Validation Tools, Assessment & Compliance

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Goal

- Contribute towards a better assessment of the Quality of Clinical Data
  - As one measurement of Data Quality is based on how closely the Data complies with a given Standard and associated Implementation Guidelines, the SDTM Validation Project initially aims to provide an agreeable mechanism to assess Data Quality based on how closely a clinical database follows the CDISC/SDTM Standard and corresponding Implementation Guide.
  - Compliance will allow faster review and enable data integration
  - Non-Compliance will break tools, slows or inhibits review and potentially will inhibit data integration
Goal

• In Scope:
  – Data and Metadata (in data files and define.xml)

• Initial focus:
  – Regulatory submissions to the FDA

• Notes:
  – Metadata in the define.xml is expected to be a superset of the metadata included in SAS XPT files
  – Define.xml schema validation is not in scope – it is assumed that a valid define.xml document is submitted. Refer to the published white paper by the CDISC/XML team
# Team Members (*)

<table>
<thead>
<tr>
<th>Name</th>
<th>Company</th>
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<td>Borowiak, Ken</td>
<td>PPD</td>
<td>Kalfas, Thomas *</td>
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<td>Cassells, Sally</td>
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<td>Malla, Amy</td>
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<td>Shinaberry, Lauren *</td>
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<td>Simpson, Trisha *</td>
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<td>Gibson, Bill *</td>
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<td>Smith, Steve</td>
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<td>Hernandez, Joyce *</td>
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<td>Image Solutions, Inc.</td>
<td>Van Reusel, Peter *</td>
<td>Business &amp; Decision</td>
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<td>Witczak, Bobbie</td>
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(*) CAB representatives
Team’s skills

- Broad Industry representation, *including the FDA*
- Strong understanding of SDTM
- Strong technical skills
- Great open cooperation (no wall flowers)
Checks from Software Tools reviewed

a) WebSDM / Phase Forward
b) OpenCDISC Validator / OpenCDISC
c) SAS Clinical Standards Toolkit / SAS
d) CheckPoint / Octagon
e) DMCC / Business & Decision
Data Package:
- SDTM annotated CRFs
- SDTM datasets
- ADaM datasets
- Define.xml (metadata)

NOTE: No regulatory authority to reject (RTF) based on failed validation rules – must be due to inability to review data

Courtesy of Peter Van Reusel, revised with input from the project team specially from Amy Malla
FDA CRT Submission Process

Data Package:
- SDTM annotated CRFs
- SDTM datasets
- ADaM datasets
- Define.xml (metadata)

Electronic Submission

WEBSDM™ and/or OpenCDISC
Load & Validation

FDA

JANUS

Reviewer Tools

NOTE: No regulatory authority to reject (RTF) based on failed validation rules – must be due to inability to review data

Courtesy of Peter Van Reusel, revised with input from the project team specially from Amy Malla
Approach

• Review the Standard Compliance checks implemented by different vendors to assess
  – differences in meaning (independent of style) vs. granularity
  – potentially missing checks
  – categories of checks (structure; content/terminology: individual and cross-column, cross-domain constraints; metadata: consistency of self-contained in SAS XPT files with define.xml plus not contained in SAS XPT files)
  – severity of failures

• Develop a uniform set of checks, where rules
  – are concise and unambiguous
  – include both data and metadata from all identified categories
  – are not ‘value’ specific
  – have consensus on severity

• Develop golden set(s) of test data and associated check’s results
  – include positive and negative tests

→ Enable CDISC/SDTM Compliance Checks Certification (pending discussion)
Challenges

• Standard is evolving
  – Definition of SDTM
  – Vocabularies (Standard Terminology) change constantly
  – Standard Terminology: suggestion or mandate?
• Agreement on definition of severity of failure
  – Error – prevent loading and/or impact reviewability?
  – Warning – may impact reviewability?
  as opposed to
  – High – prevent loading
  – Medium – may impact reviewability
  – Low – may or may not impact reviewability
• Timeline coordination and acceptance within Industry and Agency will be a future challenge
• Organizing the real work
**Results**

<table>
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<tr>
<th>Software Tool / Vendor</th>
<th>Severity</th>
<th>In WebSDM</th>
<th>Not in WebSDM</th>
<th>Unique to WebSDM</th>
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<tr>
<td>DMCC / Business &amp; Decision</td>
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<td>232</td>
<td>206</td>
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</table>

Total messages reviewed 1191

- Difference ways to categorize checks and assign severity
- List of potential new rules to be added
- Differences in rules granularity, description and message provided
- Work in progress to compile unique checks
Next Steps

- **Compiled list of checks** with preliminary questions and recommendations to FDA (*)
- FDA response to team’s questions and compiled list
- Definition of severity of failure
  - recommendation for Error - Warning
- Janus checks review
- Consolidated list of checks V1
- Public Review? (following the CDISC/COP?)
- Approval?
- Golden set(s) of test data V1

(*) work in progress
Timelines

- Optimistic/Stretch Goal: by the next North America CDISC Interchange in 2011
Strength *through collaboration.*

Q&A

Thank you!