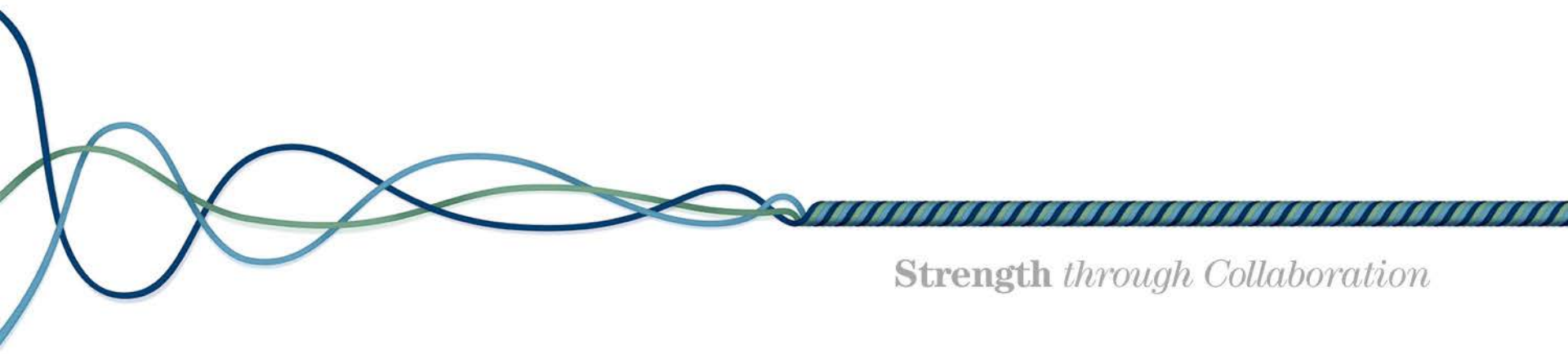
CDISC Public Webinar- Standards Updates and Additions

26 September 2017



AGENDA

- SDTM v1.7
- Q&A
- CDISC Online Education and Event Updates
  - Victor Martin, CDISC

Question and Answer

- ‘Panelist’: Question

OR

- ‘Presentation’: Question

Examples:

John: Where are standards documents in the Wiki?

OR

CDISC: When can we start registering for the Interchange?

SDTM v1.7

CDISC Webinar, 2017-10-31

Diane Wold, CDISC
Janet Reich, Amgen
Bess LeRoy, CDISC
Carey Smoak, DataCeutics

Strength *through Collaboration*

Background

- SDTM v1.7 supports two implementation guides based on the SDTM
  - The SDTM Implementation Guide for Human Clinical Trials, SDTMIG v3.3
  - The SDTM Implementation Guide for Medical Devices, SDTMIG-MD v1.1 Final
- It also includes one variable included in the SENDIG v3.1 that was missed in SDTM v1.5

Agenda

- Diane Wold
  - Interventions variable –RSDISC
  - Changes to DM, including new variables
  - Domain-specific variable MHEVDTYP
- Janet Reich
  - Changes to CO
- Bess LeRoy
  - Changes to Microbiology (MS and MB)
  - New Non-Host Organism Identifier domain
- Carey Smoak
  - Changes from SDTMIG-MD v1.0

--RSDISC, Reason for Discontinuation
DM changes
MHEVDTYP, Event Date Type

Diane Wold, CDISC

--RSDISC, Reason for Discontinuation

- New variable in the Interventions class
- Original use case was for prior treatments for the disease under study

cm.xpt

Row	CMTRT	CMCAT	CMSTDTC	CMENDTC	CMRSDISC
1	Drug X	HCV TREATMENT	2013-08-15	2013-09-22	Toxicity/Intolerance
2	Drug Y	HCV TREATMENT	2013-09-30	2014-01-17	Lack of Efficacy

- Can be used for interventions in any domain

New Demographics (DM) variables

- For most subjects, the values in ARMCD/ARM and ACTARMCD/ACTARM come from Trial Arms.
- In previous versions, special values were used for subjects who didn't follow a path in Trial Arms
  - Examples: "SCRNFAIL", "NOTASSGN", "NOTTRT".
- Information about unplanned paths will now be in new variables, so that values in ARMCD/ARM and ACTARMCD/ACTARM will now always come from Trial Arms or be null.

ARMNRS, Reason Arm and/or Actual Arm is Null

- Holds information that used to be in special values
  - "SCREEN FAILURE“
  - "NOT ASSIGNED“
  - "NOT TREATED“
  - "UNPLANNED TREATMENT"

dm.xpt

Row	USUBJID	ARMCD	ARM	ACTARMCD	ACTARM	ARMNRS	ACTARMUD
1	003					SCREEN FAILURE	
2	004					NOT ASSIGNED	
3	005	A	Drug A			NOT TREATED	

ACTARMUD, Description of Unplanned Actual Arm

- A description of actual treatment for a subject who did not receive treatment described in one of the planned trial arms.
- Example: “Drug B dispensed for part of Drug A element”

dm.xpt

Row	SUBJID	ARMCD	ARM	ACTARMCD	ACTARM	ARMNRS	ACTARMUD
1	012	A	A	A	A		
2	103	AR	A-Rescue			UNPLANNED TREATMENT	Drug B dispensed for part of Drug A element

Things that did not change

- In a trial with multiple treatments (e.g., a crossover trial), if a subject received only some of their assigned treatments, their ACTARMCD/ACTARM values reflect the entire sequence to which they were assigned.
  - Example: Randomized to AB, only received A, actual arm is still AB
- In trials with multiple assignments, if a subject did not receive all assignments, their arm and actual arm values can be truncated versions of values in Trial Arms.
  - Example: Randomized to A, did not reach second randomization to C or D. Arm and actual arm are A, rather than Trial Arms values AC or AD.

MHEVDTYP: Background

- What is meant by the start of an event is not clearly defined and depends on the kind of event.
- Examples:
  - An injury has a clear start, e.g., an accident.
  - Symptomatic diseases would usually be thought of as starting when symptoms start, e.g., a cold.
  - Asymptomatic diseases may have been present long before diagnosis, and the only available “start date” may be the date of diagnosis, e.g., cancer.

MHEVDTYP, Use Case

- Data collected about pre-specified medical history events sometimes specifies a particular kind of start date.
  - Example: “When was asthma diagnosed?”
- MHEVDTYP can be used to represent the type of date represented in MHSTDTC (or occasionally, MHENDTC).

mh.xpt

Row	USUBJID	MHSEQ	MHTERM	MHPRESP	MHOCCUR	MHDTC	MHSTDTC	EVDTYP
2	XYZ-001-001	2	ASTHMA	Y	Y	2010-10-26	2010-04-25	DIAGNOSIS

- MHEVDTYP is a domain-specific variable.

MHEVDTYP, Multiple start dates

- Occasionally, data is collected about multiple aspects of a pre-specified medical history event.
  - Example:
    - “When did asthma symptoms start?”
    - “When was asthma diagnosed?”
- The MH dataset will include a record for each value of MHEVDTP

mh.xpt

Row	USUBJID	MHSEQ	MHTERM	MHPRESP	MHOCCUR	MHDTC	MHSTDTC	EVDTYP
1	XYZ-001-001	1	ASTHMA	Y	Y	2010-09-26	2010-01	SYMPTOMS
2	XYZ-001-001	2	ASTHMA	Y	Y	2010-10-26	2010-04-25	DIAGNOSIS

MHEVDTYP, “Double Counting” Concern

- Reviewers have raised concerns about “double counting” events when there are two records for an event.
- Mitigating factors include:
  - Counting of events is usually more relevant for events during a study than for medical history events.
  - Specified starts for events are usually collected only for events that are pre-specified.
  - Specified starts for events are part of data collection, so programming can be planned to allow for multiple records.

MHEVDTYP – Alternatives

- Alternative Considered
  - Add Onset Date and Diagnosis Date
    - Does not provide for other kinds of start dates
  - Use Findings About (FA) for other dates of interest.
    - SDTMIG cautions about dates as results

- The MHEVDTYP solution does not address other events domains
  - Is one of the alternatives above better?
  - Other alternatives?

- Reviewer input is requested

CO Changes

Janet Reich, Amgen

CO Variable Addition – CODY

- Added CODY in SDTM v1.7
  - CODY is a Timing Variable Paired with CODTC
- Added CODY in IGs
  - SDTMIG v3.3
  - SENDIG v3.1
  - Prior IGs have an assumption that CODY as Perm

6. Only following Identifier and Timing variables that are permissible and may be added as appropriate when comments are not related to other domain records: COGRPID, COREFID, COSPID, VISIT, VISITNUM, VISITDY, TAETORD, CODY, COTPT, COTPTNUM, COELTM, COTPTREF, CORFTDTC.

CO Variable Addition – COEVALID

- Added COEVALID
  - COEVALID is a Variable Qualifier of COEVAL
    - To be used like --EVAL and --EVALID in Findings Class
    - Distinguishes comments from multiple evaluators
    - e.g., RADIOLOGIST 1 vs RADIOLOGIST 2

STUDYID	DOMAIN	RDOMAIN	USUBJID	COSEQ	IDVAR	IDVARVAL	COREF	COVAL	COEVAL	COEVALID	CODTC	CODY
1234	CO	RS	AB-99	1			GENERAL TIMEPOINT COMMENT	Comment text	INDEPENDENT ASSESSOR	RADIOLOGIST 1	2016-03-15	84
1234	CO	RS	AB-99	2			GENERAL TIMEPOINT COMMENT	Comment text	INDEPENDENT ASSESSOR	RADIOLOGIST 2	2016-03-15	84

QNAM Text Addition

Janet Reich, Amgen

QNAM Text Addition

- "QNAM cannot be the name of any standard ADaM variable."
  - Good principle for managing unique concepts

#	Variable Name	Variable Label	Type	Role	Description
8	QNAM	Qualifier Variable Name	Char	Topic	The short name of the Qualifier variable, which is used as a column name in a domain view with data from the parent domain. The value in QNAM cannot be longer than 8 characters, nor can it start with a number (e.g., "1TEST"). QNAM cannot contain characters other than letters, numbers, or underscores. This will often be the column name in the sponsor's operational dataset. QNAM cannot be the name of any standard ADaM variable.

Microbiology Changes
Non-Host Organism Identifier

Bess LeRoy, CDISC

Addition of the Non-host Organism Identifier (OI) Study Reference Dataset to Support Taxonomic Nomenclature

Virus Nomenclature- v1.0

1.5 DESIGN CONSIDERATIONS AND APPROACH

The purpose of this section is to review the design approach and lessons learned by mapping complex PGx and virology data. This section also serves to document issues encountered during the development process and their respective resolutions.

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5. **SPECIES and STRAIN were added to the domains to allow for the separation of genetic and genomic data from pathogens, such as viruses (that are the subject of this user guide) from genetic data on their human hosts (whose species and stain, if not human, would be submitted in the Demographics domain).**

6. **It was suggested that SUBSTRAIN and CLADE be added to the domains. However, because of ambiguous definitions and because the hierarchy used seems to differ, these potential additions were deferred until a future version.**

limited to resistance based on only one result. Virology data, on the other hand, includes multiple results, and a net assessment that summarizes these results. The use of the LB domain, which already includes examples of viral test data, was next considered but this approach was felt to create too high a burden for creating test codes which would have included the virus as part of the test name. After considering these alternatives, the team chose to create a Viral Resistance (VR) domain that includes the species and strain variables, eliminating the need to maintain pathogen-specific test names.

8. A draft SDTMIG-PGx document underwent public review in 2010. The need for new examples and domains was identified to better document the PGx Biological State (PB) and Subject Biological State (SB). These domains are included in draft form in this VR-UG and will be included SDTMIG-PGx that is currently under development.

Virus Nomenclature Issue

--NSPCES

	HIV	Influenza A	Hep C	Hep B	HPV
SPECIES level	**Species**	**Species**	**Species**	**Species**	**Species**
Subspecies Level 1	Type	Subtype	Genotype	Genotype	Type
Subspecies Level 2	Group	Strain	Subtype	Sub-genotype	
Subspecies Level 3	Subtype (or Clade)			Recombination Type	
Subspecies Level 4	Subclade				

--NSTRN?

NHOID and Non-host Organism Identifi[illegible](OI) Domain

NHOID

HIV1MC

ms.xpt

Row	STUDYID	DOMAIN	USUBJID				ISTEST	MSDRUG	MSORRES	MSORRESU	MSSTRESC
1	COINF1	MS	COINF1-01				50 Subject Result	Experimenavir	0.2	nM	0.2
2	COINF1	MS	COINF1-01				Reference trol Result	Experimenavir	0.21	nM	0.21
3	COINF1	MS	COINF1-01				C50 Fold ange from eference	Experimenavir	0.95		0.95
4	COINF1	MS	COINF1-01	4	2	HCV2C	IC50S	IC50 Subject Result	Heprevir	1.35	nM	1.35
5	COINF1	MS	COINF1-01	5	2	H77	IC50R	IC50 Reference Control Result	Heprevir	1.21	nM	1.21

NHOID	OISEQ	OIPARMCD	OIPARM	OIVAL
HIV1MC	1	SPCIES	Species	HIV
HIV1MC	2	TYPE	Type	1
HIV1MC	3	GROUP	Group	M
HIV1MC	4	SUBTYP	Subtype	C

10	STUDY123	OI	HCV2C	2	GENTYP	Genotype	2
11	STUDY123	OI	HCV2C	3	SUBTYP	Subtype	C
12	STUDY123	OI	H77	1	SPCIES	Species	HCV
13	STUDY123	OI	H77	2	GENTYP	Genotype	1
14	STUDY123	OI	H77	3	SUBTYP	Subtype	A

Advantages of OI Approach to Nomenclature

- “Bug-” and terminology agnostic
- Should work for a variety of non-host organisms
- NHOID provides a “snapshot” of bug identity
- OI dataset provides parsed details of taxonomy when needed without the need for countless new variables like –NSPCES and –NSTRN

Addition of MS Domain Specific Variables

MSAGENT: The name of the agent for which resistance is tested. The agent specified may be based on genetic markers or direct phenotypic drug sensitivity testing, MSCONC, and MSCONCU.

MSCONC: Numeric concentration of agent listed in MSAGENT.

MSCONCU: Units for value of the agent concentration listed in MSCONC.

Ability to use the Non-host Organism ID variable

How New Variables Impact MS

Row	USUBJID	MSSEQ	MSTESTCD	MSTEST	NHOID	MSAGENT	MSCONC	MSCONCU	MSORRES	MSORRESU
1	ABC-01-101	1	DS	Drug Susceptibility	MYCOBACTERIUM TUBERCULOSIS	Isoniazid	0.015	ug/L	RESISTANT	
2	ABC-01-101	2	DS	Drug Susceptibility	MYCOBACTERIUM TUBERCULOSIS	Isoniazid	0.03	ug/L	RESISTANT	
3	ABC-01-101	3	DS	Drug Susceptibility	MYCOBACTERIUM TUBERCULOSIS	Isoniazid	0.06	ug/L	SUSCEPTIBLE	
4	ABC-01-101	4	MIC	Minimum Inhibitory Concentration	MYCOBACTERIUM TUBERCULOSIS	Isoniazid			0.06	ug/L

Row	MSSTRESC	MSSTRESN	MSSTRESU	MSMETHOD	VISITNUM
1 (cont)	RESISTANT			MICRO BROTH DILUTION	1
2 (cont)	RESISTANT			MICRO BROTH DILUTION	1
3 (cont)	SUSCEPTIBLE			MICRO BROTH DILUTION	1
4 (cont)	0.06	0.06	ug/mL	MICRO BROTH DILUTION	1

Changes in the SDTMIG-MD v1.1 Final

Carey Smoak, DataCeutics

Updates for Devices

- Process to make SDTMIG-MD v1.0 final as v 1.1:
  - Change the cover page to the new version
  - Change the description of DI as a special purpose domain to a study reference datasets
    - The classification of DI was changed when we recognized that similar structures were being used for OI and PB (in the SDTMIG-PGx), and created the new category “study reference dataset” for them.
  - Change the description of DR as a special purpose domain to a relationship dataset
    - The classification of DR was because the relationship datasets seemed like a better fit.

Instructions for Reviewers

- Items to Consider During Review
  - The following statement has been added
    - “QNAM cannot be the name of any standard ADaM variable.”

  - MHEVDTYP (Medical History Event Date Type)
    - Input on alternative solutions and scope are requested
      - Add Onset Date and Diagnosis Date
      - Use Findings About (FA) for other dates of interest.
      - Avoiding multiple records in MH for a medical condition.
      - This is not a domain-specific issue – suggest a holistic one.

Public Review Information

- Review package available only on the CDISC WIKI
  - Links/Instructions were provided in the Public Review announcement email
  - https://wiki.cdisc.org/display/SDTM1DOT7/Study+Data+Tabulation+Model+v1.7

- Reviewers are requested to make any comments directly via JIRA
  - Detailed instructions are provided on the SDTM v1.7 WIKI page
  - Wiki and JIRA use the same credentials, so if you can access the TAUG in the WIKI, then you can use JIRA.

Public Review Information – cont.

- We recommend reading the SDTM in its entirety at least once before jumping to specific sections
- Keep the JIRA-SDTM page and the WIKI Study Data Tabulation Model 1.7 page open in separate windows
  - Comments can be entered without navigating back and forth between the Wiki and JIRA.
  - Always check to make sure the project selected in JIRA is SDTM.

Public Review Information – cont.

You can also make scope suggestions for future versions

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Q&A

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Location	Dates	Courses Offered:	Discount period ends:	Late fees kick(ed) in:	Host
Austin, TX	13-17 Nov 2017	SDTM, CDASH, ADaM Primer, ADaM T&A, Define-XML, Controlled Terminology, SEND, Standards from the Start, ODM, SDTM for Medical Device	13 Aug 2017	3 Nov 2017	CDISC

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Copenhagen, Denmark	2-10 Nov 2017	SEND, SDTM, ADaM Primer, ADaM T&A, Define-XML	2 Aug 2017	3 Oct 2017	
London (Reading), United Kingdom	22-26 Jan 2018	SDTM, ADaM Primer, ADaM T&A, CDASH, Define-XML	22 Oct 2017	22 Dec 2017	

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Tokyo, Japan	4-8 Dec 2017	SDTM, CDASH, ADaM Primer, ADaM T&A, Define-XML	4 Oct	4 Nov	Croit
Seoul, South Korea	5-14 Mar 2018	Standards from the Start, SDTM, CDASH, ADaM Primer, ADaM T&A, Define-XML	5 Dec 2017	5 Feb 2018	C&R RESEARCH

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Any more questions?

Thank you for attending this webinar.

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