CDISC Roadmap Outline: Further development and convergence of SDTM, ODM & Co

CDISC Ausblick: Weitere Entwicklung und Konvergenz der CDISC-Standards SDTM, ODM & Co.

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Disclaimer

Views expressed in this presentation are those of the speaker and not, necessarily, of CDISC, the CDISC ODM team, any other CDISC teams, or any other organization

Who is Jozef Aerts ?

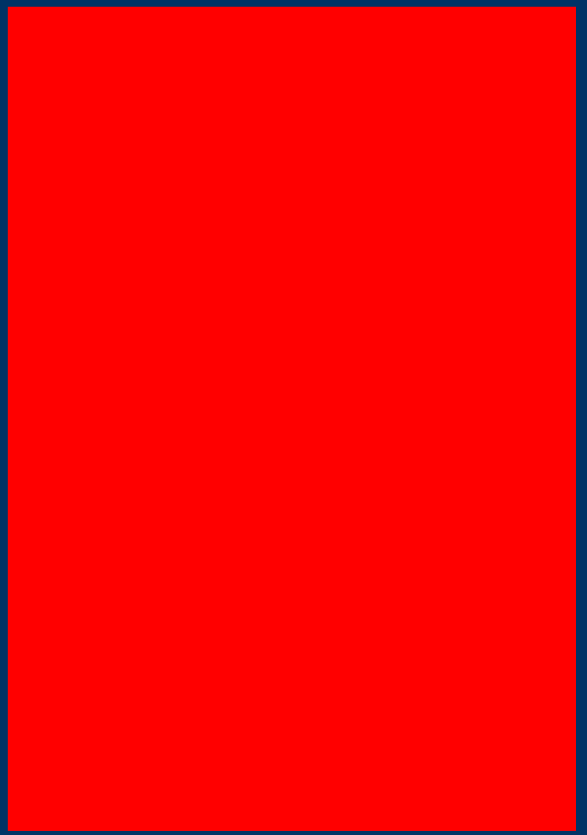
- Member of ODM team for 5 years
- Currently co-lead
- CDISC evangelist

- Independent CDISC consultant
- XML specialist
- Developer of software tools for use with CDISC standards

- Living in Singen, Baden-Württemberg

Quo Vadis CDISC ?

- Promise of “one standard” - is that possible ?



CDISC: promise of one standard

- CDISC decision 2005:
  ODM-XML will be transport vehicle / carrier for all (future) CDISC standards

- Actions: develop ODM extensions for or representations of:
  - define.pdf — DONE: define.xml
  - SDTM
  - Protocol, Trial Design Model
  - Clinical Trial Registry
  - CDASH forms
  - Lab data

Harmonization of CDISC Standards: Roadmap 2007 - 2008

- The “overall” model is in BRIDG
- XML-ization (using ODM extensions) of:
  - SDTM, ADaM
  - Trial Design Model
  - CDASH forms (?)
- Harmonization with SDTM
  - CDISC Lab
  - CDASH forms
  - Protocol and Trial Design Model

The CDISC ODM standard
(Operational Data Model)

- Standard for exchange, storage, archival, ... of clinical data, reference data and study metadata

- Metadata:
  - Study setup: visits, forms, questions, codelists, imputation methods, SDTM variables
  - Administrative data

- Reference data
  - e.g. lab normal ranges, dictionaries (MedDRA, LOINC)

- Clinical data
  - 21 CFR 11 compliant
  - Audit trails and Annotations

What is missing in the ODM ?

- Protocol information:
  - Arms
  - Epochs
  - Visit scheduling
- Mapping information with SDTM
- Incorporation of Lab data

New features of ODM 1.3

- Considerable better support for internationalization (i18n)
- Many new features of use in EDC
  - New data types
  - Machine-readable edit checks and rules
- Types data transmissions
- Grouping of Audit Records, Annotations, ...

ODM Team: 2007 plans

- Technical support for:
  - SDTM & ADaM in XML
  - define.xml 1.1
  - Trial Design in XML
- Publication of a set of "Use Cases", e.g.
  - Lab data in ODM
  - I18n
  - Use in EDC
  - ...
- In discussion: ODM implementation of CDASH forms

Plans for ODM 1.4

- Planned release: 2009 (?)
- Improved integration of SDTM
- XInclude
- Integration with Protocol
  - e.g. “ODM StudyEvent” is not the same as “Protocol Visit” or “Protocol Event”

CDISC define.xml

- Contains metadata for SDTM submission
- Version 1.1 planned
- Some issues
  - ODM knows Mandatory “Yes”, “No”
    SDTM knows Mandatory “Required”, “Expected”, “Permissible”
  - Data types: SDTM: “numeric”, “text”
    ODM: “integer”, “float”, “date”, “time”, “datetime”
  - Many relicts from SAS Transport format

Harmonisation of SDTM and ADaM

- ADaM team has regrouped about 2 years ago
- Published ADaM 2.0 (August 2006)
- ADaM and SDTM datasets have the same format
- ADaM datasets have names ADxxxx
- ADaM and SDTM “speak the same language”

SDTM & ADaM in XML

- Separate project
- Team leader: Sally Cassells
- Technical support by ODM team
- Will replace SAS Transport 5

- Will be ODM extension
- Early prototype used in SDTMWandler / SDTM-ETL
- One file per domain ?

- ADaM will be a separate extension
- May use ODM “FormalExpression” for carrying machine-readable code (e.g. SAS macros)

- Release for comment: early 2008 ?

Trial Design in XML

- Trial Design Model (TDM) first published in SDTM-IG 3.1.1.
- Defines Arms, Branches, Epochs, Trial Elements, Visits, Visit scheduling, Cycles, Transition rules ...
- XML representation needed
- Outsourced by CDISC to XML4Pharma

Trial Design in XML - requirements

- Implemented as ODM extension
- Deliverables: XML-Schema + samples + stylesheets + documentation
- User needs to be able to include all SDTM information (domains: TA, TE, TV)
- Automatic generation of SDTM tables must be possible
- Automatic generation of tabels (e.g. schedule of activities) must be possible
- Automatic generation of pictures must be possible

Trial Design in XML – an Example

```
<!-- we define two arms, one for treatment with drug A, one for treatment with drug B -->
<tdm:TrialArm TrialArmCode="ARM_A" Description="Treatment with drug A">
    <tdm:TrialCellRef TrialCellId="SCR_CELL" Sequence="1"/>
    <tdm:TrialCellRef TrialCellId="T_A_CEL" Sequence="2" BranchDescription="Randomization to drug A"/>
    <tdm:TrialCellRef TrialCellId="FUPCEL" Sequence="3"/>
    <!-- we add some visits -->
    <!-- screening visit -->
    <tdm:TrialVisitRef TrialVisitId="SCR_VIS" Mandatory="Yes" PlannedVisitNum="1" StartingTrialCellId="SCR_CELL"
        StartingTrialElementId="SCREENEL" TrialVisitStartRuleId="SCR_VIS_START_RULE" EndingTrialCellId="SCR_CELL" EndingT
        TrialVisitEndRuleId="SCR_VIS_END_RULE"/>
    <!-- first rest visit -->
    <tdm:TrialVisitRef TrialVisitId="REST_VIS" Mandatory="Yes" PlannedVisitNum="2" StartingTrialCellId="T_A_CEL"
        StartingTrialElementId="RESTEL" StartingTrialElementSequence="2" TrialVisitStartRuleId="REST_VIS_START_RULE"
        EndingTrialCellId="T_A_CEL" EndingTrialElementId="RESTEL" EndingTrialElementSequence="2" TrialVisitEndRuleId="RES
    <!-- second rest visit, during repeat of rest -->
    <tdm:TrialVisitRef TrialVisitId="REST_VIS" Mandatory="Yes" PlannedVisitNum="3" StartingTrialCellId="T_A_CEL"
        StartingTrialElementId="RESTEL" StartingTrialElementSequence="4" TrialVisitStartRuleId="REST_VIS_START_RULE"
        EndingTrialCellId="T_A_CEL" EndingTrialElementId="RESTEL" EndingTrialElementSequence="2" TrialVisitEndRuleId="RES
```

```
<!-- Trial Elements -->
<tdm:TrialElement TrialElementCode="SCREENEL" Description="Screening" StartDescription="Informed consent">
    <tdm:PlannedDuration>P7D</tdm:PlannedDuration>
</tdm:TrialElement>
<tdm:TrialElement TrialElementCode="DRUGA_EL" Description="Drug A Treatment" StartDescription="Start of treatment with drug A">
    <tdm:PlannedDuration>P3D</tdm:PlannedDuration>
</tdm:TrialElement>
<tdm:TrialElement TrialElementCode="DRUGB_EL" Description="Drug B Treatment" StartDescription="Start of treatment with drug B">
    <tdm:PlannedDuration>P3D</tdm:PlannedDuration>
</tdm:TrialElement>
```

Trial Design in XML – SDTM Info

SDTM Representation

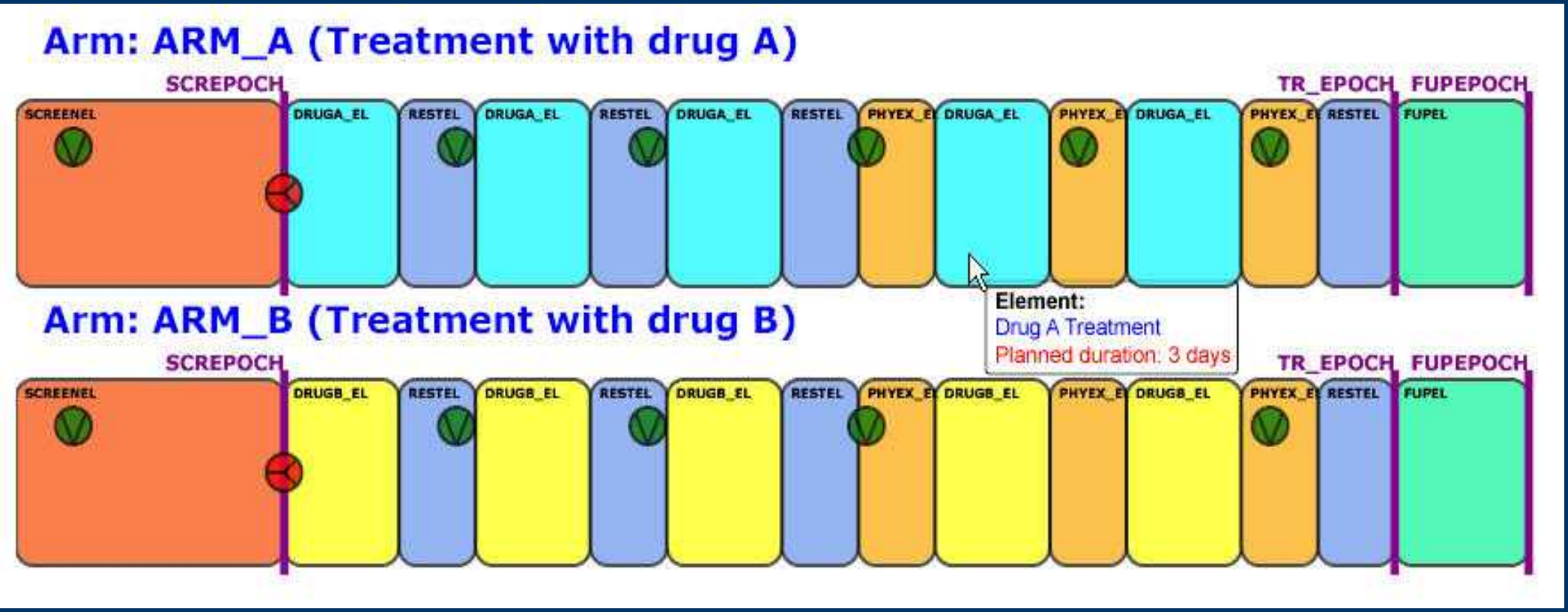
Domain: TE (Trial Elements)

STUDYID	DOMAIN	ETCD	ELEMENT	TESTRL	TEENRL	TEDUR
TDM_Repeats_Test	TE	SCREENEL	Screening	Informed consent		P7D: 7 days
TDM_Repeats_Test	TE	DRUGA_EL	Drug A Treatment	Start of treatment with drug A		P3D: 3 days
TDM_Repeats_Test	TE	DRUGB_EL	Drug B Treatment	Start of treatment with drug B		P3D: 3 days
TDM_Repeats_Test	TE	RESTEL	Rest	Start of rest for two days		P2D: 2 days
TDM_Repeats_Test	TE	PHYEX_EL	Physical Examination	Start of physical examination		P2D: 2 days
TDM_Repeats_Test	TE	FUPEL	Follow Up	Start of follow up, during 3 days and 12 hours		P3DT12H: 3 days 12 hours

Domain: TA (Trial Arms)

STUDYID	DOMAIN	ARMCD	ARM	TAETORD	ETCD	ELEMENT	TABRANCH	TATRANS	EPOCH
TDM_Repeats_Test	TA	ARM_A	Treatment with drug A	1	SCREENEL	Screening			Screening Epoch
TDM_Repeats_Test	TA	ARM_A	Treatment with drug A	2	DRUGA_EL	Drug A Treatment	Randomization to drug A		Treatment Epoch
TDM_Repeats_Test	TA	ARM_A	Treatment with drug A	3	RESTEL		Randomization to drug A	If disease progression, go to Physical Examination	Treatment Epoch

Trial Design in XML - graphics



CDASH

- Clinical Data Acquisition Standards Harmonization
- Standardization on CRFs for certain SDTM domains
- Project Leader: Rhonda Facile (CDISC)
- Including:
  - CDISC Controlled Terminology
  - SDTM Variable(s) for each input field
  - Conditional usage of fields

CDASH and ODM

- CDASH does not publish the exact phrasing of the questions
- ODM team would like to publish the CDASH forms as ODM 1.3 metadata files, for use in (e)CRFs
- Currently in discussion with CDISC Technical Leadership Committee
- Issues:
  - Translations of questions and codelist
  - To be picked up by user groups ?

	Initial Consensus Version	TLC Review	Harmonized Version	Collaborative Group Review	Reviewed Version	Public Review	Released Version 1.0
Adverse Events	December 2006	March 2007	April 2007	April-May 2007	May 2007	Q108	Q2 2008
Prior & Concomitant Medication	January 2007	March 2007	April 2007	April-May 2007	May 2007	Q108	Q2 2008
Demographics & Subject Characteristics	January 2007	March 2007	April 2007	April-May 2007	May 2007	Q108	Q2 2008
Inclusion/Exclusion Criteria	February 2007	April-May 2007	May 2007	May – June 2007	June 2007	Q108	Q2 2008
Medical History and Substance Use	February 2007	April-May 2007	May 2007	May – June 2007	June 2007	Q108	Q2 2008
Physical Exam & Vital Signs	February 2007	April-May 2007	May 2007	May – June 2007	June 2007	Q108	Q2 2008
End of Study/ Disposition	May 2007	June – July 2007	July 2007	August – Sept. 2007	September 2007	Q108	Q2 2008
Drug Accountability/ Exposure	May 2007	June – July 2007	July 2007	August – Sept. 2007	September 2007	Q108	Q2 2008
Protocol Deviations/ Comments	May 2007	June – July 2007	July 2007	August – Sept. 2007	September 2007	Q108	Q2 2008
Lab & ECG	August 2007	September-October 2007	October 2007	November-December 2007	January 2008	Q108	Q2 2008

CDISC Controlled Terminology (CT)

- Recent publications:
  - SDTM Package-1 CT (for implementation)
  - Lab Test Controlled Terminology (for implementation)
  - SDTM Package-2A (for review)

- CT used in:
  - SDTM
  - CDASH
  - define.xml templates (SDTMWandler, SDTM-ETL)

- SDTM Package-1 CT was transformed in ODM Codelists by XML4Pharma. Will probably be donated to CDISC

CDISC Lab

- Team recently regrouped – many new members
- Preparation of next release of Lab Standard
- ASCII, XML and HL7 representations
- New release will use SDTM and CDISC Controlled Terminology

CDISC Lab and ODM

- Some EDC vendors want to store Lab data exactly as they store clinical data: as ODM
- Others store lab data separately
- Lab to ODM mapping ?
  - There is no standardized way
  - ODM team may publish “best practices”

Conclusions: CDISC Standards Convergence

- All CDISC Standards need to use
  - SDTM
  - CDISC Controlled Terminology
- SDTM (SDS + SEND) will use ODM extension as carrier
- ADaM will use ODM extension as carrier
- Trial Design will use ODM as carrier, may later merge completely with ODM

Jozef 's personal Wish-List

- Controlled Terminology as ODM-XML CodeLists
- CDISC Glossary as XML (e.g. SKOS)
  - Showing relationships between terms
- Machine-readable SDTM IG
  - e.g. using DocBook
- And ...
- More customers from Germany, Switzerland and Austria

Thank you for your attention !