



EXPERTISE

SAFETY

SOLUTIONS

END TO END SDTM AUTOMATION: A METADATA CENTRIC APPROACH

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WHEN YOU NEED TO BE SURE

SGS



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



- **Introduction**
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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



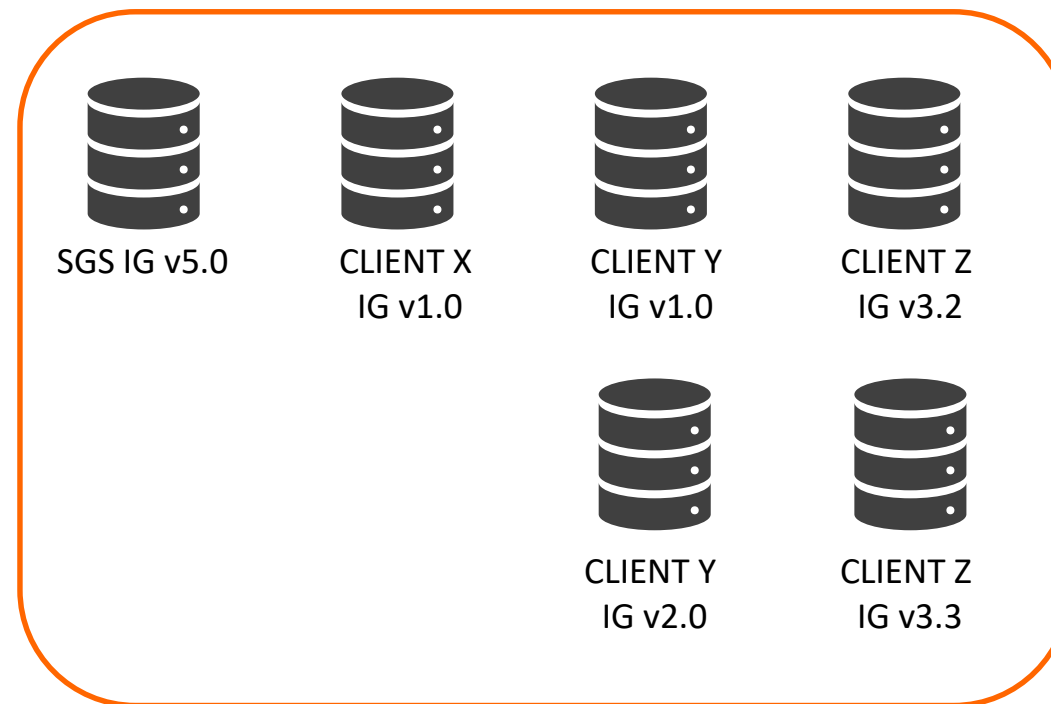
- Introduction
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MDR – METADATA REPOSITORY

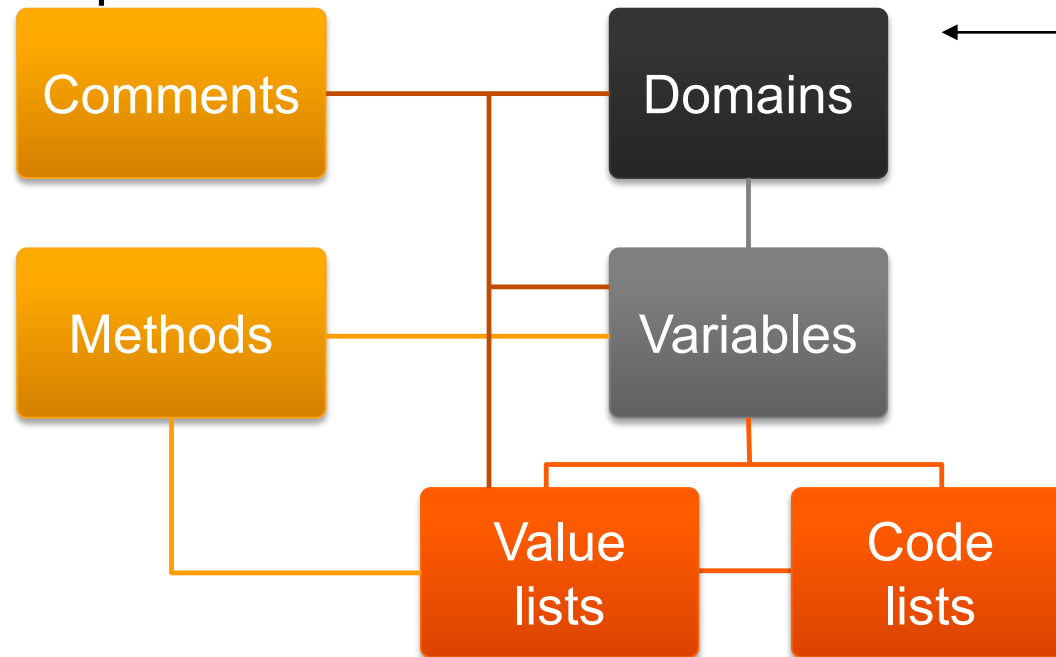
- Master source of metadata containing multiple metadata libraries.

MDR



MDR – METADATA REPOSITORY

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



SGS IG v5.0

MDR – METADATA REPOSITORY

■ 3 types of MDR libraries



SGS IG v5.0



CLIENT X
IG v1.0

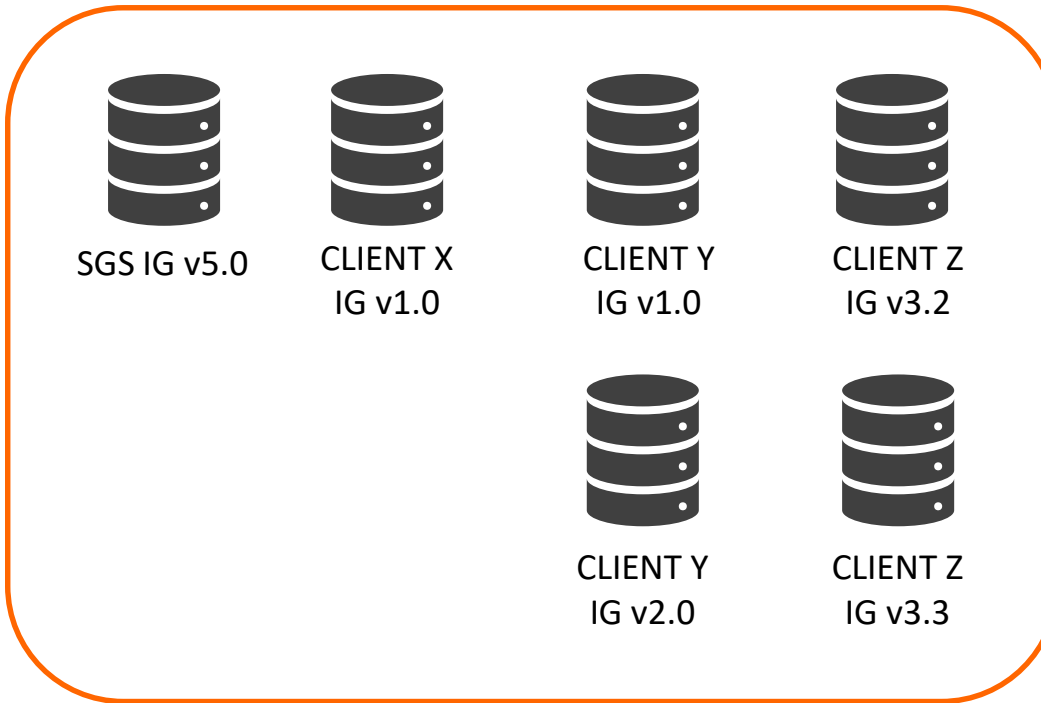


CLIE
IG CLIENT Z
IG v4.0

- Maintained by SGS
- Dictated by the client
- Maintained together with the client
- Maintained by the Client
- Implemented by SGS

MDR – METADATA REPOSITORY

MDR



Trials

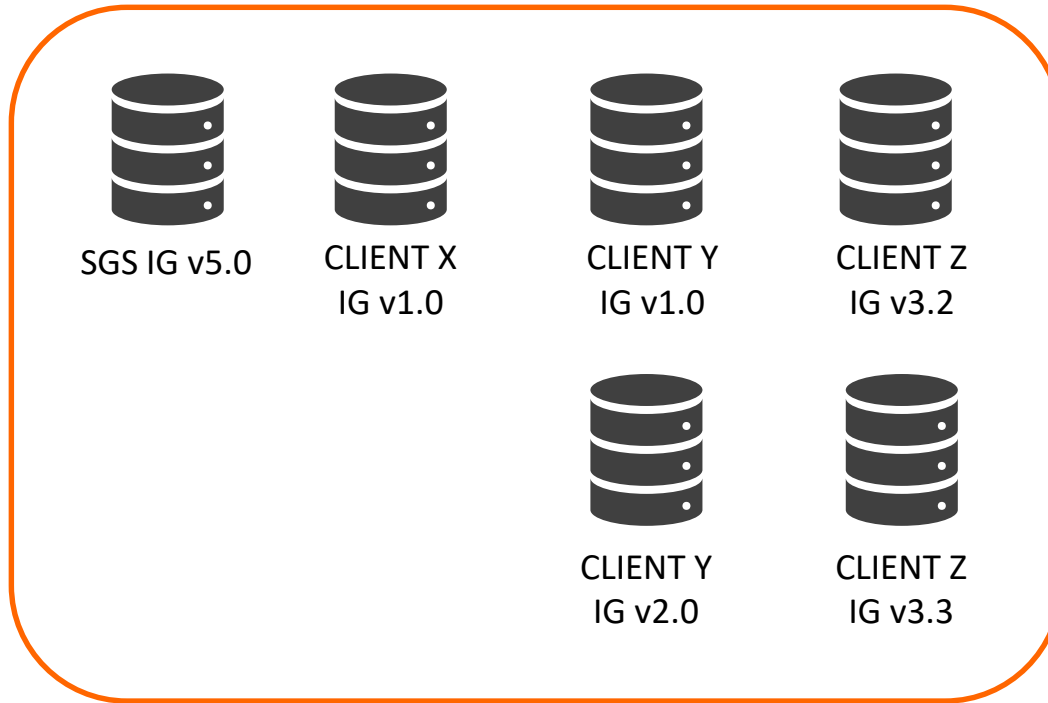




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MDR DRIVEN TOOLS

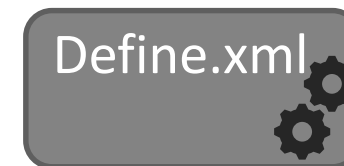
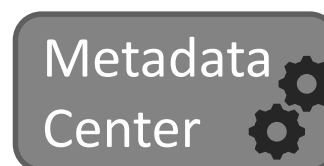
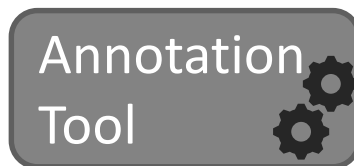
MDR



Trials



MDR Driven Tools





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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 ▾ / Req ▾ / Req ▾ BRTHDTC
2.* ✓	Subject signed informed consent on DSCAT = PROTOCOL MILESTONE	[dtmIFC] Req ▾ / Req ▾ / Req ▾ 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 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

- Domain missing



[DS - Disposition]

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

Demographics [sctDM]

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

■ Annotation properties

[DS - Disposition]

Trial A: Demographic Data and Informed Consent Records		
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



DM ▾ Page 2 20/01/2019 18:32:06 DSSTDTC
DM ▾ Page 2 20/01/2019 18:32:44 DSCAT = PROTOCOL MILESTONE
DS ▾ Page 2 20/01/2019 18:37:31 AGE
DS ▾ Page 2 20/01/2019 18:37:41 AGEU
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 ▾ / Req ▾ / Req ▾	BRTHDTC
2.* ✓	Subject signed informed consent on <i>DSCAT = PROTOCOL MILESTONE</i>	[dtmIFC] Req ▾ / Req ▾ / Req ▾	DSSTDTC
3.*	Age	[numAGE] N3 (years) <i>AGE</i>	<i>AGEU</i>



[DM - Demographics]

[DS - Disposition]

Trial A: Demographic Data and Informed Consent Record

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

[DS - Disposition]

Trial A: Demographic Data and Informed Consent Record

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 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

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



EXPERTISE

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

SGS Annot tool

roman_radelicki Feedback Switch app Logout (PROD)

HOME LIBRARIES

SGS

Properties

Annotation Types

Variables

Testcodes

Codelists

Domains

	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	VARIABLE.....#VARNAME#
Subject	CONSTANT.....#VARNAME# = #CONSTANTVALUE#
Finding	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
Other value	FREETEXT.....#FREETEXT#
	NOTE.....#FREETEXT#
Label	NOT_SUBMITTED..[Not submitted]
	REFERENCE.....For Annotations see CRF page #PAGENUMBER#
	ANNOTVERSION...#FREETEXT#
Search	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 ?

Domain

Subject

Finding

Other value

Label

Search

VS.....Vital Signs

X0.....Conversion data

X1.....Administrative data

XA.....Administrative Data

Z1.....Linking Verification

annex

ANNOTATION TOOL

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
- SSKNF.....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

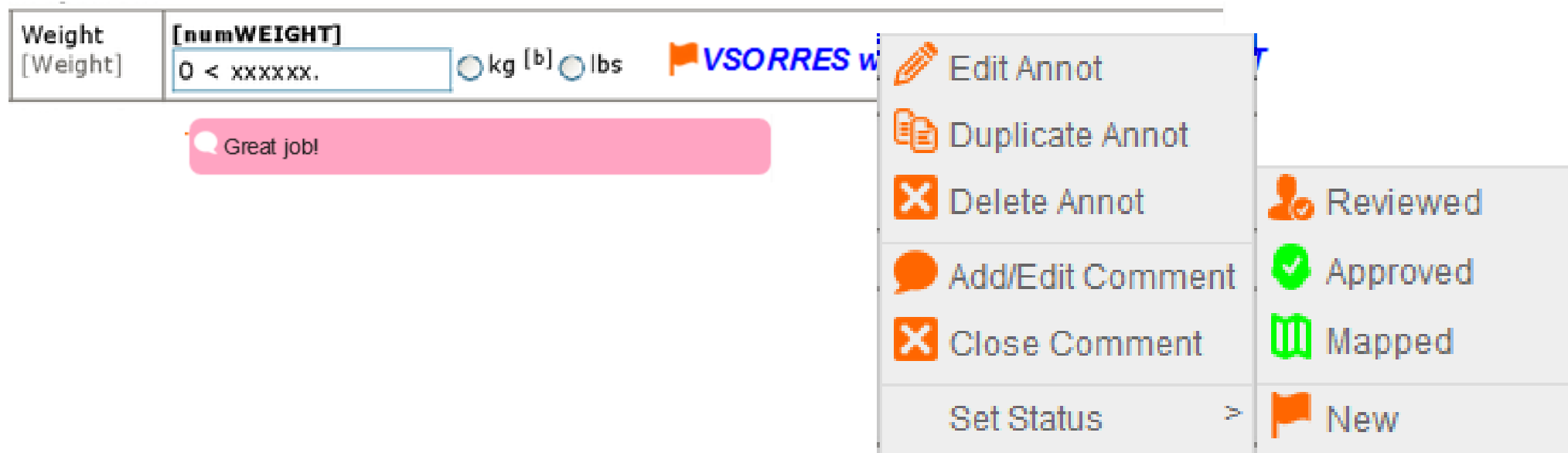
Label

Search

Search annex

■ Tracking review process

- Statuses
- Multiple users at the same time



The screenshot displays the SGS Annotation Tool interface. On the left, a form for 'Weight' is shown with a label '[numWEIGHT]' and a text input field containing '0 < xxxxxx.'. Below the input field is a pink notification bubble that says 'Great job!'. To the right of the input field are radio buttons for 'kg [b]' and 'lbs', and a blue flag icon labeled 'VSORRES w'. A context menu is open over the annotation, listing actions: 'Edit Annot' (pencil icon), 'Duplicate Annot' (document icon), 'Delete Annot' (X icon), 'Add/Edit Comment' (speech bubble icon), and 'Close Comment' (X icon). To the right of the menu is a 'Set Status' button with a right arrow. Further right is a vertical list of status options: 'Reviewed' (person icon), 'Approved' (green checkmark icon), 'Mapped' (green map icon), and 'New' (orange flag icon).



■ 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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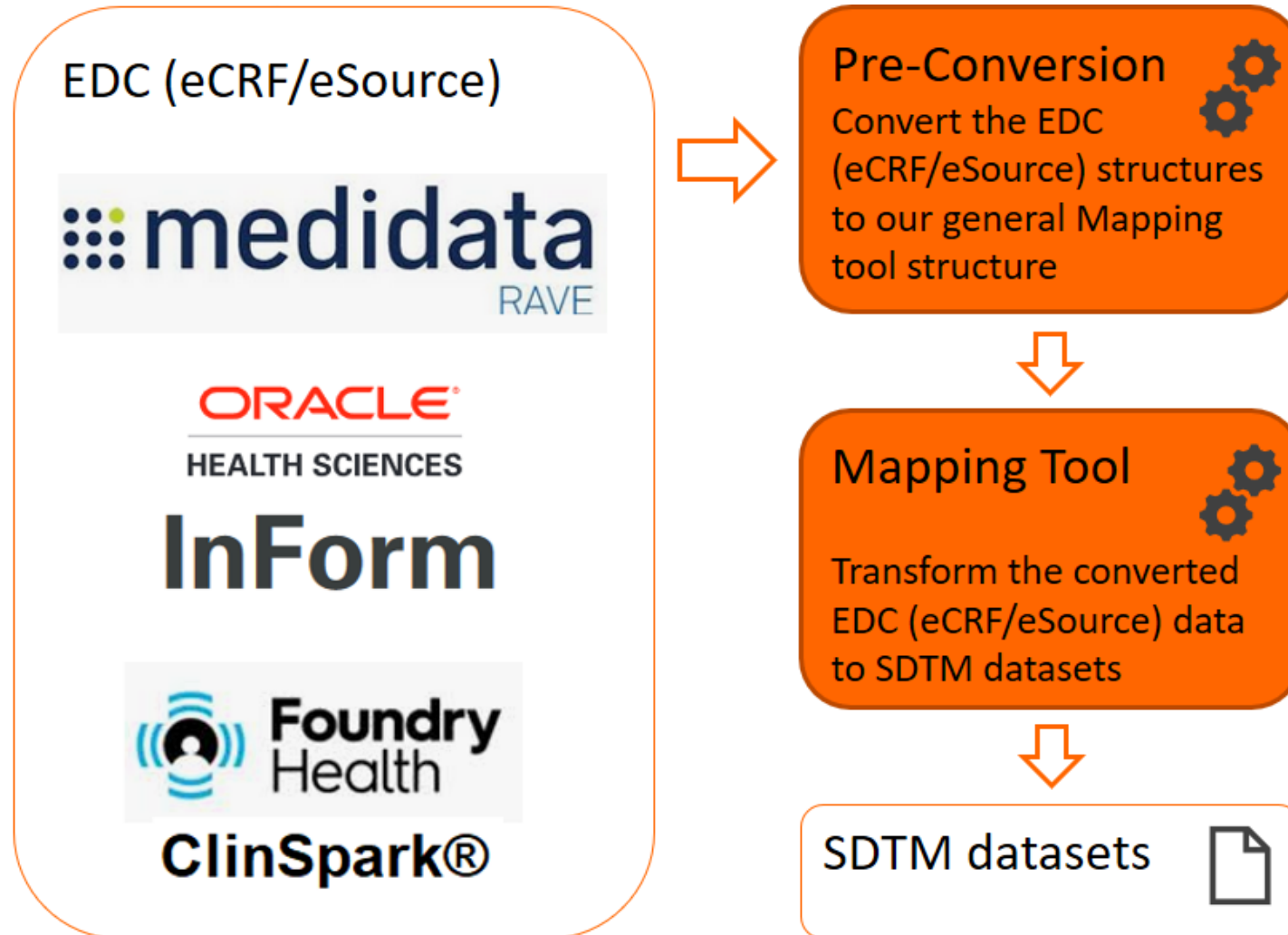


EXPERTISE

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



SDTM MAPPING TOOL



HOME

CRF

REPORTS

LIBRARIES (1142)

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



[DM - Demographics]

Demographics 1

Date of birth	DM1.DOB T	BIRTHDATE	
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	ADD	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	PARM1	PARM2	P ₁	P ₂	P ₃	CONVERTTYPE	CODE
DM1	ETHN_DEC	N	DM	ETHNIC						ANY	case when CTSS\$
DM1	DOBDT	N	DM	BRTHDTC						VALUE	upper(CTSS\$ITEM
DM1	SEX	N	DM	SEX						FIRSTCHAR	substr(upper(CT
DM1	RACE	N	DM	RACE						ANY	case when uppe



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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, ARMCOD, TAETORD
DM	Demographics	Special-Purpose	One record per subject	Tabulation	STUDYID, USUBJID
CM	Concomitant/Prior Medications	Interventions	One record per recorded intervention occurrence or const...	Tabulation	STUDYID, USUBJID, CMTRT, CMSTDTC, CMSCD
EX	Exposure	Interventions	One record per protocol-specified study treatment, const...	Tabulation	STUDYID, USUBJID, EXTRT, EXSTDTC, EXPT
AE	Adverse Events	Events	One record per adverse event per subject	Tabulation	STUDYID, USUBJID, AEDECOD, AESTDTC
DS	Disposition	Events	One record per disposition status or protocol milestone p...	Tabulation	STUDYID, USUBJID, DSDECOD, DSSTDTC, DSS
EG	ECG Test Results	Findings	One record per ECG observation per time point per visit p...	Tabulation	STUDYID, USUBJID, EGTESTCD, VISITNUM, EG
LB	Laboratory Test Results	Findings	One record per lab test per time point per visit per subject	Tabulation	STUDYID, USUBJID, LBTESTCD, LBSPEC, VISIT
VS	Vital Signs	Findings	One record per vital sign measurement per time point pe...	Tabulation	STUDYID, USUBJID, VSTESTCD, VISITNUM, VS
RELREC	Related Records	Relationship	One record per related record, group of records or dataset	Tabulation	STUDYID, RDOMAIN, USUBJID, IDVAR, IDVARV
SUPPEX	Supplemental Qualifiers for EX	Relationship	One record per IDVAR, IDVARVAL and QNAM per subject	Tabulation	STUDYID, RDOMAIN, USUBJID, IDVAR, IDVARV
SUPPLB	Supplemental Qualifiers for LB	Relationship	One record per IDVAR, IDVARVAL and QNAM per subject	Tabulation	STUDYID, RDOMAIN, USUBJID, IDVAR, IDVARV
SUPPVS	Supplemental Qualifiers for VS	Relationship	One record per IDVAR, IDVARVAL and QNAM per subject	Tabulation	STUDYID, RDOMAIN, USUBJID, IDVAR, IDVARV

■ 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

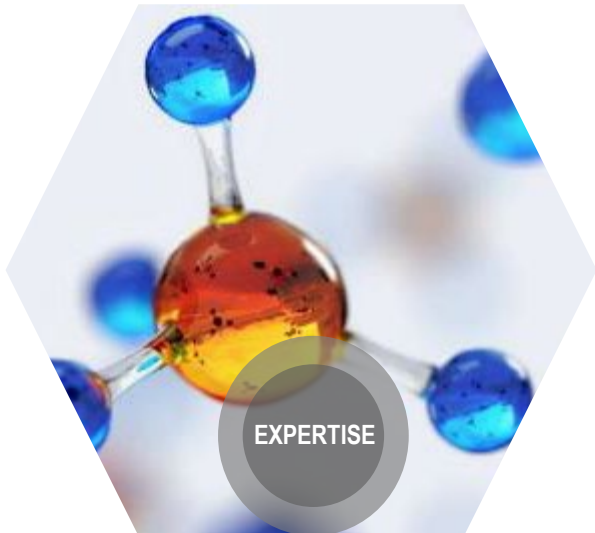
■ Audit trail

- 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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CONCLUSION

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



Thank you for your attention!



ADVANCED **CLINICAL** **RESEARCH** SOLUTIONS

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clinicalresearch@sgs.com



EUROPE: +32 15 27 32 45
AMERICAS: +1 877 677 2667



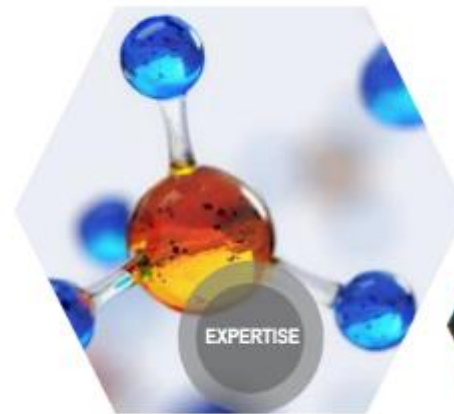
www.sgs.com/cro

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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

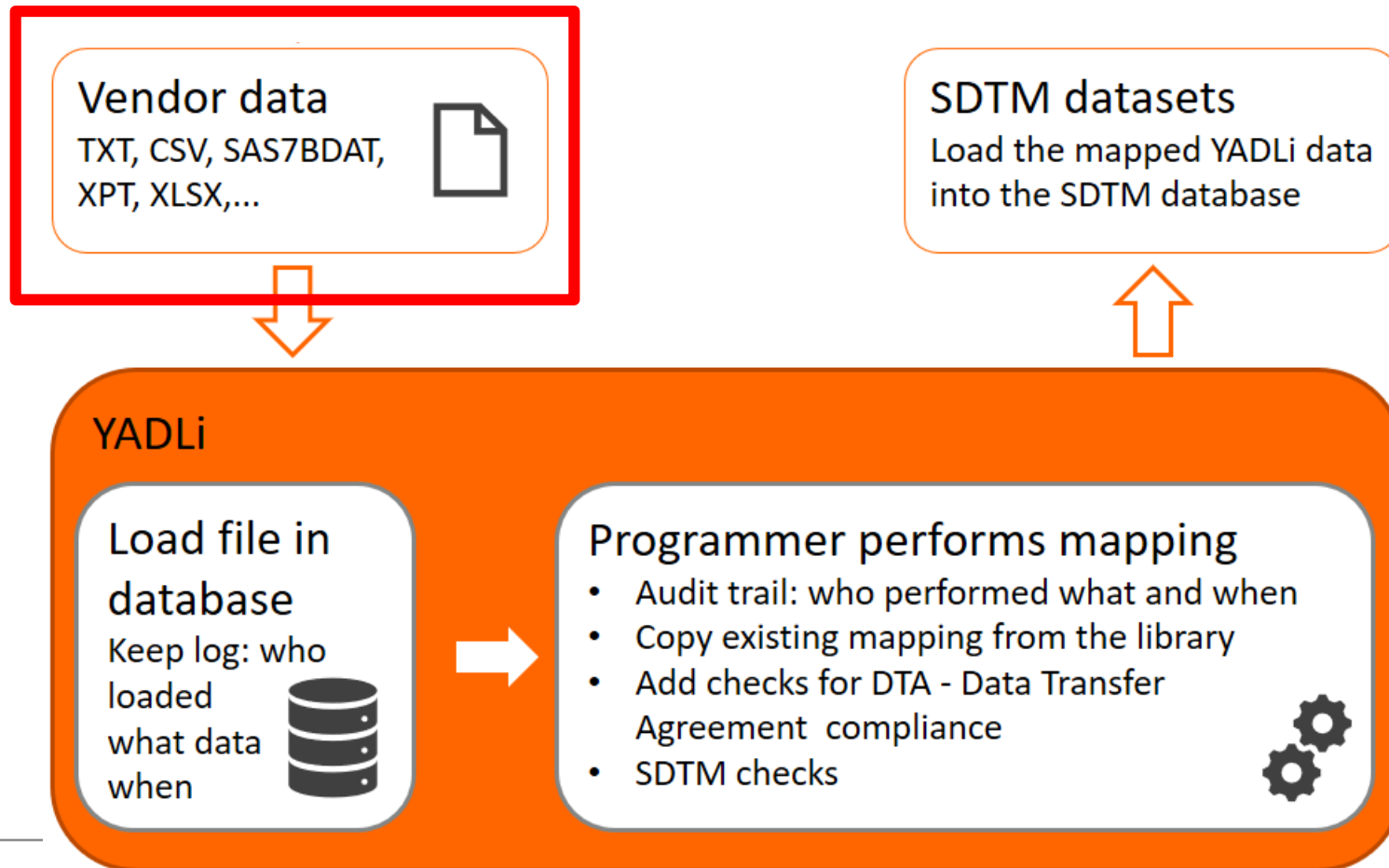


Programmer performs mapping

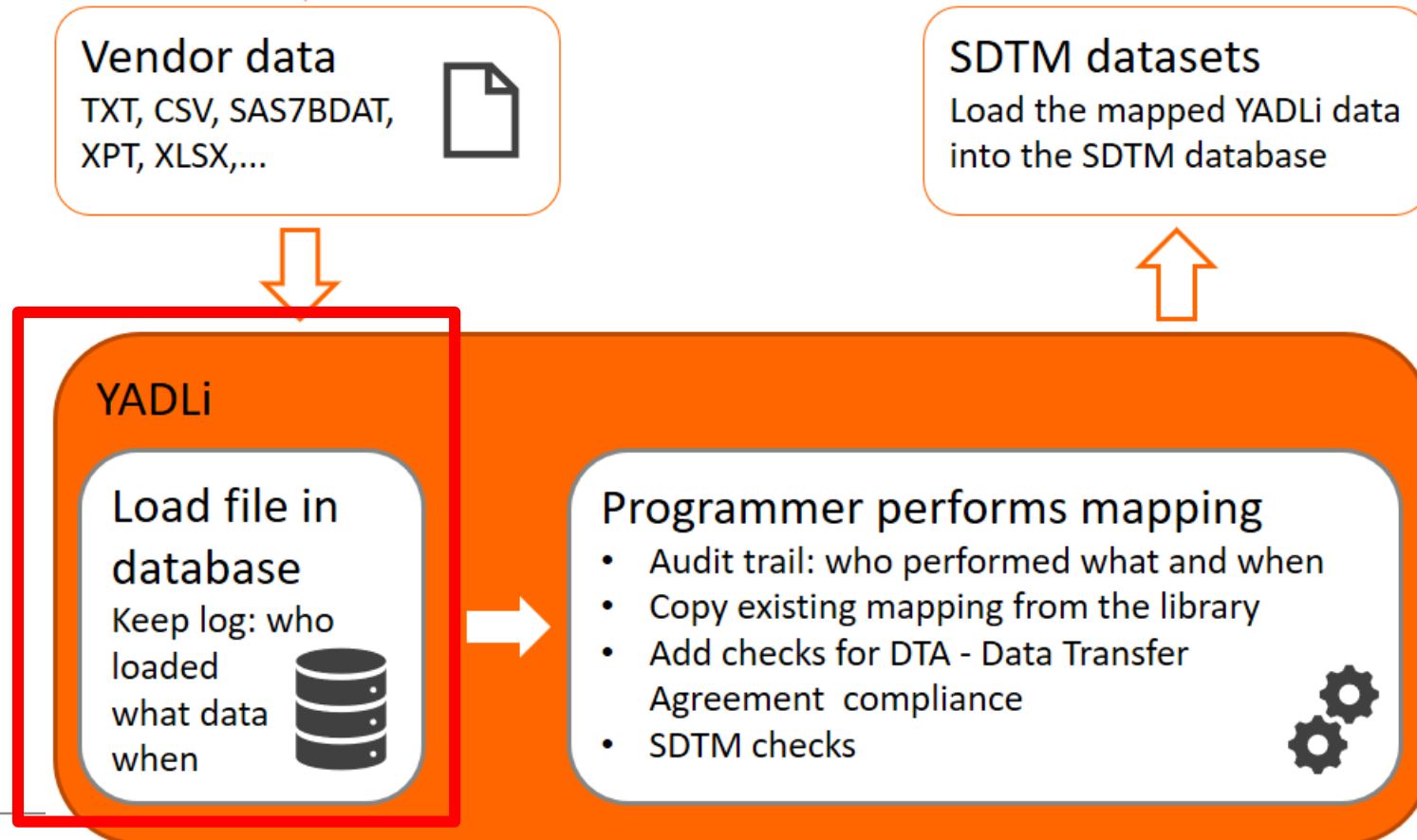
- Audit trail: who performed what and when
- Copy existing mapping from the library
- Add checks for DTA - Data Transfer Agreement compliance
- SDTM checks



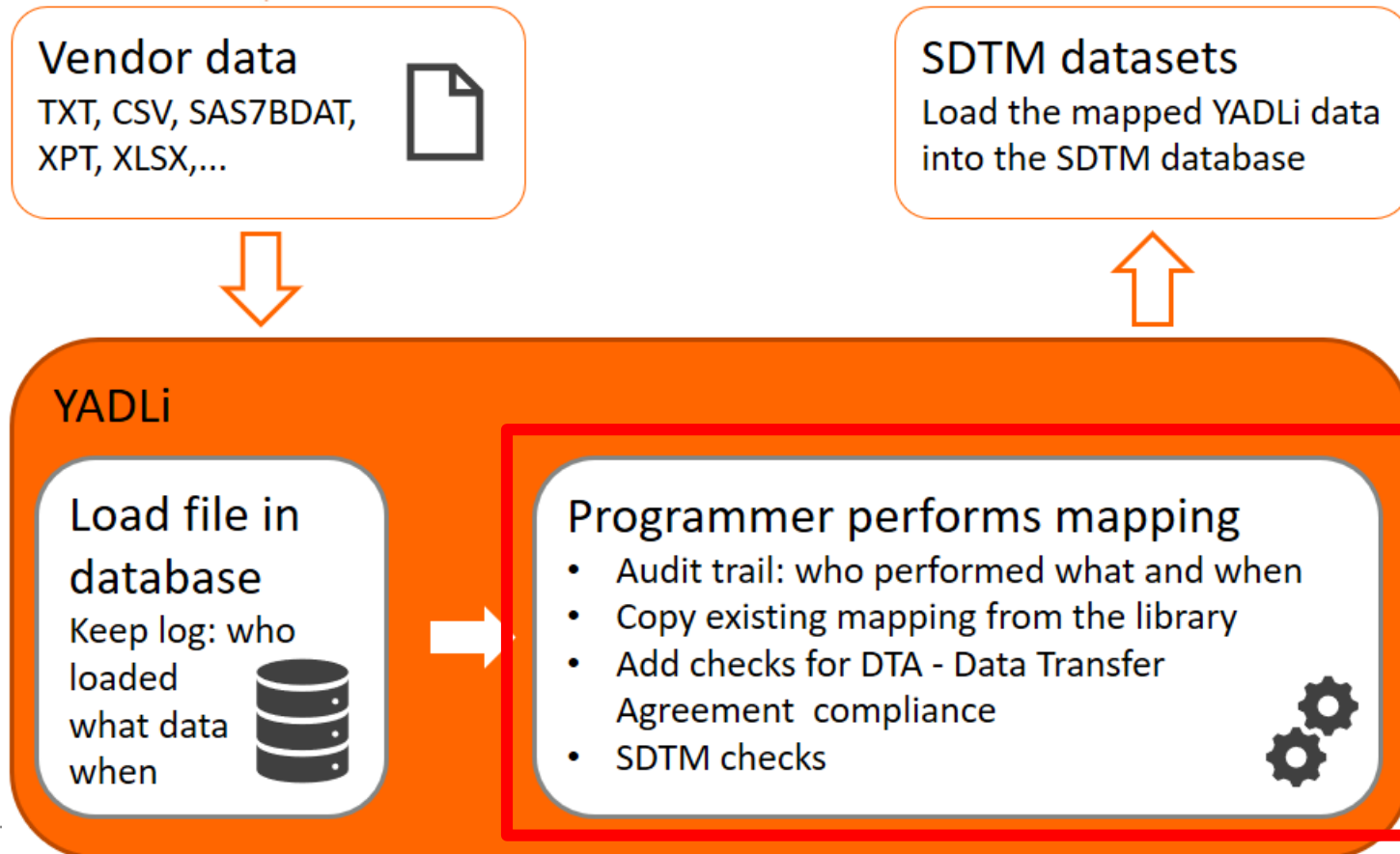
- DTA – Data Transfer Agreement
agree on format and structure



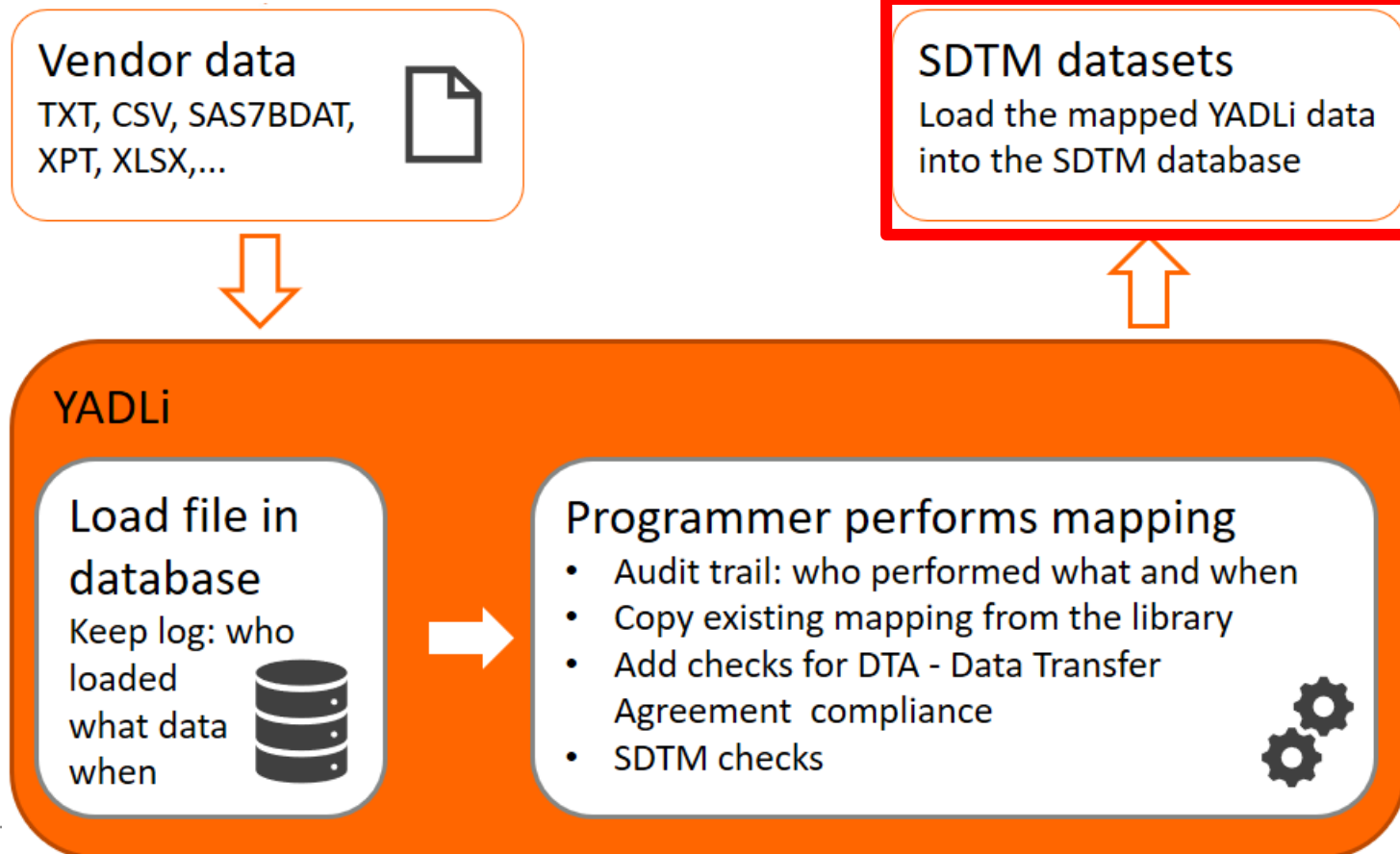
- YADLi loads the file into the database



- 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