Implementing CDISC Standards for Device-Drug Studies
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AGENDA

- What makes device data unique
  - Background of Device Standards
- Steps used to create company-wide standard
  - Beginning to end lifecycle
- DEVICE-DRUG COMBINATION Case Study
  - Description
  - Collection and SDTM Standards
  - Evolution of ADaM Standard
  - Principles for Medical Devices
- CONCLUSION
What Makes Device Data Unique?

A device has its own set of data:

- Identifiers such as manufacturer, serial #, model number
- Device event, such as calibrations, parts replacement, or malfunctions
- Device tracking, such as physical location of manufacture, implant, explant dates
- Current state of the device at certain times
Background of Device Standards

Devices can be:

Stand-alone, or part of a drug or biologic submission

CDISC standards for devices:

SDTM Medical Devices (MD) v1.0, Dec. 2012

ADaMIG MD v1.0 draft for public review, March 2018
Steps used to create company-wide standard

At our company we have beginning-to-end standards

- Each standard flows from one to the next
- It is an iterative and collaborative process
- There is alignment of variable/data mapping from CDASH to SDTM to ADaM
- There is Standards Governance Framework in place to provide compliance
Steps used to create company-wide standard (2)

Standards development lifecycle:

1. Review the existing situation by checking actual completed study dataset structures against company ADaM standard
2. Compare custom datasets to latest CDISC ADaM standard
3. Check for variables that are not part of the standard and update to follow the CDISC ADaM standard
4. Check for additional variables not in the standard that are needed for analysis
5. Roll out the updated ADaM Standards metadata and standards company’s Standards Interpretation guide
6. Define start date when a new standard becomes required as part of internal governance
7. Provide training for new standard
DEVICE-DRUG COMBINATION
Case Study

Takeda Pharmaceutical Company Limited
DESCRIPTION

- Devices can be part of a drug or biologic submission and not just stand-alone studies for device development.
- The study was based on a rare disease clinical trial with device to deliver study drug to patients. Safety data was collected on treatment and also on devices (i.e. procedures, related AEs, demographic - age at implant).
- Drug program began in 2012, after SDTM MD supplement was available and prior to ADaM MD standards.
- Device was implanted so included a surgical procedure.
- Data collection included information about the device.
- Data collection for study drug same as other clinical trials.
COLLECTION and SDTM Standards

- **Internal** CDASH library included device collection forms
- **SDTMIG MD 7** device domains for tabulation
  - Mapped data to all 7 domains for completeness
  - Mapped device-related procedures and device-related adverse events to foundational standards (AE, PR)
  - Added to supplementary qualifiers any device-related information for other foundational domains
SDTMIG Foundational and Medical Device Domains

- Device Domains highly related to each other and to Foundational Domains
- Only pure device data is stored in the device domains
### Additional SDTM Variables

<table>
<thead>
<tr>
<th>Variable Name</th>
<th>Variable Label</th>
<th>Type</th>
<th>Role</th>
<th>Abbreviated Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPDEVID</td>
<td>Sponsor Device Identifier</td>
<td>Char</td>
<td>Identifier</td>
<td>Sponsor-defined identifier for a device</td>
</tr>
<tr>
<td>--PARTY</td>
<td>Accountable Party</td>
<td>Char</td>
<td>Record Qualifier</td>
<td>Party accountable for the device or other object as a result of the activity performed in the associated --TERM variable.</td>
</tr>
<tr>
<td>PRTYID</td>
<td>Identification of specific accountable party</td>
<td>Char</td>
<td>Record Qualifier</td>
<td>Identification of the specific party accountable for the device after the action in --TERM is taken. Used in conjunction with --PARTY.</td>
</tr>
<tr>
<td>--ACNDEV</td>
<td>Action Taken with Device</td>
<td>Char</td>
<td>Record Qualifier</td>
<td>Action taken with respect to a device in a study, which may or may not be the device under study</td>
</tr>
</tbody>
</table>

These approved SDTM variables may be added to foundational SDTM domains that contain device data.
Order is SPDEVID immediately after USUBJID, other additions to the Events Observation class include --PARTY, --PRTYID (place in order after --LOC) and --ACNDEV (place in order after ACNOTH).
EVOLUTION OF ADaM Standard

• The first studies used basic foundational ADaM principles, using ADSL, Basic Data Structure and Occurrences datasets

• Study team found a problem that one subject may have one or more devices. Device data needs its own Device level data to describe a device.

Solution: The team designed a Device Identifier domain, which was called ADIDDD – Device Identifier Dataset
Mapping from ADaM legacy dataset to new Standard

**ADIDDD Dataset**
- STUDYID
- SPDEVID
- IDDN
- USUBJID
- DXSTDTC
- DXENDTC
- FAILDTC *
- FAILFL *

*unique to legacy dataset, added to standard in ADaM format

**ADDL Dataset**
- STUDYID
- SPDEVID
- USUBJID
- MODELG1
- AGEDST
- AGESTU
- DEVSDT
- DEVEDT
- DEVACFL
- DEVIPDT
- DEVXPDT
- DEVXPFL
- DXPREAS
### ADaM Device Metadata

- **Proposed Device-Specific Analysis Datasets***

<table>
<thead>
<tr>
<th>Dataset Name</th>
<th>Dataset Description</th>
<th>Dataset Structure</th>
<th>Key Variables</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADDL</td>
<td>Device-Level Analysis Dataset</td>
<td>One record per subject per device</td>
<td>USUBJID, SPDEVID</td>
<td>DEVICE-LEVEL ANALYSIS DATASET</td>
</tr>
<tr>
<td>ADXXXXXX</td>
<td>&lt;Dataset label&gt;</td>
<td>One record per record in SDTM domain (optional: per coding path, per Analysis Period and/or Phase)</td>
<td>USUBJID SPDEVID, -- SEQ</td>
<td>OCCURRENCE DATA STRUCTURE</td>
</tr>
<tr>
<td>ADXXXXXX</td>
<td>&lt;Dataset label&gt;</td>
<td>One record per subject, per device, per parameter</td>
<td>&lt;USUBJID&gt; SPDEVID, PARAM, &lt;timepoint&gt;</td>
<td>BASIC DATA STRUCTURE</td>
</tr>
</tbody>
</table>

Use foundational datasets first.
Additional datasets listed above extend the foundational standard.

* From the ADaMIG MD v1.0 Draft document
ADaM Device Metadata

- **Actual Device-Specific Analysis Datasets used**

<table>
<thead>
<tr>
<th>Dataset Name</th>
<th>Dataset Description</th>
<th>Dataset Structure</th>
<th>Key Variables</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADSL</td>
<td>Subject-Level Analysis Dataset</td>
<td>One record per subject</td>
<td>USUBJID</td>
<td>SUBJECT-LEVEL ANALYSIS DATASET</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADAE</td>
<td>Adverse Events Analysis Dataset</td>
<td>One record per subject, per adverse event</td>
<td>USUBJID, AESEQ</td>
<td>OCCURRENCE DATA STRUCTURE</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADPR</td>
<td>Procedures Analysis Dataset</td>
<td>One record per subject, per procedure, per timepoint</td>
<td>USUBJID, PARAM, AVISIT</td>
<td>BASIC DATA STRUCTURE</td>
</tr>
</tbody>
</table>

In addition, ADAE includes any device related adverse events.

.
Whenever possible use existing SDTM foundational domains to collect data, adding approved device identifiers and variables

Use additional SDTM Device domains for device-specific data. Map from approved CDASH forms.

ADaM should be built from the SDTM domains only

Use ADaM foundational standards plus additional device identifiers

Refer to ADaMIG MD for details on device-specific dataset metadata (v1.0 draft for review, March 2018)
CONCLUSION

• Standards can be developed in-house while adhering to CDISC principles
• The development of company standards and CDISC Interpretation guides is a team effort, involving multiple groups
• Using the lessons learnt from these first device-drug studies, we were able to add examples to our internal ADaM Standards metadata and Interpretation Guide
• When developing standards let the data speak!
Q&A
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