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A Critique of the Use of the Medical Device SDTM Domains in Therapeutic Area User Guides

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ABSTRACT

The Clinical Data Interchange Standards Consortium (CDISC) encompasses a variety of standards for medical research. These standards were originally developed with drug development in mind. Medical Device standards have been developed for the Submission Data Tabulation (SDTM) model. Seven SDTM domains have been developed for Medical Devices. Therapeutic Area User Guides (TAUGs) have been a recent focus to provide advice, example and explanations for collecting and submitting data for a specific disease. Interestingly, the use of the seven Medical Device SDTM domains are being used more frequently in the TAUGs than in actual device submissions. This paper will focus on the use of these seven Medical Device SDTM domains in the TAUGs. Twenty-two of the twenty-six TAUGs have examples of device data, but there are differences in these examples. Increased participation by device experts in the development of TAUGs would be beneficial to resolving these differences.

INTRODUCTION

The purpose of the Therapeutic Area User Guides (TAUGs) is to facilitate solutions using the various CDISC standards for specific diseases or conditions. Typically, the TAUGs provide advice, examples, and explanations regarding the use of CDASH, SDTM, and/or ADaM standards within the context of the specific therapeutic area.

The seven SDTM domains have been previously described (Smoak et al 2012). The medical device SDTM Implementation Guide (STDMIG-MD v1.0) is available on the CDISC website (http://www.cdisc.org/sdtmig). Briefly, the seven Medical Device domains are:

Device Identifiers (DI)

This special-purpose domain contains the data that identifies a specific device unit under study.

Device Properties (DO)

The Device Properties domain is a Findings domain and reports the characteristics of the device that are important to include in the submission, and that do not vary over the course of the study, but do not uniquely identify the device.

Device-In-Use (DU)

Device-In-Use is a Findings domain that contains the values of measurements and settings that are intentionally set on a device when it is used, and may vary from subject to subject or another target.

Device Exposure (DX)

Device Exposure is an Interventions domain that records the details of a subject's exposure to a medical device under study.

Device Events (DE)

Device Events is an Events domain that contains information about various kinds of device-related events, such as malfunctions.

Device Tracking and Disposition (DT)

The Device Tracking domain is an Events domain that represents a record of tracking events for a given device.

Device-Subject Relationships (DR)

The Device-Subject Relationships domain is a special-purpose domain that links each subject to the devices used in the study

The growth of the number of TAUGs is accelerating from one in 2011 to twenty-six in 2018. Previously, it has been shown that DI, FA and MH are the most frequently used domains in the TAUGs (Ulander and Both, 2015). The TAUGs have a variety examples of device data and provide examples of the complexity of device data (Smoak 2017). For example, software version of a device is captured in the DO domain for Parkinson's, Polycystic Kidney Disease, and QT TAUGs, while it is represented in the DU domain for the Traumatic Brain Injury TAUG (Smoak 2017). The distinction between DO and DU would be whether or not it is a static property (DO) of a device or varies based upon the subject or use instance of use (DU). While the TAUGs provide some very good uses of device data in clinical trials, there are also some differences in the device data examples in the TAUGs.

THERAPEUTIC AREA USER GUIDES AND MEDICAL DEVICES

METHOD

All of the TAUGs available on the CDISC website (https://www.cdisc.org/standards/therapeutic-areas) were downloaded. Only TAUGs with a download-able TAUG are included in this paper. This means that TAUGs which have gone through public review or are current being developed are not included in this paper.

Once the TAUGs were downloaded, I went through and looked for instances of device domains in the TAUGs. As I went through each of the TAUGs, I noticed that there were TAUGs that also mentioned device data but did not give examples. So, I also compiled this information along with the actual device data examples in the TAUGs. Appendix Table A is a compilation of all the device-related information that I found the TAUGs.

RESULTS

Twenty-two of the 26 TAUGs published as of this writing have examples of device data (Appendix Table A). Appendix Table A can be thought of as the raw data and Table 1 summarizes the information in Appendix Table A. Appendix Table A shows that there is both diversity and similarity of device data across the TAUGs. The diversity of device data is clear when looking at the examples of device data in Appendix Table A. The similarity of device data is less apparent in Appendix Table A, but eight of the TAUGs mention imaging data and six mention diagnostic assay tests.

Appendix Table A details some of the differences in the TAUGs with respect to examples of device data. The last column of this table details examples where device data is mentioned in the TAUG, but no specific example of device data is provided. For example, a PR dataset that identifies a device, but no DI dataset example is provided. While this may not be absolutely required for TAUGs to have DI for every PR that identifies a device, the purpose of the TAUG is to provide advice, examples and explanations regarding CDASH, SDTM and ADaM. Since pharmaceutical companies may not be familiar with the implementation of device data, it would be beneficial to pharmaceutical companies if the TAUGs provided actual examples for all types of device data, especially when PR identifies a device. Furthermore, there are three TAUGs (Alzheimer, Cardiovascular and Duchenne Muscular Dystrophy) which have examples of device identified in a PR dataset and associated device data in device datasets. These examples help to demonstrate how to implement device datasets when a device is identified in a PR dataset.

The differences in device data in the TAUGs are detailed here:

- Sixteen of the TAUGs have actual examples of device data:

  - These sixteen TAUGs are identified in Table 1 in the column for “DI”
- Eight of the TAUGs mention device data, but do not provide examples:
  - These eight TAUGs are identified in Table 1 in the column for “Could Have Device Domains”
  - Five of the eight TAUGs have PR datasets which mention a device, but do not identify the device in DI (see column “PR without DI” in Table 1). Examples of PR without DI include:
    - The Influenza TAUG has a PR example of assistive ventilation devices, but no example of device data for the assistive ventilation devices. In contrast, the Duchenne Muscular Dystrophy TAUG has a PR example of assistive ventilation devices and the DI dataset identifies the specific devices.
    - The Major Depressive Disorder TAUG identifies Deep Brain Stimulation (DBS) in a PR dataset, but no device data examples. In contrast, the in the Parkinson TAUG, DBS is identified in a PR dataset and there are examples of device data for five of the device domains.
  - Two of the eight TAUGs could add device data for the examples that they mention (see rows for Chronic Hepatitis C and Rheumatoid Arthritis in Table 1):
    - The Chronic Hepatitis C TAUG could add DI example data for the viral load assessments mentioned in the TAUG.
    - The Rheumatoid Arthritis TAUG could add DE where it mentions that DE could be modeled for medications which are injected using a syringe or autoinjector. Additionally, DI could be added to identify the syringe or autoinjector used.
  - One of the eight TAUGs could borrow identical examples from another TAUG (see row for COPD in Table 1).
    - The Asthma and COPD TAUGs have the same peak flow meter and spirometry examples. However, the Asthma TAUG shows examples of DI and DU whereas the COPD TAUGs omits these examples of DI and DU.
- Two of the TAUGs fall into both categories (actual examples of device data and mention device data, but do not provide examples):
  - See the rows in Table 1 for Cardiovascular and Duchenne Muscular Dystrophy TAUGs where the columns for “DI” and “Could Have Device Domains” are both populated.
  - For the Cardiovascular TAUG (see Appendix Table A), in the first example, DI is used for both balloon angioplasty and pacemaker implantation. However, in the second example, PR mentions the implantation of stents. In this example, the DI dataset could have been used to identify the stents used.
  - For the Duchenne Muscular Dystrophy TAUG (see Appendix Table A) there are four examples with actual device data and three examples without device data. The four examples which have actual device data examples are: Assistive devices (powered wheelchair), imaging, musculoskeletal assessments and assisted ventilation devices. The three that mention device data, but do not provide examples are: Cardiac assessments, muscle biopsy and Pulmonary Function Tests.
- Other differences are with respect to similar device examples across the TAUGs:
  - Eight TAUGs mention the use of imaging devices (such as CT Scans, MRI and PET Scans), but six of the eight provide imaging device examples:

- The six TAUGs that have imaging device examples are: Alzheimer's Disease, Duchenne Muscular Dystrophy, Multiple Sclerosis, Parkinson's Disease, Polycystic Kidney Disease and Traumatic Brain Injury
- The two TAUGs which mention imaging devices, but do not have examples of imaging device data are: Breast Cancer and Prostate Cancer

- Six of the TAUGs mention diagnostic assay tests (such as PCR assays), but five of the six provide diagnostic assay examples:
  - The five TAUGs that have diagnostic assay test examples are: Ebola, Influenza, Malaria, Tuberculosis and Virology
  - The one TAUG which mention diagnostic assay tests, but do not have examples of diagnostic assay tests is: Chronic Hepatitis C

Please note that in Appendix Table A and Table 1 that the Cardiovascular and Duchenne Muscular Dystrophy TAUGs fall into both categories – explicit examples of device data and examples which should have examples of device data. So, the Cardiovascular and Duchenne Muscular Dystrophy TAUGs are counted as TAUGs with DI actual device examples (n=16) and as TAUGs that should have device domains (n=8). Thus, twenty-two of the TAUGs have examples of device data because the Cardiovascular and Duchenne Muscular Dystrophy TUAGs are being counted twice.

Table 1. TAUGs and Device Domains

	DI	DO	DU	DX	DT	DE	DR	PR without DI Domain	Could Have Device Domains	None
Alzheimer's (v2)	X	X	X							
Asthma (v1)	X		X							
Breast Cancer (v1)								X	DI, DO, DT	
Cardiovascular (v1)	X							X	DI, DU	
Chronic Hepatitis C (v1)									DI	
COPD (v1)									DI, DU	
Diabetes (v1)	X									
Diabetic Kidney Disease (v1)										X
Duchenne Muscular Dystrophy (v1)	X		X	X					DI	
Dyslipidemia (v1)										X
Ebola (v1)	X									
Influenza (v1.1)	X							X	DI	
Kidney Transplant (v1)	X									
Malaria (v1)	X									
Major Depressive Disorder (v1)								X	DI	
Multiple Sclerosis (v1)	X		X							

Pain (v1.1)										X
Parkinson's (v1)	X	X	X	X		X	X			
Polycystic Kidney Disease (v1)	X	X	X				X			
Prostate Cancer (v1)								X		
QT Studies (v1)	X	X								
Rheumatoid Arthritis (v1)									DI, DE	
Schizophrenia (v1.1)										X
Traumatic Brain Injury (v1)	X	X	X							
Tuberculosis (v2)	X									
Virology (v2.1)	X									
Totals	16	5	7	2	0	1	2	5	8	4

SUMMARY

Twenty-two of the twenty-six TAUGs mention device data. However, there are differences in the presentation of the device data in the TAUGs:

- Sixteen of the TAUGs have actual examples of device data
- Eight of the TAUGs mention device data, but do not provide examples
    - Five of the eight have PR datasets which mention a device, but do not identify the device in DI
    - Two of the eight TAUGs could add device data for the examples that they mention
    - One of the eight TAUGs could borrow identical examples from another TAUG
- Two of the TAUGs fall into both categories (actual examples of device data and mention device data, but do not provide examples)
- Other differences are with respect to similar device examples across the TAUGs
    - Eight TAUGs mention the use of imaging devices
        - Six of the eight provide imaging device examples.
    - Six of the TAUGs mention diagnostic assay tests
        - Five of the six provide diagnostic assay examples

DISCUSSION AND CONCLUSIONS

While TAUGs may not be required to provide examples for every type of data that they mention, it would be helpful to pharma companies to see correct implementation of the device domains in the TAUGs. I personally get questions from pharma companies about implementation of the device domains and I have personally seen incorrect implementation of device domains by pharma companies. Hopefully, good examples in TAUGs would help with this problem of incorrect implementation of device domains by pharma companies. I realize that people who work on the TAUGs are very dedicated to producing the best TAUGs possible. So, this analysis of the TAUGs with respect to device data is not intended to put down their efforts. Rather it is intended to open further discussion and, hopefully good solutions to the problem. Part of the problem lies with the lack of device experts to spend time on reviewing the TAUGs. Over the past several months, the Medical Device Team has done a better job of reviewing TAUGs. It would be even better to have device experts involved in the development of TAUGs.

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Appendix Table A. TAUGs and Examples of Device Data

TAUG (version)	Example(s) of Device Domains in TAUG	Could Have Example(s) of Device Domains in TAUG
Alzheimer's Disease (v2)	(1) Device information from lumbar procedure to collect CSF such as spinal needles, tube lots used to store samples, freezer number and microwell plate ID for lab instrument. Examples of DI, DO. (2) Imaging devices such as MRIs. Examples of DI, DO, DU.	
Asthma (v1)	(1) Peak flow meter. Examples of DI. (2) Spirometry and the reference equation used for spirometry. Examples of DI, DU.	
Breast Cancer (v1)		(1) PR dataset for tracer chips implanted for subsequent surgery. Note: The TAUG mentions that device domains DI, DO and DT can be modeled by following SDTMIG-MD for the tracer chips. (2) PR dataset for imaging devices (MRI and CT Scan) used for tumor identification.
Cardiovascular (v1)	(1) Balloon angioplasty. Example of DI. (1) Pacemakers implantation. Examples of DI.	(1) PR datasets that identify that stents were implanted.
Chronic Hepatitis C (v1)		(1) Viral load assessments of HCV are mentioned. No examples are given. Could have DI if viral load examples were provided.
COPD (v1)		(1) Peak flow meter and spirometry. Note: The COPD TAUG uses the same device data examples as the Asthma TAUG.
Diabetes (v1)	(1) Glucose meters to measure blood glucose levels. Example of DI.	
Diabetic Kidney Disease (v1)	None	
Duchenne Muscular Dystrophy (v1)	(1) Assistive devices (powered wheelchair). Example of DI, DX.	(1) Cardiac assessments (echocardiography and cardiac MRI)

	(2) DXA scan (imaging). Example of DI, DU. (3) Musculoskeletal assessments (grip dynamometer, pinch gauge and force transducer). Examples of DI. (4) Assisted ventilation devices (CPAP and Chest Cuirass). Example of DI.	(2) Muscle biopsy (needle / incisional biopsy and freezing of sample collected) (3) Pulmonary Function Tests
Dyslipidemia (v1)	None	
Ebola (v1)	(1) Rapid Ebola virus diagnostic test (qRT-PCR). Example of DI. (2) Plate reader used for IgM Ebola antibodies. Example of DI.	
Influenza (v1.1)	(1) Rapid Influenza diagnostic test. Example of DI. (2) NA inhibition assay. Example of DI. (3) Peak flow meter. Example of DI.	(1) PR datasets that identify a mechanical ventilator device.
Kidney Transplant (v1)	(1) Flow cytometer. Example of DI. (2) Multiplex assay for anti-HLA antibodies. Examples of DI.	
Malaria (v1)	(1) G6PD activity. Examples of DI. (2) Hemoglobin point-of-care test. Example of DI. (3) Flow cytometer. Example of DI. (4) Malaria Rapid Diagnostic Test. Example of DI.	
Major Depressive Disorder (v1)		Therapies which use devices: (1) Electroconvulsive therapy (ECT) (2) Vagal nerve stimulation (VNS) (3) Deep brain stimulation (DBS) (4) Transcranial magnetic stimulation (TMS). Note: PR used to identify therapies such as ECT, VNS and TMS. Could use DI to identify the devices associated with these therapies.
Multiple Sclerosis (v1)	(1) Optical Coherence Tomography (OCT) for assessing imaging	

	biomarkers for Multiple Sclerosis. Example of DI. (2) Visual Evoked Potential (VEP) equipment using in the diagnosis and characterization of Multiple Sclerosis. Example of DI, DU.	
Pain (v1.1)	None	
Parkinson's Disease (v1)	(1) Functional neurosurgery using Deep Brain Stimulation (DBS). Examples of DI, DR, DO, DU, DE. (2) Diagnostic imaging (PET-SPECT camera) for radioligand treatment. Example of DX, DI, DR, DO, DU.	
Polycystic Kidney Disease (v1)	(1) Imaging devices such as MRI, CT and Ultrasounds. Example of DI, DO, DU, DR.	
Prostate Cancer (v1)		(1) PR dataset for imaging devices (MRI, CT Scan and Scintigraphy) that are used for tumor identification.
QT Studies (v1)	(1) ECG device. Examples of DI, DO. Note: DI is used to show that the ECG device is a composite of two devices.	
Rheumatoid Arthritis (v1)		(1) The TAUG mentions that device malfunctions could be modeled in the DE domain for Rheumatoid Arthritis medications that are injected using a syringe or autoinjector. (2) The syringe or autoinjector should also be identified as devices.
Schizophrenia (v1.1)	None	
Traumatic Brain Injury (v1)	(1) CT scan. Example of DI, DO, DU. (2) Protective devices such as seat belts, airbags, helmets and body armor. Example of DI.	
Tuberculosis (v2)	(1) Interferon-gamma release assay. Example of DI. (2) Lipoarabinomannan antigen test kit. Example of DI. (3) X-ray. Example of DI.	

	(4) Nucleic Acid Amplification Test. Example of DI. (5) Mycobacterial Detection System. Example of DI. (6) Sputum decontamination kit. Example of DI.	
Virology (v2.1)	(1) Rapid Influenza diagnostic test. Example of DI. (2) RT-PCR kit. Example of DI. (3) NA inhibition assay. Example of DI.	