END TO END SDTM AUTOMATION:
A METADATA CENTRIC APPROACH

Roman Radelicki – Team Manager Data Programming, SGS

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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
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    - Annotation Tool
    - SDTM Mapping Tool
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    - YADLi
- Conclusion
MDR – METADATA REPOSITORY

- Master source of metadata containing multiple metadata libraries.
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
MDR – METADATA REPOSITORY

- 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

- Trials
  - Client A – Trial A
    - SGS IG v5.0
  - Client B – Trial C
    - SGS IG v5.0
  - Client Y – Trial Y
    - CLIENT Y IG v2.0
OVERVIEW

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OVERVIEW

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How we used to annotate a CRF

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>DS - Disposition</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Demographics [sctDM]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1.</strong> Date of birth</td>
</tr>
<tr>
<td><strong>2.</strong> Subject signed informed consent on <strong>DSCAT = PROTOCOL MILESTONE</strong></td>
</tr>
<tr>
<td><strong>3.</strong> Age</td>
</tr>
</tbody>
</table>

<p>| | |</p>
<table>
<thead>
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<td></td>
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</table>
### ANNOTATION TOOL

- Font: Courier vs Arial

#### [DS - Disposition]

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

<table>
<thead>
<tr>
<th></th>
<th><strong>Demographics [sctDM]</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Date of birth&lt;br&gt;[dtmBRTH]&lt;br&gt;Req ✓ / Req ✓ / Req ✓&lt;br&gt;<strong>BRTHDTC</strong></td>
</tr>
<tr>
<td>2.</td>
<td>Subject signed informed consent on&lt;br&gt;DSCAT = PROTOCOL MILESTONE&lt;br&gt;[dtmIFC]&lt;br&gt;Req ✓ / Req ✓ / Req ✓&lt;br&gt;<strong>DSSTDTC</strong></td>
</tr>
<tr>
<td>3.</td>
<td>Age&lt;br&gt;[numAGE]&lt;br&gt;N3 (years) AGE  AGEU</td>
</tr>
</tbody>
</table>
**ANNOTATION TOOL**

- Size: 11 vs 18

### [DS - Disposition]

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

<table>
<thead>
<tr>
<th>Demographics [sctDM]</th>
<th></th>
</tr>
</thead>
</table>
| **1.** Date of birth | [dtmBRTH]  
| Req ✓ | Req ✓ | Req ✓ | BRTHDTC |
| **2.** Subject signed informed consent on | [dtmIFC]  
| Req ✓ | Req ✓ | Req ✓ | DSSTDTC |
| **DSCAT = PROTOCOL MILESTONE** |  |
| **3.** Age | [numAGE] N3 (years) | AGE | AGEU |
## ANNOTATION TOOL

- **Color**

### [DS - Disposition]

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

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<tr>
<td>[dtmBRTH] Req ✔ / Req ✔ / Req ✔</td>
</tr>
<tr>
<td>BRTHDTC</td>
</tr>
<tr>
<td><strong>2.</strong> Subject signed informed consent on DSCAT = PROTOCOL MILESTONE</td>
</tr>
<tr>
<td>[dtmIFC] Req ✔ / Req ✔ / Req ✔</td>
</tr>
<tr>
<td>DSSTDTC</td>
</tr>
<tr>
<td><strong>3.</strong> Age</td>
</tr>
<tr>
<td>[numAGE] N3 (years) AGE AGEU</td>
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</tbody>
</table>
### Trial A: Demographic Data and Informed Consent Recording (DM) [frmDM]

#### Demographics [sctDM]

<table>
<thead>
<tr>
<th>Field</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. * Date of birth</td>
<td>BRTHDTC</td>
</tr>
<tr>
<td>2. * Subject signed informed consent on</td>
<td>DSSTDTC</td>
</tr>
<tr>
<td>3. * Age</td>
<td>AGED</td>
</tr>
</tbody>
</table>

**Domain missing**
ANNOTATION TOOL

- Annotation properties
## ANNOTATION TOOL

- Domain colors

### [DS - Disposition]

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

**Demographics [sctDM]**

<p>| | | | |</p>
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<tbody>
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<td>Date of birth</td>
<td>[dtmBRTH]</td>
<td>Req ✓ / Req ✓ / Req ✓</td>
</tr>
<tr>
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<td>Subject signed informed consent on <strong>DSCAT = PROTOCOL MILESTONE</strong></td>
<td>[dtmIFC]</td>
<td>Req ✓ / Req ✓ / Req ✓</td>
</tr>
<tr>
<td>3</td>
<td>Age</td>
<td>[numAGE]</td>
<td>N3 (years) AGE AGEU</td>
</tr>
</tbody>
</table>

**Annotations:**
- BRTHDTC
- DSSTDTC
**ANNOTATION TOOL**

**[DM - Demographics]**

**[DS - Disposition]**

<table>
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<td>3. * Age</td>
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</tbody>
</table>

| [dtnBRTH]                                           |
| Req ✔ / Req ✔ / Req ✔                               |

**[DS - Disposition]**

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</tr>
<tr>
<td>3. * Age</td>
</tr>
</tbody>
</table>

| [dtnIFC]                                           |
| Req ✔ / Req ✔ / Req ✔                               |

**[DM - Demographics]**

| [dtnBRTH]                                           |
| Req ✔ / Req ✔ / Req ✔                               |

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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
ANNOTATION TOOL

- Annotation type demo
  - Weight of a subject
  - TESTCD
## Annotation Tool

### Add Annotation

<table>
<thead>
<tr>
<th>Annotation type</th>
<th>Domain</th>
</tr>
</thead>
<tbody>
<tr>
<td>VARIABLE........</td>
<td>#VARNAME#</td>
</tr>
<tr>
<td>CONSTANT.........</td>
<td>#VARNAME# = #CONSTANTVALUE#</td>
</tr>
<tr>
<td>VARIABLE2.......</td>
<td>#VARNAME# = #CONSTANTVALUE#</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Subject</th>
</tr>
</thead>
<tbody>
<tr>
<td>TESTCD.........</td>
</tr>
<tr>
<td>TESTCD2........</td>
</tr>
<tr>
<td>TESTCD3........</td>
</tr>
<tr>
<td>TESTCD4........</td>
</tr>
<tr>
<td>SUPP...........</td>
</tr>
<tr>
<td>SUPP2...........</td>
</tr>
<tr>
<td>SUPP3...........</td>
</tr>
<tr>
<td>SUPP4...........</td>
</tr>
<tr>
<td>COVAL...........</td>
</tr>
<tr>
<td>RELREC...........</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FREETEXT......</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Label</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOT_SUBMITTED [Not submitted]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Search</th>
</tr>
</thead>
<tbody>
<tr>
<td>REFERENCE......</td>
</tr>
<tr>
<td>ANNOTVERSION....</td>
</tr>
<tr>
<td>CRFVERSION.....</td>
</tr>
<tr>
<td>DOMAIN........</td>
</tr>
</tbody>
</table>
ANNOTATION TOOL

ADD ANNOTATION

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

Domain

Subject

Author

Finding

Other value

Label

Search

Search annex
Tracking review process

- Statuses
- Multiple users at the same time
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
ANNOTATION TOOL

- **Challenges**
  - Screen vs exported PDF file

- **Opportunities**
  - Further automatisation: auto copy annotations from the library or previously annotated CRF’s
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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)**
  - medidata RAVE
  - ORACLE HEALTH SCIENCES
  - InForm
  - Foundry Health 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**
### Demographics 1

<table>
<thead>
<tr>
<th></th>
<th>DM1.DOBDT</th>
<th>BRTHDT</th>
<th>DM1.RACE</th>
<th>RACE = NOT ALLOWED TO ASK AS PER LOCAL REGULATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of birth</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex at birth</td>
<td>DM1.SEX</td>
<td>SEX</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td>DM1.RACE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specify race:</td>
<td>DM1.RACES</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td>DM1.ETHN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>ETHNIC</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Male
- Female
- Not allowed to ask per local regulations
- Please specify:
- Not allowed to ask per local regulations
- Hispanic or Latino
- Not Hispanic or Latino
- ETHNIC = NOT ALLOWED TO ASK AS PER LOCAL REGULATIONS
SDTM MAPPING TOOL

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

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  - Metadata Center
  - YADLi
- Conclusion
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

Variables

MDR - DS

<table>
<thead>
<tr>
<th>Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSGRPID</td>
</tr>
<tr>
<td>DSREFID</td>
</tr>
<tr>
<td>DSSPID</td>
</tr>
<tr>
<td>DSSCAT</td>
</tr>
<tr>
<td>EPOCH</td>
</tr>
<tr>
<td>DSDTC</td>
</tr>
<tr>
<td>STUDYID</td>
</tr>
<tr>
<td>USUBJID</td>
</tr>
<tr>
<td>DSTERM</td>
</tr>
<tr>
<td>DSCAT</td>
</tr>
<tr>
<td>DSSTDY</td>
</tr>
<tr>
<td>DOMAIN</td>
</tr>
<tr>
<td>DSSEQ</td>
</tr>
<tr>
<td>DSDECOD</td>
</tr>
<tr>
<td>DSSTDTC</td>
</tr>
</tbody>
</table>

Trial
### 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>STUDYID, ARMCO, TAETORD</td>
</tr>
<tr>
<td>DM</td>
<td>Demographics</td>
<td>Special-Purpose</td>
<td>One record per subject</td>
<td>Tabulation</td>
<td>STUDYID, USUBID</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>STUDYID, USUBID, CMTRT, CMSTDTD, CMSO, CMSTRT</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>STUDYID, USUBID, EXTRT, EXSTDTD, EXPTT</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>STUDYID, USUBID, AEDECOD, AESTDTC</td>
</tr>
<tr>
<td>DS</td>
<td>Disposition</td>
<td>Events</td>
<td>One record per disposition status or protocol milestone p...</td>
<td>Tabulation</td>
<td>STUDYID, USUBID, DSDECOD, DSSTDTD, DSSPE</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 p...</td>
<td>Tabulation</td>
<td>STUDYID, USUBID, ECGTESTCD, VISITNUM, EGFTC, ECGVTS</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>STUDYID, USUBID, LBTESTCD, LBSPEC, VISTNUM, VBTS</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>STUDYID, USUBID, VSTESTCD, VISITNUM, VSPTS</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>STUDYID, RDOMAIN, USUBID, IDVAR, IDVARU</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>STUDYID, RDOMAIN, USUBID, IDVAR, IDVARU</td>
</tr>
<tr>
<td>SUPPLB</td>
<td>Supplemental Qualifiers for LB</td>
<td>Relationship</td>
<td>One record per IDVAR, IDVARVAL and QNAM per subject</td>
<td>Tabulation</td>
<td>STUDYID, RDOMAIN, USUBID, IDVAR, IDVARU</td>
</tr>
<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>STUDYID, RDOMAIN, USUBID, IDVAR, IDVARU</td>
</tr>
</tbody>
</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 CENTER

- 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!
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- **MDR driven tools**
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  - Metadata Center
  - **YADLi**
- Conclusion
YADLI

- **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
YADLI

- DTA – Data Transfer Agreement
  agree on format and structure

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 loads the file into the database

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
Programmer maps the data to SDTM

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 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
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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