Software Tools for working with CDISC ODM, SDTM, Lab and define.xml

Jozef Aerts
XML4Pharma
A software overview is always ...

- Incomplete
- Biased
- So ...

The opinions of the author expressed herein do not necessarily state or reflect those of CDISC, SAS, or any other organization. Reference herein to any specific commercial products, process, or service by trade name, trademark manufacturer, or otherwise, does not necessarily constitute or imply its endorsement, recommendation, or favoring CDISC or SAS.
The CDISC Models

- **CDISC ODM**: Standard for exchange, storage and archiving of clinical study data and metadata
- **CDISC Lab**: Exchange of laboratory data
  - ASCII, XML, SAS, HL7 implementation
- **CDISC SDTM**: Standard for submission of clinical data sets to the FDA
- **CDISC CRT-DDS (define.xml)**: Case Report Tabulations Data Definition Specification
CDISC end-to-end

Protocol → CDISC ODM Study Description → Rel. Database

CDMS → XML Database

CRO DB

eCRF

XML-Signature

Investigators copy of submitted e-CRF

Investigator: Investigator
Form: Physical Exam
Group: Physical Exam, General

Group code: 0.00.00.0

<table>
<thead>
<tr>
<th>Question Code</th>
<th>Question Text</th>
</tr>
</thead>
<tbody>
<tr>
<td>H-DX010</td>
<td>Diagnosis</td>
</tr>
<tr>
<td>H-DX020</td>
<td>History</td>
</tr>
<tr>
<td>H-SEX</td>
<td>Sex</td>
</tr>
<tr>
<td>H-AGE</td>
<td>Age</td>
</tr>
<tr>
<td>H-BIRTH</td>
<td>Birthdate</td>
</tr>
<tr>
<td>H-HEIGHT</td>
<td>Height</td>
</tr>
<tr>
<td>H-WEIGHT</td>
<td>Weight</td>
</tr>
<tr>
<td>H-BP</td>
<td>Blood Pressure</td>
</tr>
<tr>
<td>H-HB</td>
<td>Hb</td>
</tr>
<tr>
<td>H-STATUS</td>
<td>Status</td>
</tr>
</tbody>
</table>

Group code: 0.00.00.1

<table>
<thead>
<tr>
<th>Group Code</th>
<th>Group Name</th>
<th>Question Code</th>
<th>Question Text</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00.00.1</td>
<td>Physical Exam, Body System</td>
<td>H-BODY</td>
<td>Body Information</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group Code</th>
<th>Group Name</th>
<th>Question Code</th>
<th>Question Text</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00.00.2</td>
<td>Physical Exam, Blood Pressure</td>
<td>H-BP</td>
<td>Blood Pressure Information</td>
</tr>
<tr>
<td>0.00.00.3</td>
<td>Physical Exam, Hb</td>
<td>H-HB</td>
<td>Hb Information</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group Code</th>
<th>Group Name</th>
<th>Question Code</th>
<th>Question Text</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00.00.4</td>
<td>Physical Exam, Status</td>
<td>H-STATUS</td>
<td>Status Information</td>
</tr>
</tbody>
</table>
CDISC end-to-end

CRO

Rel.Database
XML Database
CDMS

Lab data

WS

Sponsor

Define.xml

ADaM
SDTM

SAS
Transport 5

FDA
Protocols

• No CDISC Protocol Standard yet
• So no tools yet
• CDISC ODM Study setup should be automatically generated from the (CDISC) Protocol document
Tools to create ODM Study Setups

• Create Item, ItemGroup definitions, Forms, Visits ..., and save them as ODM

• Tools available:
  – **Origin** (Formedix)
  – **XC Designer** (DataLabs)
  – **ODMDDesigner** (XML4Pharma)
CDISC ODM based CMD / EDC systems

- Commercial
  - Marvin (Xclinical)
  - Express (Formedix)

- Open Source:
  - Visitrial (Granite Health Systems)

- Many other export ODM Data
- Some import ODM Data
CDISC ODM and eCRF

• The ODM Study definition contains all information to automatically create eCRFs

• This has been implemented by a good number of eCRF vendors

• Demo application (using XForms) at: www.XML4PharmaServer.com
Why use ODM for eCRF?

- Format already CDISC
- Easily appendable to ODM file for transfer
- All information is there
- Ideal for native XML database
- Standard XML tools usable
  - XML-Signature, XML-Security
  - Web Services
  - ...
Standard XML tools (usable for ODM)

- **XML-Signature, XML-Security**
  - Many implementations available: Apache, IBM, Verisign, Microsoft ...

- **Web Services**
  - Many implementations available: Apache Axis, .Net, Perl, C++, ...

- **Native XML databases:**
  - Tamino ... eXist ... ... Oracle

Demos of all these available at www.XML4PharmaServer.com
CDISC ODM and conformity

- 70-80% of the rules can be described in the XML-Schema
- 20-30% can only be described in the spec itself

- Use a Conformity Checker
  - ODMConform (Assero)
  - ODMChecker (XML4Pharma)
Results from checking the CDISC ODM Document

Checking ODM file
C:\CDISC_ODM_Checker\CDISC_ODM_Checker_v0.6\testfiles\ODM1.2\CTChicago_XSchema_not_conform.xml

Level 1 ERROR when reaching line 3
Incorrect value for attribute
Found: “Absent”
The attribute should have one from the following list of values:
All, Metadata, AdminData, ReferenceData, AllClinicalData, SingleSite, SingleSubject

Level 1 ERROR when reaching line 3
The value “Absent” of attribute “Granularity” on element “ODM” is not valid with respect to its type, “Granularity”.

Level 2 WARNING when reaching line 3
ODM Version mismatch
No “ODMVersion” attribute was found although the presence of an XML-Schema indicates that the ODM Version is 1.2
Documents based on ODM 1.2 should have ODMVersion="1.2"
ODM Version 1.2 will be supposed further

Level 1 ERROR when reaching line 69
The value “AExxxxxxxxxxxxx” of attribute “SASDatasetName” on element “ItemGroupDef” is not valid with respect to its type, “sasName”.
The attribute length is more than 8 characters or contains invalid characters.
Tools for working with CDISC Lab files

- Implementations: ASCII, XML, SAS, HL7
- PHT has/had a CDISC Lab Viewer
- Covance is forerunner
- CDISC Lab Checker
  - ASCII version
  - XML version
- Server implementation running at Gereq
Tools for working with CDISC Lab files

• Lab ASCII to Lab XML Converter
  – Available online

• Conversion from Lab (XML) to ODM
  – Use XSLT
  – Several demo stylesheets available from different consultants
Working with ODM in SAS

- SAS Proc CDISC

- Tekoa Toolkit and Tekoa Statistical Reporting from Zürich Biostatistics (ZBI)
From ODM to submission

- How do we convert ODM into submission data?
- SDTM is a specification, not a format
- Submission data in define.xml and SAS Transport 5
- Later: ALL data in define.xml
Convert ODM into SDTM

• Use SAS, or ...

• Use other commercial software
  – OC2SDS (Oracle Clinical)
  – WebSDM (Lincoln Techn.)

• Write custom software
  – Some CDMS vendors do ...
  – Some sponsors / end-users do ...
ODM to SDTM Considerations

- Where implement SDTM in the chain?
- Several scenarios are possible
Using SDTM from the start on

Protocol Database

More work to do here

STDM

Less work to do here

ODM Study Design

Submission
<table>
<thead>
<tr>
<th>Domain Code</th>
<th>Domain Name</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>CM</td>
<td>Demographics</td>
<td>Special-PurposeDomains</td>
</tr>
<tr>
<td>SO</td>
<td>Comments</td>
<td>Special-PurposeDomains</td>
</tr>
<tr>
<td>CM</td>
<td>Concomitant Medications</td>
<td>Interventions</td>
</tr>
<tr>
<td>DV</td>
<td>Exposure</td>
<td>Interventions</td>
</tr>
<tr>
<td>SU</td>
<td>Substance Use</td>
<td>Interventions</td>
</tr>
<tr>
<td>AE</td>
<td>Adverse Events</td>
<td>Events</td>
</tr>
<tr>
<td>DS</td>
<td>Disposition</td>
<td>Events</td>
</tr>
<tr>
<td>MH</td>
<td>Medical History</td>
<td>Events</td>
</tr>
<tr>
<td>DV</td>
<td>Protocol Deviations</td>
<td>Events</td>
</tr>
<tr>
<td>DA</td>
<td>Drug Accountability</td>
<td>Findings</td>
</tr>
<tr>
<td>EG</td>
<td>ECG Tests</td>
<td>Findings</td>
</tr>
<tr>
<td>IE</td>
<td>Inclusion/Exception</td>
<td>Findings</td>
</tr>
<tr>
<td>LB</td>
<td>Laboratory Tests</td>
<td>Findings</td>
</tr>
<tr>
<td>MB</td>
<td>Microbiology</td>
<td>Findings</td>
</tr>
<tr>
<td>Q8</td>
<td>Questionnaires</td>
<td>Findings</td>
</tr>
<tr>
<td>PC</td>
<td>Pharmacokinetics Concentr.</td>
<td>Findings</td>
</tr>
<tr>
<td>PP</td>
<td>Pharmacokinetics Parameter</td>
<td>Findings</td>
</tr>
<tr>
<td>PE</td>
<td>Physical Examinations</td>
<td>Findings</td>
</tr>
<tr>
<td>SC</td>
<td>Subjects Characteristics</td>
<td>Findings</td>
</tr>
<tr>
<td>VS</td>
<td>Vital Signs</td>
<td>Findings</td>
</tr>
<tr>
<td>TE</td>
<td>Trial Elements</td>
<td>Trial Design Domains</td>
</tr>
<tr>
<td>TA</td>
<td>Trial Arms</td>
<td>Trial Design Domains</td>
</tr>
<tr>
<td>TV</td>
<td>Trial Visits</td>
<td>Trial Design Domains</td>
</tr>
<tr>
<td>SE</td>
<td>Subject Elements</td>
<td>Trial Design Domains</td>
</tr>
<tr>
<td>SV</td>
<td>Subject Vists</td>
<td>Trial Design Domains</td>
</tr>
<tr>
<td>TI</td>
<td>Trial Inclusion/Exclusion</td>
<td>Trial Design Domains</td>
</tr>
<tr>
<td>TS</td>
<td>Trial Summary</td>
<td>Trial Design Domains</td>
</tr>
<tr>
<td>SUPPQUAL</td>
<td>Supplemental Qualifiers</td>
<td>Special-PurposeDomains</td>
</tr>
<tr>
<td>RELREC</td>
<td>Relate Records</td>
<td>Special-PurposeDomains</td>
</tr>
<tr>
<td>OTHER</td>
<td>Other</td>
<td>Other</td>
</tr>
</tbody>
</table>
Tools for working with Define.xml

• The standard is young, so ...
• Viewing: the CDISC distribution already comes with a stylesheet for viewing as HTML in a browser
• CDISC ODMChecker will be extended for define.xml files
• A editing tool is currently in development
Should SAS Clinical Developers learn XML?

- SAS Transport 5 is obsolete within 3-4 years
- The FDA is going ... XML
- SAS is going ... XML
- XML is THE exchange data format

- October 2004: DIA Meeting Washington: 2/3 of the XML course attendees were SAS developers
Thank you for your attention

Jozef Aerts
XML4Pharma

www.XML4Pharma.com
www.XML4PharmaServer.com