END TO END SDTM AUTOMATION
A METADATA CENTRIC APPROACH

Roman Radelicki
Team Manager Data Programming
PhUSE US Connect 2019, February 25th
OVERVIEW

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

- **Introduction**

- MDR – metadata repository

- MDR driven tools
  - Annotation Tool
  - SDTM Mapping Tool
  - Metadata Center
  - YADLi

- Conclusion
What is the key to creating clinical databases that are compliant with CDISC SDTM standards?

- Metadata driven approach
- Seamless integration of processes and people
OVERVIEW

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

- Master source of metadata containing multiple metadata libraries.

MDR

- SGS IG v5.0
- CLIENT X IG v1.0
- CLIENT Y IG v1.0
- CLIENT Z IG v3.2
- CLIENT Y IG v2.0
- CLIENT Z IG v3.3
MDR – METADATA REPOSITORY

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

- 3 types of MDR libraries
  - Maintained by SGS
  - Dictated by the client
    - Maintained together with the client
  - Maintained by the Client
    - Implemented by SGS
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- Conclusion
How we used to annotate a CRF
**ANNOTATION TOOL**

- Font: Courier vs Arial

---

<table>
<thead>
<tr>
<th>Trial A: Demographic Data and Informed Consent Recording (DM) [frmDM]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics [sctDM]</strong></td>
</tr>
<tr>
<td>1.* Date of birth</td>
</tr>
<tr>
<td>[dtmBRTH]</td>
</tr>
<tr>
<td>Req ✓ / Req ✓ / Req ✓</td>
</tr>
<tr>
<td><strong>BRTHDTC</strong></td>
</tr>
<tr>
<td>2.* Subject signed informed consent on</td>
</tr>
<tr>
<td><strong>DSCAT = PROTOCOL MILESTONE</strong></td>
</tr>
<tr>
<td>[dtmIFC]</td>
</tr>
<tr>
<td>Req ✓ / Req ✓ / Req ✓</td>
</tr>
<tr>
<td><strong>DSSTDTC</strong></td>
</tr>
<tr>
<td>3.* Age</td>
</tr>
<tr>
<td>[numAGE]</td>
</tr>
<tr>
<td>N3 (years) AGE AGEU</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>1.*</td>
</tr>
<tr>
<td>[dtmBRTH]</td>
</tr>
<tr>
<td>Req</td>
</tr>
<tr>
<td>2.*</td>
</tr>
<tr>
<td>[dtsIFC]</td>
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</tr>
<tr>
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</tr>
<tr>
<td>N3</td>
</tr>
</tbody>
</table>

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

**Demographics [sctDM]**

- Size: 11 vs 18
## ANNOTATION TOOL

- Color

### [DS - Disposition]

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

### Demographics [sctDM]

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>1.</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>[dtmBRTH]</td>
</tr>
<tr>
<td>2.</td>
<td>Subject signed informed consent on <strong>DSCAT = PROTOCOL MILESTONE</strong></td>
<td><strong>DSSTDTC</strong></td>
</tr>
<tr>
<td></td>
<td></td>
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<td>Age</td>
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## Annotation Tool

- Domain missing

<table>
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<td>AGE AGEU</td>
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</table>
### Annotation properties

#### DS - Disposition

**Trial A: Demographic Data and Informed Consent**

**Demographics [sctDM]**

<table>
<thead>
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<td>(years)</td>
<td>AGE</td>
</tr>
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</table>

**DSCAT = PROTOCOL MILESTONE**

- DS
- AGE
- N3
- AGEU

**Supplemental**

- SUPPQS
- BRTHDTC
## ANNOTATION TOOL

- Domain colors

### [DS - Disposition]

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- [ ] Req

**[dtmIFC]**
- [ ] Req
- [ ] Req
- [ ] Req

**[numAGE]**
- N3 (years) **AGE AGEU**
**Sgs Annotation Tool**

### [DM - Demographics]

**[DS - Disposition]**

#### Trial A: Demographic Data and Informed Consent Records

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**[DS - Disposition]**

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<tr>
<td>3. * Age</td>
<td>[numAGE] N3 (years)</td>
</tr>
</tbody>
</table>

---

**DSCAT = PROTOCOL MILESTONE**

---

**AGE**

---

**AGEU**
ANNOTATION TOOL

- 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 Tool

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

### Annot Tool

<table>
<thead>
<tr>
<th>Annotype</th>
<th>Textfont</th>
<th>Objectype</th>
<th>Fillcolor</th>
<th>Annotcolor</th>
<th>Annotformat</th>
<th>FontWeight</th>
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<td>#VARNAME#</td>
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<tr>
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<td>Arial</td>
<td>FreeText</td>
<td>-</td>
<td>#FF0000</td>
<td>SUPP#DOMAIN#.QVAL when QNAM = #QNAM#</td>
<td>bold</td>
<td>italic</td>
<td>11</td>
<td>0</td>
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<td>TESTCD</td>
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<td>FreeText</td>
<td>-</td>
<td>#0000FF</td>
<td>#DOMAIN#ORRES when #DOMAIN#TESTCD = #FINDING#</td>
<td>bold</td>
<td>italic</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>NOT_SUBMITTED</td>
<td>Arial</td>
<td>FreeText</td>
<td>-</td>
<td>#0000FF</td>
<td>[Not submitted]</td>
<td>bold</td>
<td>italic</td>
<td>11</td>
<td>0</td>
</tr>
</tbody>
</table>
**ANNOTATION TOOL**

- Annotation type demo
  - Weight of a subject
  - TESTCD
ANNOTATION TOOL

ADD ANNOTATION

Annotation type

Domain

Subject

Finding

Author

Other value

Label

Search

Search annex
ANNOTATION TOOL
ANNOTATION TOOL

ADD ANNOTATION

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

Domain: VOID ...

Subject: 

Author: 

Finding: 

Other value: 

Label: 

Search: Search annex
## Annotation Tool

### Add Annotation

<table>
<thead>
<tr>
<th>Annotation Type</th>
<th>Test CD...........#DOMAIN#ORRES when #DOMAIN#TESTCD = #FINDING#</th>
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<tbody>
<tr>
<td>Domain</td>
<td>Microbiology Susceptibility</td>
</tr>
<tr>
<td>Subject</td>
<td>Pharmacokinetic Concentrations</td>
</tr>
<tr>
<td>Finding</td>
<td>Pharmacodynamics</td>
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<tr>
<td></td>
<td>Physical Examination</td>
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<td></td>
<td>Pharmacokinetic Parameters</td>
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<td></td>
<td>Questionnaires</td>
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<td></td>
<td>Respiratory System Findings</td>
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<td>Reproductive System Findings</td>
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<tr>
<td></td>
<td>Disease Response</td>
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<tr>
<td></td>
<td>Subject Characteristics</td>
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<tr>
<td></td>
<td>Skin Response</td>
</tr>
<tr>
<td></td>
<td>Subject Status</td>
</tr>
<tr>
<td></td>
<td>Tumor Results</td>
</tr>
<tr>
<td></td>
<td>Tumor Identification</td>
</tr>
<tr>
<td>Other Value</td>
<td>Vital Signs</td>
</tr>
<tr>
<td>Label</td>
<td>conversion data</td>
</tr>
<tr>
<td>Search</td>
<td>Administrative data</td>
</tr>
<tr>
<td></td>
<td>Administrative Data</td>
</tr>
<tr>
<td></td>
<td>Linking Verification</td>
</tr>
</tbody>
</table>
ANNOTATION TOOL

ADD ANNOTATION

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

Domain: VS...........Vital Signs

Subject: 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
- BODLENGTH.....Body Length
- BODYFAT........Adipose Tissue; Body Fat; Fat Tissue
- BODYFATM.......Body Fat Measurement
- BSA............Body Surface Area
- DIABP..........Diastolic Blood Pressure
- ENRGRXLP.....Energy Expenditure
- EWEIGHT.......Estimated Weight
- FARMCIR........Forearm Circumference
- FRMSIZE........Body Frame Size

Other value

Label

Search
ANNOTATION TOOL

- Tracking review process
  - Statuses
  - Multiple users at the same time
ANNO\:TATION TOOL

Advantages

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

- Challenges
  - Screen vs exported PDF file

- Opportunities
  - Further automatisation: auto copy annotations from the library or previously annotated CRF’s
OVERVIEW

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

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

- **EDC (eCRF/eSource)**
- **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
SDTM MAPPING TOOL

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

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

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

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

- 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

Vendor data
TXT, CSV, SAS7BDAT, XPT, XLSX,...

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YADLi loads the file into the database

Vendor data
TXT, CSV, SAS7BDAT, XPT, XLSX,...

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Programmer maps the data to SDTM

Vendor data
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YADLi produces output that can be used in SDTM datasets

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
YADLI

- 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!
Questions?

Join us at the SGS booth 13