CDISC MDUFA V Presentation

Presented by
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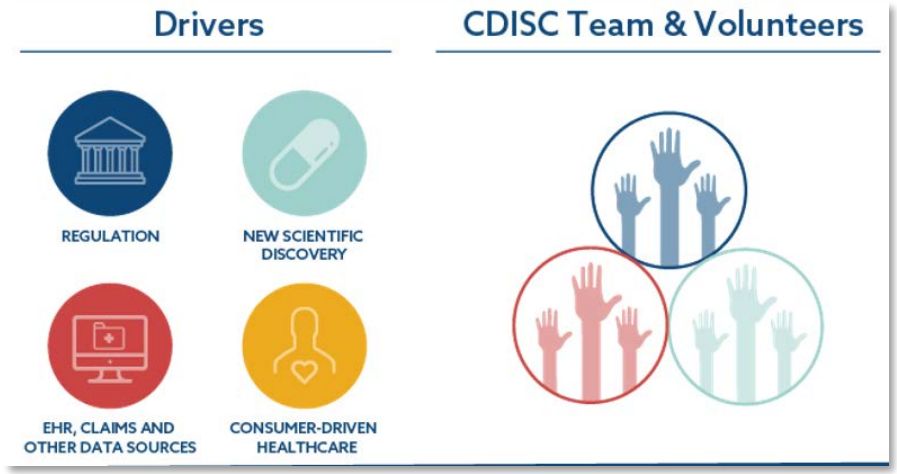
What is CDISC?



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

CDISC Foundational Standards

Data Collection
CDASH

Data Organization
SDTM

Data Analysis
ADaM

Data Transfer
XML

Controlled Terminology

CDISC Medical Device Standards

Study Reference	**Device Identifiers (DI)**	Consistent unique sponsor-defined identifier that links data across domains.
Device Characteristics	**Device Properties (DO)**	Important unvarying device characteristics that are not identifiers
	Device-In-Use (DU)	Measurements and settings intentionally set that may vary between uses of a device
Device Treatment	**Device Exposure (DX)**	Subject's exposure to a medical device under study
Events	**Device Events (DE)**	Reportable device-related occurrences such as malfunctions and calibrations
	Tracking and Disposition (DT)	Physical locations of device, either at each movement or just final status
Representing Relationships	**Device-Subject Relationship (DR)**	Look-up table providing single consistent link between each device and subject

CDRH Challenges

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

Trial Data Issues

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

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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)

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Missing data

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

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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 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

Protocol Deviations

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

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