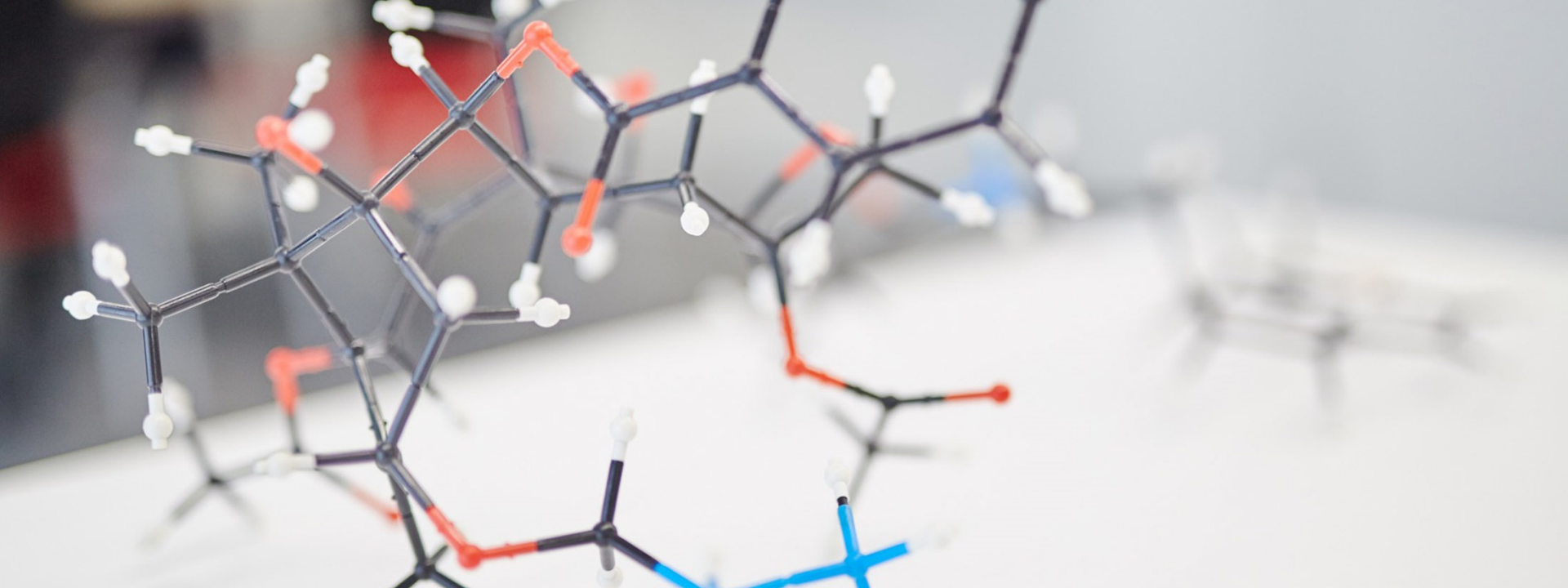




Implementing CDISC Standards for Device-Drug Studies

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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:



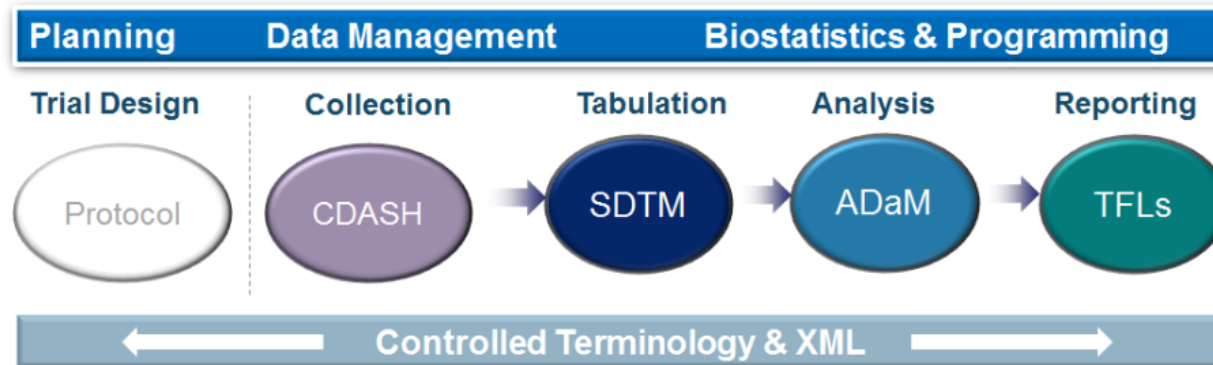
SDTM Medical Devices
(MD) v1.0, Dec. 2012



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



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DESCRIPTION

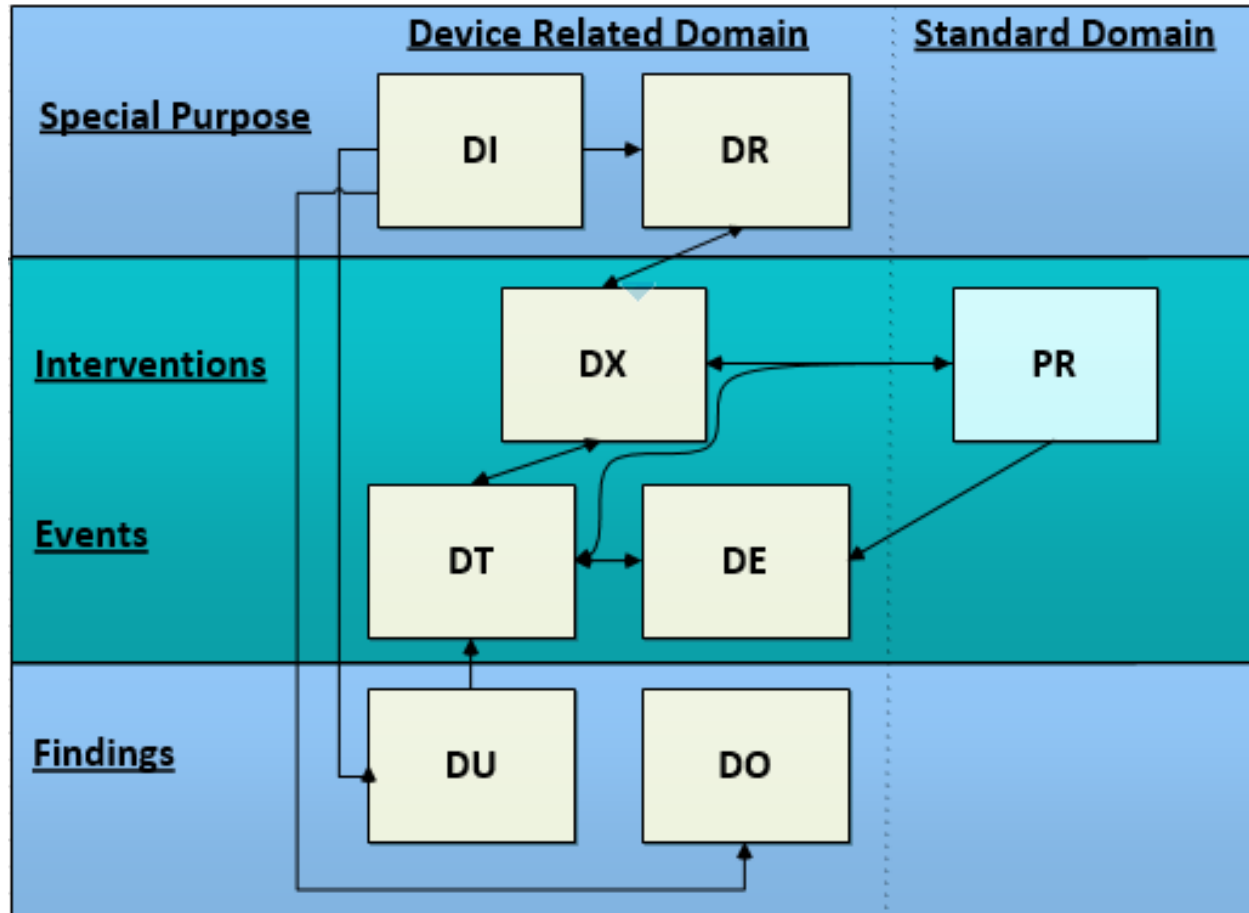
- Devices can be part of a drug or biologic submission and not just stand-alone studies for device development.
- The study was based on a rare disease clinical trial with device to deliver study drug to patients. Safety data was collected on treatment and also on devices (i.e. procedures, related AEs, 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

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

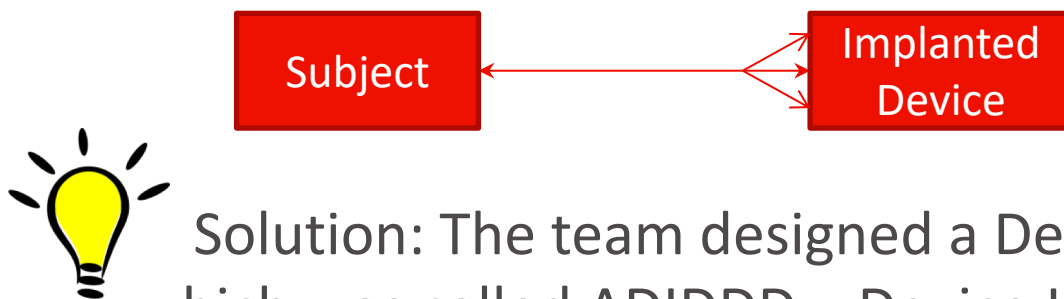
These approved SDTM variables may be added to foundational SDTM domains that contain device data.

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).

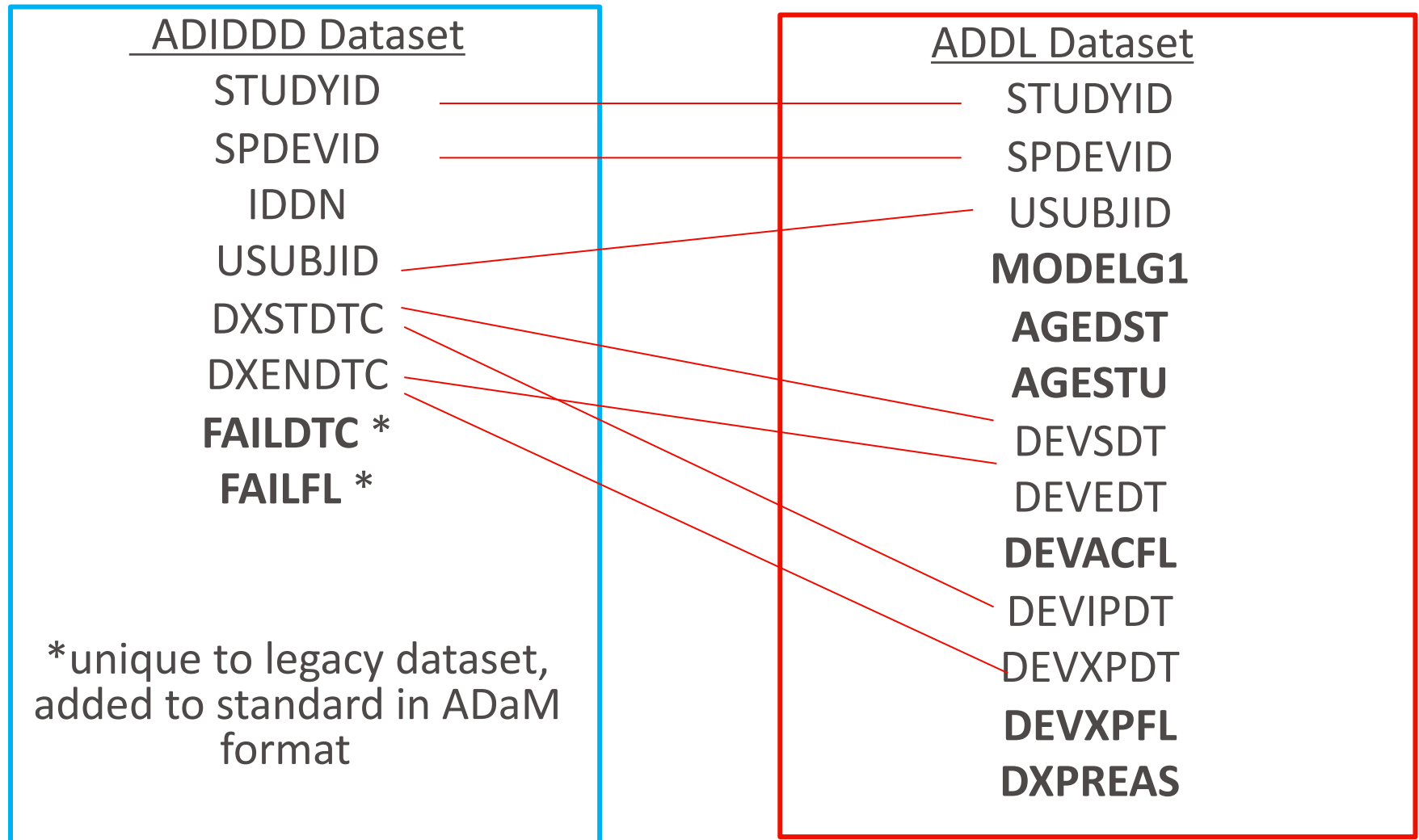
EVOLUTION OF ADaM Standard

- 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



ADaM Device Metadata

- Proposed Device-Specific Analysis Datasets*

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

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

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

In addition, ADAE includes any device related adverse events.

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SDTM and ADaM Principles for Medical Devices

- 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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