What is CDISC?

Non-profit standards development organization

Community consensus standards development for clinical & translational research

Ongoing global research support in the Americas, Europe, Japan, China, India, Korea and other regions

Standards downloaded in 90+ countries

Drivers
- REGULATION
- NEW SCIENTIFIC DISCOVERY
- EHR, CLAIMS AND OTHER DATA SOURCES
- CONSUMER-DRIVEN HEALTHCARE

CDISC Team & Volunteers
CDISC Foundational Standards

- Data Collection: CDASH
- Data Organization: SDTM
- Data Analysis: ADaM
- Data Transfer: XML

Controlled Terminology
### CDISC Medical Device Standards

<table>
<thead>
<tr>
<th>Dimension</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study Reference</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Device Identifiers</strong></td>
<td>Consistent unique sponsor-defined identifier that links data across domains.</td>
</tr>
<tr>
<td><strong>Device Properties</strong></td>
<td>Important unvarying device characteristics that are not identifiers.</td>
</tr>
<tr>
<td><strong>Device-In-Use</strong></td>
<td>Measurements and settings intentionally set that may vary between uses of a device.</td>
</tr>
<tr>
<td><strong>Device Exposure</strong></td>
<td>Subject’s exposure to a medical device under study.</td>
</tr>
<tr>
<td><strong>Device Events</strong></td>
<td>Reportable device-related occurrences such as malfunctions and calibrations.</td>
</tr>
<tr>
<td><strong>Tracking and Disposition</strong></td>
<td>Physical locations of device, either at each movement or just final status.</td>
</tr>
<tr>
<td><strong>Device-Subject Relationship</strong></td>
<td>Look-up table providing single consistent link between each device and subject.</td>
</tr>
</tbody>
</table>
CDRH Challenges

- Trial Data Issues
- Data Traceability
- Missing data
- Patient Accountability
- Missing coding tools
- Protocol Deviations

Source: Presentation by Dr. Rajesh Nair, CDRH, 2014, AdvaMed meeting; Poster by Dr. Nair, Kit Howard, Carey Smoak, Fred Wood, 2015, CDISC US Interchange
# Trial Data Issues

## CDRH Reviewer Requests

<table>
<thead>
<tr>
<th>CDRH Reviewer Requests</th>
<th>CDISC Solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Include electronic datasets in PMA submission</td>
<td>• SDTM and ADaM provide subject-and device-level tabulation and analysis datasets</td>
</tr>
<tr>
<td></td>
<td>• Data transmitted in SAS transport files</td>
</tr>
<tr>
<td>• Adverse Event listings for medical reviewers</td>
<td>• Standardized AE data support listings from data visualization tools</td>
</tr>
<tr>
<td>• Study endpoints analysis dataset(s) and raw data to minimize complicated manipulations and merges required to validate results</td>
<td>• ADaM defines key effectiveness/safety analysis datasets, and permits inclusion of any/all relevant variables</td>
</tr>
<tr>
<td>• Include basic demographic variables and important covariates in analysis datasets</td>
<td>• ADaM datasets are “one proc away” from running analyses</td>
</tr>
<tr>
<td>• Define/README file for datasets and program files</td>
<td>• Define-xml provides structure to document all datasets</td>
</tr>
<tr>
<td>• Document datasets and code sufficiently</td>
<td></td>
</tr>
</tbody>
</table>

Source: Presentation by Dr. Rajesh Nair, CDRH, 2014; AdvaMed meeting; Poster by Dr. Nair, Kit Howard, Carey Smoak, Fred Wood, 2015, CDISC US Interchange
Takeaway Points

- Can reduce review timelines (FAIR data) and increase efficiency in the submission/review process
- Supports cross-company integrated analyses, e.g., to identify safety signals
- Can increase ability to perform ad hoc analyses internally
- Easier to perform cross-study comparisons when the data structure is consistent
- Allow connections to other data sources (Including RWD)
- Can develop standard review tools based in a consistent, predictable data structure
- Some device companies are early adopters of CDISC standards
Thank You!
Additional Slides: CDRH Challenges
Data Traceability

**Issue**: Lack of data traceability means cannot assess data validity

**CDRH Reviewer Requests**
- Provide mechanism to trace each data point from the study report back to the CRF

**CDISC Solutions**
- ADaM, SDTM, associated define-xml and CDASH-conformant CRFs are specifically designed for this: hyperlink each variable to associated algorithm(s), source dataset(s), controlled terms and annotated CRF(s)

Source: Presentation by Dr. Rajesh Nair, CDRH, 2014 2014, AdvaMed meeting; Poster by Dr. Nair, Kit Howard, Carey Smoak, Fred Wood, 2015, CDISC US Interchange
Issue: Missing data may impact validity of conclusions, choice of statistical model

CDRH Reviewer Requests
- Show why and when data are missing (missed visits, value not recorded, etc.)
- No undisclosed data omissions; justify all data omissions
- Clearly note all imputed data

CDISC Solutions
- SDTM and ADaM define-xml:
  - Origin of each variable is defined as collected, derived or imputed
  - Algorithms for all derivations and imputations included
  - Can show what data were included or omitted and why
- CDASH can indicate what data were missing, with associated dates

Source: Presentation by Dr. Rajesh Nair, CDRH, 2014, AdvaMed meeting; Poster by Dr. Nair, Kit Howard, Carey Smoak, Fred Wood, 2015, CDISC US Interchange
**Patient Accountability**

**Issue:** Hard to determine accountability for all subjects

**CDRH Reviewer Requests**
- Provide patient accountability charts with discussions of missing data

**CDISC Solutions**
- CDASH and SDTM: Subject Disposition domain captures status of each subject at each defined time point, which can be used to produce accountability charts; see also “Missing Data” slide

Source: Presentation by Dr. Rajesh Nair, CDRH, 2014, AdvaMed meeting; Poster by Dr. Nair, Kit Howard, Carey Smoak, Fred Wood, 2015, CDISC US Interchange
Missing coding tools

**Issue:** Hard to identify, determine impact

**CDRH Reviewer Requests**
- Include Proc Format program that creates the format catalog

**CDISC Solutions**
- Controlled Terminology contains standard "formats"
- define-XML contains customized ones and external terms

Source: Presentation by Dr. Rajesh Nair, CDRH, 2014 2014, AdvaMed meeting; Poster by Dr. Nair, Kit Howard, Carey Smoak, Fred Wood, 2015, CDISC US Interchange
**Issue**: Hard to identify, determine impact

**CDRH Reviewer Requests**
- Summary tables by type of deviation (major/minor)
- Protocol deviations by investigational site

**CDISC Solutions**
- SDTM: designed to facilitate summary table production;
- CDASH: defines deviation data capture, including narratives; facilitates categorization

*Source: Presentation by Dr. Rajesh Nair, CDRH, 2014, AdvaMed meeting; Poster by Dr. Nair, Kit Howard, Carey Smoak, Fred Wood, 2015, CDISC US Interchange*