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SDTMIG v3.3: New domains – new benefits

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ABSTRACT

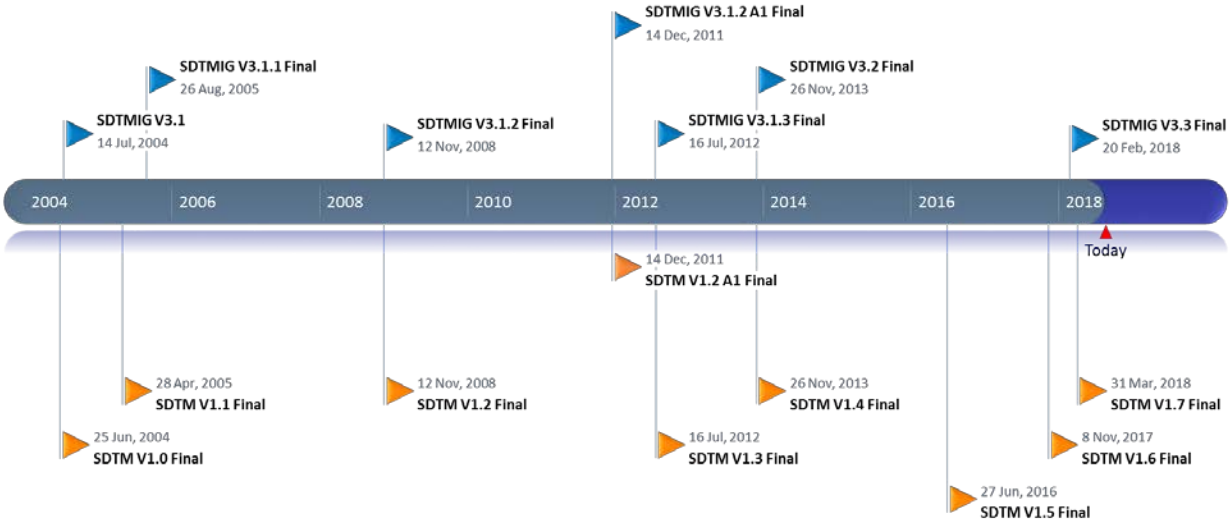
In 2018 CDISC will release SDTM v1.7 and SDTMIG v3.3. New variables will be introduced that will make it easier to represent the captured data or better diversify the data. Besides that, the new Implementation Guide will contain some new domains. In this paper we want to guide you through the newly published domains, their use and advantages.

Several Therapeutic Area User Guides (TAUGs) have been published over the last years. In these TAUG new domains and variables have been suggested. For example, the TAUG for Asthma has been published as a provisional version. The new domains indicated in this TAUG like Respiratory System Findings (RE) and Procedure Agents (AG) could be used but they had to be considered as custom domains. With the publication of SDTMIG v3.3 those domains have now been standardized and can be used as standard domains with fixed variables names.

INTRODUCTION

The paper will give a bit of history about the Study Data Tabulation Model (SDTM) and its associated Implementation Guide for Human Clinical Trials (SDTMIG). Further in the paper we will describe the different new domains that have been published. These new domain did not appear out of thin air but have previously been described in the TAUGs.

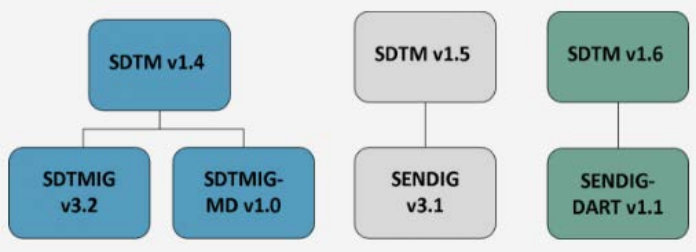
A HISTORY OF SDTM



The first modern version of the model was published in 2004 together with Implementation Guide version 3.1. Over the course of the next 10 years several models and IGs have been published at the same time. At the end of 2013 we could see a difference in the naming convention; while the model continued using the same numbering at that moment the version of the IG was considered more major and the numbering changed. Besides supporting the SDTMIG V3.2, model V1.4 was also created to support the SDTMIG-MD V1.0 (implementation guide for Medical Devices).

In 2011 there was a small release of an Amendment to the model and IG of version 1.2. This Amendment 1 included new variables for the Demographics (DM) domain and for the Events domain class, mainly for the Adverse Events (AE) domain. New variables were included to upgrade the MedDRA dictionary coding from the Supplemental Qualifier to the parent domain.

In 2016 and 2017, two new versions of the model have been released but no associated implementation guide. These 2 models were published mainly to support the Standard for the Exchange of Non-clinical Data (SEND). V1.5 was released to support SENDIG V3.1 and V1.6 was released to support SENDIG-DART V1.1 (Developmental And Reproductive Toxicology).



SDTMIG 3.3

At the beginning of 2018 version 1.7 of the model and version 3.3 of the IG have been completed by the SDS team. "SDS" stands for Submission Data Standards. The SDS team is responsible for developing and maintaining the SDTMIG. The 2 documents have been finalized but they have not yet been published. The documents have first been published for provisional use: provisional use means that the standard has been published for initial use, and is dependent upon completion of other standards:

- The SDTM Model
- Controlled Terminology (codelists referenced in the SDTMIG are published)
- Conformance Rules
- Metadata in SHARE
- Educational learning objectives

SDTMIG v3.3 is grandfathered such that it will be published as Final (as opposed to Provisional) even though the SDS team is still working on the associated conformance rules. This is an exceptional rule for 2018 as the SDTM standard already passed the public review. The standard has passed the cross-team internal review and been approved by the Standards Review Council (SRC) or the Global Governance Group (GGG) so it could proceed to public review.

According to the standard release schedule the SDTM and SDTMIG will be publically released the first week of November.

NEW VARIABLES

As there are several new versions of the model since the last new IG a lot of new variables have been created. These variables appear in the new domains that will be explained in the next section of this paper. As there are quite some new variables it would be enough information for an extra paper/presentation. An overview of the different new variables can be found in the back-up slides of the presentation.

ORIGIN OF NEW DOMAINS

The new domains described in the next section have previously been described in the different TAUGs. The examples shown underneath are coming from the TAUGs of Diabetes, Asthma, Alzheimer, Multiple Sclerosis … These TAUGs have first been published in 2013 and 2014. This means that all these domains have first been described almost 5 years ago and even before the publication of the previous implementation guide.

NEW DOMAINS

Since the IG V3.2, ten new domains have been generated:

- Trial Design
    - Trial Disease Milestones (TM)
- Special Purpose
    - Subject Disease Milestones (SM)
- Interventions
    - Procedures 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)

In the IG it is stated: “The Morphology domain was introduced in SDTMIG v3.2 when the SDS team planned to represent morphology and physiology findings in separate domains: morphology findings in the MO domain and physiology findings in separate domains by body systems. Since then, the team found that separating morphology and physiology findings was more difficult than anticipated and provided little added value. This led to the decision to expand the body system-based domains to cover both morphology and physiology findings and to deprecate MO in a future version of the SDTMIG”. So all of the new findings domains are “”sub-domains” of the MO domain but system based. One of these domains already existed which is Reproductive System Findings (RP).

TM - TRIAL DISEASE MILESTONES

This domain is used to describe Disease Milestones, which are observations or activities anticipated to occur in the course of the disease under study, and which trigger the collection of data.

Row	STUDYID	DOMAIN	MIDSTYPE	TMDEF	TMRPT
1	XYZ	TM	DIAGNOSIS	Initial diagnosis of diabetes, the first time a physician told the subject they had diabetes	N
2	XYZ	TM	HYPOGLYCEMIC EVENT	Hypoglycemic Event, the occurrence of a glucose level below (threshold level)	Y

In this diabetes study, initial diagnosis of diabetes and the hypoglycemic events that occur during the trial have been identified as Disease Milestones of interest

MIDSTYPE: Disease milestone type is indicating the type of milestone

TMDEF is the definition of the milestone

TMRPT is the milestone repetition indicator: the value is N when it’s a unique event and Y when the event could be repeated

SM - SUBJECT DISEASE MILESTONES

This domain is designed to record the timing, for each subject, of Disease Milestones that have been defined in the Trial Disease Milestones (TM) dataset.

Row	STUDYID	DOMAIN	USUBJID	SMSEQ	MIDS	MIDSTYPE	SMSTDTC	SMENDTC	SMSTDY	SMENDY
1	XYZ	SM	001	1	DIAG	DIAGNOSIS	2005-10			
2	XYZ	SM	001	2	HYPO1	HYPOGLYCEMIC EVENT	2013-09-01T11:00		25	
3	XYZ	SM	001	3	HYPO2	HYPOGLYCEMIC EVENT	2013-09-24T8:48		50	
4	XYZ	SM	002	1	DIAG	DIAGNOSIS	2010-05-15		-1046	

In this study, the Disease Milestones of interest were initial diagnosis and hypoglycemic events, as shown in the TM example.

AG – PROCEDURE AGENTS

A domain for the agents administered to the subject as part of a procedure or assessment, as opposed to drugs, medications, and therapies administered with therapeutic intent.

Row	STUDYID	DOMAIN	USUBJID	AGSEQ	AGTRT	AGPRESP	AGOCCUR	AGDOSE	AGDOSU	AGROUTE	VISIT	AGENDTC
1	XYZ	AG	XYZ-001-001	1	SALINE	Y	Y	0	SQ-u/mL	RESPIRATORY (INHALATION)	SCREENING	2010-11-07T10:56:00
2	XYZ	AG	XYZ-001-001	2	GRASS	Y	Y	250	SQ-u/mL	RESPIRATORY (INHALATION)	SCREENING	2010-11-07T11:19:00
3	XYZ	AG	XYZ-001-001	3	GRASS	Y	Y	1000	SQ-u/mL	RESPIRATORY (INHALATION)	SCREENING	2010-11-07T11:43:00
4	XYZ	AG	XYZ-001-001	4	GRASS	Y	Y	2000	SQ-u/mL	RESPIRATORY (INHALATION)	SCREENING	2010-11-07T12:06:00

This example captures data about the allergen administered to the subject as part of a bronchial allergen challenge (BAC) test. Prior to the BAC, the subject had a skin-prick allergen test to help identify the allergen to be used for the BAC test. It identified grass as the allergen to be used in the BAC test. Data from the allergen skin test are not shown, but the CRF for the BAC includes collection of the allergen chosen for use in the BAC. A predetermined set of ascending doses of the chosen allergen was used in the screening BAC test. The results of the screening BAC are not shown, but would be represented in the RE domain.

ML – MEAL DATA

The Meal Data domain model reflects collected details describing a subject's food product consumption.

Row	STUDYID	DOMAIN	USUBJID	MLSEQ	MLTRT	MLCAT	MLPRESP	MLOCCUR	MLDOSE	MLDOSU	MLSTDTC	MLENDTC	RELMIDS	MIDS	MIDSDTC
1	XYZ	ML	XYZ-001-001	1	SNACK	HYPOGLYCEMIA EVALUATION	Y	Y			2015-06-03T14:15		LAST MEAL PRIOR TO	HYPO1	2015-06-03T19:20
2	XYZ	ML	XYZ-001-001	2	NUTRITIONAL DRINK	HYPOGLYCEMIA EVALUATION	Y	Y	8	oz	2015-09-03T08:30		LAST MEAL PRIOR TO	HYPO2	2015-09-03T17:00
3	XYZ	ML	XYZ-001-001	3	MEAL	HYPOGLYCEMIA EVALUATION	Y	Y			2015-12-31T19:00		LAST MEAL PRIOR TO	HYPO3	2016-01-01T10:30

Data was collected about the last meal before each hypoglycemic event.

CV – CARDIOVASCULAR SYSTEM FINDINGS

A domain for morphological and physiological findings related to the cardiovascular system, including the heart, blood vessels, and lymphatic vessels.

Row	STUDYID	DOMAIN	USUBJID	CVSEQ	CVGRPID	CVTESTCD	CVTEST	CVORRES	CVSTRESC	CVLOC	CVMETHOD	VISITNUM	VISIT	CVDTC
1	ABC123	CV	002-2004	1	2	ANEURIND	Aneurysm Indicator	Y	Y	THORACIC AORTA	TRANSTHORACIC ECHOCARDIOGRAPHY	2	BASELINE	2015-06-09T14:20
2	ABC123	CV	002-2004	2	2	DISECIND	Dissection Indicator	Y	Y	THORACIC AORTA	TRANSTHORACIC ECHOCARDIOGRAPHY	2	BASELINE	2015-06-09T14:20
3	ABC123	CV	002-2004	3	2	STANFADC	Stanford AoD Classification	CLASS A	CLASS A	THORACIC AORTA	TRANSTHORACIC ECHOCARDIOGRAPHY	2	BASELINE	2015-06-09T14:20
4	ABC123	CV	002-2004	4		ANEURIND	Aneurysm Indicator	N	N	SUPRARENAL AORTA	TRANSTHORACIC ECHOCARDIOGRAPHY	2	BASELINE	2015-06-09T14:20
5	ABC123	CV	002-2004	5		ANEURIND	Aneurysm Indicator	N	N	INFRARENAL AORTA	TRANSTHORACIC ECHOCARDIOGRAPHY	2	BASELINE	2015-06-09T14:20

The example shows various findings related to the aortic artery. This example also shows the evaluation for the presence or absence of abdominal aortic aneurysms. The suprarenal, infrarenal, and thoracic sections of the aorta were examined for aneurysms. This level of anatomical location detail can be found in CVLOC. The records in rows 1 to 3 are related assessments regarding an aneurysm in the thoracic aorta and are grouped together using the CVGRPID variable.

MK – MUSCULOSKELETAL SYSTEM FINDINGS

A domain for morphological and physiological findings related to the system of muscles, tendons, ligaments, bones, joints, and associated tissues.

Row	STUDYID	DOMAIN	USUBJID	MKSEQ	MKTESTCD	MKTEST	MKORRES	MKSTRESC	MKSTRESN	MKLOC	MKLAT	MKMETHOD	VISITNUM	VISIT	MKDTC
1	DEF	MK	DEF-138	1	TNDRIND	Tenderness Indicator	Y	Y		TEMPOROMANDIBULAR JOINT	RIGHT	PHYSICAL EXAMINATION	2	WEEK 4	2012-09-30
2	DEF	MK	DEF-138	2	SWLLIND	Swollen Indicator	Y	Y		TEMPOROMANDIBULAR JOINT	RIGHT	PHYSICAL EXAMINATION	2	WEEK 4	2012-09-30
3	DEF	MK	DEF-138	3	TNDRIND	Tenderness Indicator	N	N		TEMPOROMANDIBULAR JOINT	LEFT	PHYSICAL EXAMINATION	2	WEEK 4	2012-09-30
4	DEF	MK	DEF-138	4	SWLLIND	Swollen Indicator	N	N		TEMPOROMANDIBULAR JOINT	LEFT	PHYSICAL EXAMINATION	2	WEEK 4	2012-09-30

This example illustrates the data collected for the Swollen/Tender Joint Count assessment, specifically the 68-joint count. After determining whether each joint is swollen or tender, the assessment includes adding up the number of "Yes" responses for swollen joints and tender joints to obtain a total count for swollen joints and tender joints. Total counts were not collected on the CRF since they were to be derived in ADaM datasets. Data collection included a field for marking a joint "Not Evaluable" when that joint met a condition (e.g., infection of the overlying tissue or skin, grossly edematous, fused) which precluded joint assessment. As specified by the protocol and the protocol-related joint assessor training. A field for the reason that a joint was not evaluable was not needed. Note that there was a

field for marking a joint assessment as "Not Done"; this was to be used if the joint assessor overlooked or missed that joint while performing the joint assessment.

The data collected are represented in the Musculoskeletal System Findings (MK) domain. Each joint location is specified in MKLOC with laterality ("RIGHT" or "LEFT") in MKLAT. Since the evaluation includes a large number of joints that would result in many records, only a subset of the data collected is shown.

NV – NERVOUS SYSTEM FINDINGS

A domain for physiological and morphological findings related to the nervous system based on neurological examinations or procedures, involving the brain, spinal cord, the cranial and spinal nerves, autonomic ganglia, and plexuses.

Row	STUDYID	DOMAIN	USUBJID	SPDEVID	NVSEQ	NVREFID	NVLNKID	NVTESTCD	NVTEST	NVORRES	NVORRESU	NVLOC	NVDIR	NVMETHOD	NVDTC
1	ABC123	NV	AD01-101	22	1	1236	03	SUVR	Standard Uptake Value Ratio	0.95	RATIO	PRECUNEUS		PET/CT SCAN	2012-05-22
2	ABC123	NV	AD01-101	22	2	1236	03	SUVR	Standard Uptake Value Ratio	1.17	RATIO	CINGULATE CORTEX	POSTERIOR	PET/CT SCAN	2012-05-22
3	ABC123	NV	AD01-102	22	1	1237	04	SUVR	Standard Uptake Value Ratio	1.21	RATIO	PRECUNEUS		PET/CT SCAN	2012-05-22
4	ABC123	NV	AD01-102	22	2	1237	04	SUVR	Standard Uptake Value Ratio	1.78	RATIO	CINGULATE CORTEX	POSTERIOR	PET/CT SCAN	2012-05-22
5	ABC123	NV	AD01-103	44	1	1238	05	SUVR	Standard Uptake Value Ratio	1.52	RATIO	PRECUNEUS		FDGPET	2012-05-22
6	ABC123	NV	AD01-103	44	2	1238	05	SUVR	Standard Uptake Value Ratio	1.63	RATIO	CINGULATE CORTEX	POSTERIOR	FDGPET	2012-05-22

The example demonstrates the SDTM-based modeling of the nervous system information collected and generated (as described above) from separate PET or PET/CT procedures. This example shows measures for standard uptake value ratios taken from three PET scans. SPDEVID shows the scanner used. NVLNKID can be used to link back to the imaging procedure record in the PR domain (PRLNKID), as well as to the tracer administration record in the AG domain (AGLNKID). AGLNKID would be used to determine which tracer uptake is being measured (SUVR), and therefore to which biomarker the findings pertain. NVDTC corresponds to the date of the PET or PET/CT procedure from which these results were obtained.

OE – OPHTHALMIC EXAMINATIONS

The OE domain is for findings related to tests that measure a person's ocular health and visual status, to detect abnormalities in the components of the visual system, and to determine how well the person can see.

Row	STUDYID	DOMAIN	USUBJID	FOCID	OESEQ	OETESTCD	OETEST	OEORRES	OESTRESC	OELOC	OELAT	OEDIR	OEMETHOD	OEDTC
1	XXX	OE	XXX-450-110	OS	1	INTP	Interpretation	NORMAL	NORMAL	LENS	LEFT		SLIT LAMP	2012-03-20
2	XXX	OE	XXX-450-110	OD	2	INTP	Interpretation	ABNORMAL	ABNORMAL	LENS	RIGHT		SLIT LAMP	2012-03-20
3	XXX	OE	XXX-450-110	OD	3	OEEXAM	Ophthalmic Examination	RED SPOT VISIBLE	RED SPOT VISIBLE	CONJUNCTIVA	RIGHT	MULTIPLE	SLIT LAMP	2012-03-20

This example shows a general anterior segment examination performed on each eye at one visit, with the purpose of evaluating general abnormalities.

RE – RESPIRATORY SYSTEM FINDINGS

A domain for morphological and physiological findings related to the respiratory system, including the organs that are involved in breathing, such as the nose, throat, larynx, trachea, bronchi, and lungs.

Row	STUDYID	DOMAIN	USUBJID	SPDEVID	RESEQ	RETESTCD	RETEST	REORRES	REORRESU	REORREF	...	VISITNUM	VISIT	REDTC
1	XYZ	RE	XYZ-001-001	ABC001	1	FEV1	Forced Expiratory Volume in 1 Second	2.73	L	3.37		2	VISIT 2	2013-06-30
2	XYZ	RE	XYZ-001-001	ABC001	2	FVC	Forced Vital Capacity	3.91	L	3.86		2	VISIT 2	2013-06-30
3	XYZ	RE	XYZ-001-001	ABC001	3	FEV1PP	Percent Predicted FEV1	81	%			2	VISIT 2	2013-06-30

4	XYZ	RE	XYZ-001-001	ABC001	4	FVCPP	Percent Predicted Forced Vital Capacity	101.3	%			2	VISIT 2	2013-06-30
5	XYZ	RE	XYZ-001-001	DEF999	5	PEF	Peak Expiratory Flow	6.11	L/s	7.33		4	VISIT 4	2013-07-17

This example shows results from several spirometry tests using either a spirometer or a peak flow meter. When spirometry tests are performed, the subject usually makes several efforts, each of which produces results, but only the best result for each test is used in analyses. In this study, the sponsor collected only the best results. The Device Identifiers (DI) domain was submitted for device identification, and the Device In-Use (DU) domain was submitted to provide information about the use of the device.

Because the original and standardized units of measure are identical in this example, RESTRESC, RESTRESN, RESTRESU, and RESTREFN are not shown. Spirometry test values are compared to a predicted value, rather than a normal range. Predicted values are represented in REORREF which is a new variable that was added in SDTM V1.5.

UR – URINARY SYSTEM FINDINGS

A domain for morphological and physiological findings related to the urinary tract, including the organs involved in the creation and excretion of urine, such as the kidneys, ureters, bladder, and urethra.

Row	STUDYID	DOMAIN	USUBJID	URSEQ	URTESTCD	URTEST	URORRES	URORRESU	URSTRESC	URSTRESN	URSTRESU	URLOC	URLAT	URDIR	URMETHOD	URDTC
1	ABC	UR	ABC-001-011	1	LENGTH	Length	12.6	cm	126	126	mm	KIDNEY	LEFT		CT SCAN	2016-03-30
2	ABC	UR	ABC-001-011	2	COUNT	Count	2		2	2		RENAL ARTERY	LEFT		CT SCAN	2016-03-30
3	ABC	UR	ABC-001-011	3	COUNT	Count	1		1	1		RENAL VEIN	LEFT		CT SCAN	2016-03-30
4	ABC	UR	ABC-001-011	4	HEMAIND	Hematoma Indicator	ABSENT		ABSENT			KIDNEY			CT SCAN	2016-03-30
5	ABC	UR	ABC-001-011	5	SGDMGIND	Surgical Damage Indicator	PRESENT		PRESENT			KIDNEY, CORTEX	LEFT	SUPERIOR	CT SCAN	2016-03-30

This example shows measurements of the kidney, number of renal arteries and veins, and presence/absence results for pre-specified abnormalities of the kidneys. These findings were made using CT imaging.

CONCLUSION

The use of provisional standards is encouraged but with an appropriate risk assessment. Once the standard gets released as final, updates might have occurred that will not be mentioned. When new standards are published have a look at the revision history at the end of the document and/or the differences file which is published on the SHARE.

REFERENCES

Standards in development: https://www.cdisc.org/standards/in-development
Standards Updates Table: https://wiki.cdisc.org/display/TEAM/Standards+Updates+Table

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