The ODM and Define.xml

PhUSE

Dave Iberson-Hurst
Assero Limited
dave.iberson-hurst@assero.co.uk

© CDISC & Assero Limited, 2005
ODM and Define.xml

- History
- The ODM
- ODM Touch Points
- Define.xml
- The Future
- Summary
Outline

• History
• The ODM
• ODM Touch Points
• Define.xml
• The Future
• Summary

ODM and Define.xml
Operational Data Model (ODM)

- Support data interchange and archive
- Represent an entire clinical study
- Comply with 21 CFR Part 11 (and associated regulatory requirements)
- Be compatible with clinical data applications
- Platform and Vendor neutral
History

CDISC Volunteer Group

DIA SIAC Formed

CDISC Europe

CDISC Incorporated

CDISC Japan

SDTM into guidance

Define.XML guidance

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>CDISC Volunteer Group Formed</td>
</tr>
<tr>
<td>1998</td>
<td>DIA SIAC Formed</td>
</tr>
<tr>
<td>1999</td>
<td>CDISC Europe Formed</td>
</tr>
<tr>
<td>2000</td>
<td>CDISC Incorporated</td>
</tr>
<tr>
<td>2001</td>
<td>SDTM into guidance</td>
</tr>
<tr>
<td>2002</td>
<td>Define.XML guidance</td>
</tr>
<tr>
<td>2003</td>
<td>ODM V1.0</td>
</tr>
<tr>
<td>2004</td>
<td>ODM V1.1</td>
</tr>
<tr>
<td>2005</td>
<td>ODM V1.2</td>
</tr>
<tr>
<td>2005</td>
<td>ODM V1.3</td>
</tr>
</tbody>
</table>
Outline

ODM and Define.xml

- History
- The ODM
- ODM Touch Points
- Define.xml
- The Future
- Summary
Site Details
Site No.: ________

Subject's Characteristics
Number: ________
Sex:   M [ ]   F [ ]
Height: ________ cm
Weight: ________ kg
Site Details
Site No.: ___5___

Subject's Characteristics
Number: ___12___
Sex: M [Y] F [ ]
Height: ___1560___ cm
Weight: ___87.2___ kg
Site Details
Site No.: ___5___

Subject's Characteristics
Number: ___12___
Sex: M [Y] F [ ]
Height: ___1560___ cm ABC 1/1/2005
Weight: ___87.2___ kg
• History
• The ODM
• **ODM Touch Points**
• Define.xml
• The CDI SC Standard
• The Future
• Summary
Email

Outlook

Thunderbird
• Email Content
  – From
  – To
  – Subject
  – Body
• Standards
  – SMTP & POP3
Standards

• Standards exist at varying levels within a hierarchy
• We do not necessarily need to understand the inner workings to benefit from them
• The CDISC Models sits at different levels
  – SDTM & ADaM are about “content”, ways of organising
  – LAB and ODM have a physical form, they are based on XML
<table>
<thead>
<tr>
<th>CRF Forms &amp; Data</th>
<th>Lab Data</th>
<th>Tabulations</th>
<th>Analysis Datasets</th>
</tr>
</thead>
<tbody>
<tr>
<td>ODM</td>
<td>LAB</td>
<td>SDTM</td>
<td>ADaM</td>
</tr>
<tr>
<td>XML</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Touch Points

CRO

Sponsor

Investigator

Subject

LABs
Set Up

- Use of the ODM Metadata to configure tools
- eCRF systems
  - Several vendors using ODM-based mechanisms
- eDiary systems
  - At least one system uses ODM for configuration purposes
- ODM Version 1.3 being developed to include additional support
# Electronic Configuration (ACRO)

## SPONSOR NAME

<table>
<thead>
<tr>
<th>Protocol No.</th>
<th>Investigator No.</th>
<th>Subject No.</th>
<th>Subject Initials</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC123</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## ADVERSE EVENTS

Has the subject experienced any adverse events?  
1 Yes  0 No  0 If Yes, describe below.

<table>
<thead>
<tr>
<th>Event No.</th>
<th>Adverse Event</th>
<th>Start Date</th>
<th>Stop Date</th>
<th>Was Event Serious?</th>
<th>Severity</th>
<th>Is there a reasonable possibility that the AE may have been caused by the study drug(s)?*</th>
<th>Action Taken with Study Drug</th>
<th>Subject Outcome</th>
</tr>
</thead>
</table>
|           |               |            |           |                    |          | 0 - None  
1 - Study drug regimen changed  
2 - Temporarily stopped study drug  
3 - Study drug discontinued  
0 - Subject remains in study  
1 - Withdrawn from study  
2 - Lost to follow-up  
3 - Death | 0               | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

*Please list one event per line*  
Either provide a stop date or mark box (✓) if event is continuing  

day  
month  
year

---

*A "reasonable possibility" means you cannot rule out a relationship between the event and the study drug.*
### Adverse Event Form (ACRO)

**Visit:** Adverse Event  
**Subject ID:** 00011:SAW

#### Common

- Site #:  
- Subject ID #:  
- Visit Date: 11

#### Adverse Events Occurred

- Has the subject experienced any adverse events:  
  - No  
  - Yes

#### Adverse Event

- Event No.:  
- Adverse event:  
- Start Date: 11  
- Stop Date: 11  
- Mark if event is still continuing:  
  - No  
  - Yes  
- Was event serious:  
  - No  
  - Yes  
- Severity:  
  - Mild  
  - Moderate  
  - Severe  
- Is there a reasonable possibility that the AE may have been caused by the study drug:  
  - No  
  - Yes  
- Action taken with study drug:  
  - None  
  - Study drug regimen changed  
  - Temporarily stopped study drug  
  - Study drug discontinued

- Subject outcome:  
  - Subject remains in study  
  - Withdrawn from study  
  - Lost to follow-up  
  - Death
Acquisition

Sponsor

- EDC
- EHR
- Paper

Site A

Site B

Site C
• ODM allows for integration of multiple data sources
Example Development

- ODM being leveraged to integrate an EHR with sponsor systems
- ODM being employed to help meet regulatory requirements
• Investigator is obliged to
  – Maintain source data (accurate)
  – Retain source data
  – Prevent its destruction
  – Allow access to inspectors
• One of the original use cases for the model
• Ability to interchange Metadata and / or Clinical Data
• Submission MetaData
  – Currently uses PDF mechanism – Define.PDF
  – ODM version – Define.XML

• Submission Datasets
  – Currently SAS XPORT Transport (XPT)
  – ODM support being developed

• CRF Data and Audit Trail
  – Currently paper or PDF
  – CDISC ODM?

• Annotated CRF
  – Currently PDF
  – CDISC ODM?
CDISC Archive

ODM XML
Metadata
Data
ODM XML
Audit

?
• Data should be archived in an electronic form
• The archive should contain the trial metadata
• The archive should permit the data to be used in trial reconstruction
• The archive mechanism should allow for both sponsor (full) and investigator (subset) archives
• The data archive should be supportable for periods of 20 years or more
• The data archive should prevent unauthorised access
• The data archive should prevent changes being made to the data
• The data archive should contain the audit trail
• The data migration process should preserve the quality and integrity of the data
• The data archive should permit the regulatory authorities to inspect the data
ODM & Archive

- Electronic
- MetaData
- Reconstruction
- Full and Partial Archives
- Long-term
- Unauthorised Access [X]
- Changes
- Audit
- Quality & Integrity
- Inspection
ODM as the Backbone

CRO

Sponsor

Investigator

Subject

LABs

FDA
Outline

• History
• The ODM
• ODM Touch Points
• Define.xml
• The Future
• Summary
Case Report Tabulation Data Definition Specification (define.xml)

This document specifies the standard for providing Case Report Tabulations Data Definitions in an XML format for submission to a regulatory authority such as the U.S. Food and Drug Administration (FDA).
• Sponsor needs to submit
  – Metadata
  – Data
  – FDA’s Electronic Common Technical Document (eCTD)

• Metadata can employ
  – The Case Report Tabulation – Data Definition Specification (Define.XML), standard
  – The ODM as the transport mechanism

• Data will employ
  – The SDTM standard
  – Currently use SAS transport files as the transport mechanism
• For the wine connoisseur, it is all about the wine.
• The bottle and the glass are means of transporting the wine from the vineyard to the table.
• The wine label provides important information about the wine, the contents of the bottle.
• SDTM is our wine, the important content.

• ODM is the bottle, containing the SDTM data. Currently SAS transport files are used.

• Define.XML is our label, telling us what SDTM we have. A machine-readable format that replaces Define.PDF for transmitting submission metadata.
Submission

• Submissions Data Tabulation Model (SDTM)
  – Referenced in FDA Guidance as of 21 July 04

• Federal Register announcement
  – Department of Health and Human Services, Semiannual Regulatory Agenda (26818 Federal Register / Vol. 70, No. 93 / Monday, May 16, 2005 / Unified Agenda)
  – “The proposal would revise our regulations to require that CSD [Clinical Study Data] submitted for NDAs, ANDAs, BLAs, and their supplements and amendments be provided in electronic format and require the use of standard data structure, terminology, and code sets.”

• Define.XML
  – Referenced in FDA Guidance as of 18 March 05
ODM Transport

ODM XML

MetaData  Data  CRF  Audit
Define.XML leveraged the ODM

CRF

SDTM

ODM XML
Define.xml would be supplied in support of the Data Tabulations

Replace with module name, e.g., m5

Replace with study identifier, e.g., 123-070

Contains analysis datasets, annotated CRF, data definition
Contains program files
Contains annotated ECG waveform datasets
Contains data listing datasets, annotated CRF, data definition
Contains subject profiles
Contains data tabulation datasets, annotated CRF, data definition
The Big Question

• How do we “link” the data from collection through to the submission by the sponsor?
The Flow

CDISC Example Study

Baseline

Demographics

Race

Caucasian

Black

Asian

Other

Smoking History

Number of cigarettes per day

< 10 cigarettes / day

20 cigarettes / day

> 20 cigarettes / day

Drinking History

Number of alcoholic drinks per day

< 1 drink / day

2 drinks / day

> 2 drinks / day

Physical Exam

Systolic Blood Pressure

Diastolic Blood Pressure

ODM Metadata

MetaData

Data

define.xml
Outline

• History
• The ODM
• ODM Touch Points
• Define.xml

• The Future
• Summary
The Next Step

CDISC

CRF
SDTM
SDTM

ODM XML

Data
Audit
MetaData
Define.XML
Data
<table>
<thead>
<tr>
<th>Lab Data</th>
<th>CRF Forms &amp; Data</th>
<th>Tabulations</th>
<th>Analysis Datasets</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAB</td>
<td>ODM</td>
<td>SDTM</td>
<td>ADaM</td>
</tr>
</tbody>
</table>

**CDISC Models In Unison**

**ODM**

**XML**
CDISC Models In Unison

CRF & LAB

Tabulations
Analysis Datasets

ODM
XML
CDISC Models In Unison

- **Content**
  - CRF & LAB Data
  - Tabulations & Analysis Datasets

- **Standards**
  - SDTM, ADaM, ODM, LAB
Data Flow using the CDISC Std

Protocol Representation
- Trial Design (SDTM) Analysis Plan

Patient Info
- CRF - Clinical Trial Data (defined by SDTM)

Administrative, Tracking, Lab Acquisition Info

CRF, Analysis Data

Operational & Analysis Database

Integrated Reports
- SDTM Data, Analysis Data, Metadata

Clinical Trial Protocol
- (e)Source Document

ODM Transport
- SDTM & Analysis Data (content)
- Protocol Information (content)
- Source Data (other than SDTM/CRF data)
Outline

• History
• The ODM
• ODM Touch Points
• Define.xml
• The Future
• Summary
Summary

• ODM and define.xml are important components in the FDA’s move to an XML world

• The ODM is the transport backbone for the CDISC standard