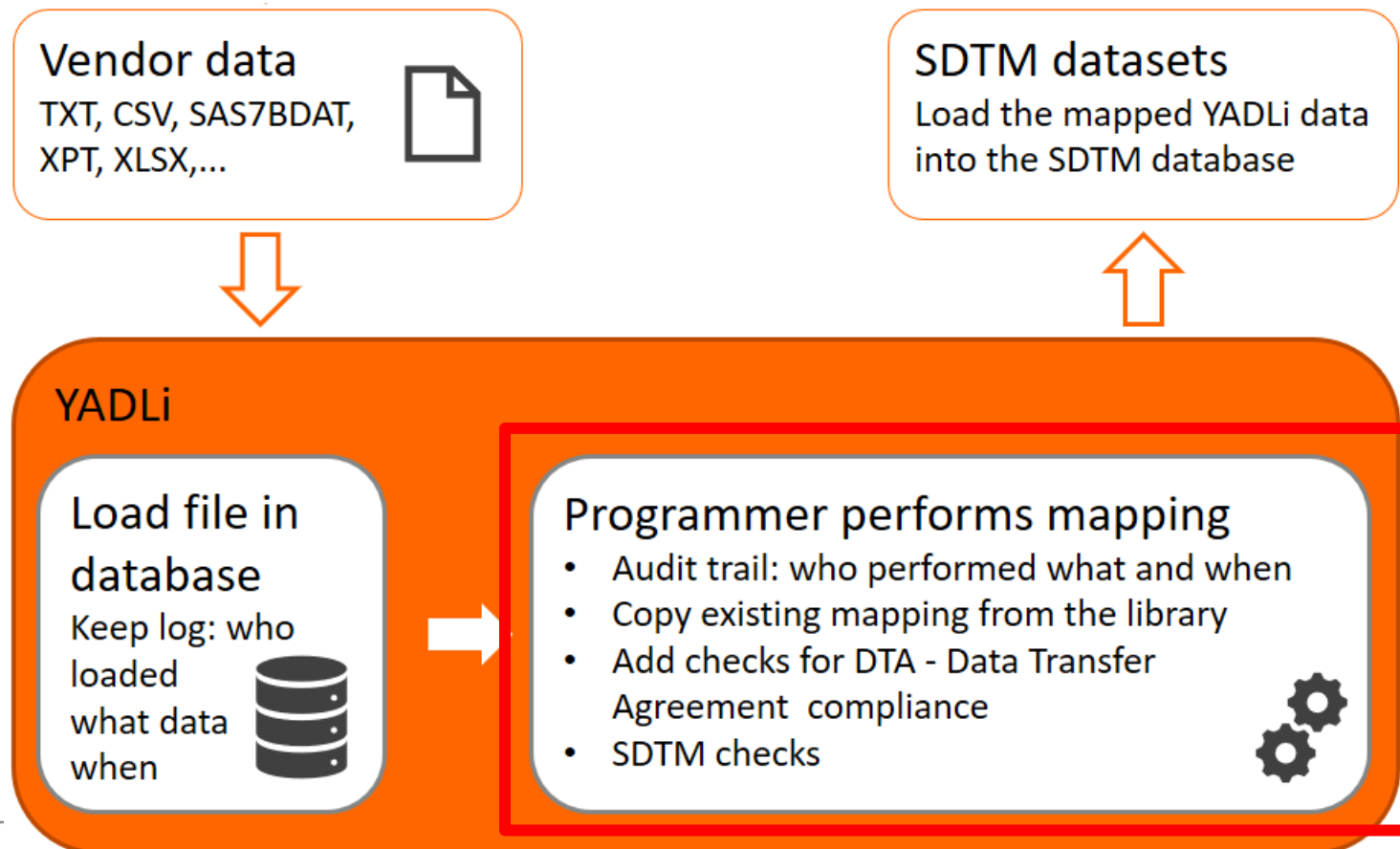
- DTA – Data Transfer Agreement
agree on format and structure



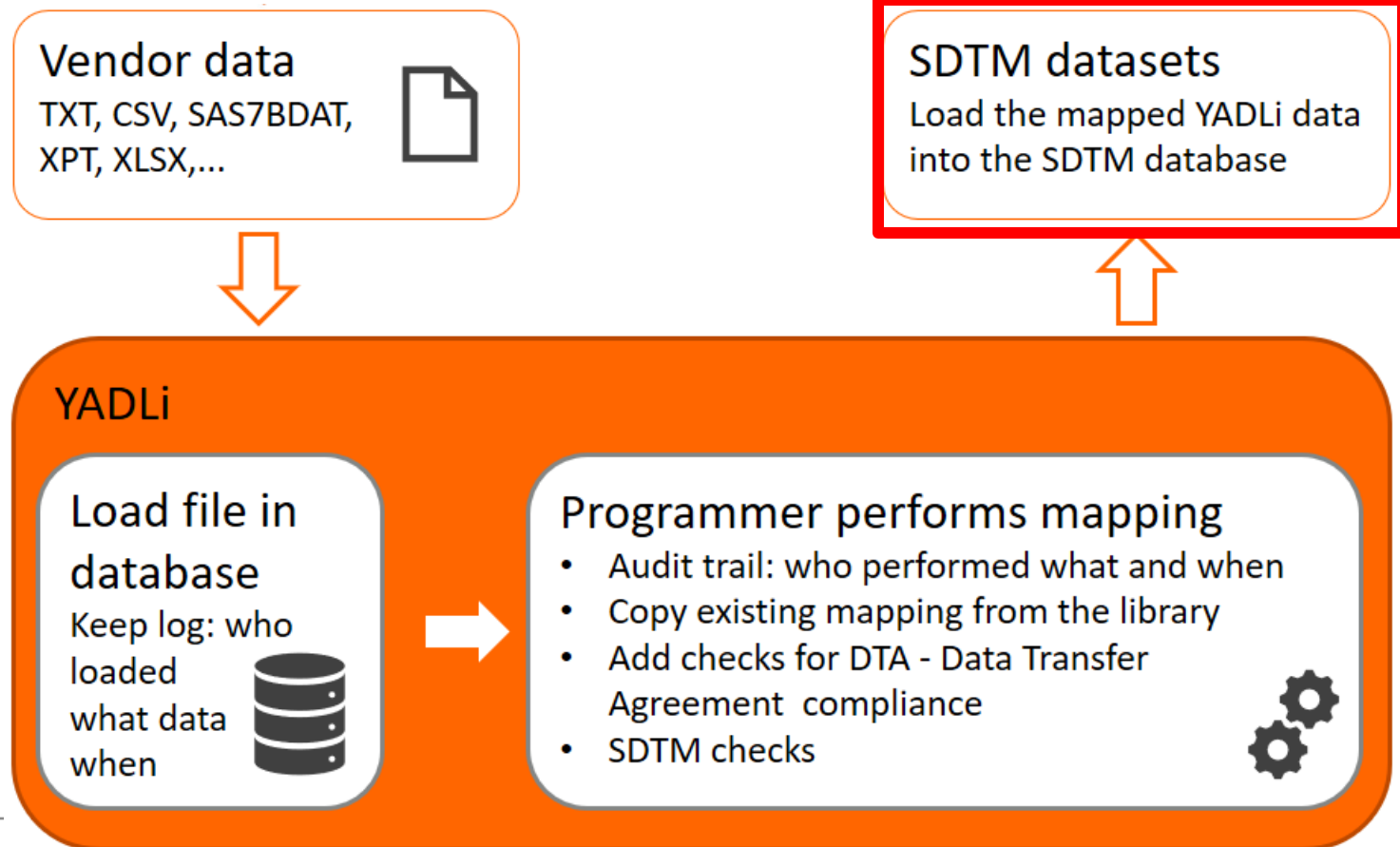
- YADLi loads the file into the database



- Programmer maps the data to SDTM



- YADLi produces output that can be used in SDTM datasets



- Best features
 - Handles any type of format
 - Logging and traceability
- Challenge
 - Load any kind of format and structure
- Opportunity
 - Further integration into the SDTM mapping tool

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CONCLUSION

- MDR to automate SDTM workflows paid off
- Road hasn't been easy
- Work in progress



Thank you for your attention!

BROAD CLINICAL RESEARCH SOLUTIONS

Questions ?



Join us at the SGS booth 13

CONTACT US

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