“CONNECT and CREATE”
Connect Standards and Enable Protocol Authoring

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Paper DH05

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Our Vision

PULSE – Global Medical Standards Tool

SSD
Structured Study Definition
(Protocol Designer Tool)

EDC
Medidata Rave eCRF based on Standard CRF & ESC

CIE
Statistical Analysis & Standard TLF Reporting

Document Management
Structured CSR

Conduct of Clinical Studies in end-to-end process
To achieve this vision, Bayer focused on two key areas within the Global Medical Standards toolset initiative:

- **Standards Management System**
  - Standards Taxonomy (directory) setup
  - Standards Data Flow
  - Standards Visualization and Reporting

- **Standards Content**
  - Create Standards Content Structure
  - Connect Standards
Approach

Phased Approach

- **Base**
  - Taxonomy definition, data structure and codelists
  - Processes for standards management, governance

- **PULSE 1.0**
  - July 2013

- **PULSE 1.1**
  - Sept 2014

- **PULSE 2.0**
  - Q1, 2016
  - Provision of standards to other systems
  - Performance patch

- **Associate**
  - Include additional scopes of standard elements
  - Linkage between standard elements (forward and backwards)

- **MDR Viewer 1.0**
  - Q1, 2016

- **PULSE 3.0**
  - Future
  - Full end-to-end standards from protocol to CSR

- **Extend**
  - Consumer read access for data view and reporting
Future State: Connect Activity to Protocol Authoring

Structured Study Design

- List of Activities
  - Select Activities for Protocol
  - Protocol Authoring

Medical Standards Management

- Global Medical Standards
- TA Standards
- Compound Standards
- Study Standards

Activities

Confirmed Study Activities

Automated Selection of Study Standards
Current – Future situation

CMDF = Clinical Metadata Foundation

Standard elements:
- Annotated CRF
- Edit checks
- Database operational
- EDC forms

Protocol activity:
- Codelist
- CMDF
- Medical item
- CRF
Clinical Metadata Foundation (CMDF)

- Superset of all variables and all datasets, grouped according to context
  - Medical topic
  - Common variables
Standard elements – CMDF (2)

- Provide Metadata Structure for different scopes e.g.
  - SDTM
  - ADS
  - Foundation
  - Source plus
Protocol Activity

Protocol activity

- Describes the activity in a protocol such as the procedure or the measurement performed at the Clinical Research Site to obtain clinical data for the study result.
- Combines medical items and standard protocol text
- Deliverable for standard protocol tool and initiator for complete study set up

<table>
<thead>
<tr>
<th>Activities Context</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activity Name</td>
</tr>
<tr>
<td>------------------</td>
</tr>
<tr>
<td>Vital Signs_Brief</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Vital Signs_ex</td>
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</tr>
</tbody>
</table>
Standard element

Medical item

- Main driver for linkage of different standard objects
- Developed and maintained by medical team
- Grouped according to medical context
- Reflects data fields on CRF with relevant subset of codes
- Contains medical item specific attributes like CRF label, field help text, implementation instructions
- Has references to CMDF variables and their codelists
- Defines the relevant subset of codelist
- Is used as reference object for protocol activities, edit checks and EDC forms
Example:

**Activity (V1)**
- **Activity group**: Adverse event
- **Activity**: Adverse event assessment
- **Description**: Adverse events will start immediately after signing the informed consent until the follow-up visit.

**EDC (V1)**

<table>
<thead>
<tr>
<th>EDC form</th>
<th>Form</th>
<th>FormOID</th>
<th>Formname</th>
</tr>
</thead>
<tbody>
<tr>
<td>AE</td>
<td>AE</td>
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</table>

<table>
<thead>
<tr>
<th>Field</th>
<th>FieldID</th>
<th>FieldLabel</th>
<th>FormOID</th>
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</thead>
<tbody>
<tr>
<td>AE_term</td>
<td>AE</td>
<td>AE</td>
<td>AE</td>
</tr>
<tr>
<td>Intensity</td>
<td>AESEV</td>
<td>AESEV1</td>
<td>AE</td>
</tr>
<tr>
<td>AE_term</td>
<td>AE</td>
<td>AE</td>
<td>AE</td>
</tr>
<tr>
<td>Severity</td>
<td>AESEV1</td>
<td>AESEV1</td>
<td>AE</td>
</tr>
</tbody>
</table>

**Edit checks (V1)**

<table>
<thead>
<tr>
<th>Edit check number</th>
<th>Edit check type</th>
<th>Error message</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>AE0070</td>
<td>AE</td>
<td>AE value is invalid or missing</td>
<td>AE</td>
</tr>
</tbody>
</table>

**Medical item (V1)**
- **Adverse event**

<table>
<thead>
<tr>
<th>Medical item name</th>
<th>MI label</th>
<th>Justification</th>
<th>Fieldhelp text</th>
<th>Codelist</th>
</tr>
</thead>
<tbody>
<tr>
<td>AE</td>
<td>AE</td>
<td>Intensity</td>
<td>required by authorities for safety analysis</td>
<td>AESEV</td>
</tr>
</tbody>
</table>

**CMDF**

<table>
<thead>
<tr>
<th>Variable</th>
<th>VariableLabel</th>
<th>Type</th>
<th>Codelist</th>
<th>Scope</th>
<th>Dataset</th>
</tr>
</thead>
<tbody>
<tr>
<td>AESEV(V1)</td>
<td>Severity/Int</td>
<td>AE</td>
<td>AESEV1</td>
<td>AE</td>
<td>AE</td>
</tr>
<tr>
<td>AESEV1(N)</td>
<td>Severity/Int</td>
<td>N</td>
<td>AESEV</td>
<td>OAD, AD, AOD, ADE, AD, AE</td>
<td>AE</td>
</tr>
</tbody>
</table>

**Codelist (V1)**

<table>
<thead>
<tr>
<th>Codelist name</th>
<th>CodelistLabel</th>
<th>Extension</th>
</tr>
</thead>
<tbody>
<tr>
<td>AESEV</td>
<td>Severity of AE</td>
<td>N</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Code</th>
<th>Decode</th>
<th>Version</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>mild</td>
<td>V1</td>
</tr>
<tr>
<td>2</td>
<td>Moderate</td>
<td>V1</td>
</tr>
<tr>
<td>3</td>
<td>severe</td>
<td>V1</td>
</tr>
</tbody>
</table>
Automated study set up

Linked standard objects allow automated study set up:

In other words, selection of Protocol Activities will automatically drive the study standards setup and provide all standard objects for

Protocol Activities
EDC forms and items
Data base structures
Codelists
Edit checks
Table, Listings and Figure specs
Mappings and derivations

- Activity
  - Medical items
    - Date
    - Time
    - Test
    - SDTM variables
    - ADS variables
    - ...
  - Variables
    - Controlled terminology subsets
    - ADS codelists
  - Codelist
    - EDC form
  - Edit checks
Summary

• Create structure standard objects to enable end to end study set up (Protocol to CSR)
• Consider Standards Hierarchy from Global to Study level
• Build connections between standard elements (forward and backward links)
• Enable flexibility via Metadata supersets
• Allows Standards Maintenance and Governance
• Allows Reporting and Visualization of Standards elements
• Enable automated study set up via referencing protocol activities
Questions?

Thank you,

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