CDISC Italian User Network 2019

Milan, Italy | 22 February 2019

SDTM Ig 3.3
A Closer Look

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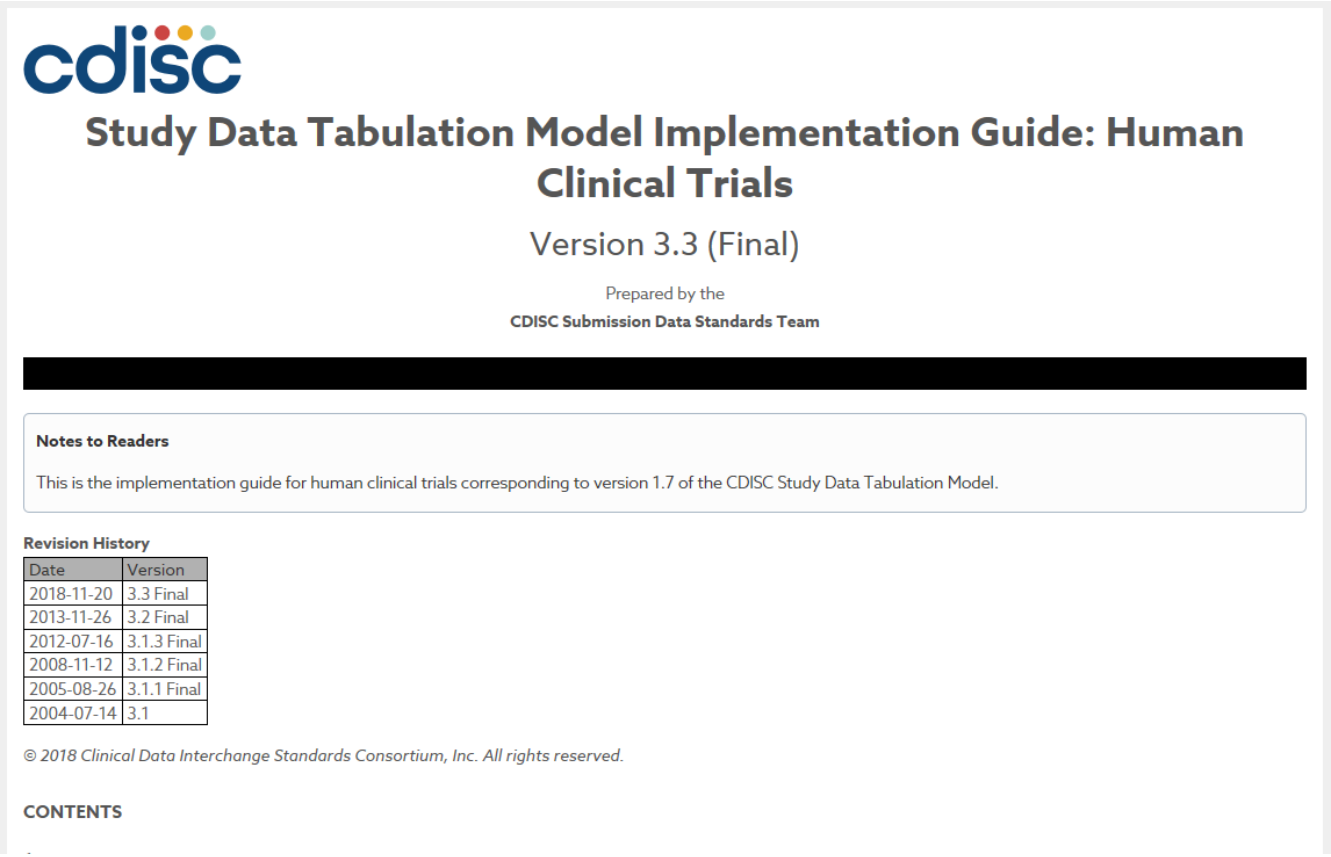
Agenda

- Introduction
- Evolution of SDTM Model and Implementation Guidance
- New Subject Domains
- New Trial Design and Special Purpose Domains
- Section by Section comparison
  - New Variables
  - Key Changes in Metadata
  - Improvements / Clarifications
  - Significant Changes in Individual Domains
  - Other Changes
  - What questions the Ig doesn’t answer yet
- Conclusions

Introduction

https://www.cdisc.org/standards/foundational/sdtmig/sdtmig-v3-3



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Study Data Tabulation Model Implementation Guide: Human Clinical Trials

Version 3.3 (Final)

Prepared by the

CDISC Submission Data Standards Team

Notes to Readers

This is the implementation guide for human clinical trials corresponding to version 1.7 of the CDISC Study Data Tabulation Model.

Revision History

Date	Version
2018-11-20	3.3 Final
2013-11-26	3.2 Final
2012-07-16	3.1.3 Final
2008-11-12	3.1.2 Final
2005-08-26	3.1.1 Final
2004-07-14	3.1

CONTENTS

- Only Html Version
- Excel metadata available in CDISC/SHARE (including a Diff file)

Introduction

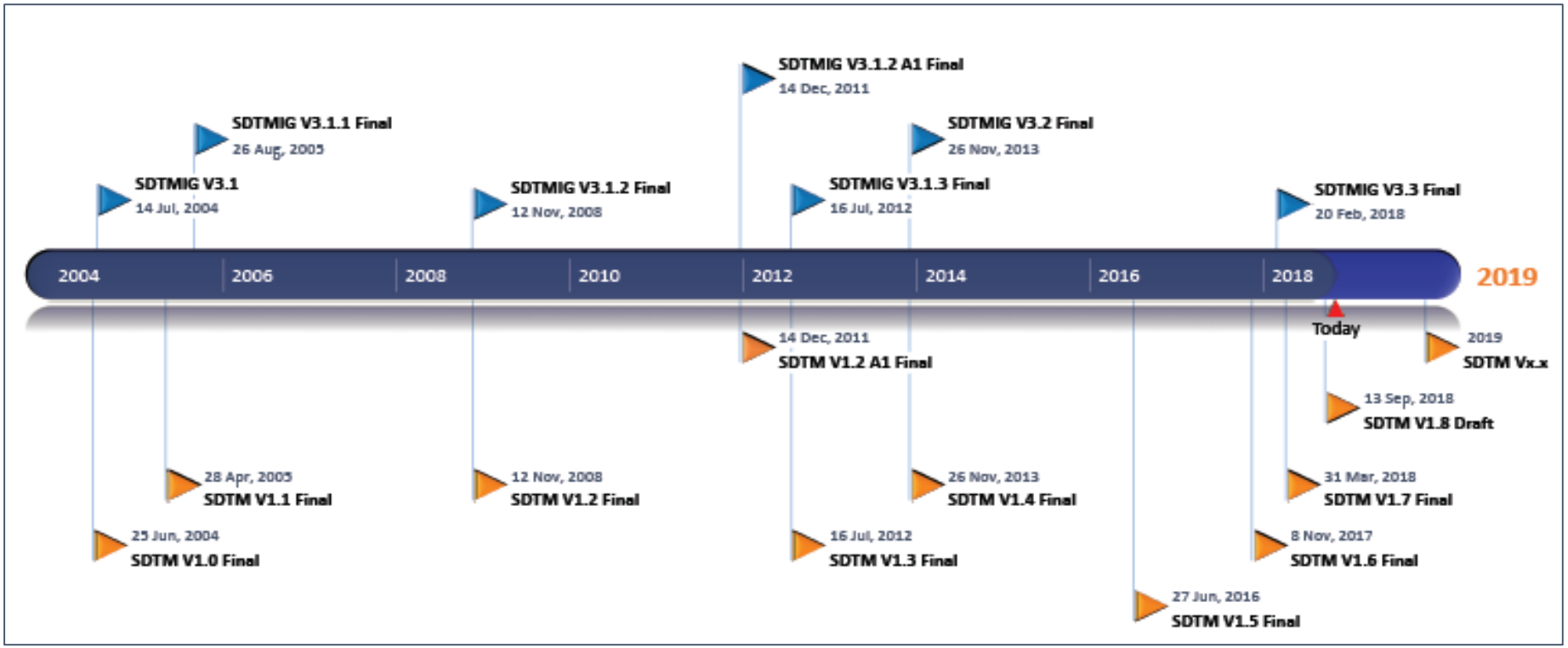
The Diff file available in CDISC/SHARE

C	D	E	F	G	H	
Action	**Impact**	**Observation Cla**	**Domai**	**Variable**	**Attribute (updated)**	**Attribute (previous)**
Update	CDISC Notes	Events	AE	AESCAN	Was the serious event associated with the development of cancer? Valid values are "Y" and "N". This is a legacy seriousness criterion. It is not included in ICH E2A.	Was the serious event ass cancer?
Update	CDISC Notes	Events	AE	AESCONG	Was the serious event associated with congenital anomaly or	Was the serious event ass

Add
Drop
Update

CDISC Notes
Core
CT Codelist/Formats
Domain
Role
Type
Variable
Variable Label

Evolution of SDTM Model and Implementation Guidance



SDTMIG v3.3: New domains – new benefits, Nick De Donder, PhUSE 2018

New Domains

- Interventions
  - Procedure Agents (AG)
  - Meal Data (ML)

- Findings
  - Cardiovascular System Findings (CV)
  - Musculoskeletal System Findings (MK)
  - Nervous System Findings (NV)
  - Ophthalmic Examinations (OE)
  - Respiratory System Findings (RE)
  - Urinary System Findings (UR)

- Trial Design
  - Trial Design Milestones (TM)

- Special Purpose
  - Subject Disease Milestones (SM)

New Subject Domains

Interventions

Domain Name	Domain Label	When to be used
AG	Procedures Agents	To record agents administered to the subject as a part of a procedure or assessment (e.g., data about allergen administered as a part of a bronchial allergen challenge (BAC) test)
ML	Meal Data	To record collected data describing a subject's food consumption (e.g. data collected about the meals before each hypoglycemic event)

New Subject Domains

Findings (1/3)

The following domains are « Morphology/Physiology Domains » and come from TAUGs

Domain Name	Domain Label	When to be used
CV	Cardiovascular System Findings	To record morphological and physiological findings related to the cardiovascular system (including the heart and blood and lymphatic vessels)
MK	Musculoskeletal System Findings	To record morphological and physiological findings related to the muscles, tendons, ligaments, bones, joints and associated tissues
NV	Nervous System Findings	To record morphological and physiological findings related to the nervous system based on neurological examinations or procedures, involving the brain, spinal cord, cranial and spinal nerves, etc.

New Subject Domains

Findings (2/3)

Domain Name	Domain Label	When to be used
OE	Ophthalmic Examinations	To record findings related to tests measuring ocular health and visual status
RE	Respiratory System Findings	To record morphological and physiological findings related to the respiratory system (including nose, throat, larynx, trachea, bronchi and lungs)
UR	Urinary System Findings	To record morphological and physiological findings related to the urinary tract (including kidneys, ureters, bladder and urethra)

MO domain will probably be deprecated in a later version of SDTMIG

New Subject Domains

Findings (3/3)

The following domain belong to the category of « Questionnaires, Ratings and Scales »

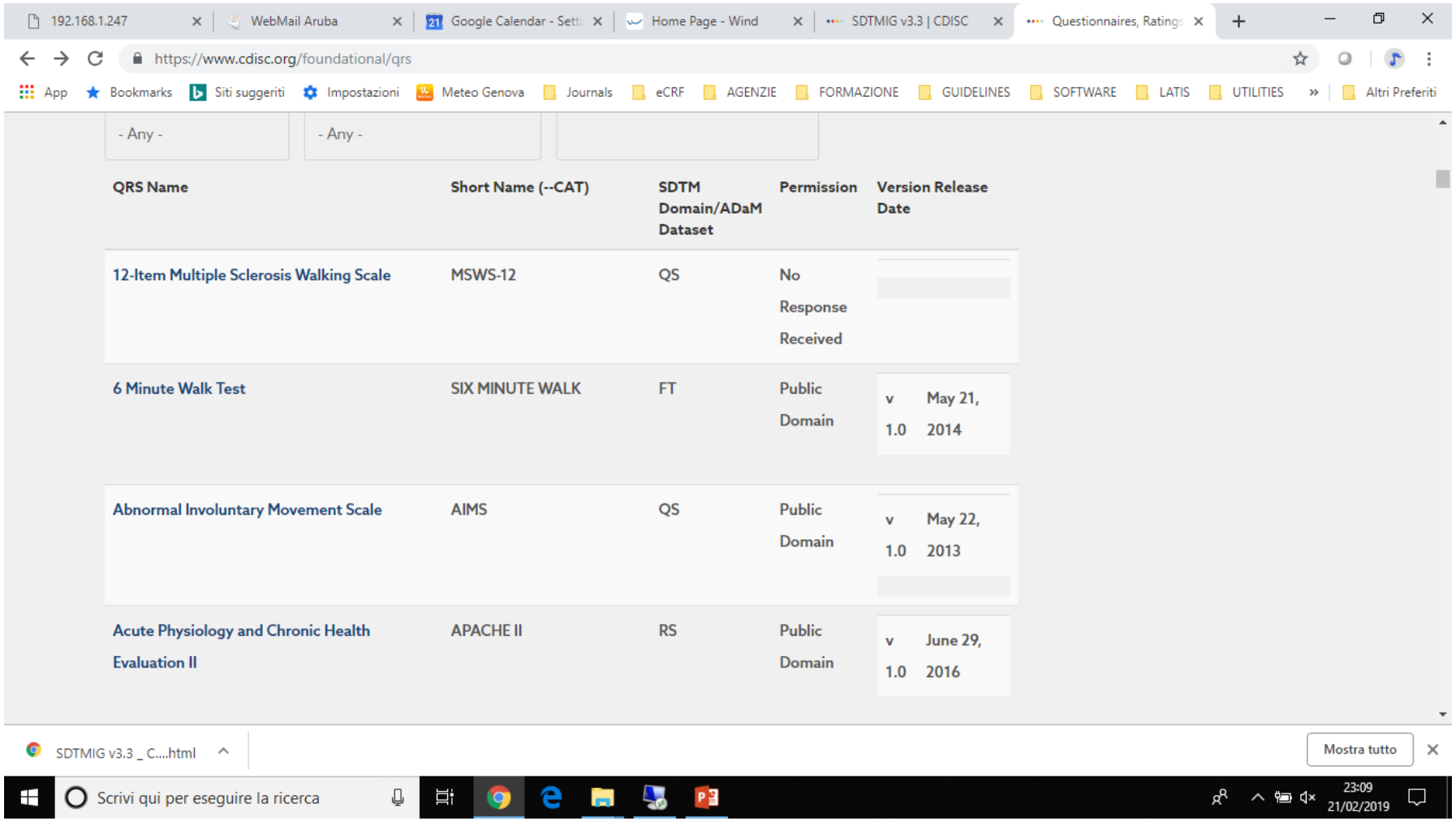
Domain Name	Domain Label	When to be used
FT	Functional Tests	To record data for named, stand-alone, task-based evaluations designed to provide an assessment of mobility, dexterity, or cognitive ability.

This category already includes other domains:

QS – To record data about the assessment of a concept

RS – To record data about disease response to therapy or clinical classification based on published criteria

Questionnaires, Ratings and scales



New Trial Design Domain

Domain Name	Domain Label	When to be used
TM	Trial Disease Milestones	To describe disease milestones, i.e. observations or activities anticipated to occur in the course of the disease under study.

New Special Purpose Domain

Domain Name	Domain Label	When to be used
SM	Subject Disease Milestones	To record the timing, for each subject, of disease milestones defined in the TM dataset

New Variables

4.5.9 Baseline Values (--LOBXFL vs –BLFL)

- --LOBXFL (Last Observation Before Exposure Flag): Unique definition (Role=expected/permissible)

  Last non-missing value prior to RFXSTDTC

- --BLFL: added (and defined) by the sponsor (Role=~~expected~~ permissible)

Key Changes in Metadata

- New permissible variables added to domains i.e.
  - EPOCH/TAETORD in all Events/Findings/Interventions
  - SESTDY/SEENDY in SV

In future no more « annoying » P21 Warnings/Errors to justify in the cSDRG

- New variables, some examples
  - CMADJ (Reason for dose adjustment - *Perm*)
  - CMRSDISC (Reason for CM discontinuation - *Perm*)

Key Changes in Metadata

- PC and PP now have the same CT for unit (PKUNIT)

Code	Codelist Code	Codelist Name	CDISC Submission Value	CDISC Synonym(s)
C67306	C71620	Unit	ug/L	Microgram per Liter; Milligram per Cubic Meter; Nanogram per Milliliter; mcg/L; mg/m3; **ng/mL**; ug/L

Code	Codelist Code	Codelist Name	CDISC Submission Value	CDISC Synonym(s)
C67306	C85494	PK Units of Measure	ng/mL	Microgram per Liter; Milligram per Cubic Meter; Nanogram per Milliliter; mcg/L; mg/m3; ng/mL; **ug/L**

Improvements / Clarifications

4.1.3.1 EPOCH Variable Guidance

- For Findings it should be based on the –DTC
- For Observations / Interventions it should be based on the --STDTC variable, since this is the start of the Intervention or Event
- Sponsor should not impute EPOCH values, but should, where possible, assign EPOCH values on the basis of CRF instructions and
- If it is not possible to determine the EPOCH; EPOCH should be left Null

Improvements / Clarifications

4.5.3.2 Text Strings Greater than 200 Characters in Other Variables

General Observation Class & SUPP	CO.COVAL	TS.TSVAL	TI.IETEST and IE.IETEST
First 200 chars in the variable and each additional 200 chars SUPP--	Fist 200 chars in COVAL and each additional 200 chars in COVAL1 to COVALn	First 200 chars in TSVAL and each additional 200 chars TSVAL1 to TSVALn.	If criteria >200 chars meaningful text in IETEST and describe the full text in the study metadata.
When splitting a text string into several records, the text should be split between words to improve Readability			Not Applicable
QLABEL should be the original domain variable label	Label for COVAL1-COVALn should be « Comment »	Label for TSVAL1-TSVALn « Parameter Value »	Not Applicable

Improvements / Clarifications

4.3.3 Controlled Terminology Values

A clarification was added with respect to subset-CT:

When a domain or dataset specification includes a codelist for a variable, not every value in that codelist may have been part of planned data collection; only values that were part of planned data collection should be included in the define-XML document.

This means for example if a variable has assigned a standard generic CT such as UNIT, not all units in the CT should be reported i.e. CMUNIT can be a subset standard UNIT CT

Significant Changes in Individual Domains

5.2 DM - Demographics

- Added ARMNRS to specifcy the reason why ARM is null
- and ACTARMUD to describe unplanned actual arm

Row	STUDYID	DOMAIN	USUBJID	ARMCD	ARM	ACTARMCD	ACTARM	ARMNRS	ACTARMUD
1	ABC	DM	001	A	Drug A	A	Drug A		
2	ABC	DM	002	B	Drug B	B	Drug B		
3	ABC	DM	003					SCREEN FAILURE	
4	ABC	DM	004					NOT ASSIGNED	
5	ABC	DM	005	A	Drug A			ASSIGNED, NOT TREATED	

- ARM/ARMCD Null when subject not randomized (aligned with FDA TCG)
- ACTARM/ACTARMCD Null when subject not treated
- ARM/ACTARM for multi-stage trial (i.e. cross-over)
- ARM/ARMCD/ACTARM/ACTARMCD are now Expected (before Required)
- ~~SUPPDM.QNAM=ITT/PPROT/etc.~~ Study Population flags only in ADAM

Significant Changes in Individual Domains

6.2.3 DS - Disposition

Clarifying text in the «Assumptions» section about **«Study Participation» vs «Study Treatment »** disposition event:

- **DSSCAT = "STUDY PARTICIPATION"** is used to represent disposition of study participation.
- **DSSCAT = "STUDY TREATMENT"** can be used as a generic identifier when a study has only a single treatment.
- If a study has multiple treatments, then **DSSCAT should name the individual treatment**.

Row	STUDYID	DOMAIN	USUBJID	DSSEQ	DSTERM	DSDECOD	DSCAT	DSSCAT	DSSTDTC	EPOCH
1	XXX	DS	XXX-767-001	1	PERSISTENT HIGH-LEVEL POSITIVE CULTURES, PER PROTOCOL, LEVOFLOXACIN REMOVAL RECOMMENDED	PHYSICIAN DECISION	DISPOSITION EVENT	LEVOFLOXACIN	2016-02-15	TREATMENT 1
2	XXX	DS	XXX-767-001	2	COMPLETED	COMPLETED	DISPOSITION EVENT	ISONIAZID	2016-02-15	TREATMENT 1
3	XXX	DS	XXX-767-001	3	COMPLETED	COMPLETED	DISPOSITION EVENT	STUDY PARTICIPATION	2016-02-25	TREATMENT 1
4	XXX	DS	XXX-767-001	4	COMPLETED	COMPLETED	DISPOSITION EVENT	ISONIAZID	2016-03-14	TREATMENT 2
5	XXX	DS	XXX-767-001	5	COMPLETED	COMPLETED	DISPOSITION EVENT	STUDY PARTICIPATION	2016-03-24	TREATMENT 2

- EPOCH can be now used for any DSCAT (before restriction on DISPOSITION EVENT)

Other Changes

9. Study References (New Section)

Used when it is necessary to establish study-specific terminology that will be used in subject data

- Device Identifier (DI): establishes identifiers for devices, used to populate the variable SPDEVID. Domain specification, assumptions and examples → SDTMIG-MD
- Non-host Organisms Identifiers (OI): to store the taxonomic nomenclature of microbes or parasites either experimentally determined during the study or previously known (e.g., lab strains used as reference)
- Identifiers for Pharmacogenomic/genetic Biomarkers (PB), which are composed of groups of genetic variations → Domain specification, assumptions and examples in SDTMIG-PGx

Other Changes

Other SDTM Guidance to consider mentioned in the Ig:

- SDTMIG-AP (Associated Persons)
- SDTMIG-MD (Medical Devices)
- SDTMIG-PGx (Pharmacogenomics/Genetics for data about biospecimens)

Version of SDTM domains

- 3.3 if domain changed from previous version 3.3 (further rules to develop)
- 1.0 for new domain
- 3.2 if domain did not change from previos version 3.2

Other Changes

- 6.3.12 Physical Examination: Clarified to limit the use of PE in tradition physical examination: Evaluation of targeted body systems (e.g., cardiovascular, endocrine, ophthalmic, reproductive) as part of therapeutic specific assessments should be represented in an appropriate body system domain (e.g., CV, ED, OE, RP).

- 6.3.13.3: Disease Response and Clinical Classification: Scope of RS (a domain for the assessment of disease response to therapy) is to record any situation where clinical classification based on published criteria is used (not only for oncology disease)

- 6.3.16 Tumor/Lesions Domain: Scope of TU/TR extended to any situation where lesions measurement is needed (not only for oncology disease)

- 7.1.2 Definitions of Trial Design Concepts (new section): Provides clarifications on Trial Design Elements, e.g., Epoch, Study Cells, Element, etc.

What questions the Ig doesn't answer yet

Multiple screen-failures / registrations in the same study

From FDA TCG

- For subjects with **multiple enrollments** within a single study, the primary enrollment should be submitted in DM. Additional enrollments should be included in a custom domain with a similar structure to DM
- For subjects with **multiple screenings** and no subsequent enrollment, include the primary screening in DM with additional screenings in a custom domain with a structure similar to DM.
- For subjects with **multiple screenings and subsequent enrollment**, include the enrollment in DM with screenings in a custom domain with a structure similar to DM

Not yet clear indications in SDTM Ig how to handle this

Conclusions

- SDTM Standards in Development
  - SDTMIG v3.3 Conformance Rules (in progress)
  - SDTMIG-Medical Devices v1.1 (public review completed)
  - SDTMIG-PGx v1.1 (in progress)
  - SDTM Metadata Submission Guidelines (MSG) v2.0 (in progress)

SDTM 'Diff' Course

½ day course to cover the differences between SDTM standard versions v1.4 to v1.7 and SDTM Ig v3.2 to v3.3

http://www.cvent.com/events/cdisc-2019-europe-interchange/event-summary-bbde371c70f54daea88ded300a230f43.aspx


感謝你
Danke
Gracias
Grazie
Merci
Thanks!
THANK
YOU!