OpenStudyBuilder – Status & Workshop on EDC Integrations

COSA Spotlight Q1 – 26 March 2024
Nicolas de Saint Jorre
Introduction
What is the OpenStudyBuilder?...

A NEW APPROACH TO STUDY SPECIFICATION

• Compliance with external and internal standards
• Facilitates automation and content reuse
• Ensures a higher degree of end-to-end consistency

3 ELEMENTS OF OpenStudyBuilder

• Clinical Metadata and Study Definition Repository (central repository for all study specification data)
• OpenStudyBuilder application / Web UI
• API layer (allowing interoperability with other applications) (DDF API Adaptor – enabling DDF SDR Compatibility)
# OpenStudyBuilder Components

<table>
<thead>
<tr>
<th>STUDIES</th>
<th>LIBRARY</th>
</tr>
</thead>
<tbody>
<tr>
<td>TITLE</td>
<td>CONTROLLED</td>
</tr>
<tr>
<td>CRITERIA</td>
<td>TERMINOLOGY</td>
</tr>
<tr>
<td>REGISTRY IDENTIFIERS</td>
<td>MEDICAL</td>
</tr>
<tr>
<td>INTERVENTIONS</td>
<td>DICTIONARIES</td>
</tr>
<tr>
<td>STRUCTURE</td>
<td>(e.g., MedDRA)</td>
</tr>
<tr>
<td>PURPOSE</td>
<td>CONCEPTS</td>
</tr>
<tr>
<td>POPULATION</td>
<td>(ACTIVITIES,</td>
</tr>
<tr>
<td></td>
<td>UNITS, CRFs,</td>
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<tr>
<td></td>
<td>COMPOUNDS)</td>
</tr>
<tr>
<td>ACTIVITIES</td>
<td>SYNTAX</td>
</tr>
<tr>
<td></td>
<td>TEMPLATES</td>
</tr>
<tr>
<td></td>
<td>DATA EXCHANGE</td>
</tr>
<tr>
<td></td>
<td>STANDARDS</td>
</tr>
</tbody>
</table>
Goal of OpenStudyBuilder

Metadata driven
End-2-End Automation!
Connectivity is key!

<table>
<thead>
<tr>
<th>CDISC</th>
<th>ODM</th>
<th>Define.xml</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDASH</td>
<td>SDTM</td>
<td>ADaM</td>
</tr>
<tr>
<td>CDASHIG</td>
<td>SDTMIG</td>
<td>ADAIG</td>
</tr>
<tr>
<td>COSMoS</td>
<td>Controlled</td>
<td>Terminology</td>
</tr>
</tbody>
</table>

**Sponsor Library**

**Dictonaries**
- SNOMED
- MeDDRA
- MED-RT
- UNII
- LOINC
- UCUM

**Software Tools**
- Word Addin
- DDF Adaptor
- Any DDF Compatible System
- TFL Builder

**Output Formats**
- Sponsor version
- M11 version
- CPT version
- Ct.gov...

As ODM or CSV
Blank CRF
Annotated CRF
With Vendor Extensions

As Define.xml
(pre-version for both SDTM and ADaM)
Connectivity is key!

- Standards & Study Definitions
- API & DDF API
- OpenStudyBuilder Application
- Protocol (Word Add-In coming as open-source)
- Electronic Data Capture
- Scripts, CTMS, other MDR, SCE, TLF Builder, ...
Protocol Generation

StudyBuilder ribbon (Word add-in)

- One-way connection
- Code recognizes the document type
- User-friendly ribbon and ‘fly-out’ in Word
- Styles ensure proper formatting in Word
1.2 Flowchart

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Screening</th>
<th>Treatment</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visit short name</td>
<td>V1</td>
<td>V6</td>
<td>V11</td>
</tr>
<tr>
<td>Study day</td>
<td>-14</td>
<td>29</td>
<td>183</td>
</tr>
<tr>
<td>Visit window (days)</td>
<td>±0</td>
<td>±1</td>
<td>±1</td>
</tr>
<tr>
<td>Randomisation</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>End of Study</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body Measurements</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Eligibility Criteria</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Laboratory Assessments</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

Structured content including SoA will be transferred to the content controls Word based Protocol Template.
CRF Standards & Metadata

Manage
Standard & Study CRF

Including rules, checks
Support vendor extensions

EDC Setup, Test, Execution

Finetuning, Layout
OpenStudyBuilder to drive EDC setup

A COSA Workshop
CDISC Interchange 2024

Use OpenStudyBuilder to drive EDC setup - a COSA Workshop
23 April 2024 9:00-16:00, Berlin, Germany
Problem Statement

Data Exchange Formats

- CDASH
- ODM.XML
- USDM
- Biomedical Concepts

Implementation

- Native formats
- Limited interface capabilities
- Limited selection of standards
- Custom extensions
Workshop Focus

- Challenges & Opportunities
  - ODM.XML integrations
  - API based integrations

- Knowledge exchange
  - OpenStudyBuilder functionality
  - Integration status, challenges and opportunities from EDC vendors

- Discussion
  - Integration strengths, weaknesses, opportunities & threats
  - Options and next steps
Workshop Agenda

- Information Exchange
  - Introduction
  - OpenStudyBuilder status with CRF & SoA for EDC & plans
  - EvidentIQ ODM.xml integration (Marvin EDC)
  - Veeva EDC integration via SDS files and future API integration
  - Oracle ClinicalOne API integration & EvidentIQ ePRO API integration
  - The potential future of API standards

- Breakouts
  - Discuss strengths, weaknesses, opportunities & threats
  - Options and next steps

- Share and discuss in plenum
CRF for EDC Status & Questions
# eCRF API endpoints

<table>
<thead>
<tr>
<th>Category</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ODM Study Events</td>
<td></td>
</tr>
<tr>
<td>ODM Forms</td>
<td></td>
</tr>
<tr>
<td>ODM Item Groups</td>
<td></td>
</tr>
<tr>
<td>ODM Item</td>
<td></td>
</tr>
<tr>
<td>ODM Conditions</td>
<td></td>
</tr>
<tr>
<td>ODM Methods</td>
<td></td>
</tr>
<tr>
<td>ODM Formal Expressions</td>
<td></td>
</tr>
<tr>
<td>ODM Descriptions</td>
<td></td>
</tr>
<tr>
<td>ODM Aliases</td>
<td></td>
</tr>
<tr>
<td>ODM Vendor Namespaces</td>
<td></td>
</tr>
<tr>
<td>ODM Vendor Attributes</td>
<td></td>
</tr>
<tr>
<td>ODM Vendor Elements</td>
<td></td>
</tr>
<tr>
<td>ODM Metadata Import/Export</td>
<td></td>
</tr>
</tbody>
</table>
CRF Specification in the Library

- **Study Events**
- **Forms**
- **ItemGroups**
- **Items**
- **eCRF specs**
- **Vendor Extensions**
- **Alias**
- **eCRF views**
Form def. as ODM (Vendor Extensions + Alias)
ItemGroup def. as ODM (Vendor Extensions + Alias)
Item def. as ODM (Vendor Extensions + Alias) 1/2
Vendor Extensions
Concept: CRFs

Templates used to defined multiple CRF version

Annotated CRF following MSG 2.0 standard

ODM.xml with vendor extensions (or CSV)

PDF format
Vendor Extension in ODM

Please complete this Vital Signs form before starting the treatment.

Vital signs form

Please complete the Vital Signs item group at each expected time point.

Vital signs

Pulse

Pulse

beats/min
Odm.xml API endpoint

Level of Metadata in the ODM (uid):
- StudyEvent
- Form
- ItemGroup

Target Type:
- StudyEvent
- Form
- ItemGroup

Status of the metadata
PDF or CSV
Stylesheet ref.
**API Endpoints to work with the SoAs...**

<table>
<thead>
<tr>
<th>Method</th>
<th>Endpoint</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>GET</td>
<td>/studies</td>
<td>Returns all studies in their latest/oldest version.</td>
</tr>
<tr>
<td>POST</td>
<td>/studies</td>
<td>Creates a new Study Definition.</td>
</tr>
<tr>
<td>GET</td>
<td>/studies/headers</td>
<td>Returns possible values from the database for a given header.</td>
</tr>
<tr>
<td>GET</td>
<td>/studies/{uid}/fields-audit-trail</td>
<td>Returns the audit trail for the fields of a specific study definition identified by ‘uid’.</td>
</tr>
<tr>
<td>GET</td>
<td>/studies/{uid}/audit-trail</td>
<td>Returns the audit trail for the subparts of a specific study definition identified by 'uid'.</td>
</tr>
<tr>
<td>GET</td>
<td>/studies/{uid}/protocol-title</td>
<td>Retrieve all information related to Protocol Title.</td>
</tr>
<tr>
<td>PATCH</td>
<td>/studies/{uid}/copy-component</td>
<td>Copy study form from another study.</td>
</tr>
<tr>
<td>GET</td>
<td>/studies/{uid}/time-units</td>
<td>Gets a study preferred time unit.</td>
</tr>
<tr>
<td>PATCH</td>
<td>/studies/{uid}/time-units</td>
<td>Edits a study preferred time unit.</td>
</tr>
<tr>
<td>PATCH</td>
<td>/studies/{uid}/order</td>
<td>Reorder Study Subparts within a Study Parent Part.</td>
</tr>
<tr>
<td>GET</td>
<td>/studies/{uid}/design.svg</td>
<td>Builds and returns a Study Design visualization image in SVG format.</td>
</tr>
<tr>
<td>GET</td>
<td>/studies/{uid}/flowchart/coordinates</td>
<td>Returns uid to [x,y,coordinates] coordinates mapping of items included in SoA Protocol Flowchart table.</td>
</tr>
<tr>
<td>GET</td>
<td>/studies/{uid}/flowchart</td>
<td>Protocol, Detailed or Operational SoA table with footnotes as JSON.</td>
</tr>
<tr>
<td>GET</td>
<td>/studies/{uid}/flowchart.html</td>
<td>Builds and returns an HTML document with Protocol, Detailed or Operational SoA table with footnotes.</td>
</tr>
<tr>
<td>GET</td>
<td>/studies/{uid}/flowchart.docx</td>
<td>Builds and returns a DOCX document with Protocol, Detailed or Operational SoA table with footnotes.</td>
</tr>
<tr>
<td>GET</td>
<td>/studies/{uid}/detailed-soa-history</td>
<td>Returns the history of changes performed to a specific detailed SoA.</td>
</tr>
<tr>
<td>GET</td>
<td>/studies/{uid}/detailed-soa-exports</td>
<td>Exports the Detailed SoA content.</td>
</tr>
<tr>
<td>GET</td>
<td>/studies/{uid}/operational-soa-exports</td>
<td>Exports the Operational SoA content.</td>
</tr>
<tr>
<td>GET</td>
<td>/studies/{uid}/protocol-soa-exports</td>
<td>Exports the Protocol SoA content.</td>
</tr>
</tbody>
</table>
SoA and Biomedical Concepts...
Schedule of Activities (SoA) at multiple levels

**Protocol SoA**
- For the high level SoA in protocol section 1.2
- Main purpose is for the investigator and site staff to get an overview of the operational schedule

**Detailed SoA**
- Specifying the semantic data observations to be collected in the study – but not specific to representation in ADaM, SDTM or data collection
- Will be part of protocol section 8 and appendixes or other supplementary documents

**Operational SoA**
- The data specification to support data collection specification
- Correspond to our existing legacy BCs (Topic Codes)
- Will also related to specific ADaM PARAM/PARAMCD

**Data Capture / Collection Specification**
- How data is to be collected in the study and when
- What is pre-set, what is collected and how
Detailed SoA
The detailed SoA describe scheduling of the specific Activities and their grouping for the study.

Each level in the Activity hierarchy can be selected for display in the “Protocol SoA”.
Protocol and Operational SoA

### Study Activities (CDISC DEV-0)

<table>
<thead>
<tr>
<th>Activity Instructions</th>
<th>Protocol SoA</th>
<th>Activity Instructions</th>
<th>Protocol SoA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protocol SoA</td>
<td></td>
<td>Protocol SoA</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study Activities</th>
<th>Detailed SoA</th>
<th>SAP overrides</th>
<th>Protocol SoA</th>
<th>Activity Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Activities</td>
<td></td>
<td></td>
<td>Protocol SoA</td>
<td>Activity Instructions</td>
</tr>
</tbody>
</table>

#### Study Data Specifications (CDISC DEV-0)

<table>
<thead>
<tr>
<th>Study Activity</th>
<th>Operational SoA</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Study Activity Data Specifications</th>
<th>Operational SoA</th>
</tr>
</thead>
</table>

### Screen and Treatment

<table>
<thead>
<tr>
<th>Visit short name</th>
<th>Screening</th>
<th>Treatment</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>V1</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>V2</td>
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<td>V3</td>
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<td>V4</td>
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<td>V9</td>
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<td></td>
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<tr>
<td>V10</td>
<td></td>
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</tr>
</tbody>
</table>

#### End of Study

- General
  - Physical Examination - early phase
  - Self-Measured Plasma Glucose
- Body Measurements
  - Body Measurements
- Eligibility Criteria
  - Eligibility Criteria
- Laboratory Assessments
  - Glucose Metabolism
  - Lipids
  - Biochemistry
- Haematology
  - Ac Requiring Additional Data
    - Laboratory Assessment
    - Advance Event
    - Vital Signs
    - Vital Signs
    - Medical History/Concomitant Illness
      - Medical History/Concomitant Illness
      - Informed Consent and Demography
      - Informed Consent and Demography
### Study Activities (CDISC DEV-0)

**Protocol SoA**

**SoA layout:** Operational SoA

**Preferred time unit:** Week

**Follow-up**

<table>
<thead>
<tr>
<th>Visit short name</th>
<th>Study week</th>
<th>Visit window (days)</th>
<th>SUBJECT RELATED INFORMATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visit short name</td>
<td>Study week</td>
<td>Visit window (days)</td>
<td>SUBJECT RELATED INFORMATION</td>
</tr>
<tr>
<td>Visit short name</td>
<td>Study week</td>
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<td>Visit window (days)</td>
<td>SUBJECT RELATED INFORMATION</td>
</tr>
<tr>
<td>Visit short name</td>
<td>Study week</td>
<td>Visit window (days)</td>
<td>SUBJECT RELATED INFORMATION</td>
</tr>
</tbody>
</table>

**ADAM Parameter Code**

<table>
<thead>
<tr>
<th>Topic Code</th>
<th>ADAM Parameter Code</th>
<th>Screening</th>
<th>Treatment</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visit short name</td>
<td>Study week</td>
<td>Visit window (days)</td>
<td>SUBJECT RELATED INFORMATION</td>
<td></td>
</tr>
<tr>
<td>Visit short name</td>
<td>Study week</td>
<td>Visit window (days)</td>
<td>SUBJECT RELATED INFORMATION</td>
<td></td>
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<td></td>
</tr>
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<td>Visit window (days)</td>
<td>SUBJECT RELATED INFORMATION</td>
<td></td>
</tr>
<tr>
<td>Visit short name</td>
<td>Study week</td>
<td>Visit window (days)</td>
<td>SUBJECT RELATED INFORMATION</td>
<td></td>
</tr>
</tbody>
</table>

**Randomisation**

<table>
<thead>
<tr>
<th>Randomisation</th>
<th>Randomized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomisation Date</td>
<td>RANDOMISATION_DATE</td>
</tr>
<tr>
<td>Randomisation Date</td>
<td>RANDDOT</td>
</tr>
<tr>
<td>Randomisation Date</td>
<td>X</td>
</tr>
</tbody>
</table>

**End of Study**

<table>
<thead>
<tr>
<th>End of Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>End of Study</td>
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<td>End of Study</td>
</tr>
<tr>
<td>End of Study</td>
</tr>
<tr>
<td>End of Study</td>
</tr>
</tbody>
</table>

**General**

- Cardiovascular System
- Abdomen
- Central and Peripheral Nervous System
- Gastrointestinal System incl. Mouth
- General Appearance
- Musculoskeletal System
- Respiratory System

**Body Measurements**

<table>
<thead>
<tr>
<th>Body Measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
</tr>
<tr>
<td>Body Weight</td>
</tr>
<tr>
<td>Height</td>
</tr>
<tr>
<td>Height</td>
</tr>
</tbody>
</table>

**Eligibility Criteria**

<table>
<thead>
<tr>
<th>Eligibility Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eligibility Criteria Met</td>
</tr>
<tr>
<td>Subject Eligible to Continue the Trial</td>
</tr>
</tbody>
</table>

**Protocol SoA** displaying the selected activity level of detail as a preview.

Produce a copy of the SoA compatible with Word.
M11 – Section 8 = Detailed SoA

1. Protocol summary
2. Introduction
3. Trial objectives, endpoints and estimands
4. Trial design
5. Trial population
6. Trial intervention and concomitant therapy
7. Discontinuation of trial intervention and participant withdrawal from trial
8. Trial assessments and procedures
9. Statistical considerations
10. General considerations: regulatory, ethical, and trial oversight
11. GENERAL CONSIDERATIONS: RISK MANAGEMENT AND QUALITY assurance
12. Appendix: adverse events and serious adverse events – definitions, severity, and causality
13. Appendix: definitions and supporting operational details
14. Appendix: glossary of terms
15. Appendix: references
Selection process of Activities for SoA

For Protocol Outline / Protocol
- Select Activities in relevant grouping
- When selecting an Activity within a specific grouping, then this will drive ActivityInstance – this should be visible for Protocol Writers (like a COL)
  - Some ActivityInstances can be marked as default for an Activity, and will then be pre-selected
  - Some ActivityInstances can be marked as mandatory – and cannot be un-selected
- Select what to display or hide in high-level Protocol SoA

For Operational Data Specification
- Confirm or Select Activity Instances for each selected Activity
- If the correct ActivityInstance will change Grouping – this will require a change to the Protocol SoA – this will then

For Data Collection Specification
- The data collection specification
  - Lab specs
  - CRF
  - Other eSources
  - What is pre-set
From Activity to Activity Instance
Activity to Activity Instance to Activity Item – As Biomedical Concept (COSMOS project from CDISC)
Digital Data Flow Adaptor (TransCelerate DDF)
Our vision
Status of the OpenStudyBuilder

- Already working:
  - Protocol SoA
  - Detailed SoA
  - eCRF in the Library
  - Vendor Extensions
  - Alias
  - Models integration (like SDTM/SDTMIG with version control in the Library)

- Work in progress:
  - Operational SoA
  - Connection between Activity Instances with Activity Items to eCRF, SDTM domains and variables, ADaM domains and variables with a sharing CT management and units
  - Integration of external data like Labs

- What is planned:
  - eCRF at the Study level (with integration to the Operational SoA
  - Production of the define.xml (pre version) based on the Protocol SoA and Detailed SoA
Questions to discuss

- Extensions / configurations required for vendors
  - Additional attributes, e.g. to link to systems & versions
  - ODM.xml additional information
  - API endpoints, additional requirements

- General aspects
  - API versioning
  - Continuous development challenges, up versioning
  - Adoptions & implications according license

- Standards
  - Additional standard requirements, recommendations, wishes
Additional Information
CDISC Interchange 2024

Use OpenStudyBuilder to drive EDC setup - a COSA Workshop
23 April 2024 9:00-16:00, Berlin, Germany
CDISC Interchange 2024

Use OpenStudyBuilder as MDR Meetup
23 April 2024 17:00-18:00, Berlin, Germany
➢ Reach out to OpenStudyBuilder@gmail.com

Meet us at the Interchange
24-25 April 2024
➢ Reach us at the COSA booth for demonstration and exchange

From OpenStudyBuilder to the Digital Data Flow - USDM Format
15 April 2024 – 14:40-15:00, Presentation
OpenStudyBuilder

The OpenStudyBuilder is an open-source project for clinical study specifications. This tool is a new approach for working with studies that once fully implemented will drive end-to-end consistency and more efficient processes - all the way from protocol development and CRF design - to creation of datasets, analysis, reporting, submission to health authorities and public disclosure of study information.

https://openstudybuilder.com/
Links

• Project Homepage: https://openstudybuilder.com/
• Newsletter: https://www.linkedin.com/newsletters/openstudybuilder-6990328054849916928/
• YouTube Demonstration (30'): https://youtu.be/dL5CY0BwfEs
• GitLab (Solution, Description): https://gitlab.com/Novo-Nordisk/nn-public/openstudybuilder
• Slack: https://join.slack.com/t/openstudybuilder/shared_invite/zt-19mtauzc-jvrhtmy7hGstgyiIvB1Wsw
• E-Mail: openstudybuilder@gmail.com

Sandbox:
• Mail openstudybuilder@neotechnology.com – Subject “Request Sandbox access”
• Note: when add/modify/delete, you mail might be exposed in the version history
Thanks!

Questions?