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ADaM for Medical Devices: Extending the Current ADaM Structures

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ABSTRACT

The current ADaM structures were designed and developed for common drug and biologic studies, which are focused on the subject (USUBJID). In fact, variable USUBJID is a requirement in all standard ADaM dataset structures. Additionally, the ADSL structure of one-record-per-subject is a requirement for submission of drug and biologic studies.

Within medical device studies, subject may or may not be of interest, and USUBJID may not even be collected. Instead, the unique device identifier (SPDEVID) is the primary identifier of interest. This means that the current ADaM structures are usually not a good fit for the analysis needs of medical device studies. This presentation will highlight how ADaM can be extended to work with medical devices data. It focuses on content in an ADaM document, in development at the time of this writing, that is designed specifically to address medical device analysis needs.

INTRODUCTION

This paper describes analysis dataset structures that, at the time of this writing, are in development by the CDISC ADaM team to address the analysis of medical device studies. These structures are:

- ADDL: A Device-Level Analysis Dataset
- Modified BDS: Similar in structure to ADaM BDS, but with different requirements for identifiers
- Modified OCCDS: Similar in structure to ADaM OCCDS, but with different requirements for identifiers

Within this paper, the important variables from each of these proposed medical device standard structures are described, and the proposed structures are compared to existing ADaM standard structures for human drug and biologic clinical studies.

These proposed structures are needed to support analyses that differ from those in studies of drugs and biologics. Some unique medical device analyses include:

- Analysis of Devices
- Analysis of Subjects within each Device
- Analysis of Device Adverse Events
- Time-to-Device-Event Analysis

To fully understand this paper, you are expected to have some knowledge of medical device studies and analysis needs. Additionally, you need to know a little about CDISC, especially ADaM and SDTM. See the Recommended Reading section at the end of this paper for a list of CDISC standards documents most pertinent to this paper. Any CDISC standard document can be downloaded for free from the either the CDISC website https://www.cdisc.org/ or wiki page https://wiki.cdisc.org/.

SUBJECT-LEVEL ANALYSIS DATASET (ADSL)

In human clinical studies of drugs and biologics, ADSL is a required dataset. It is used directly to produce subject-level analyses, such as demographic summaries, plus provides denominator counts for other tables, such as those summarizing subject data over different timepoints.

When subject data is collected in a medical device study, there would be these same needs for an ADSL dataset. When subject-level data is not collected, ADSL would not make sense to include. Therefore, in a medical device study, ADSL is a conditionally-required dataset.

DEVICE-LEVEL ANALYSIS DATASET (ADDL)

ADDL is being developed to serve a similar purpose in medical device study analysis as the ADSL structure in human drug and biologic clinical studies. It can be used directly to produce device-level analyses, such as device demographic summaries. It also can easily provide denominator counts for other tables, such as those that summarize device data over different timepoints.

ADDL STRUCTURE

In the proposed ADDL, the unique device identifier (SPDEVID) must be included. Depending on the analysis need, the unique subject identifier (USUBJID) may also be included. This means that SPDEVID is a required variable, while USUBJID is conditionally required.

The variable USUBJID can be included for two different reasons. The first is when multiple devices are used on the same subject, perhaps to study how a subject performs with each device. USUBJID can also be included when multiple subjects use the same device, such as a device to measure subject lab results.

Note that ADaM has no rules around variable order within a dataset, or sort order of rows. How you arrange variables and sort rows in ADDL dataset may or may not be related to whether subjects had multiple devices, or devices were used by multiple subjects.

To help visualize, consider dataset metadata for each of the possible scenarios.

First the case where there is no subject identifier:

Dataset Name	Dataset Description	Dataset Location	Dataset Structure	Key Variables of Dataset
ADDL	Device-Level Analysis Dataset	addl.xpt	one record per device	SPDEVID

Figure 1: ADDL for Devices (no Subjects)

Next, when sorting by device, then subject:

Dataset Name	Dataset Description	Dataset Location	Dataset Structure	Key Variables of Dataset
ADDL	Device-Level Analysis Dataset	addl.xpt	one record per device per subject	SPDEVID, USUBJID

Figure 2: ADDL Sorted by Device and Subject

And finally,when sorting by subject, then device:

Dataset Name	Dataset Description	Dataset Location	Dataset Structure	Key Variables of Dataset
ADDL	Device-Level Analysis Dataset	addl.xpt	one record per subject per device	USUBJID, SPDEVID

Figure 3: ADDL Sorted by Subject and Device

The choice of ADDL structure is dependent on the study. If subject information is not collected, then use the first scenario. If subject level is collected, then determine the sort order of devices and subjects that best suits your study's analysis needs.

Similar to ADSL in human clinical studies, ADDL was designed so that its data can be combined with other device datasets, such as ADaM and SDTM, by using the appropriate merge or join key(s). With ADSL, the merge or join key is simply USUBJID. With ADDL, the merge or join key is at least SPDEVID, plus conditionally USUBJID, when USUBJID is included in ADDL.

ADDL VARIABLES

The most important identifiers for the proposed ADDL standard structure, SPDEVID and USUBJID, were mentioned in the above section: SPDEVID is required, and USUBJID is conditionally required. One other identifier, SITEID, is also required in the proposed ADDL, even if it is the same value across all rows in the dataset. All of these identifiers exist in SDTM, and would be copied unchanged into ADDL.

In the proposed ADDL structure, the start and end date variables (DEVSDT and DEVEDT) are required, however the definitions of DEVSDT and DEVEDT will depend on the study. For example, DEVSDT could be the date a device with implanted and DEVEDT the date explanted, or DEVSDT could be the date the device was turned on and DEVEDT the date turned off. Other dates may be included in addition to, but not instead of, DEVSDT and DEVEDT; this allows you to count on the pair of variables DEVSDT and DEVEDT to define the start and end of device use, regardless of study.

In long-term studies of subjects with multiple devices, it might be useful, especially when subject age could affect efficacy, to capture the age of the subject at the start of each device exposure. AGEDST is the proposed name for the age of the subject at the start of the device, and this is a permissible variable.

Most of the source data needed for ADDL can be found in SDTM domains DI (Device Identifiers), DR (Device-Subject Relationships), PR (Procedures), and DX (Device Exposure).

ADDL EXAMPLE

The following example shows a few rows of an ADDL with multiple devices per subject:

Row	USUBJID	SPDEVID	MODEL	MODELG1	MODELG1N	TYPEGR1	BRTHDT	AGEDST
	Unique Subject Identifier	Sponsor Device Identifier	Model	Device Model Group 1	Device Model Group 1 (N)	Device Type Group 1	Date of Birth	Subject Age at First Exposure to Device
1	1001	G003	Model 1	Model A	1	GENERATOR	1940-01-01	59
2	1001	G2002	Model 2	Model A	1	GENERATOR	1940-01-01	71
3	1001	W0101	Model 123	Model B	2	WIRE	1940-01-01	59

Row	DEVSDT	DEVEDT	DEVIPDT	DEVXPDT	DEVONDT	DEVOFDT	DEVRPDT	DEVMDDT
	Date of First Exposure to Device	Date of Last Exposure to Device	Date Device Implanted	Date Device Explanted	Date Device Turned On	Date Device Turned Off	Date Device Repositioned	Date Device Modified
1	1999-12-01	2011-06-06	1999-12-01	2011-06-06	1999-12-15	2011-03-03	2008-04-01	
2	2011-06-06		2011-06-06		2011-06-06			
3	1999-12-01		1999-12-01		1999-12-15			2014-05-05

Figure 4: Example ADDL Dataset

Additional variables, not shown above, could include flags that denote whether a device was implanted, explanted, etc., which would enable counting for summary tables.

OCCURRENCE DATA STRUCTURE (OCCDS) FOR MEDICAL DEVICES

The proposed Medical Device version of OCCDS is very similar to the current ADaM OCCDS structure. The only differences have to do with the identifier requirements.

OCCDS STRUCTURE AND VARIABLES

The current ADaM OCCDS structure requires USUBJID, which as explained above may not be collected in medical device studies. In the proposed Medical Device version of OCCDS, the variable SPDEVID is required, and the USUBJD requirement has been changed to conditionally required.

There is only one other variable in the proposed Medical Devices OCCDS that is different from the current ADaM OCCDS: ASEQ. The CDISC Notes in the current ADaM OCCDS structure explain that this assigned sequence number ASEQ must be unique within a subject (USUBJID). In the proposed Medical Device OCCDS, sequence number uniqueness is instead required within SPDEVID.

Because of these changes to the dataset identifiers, dataset meta is affected. In the proposed Medical Device OCCDS, SPDEVID is a key variable.

OCCDS EXAMPLE

The following example shows a few rows of a Medical Device OCCDS dataset containing device events:

Row	USUBJID	SPDEVID	DEVSDT	DEVEDT	DETERM	DESTDTC	ASTDT
1	1001	G003	1999-12-01	2011-06-06	POWER CONDITIONING ISSUE	2009-12-28	2009-12-28
2	1001	W0101	1999-12-01		BENT	2013-08-08	2013-08-08

Figure 5: Example OCCDS for Device Events Analysis

Note that:

1. Variables USUBJID and SPDEVID are keys that would be used to merge or join input datasets ADDL and SDTM DE.
2. Variables DEVSDT and DEVEDT would be copied from ADDL.
3. Variables DETERM and DESTDTC would be copied from SDTM DE.
4. Variable ASTDT is a numeric date, derived from the character DESTDTC.
5. This example dataset contains just device events from SDTM domain DE. Other adverse events, not associated with a device, would be found in SDTM AE, and analysed without SPDEVID.

This type of dataset could be used to produce a summary table of device events.

BASIC DATA STRUCTURE (BDS) FOR MEDICAL DEVICES

The proposed Medical Device version of BDS is very similar to the current ADaM BDS structure. The only differences have to do with the identifier requirements.

BDS STRUCTURE AND VARIABLES

The current ADaM BDS structure requires USUBJID, which as explained above may not be collected in medical device studies. In the proposed Medical Device version of BDS, the variable SPDEVID is required, and the USUBJD requirement has been changed conditionally required.

There is only one other variable in the proposed Medical Devices BDS that is different from the current ADaM BDS: ASEQ. The CDISC Notes in the current ADaM BDS structure explain that this assigned sequence number ASEQ must be unique within a subject (USUBJID). A similar requirement is needed for device studies, so in the proposed Medical Device BDS, sequence number uniqueness is required within SPDEVID.

Because of these changes to the dataset identifiers, dataset meta is affected. In the current BDS structure, the dataset is structed as one or more records per subject, per analysis parameter, per analysis timepoint, where timepoint is optional. The proposed structure for the Medical Device version of BDS is one or more records per device, per subject, per analysis parameter, per analysis timepoint, where subject and timepoint are optional.

BDS EXAMPLE

The following example shows a few rows of a Medical Device BDS dataset for time-to-device-event analysis:

Row	USUBJID	SPDEVID	PARAM	PARAMCD	STARTDT	ADT	AVAL	CNSR
1	1001	G003	TIME TO FIRST DEVICE EVENT (MONTHS)	TTFDE	1999-12-01	2011-06-06	138	0
2	1001	G2002	TIME TO FIRST DEVICE EVENT (MONTHS)	TTFDE	2011-06-06	2016-08-10	62	1
3	1001	W0101	TIME TO FIRST DEVICE EVENT (MONTHS)	TTFDE	1999-12-01	2013-08-08	164	0

Row	EVENTDESC	SRCDOM	SRCVAR	SRCSEQ
1	DEVICE REPOSITIONED	ADDATES	ADT	2
2	END OF STUDY	ADDATES	ADT	10
3	DEVICE BENT	ADDATES	ADT	8

Figure 6: Example BDS for Time-to-Device-Event Analysis

Notes:

1. This time-to-device-event dataset looks very similar to a typical time-to-event dataset found in drug and biologic studies. The only difference here is the inclusion of SPDEVID.
2. SRCDOM for all rows is ADDATES. This idea of using an intermediate dataset called ADDATES to collect all the dates that could be used as events or censoring was first published in the Prostate Cancer Therapeutic Area User Guide (Provisional, April 2017).

The example ADDATES for the above time-to-device-event dataset is:

Row	USUBJID	SPDEVID	ASEQ	ADT	ADTDESC	ADTDESCD	SRCDOM	SRCVAR	SRCSEQ
1	1001	G003	1	1999-12-01	Date of First Exposure to Device	DEVSDT	ADDL	DEVSDT	1
2	1001	G003	2	2008-04-01	Date Device Repositioned	DEVRPDT	ADDL	DEVRPDT	1
3	1001	G003	3	2009-12-28	Date of Device Event	ASTDT	ADDE	ASTDT	1
4	1001	G003	4	2011-03-03	Date Device Turned Off	DEVOFDT	ADDL	DEVOFDT	1
5	1001	G003	5	2011-06-06	Date Device Explanted	DEVXPDT	ADDL	DEVXPDT	1
6	1001	G2002	6	2011-06-06	Date of First Exposure to Device	DEVSDT	ADDL	DEVSDT	2
7	1001	W0101	7	1999-12-01	Date of First Exposure to Device	DEVSDT	ADDL	DEVSDT	3
8	1001	W0101	8	2013-08-08	Date of Device Event	ASTDT	ADDE	ASTDT	2
9	1001	W0101	9	2014-05-05	Date of Device Modified	DEVMDDT	ADDL	DEVMDDT	3
10	1001		10	2016-08-10	End of Study Date	EOSDT	ADSL	EOSDT	.

Figure 7: Example ADDATES Intermediate Dataset

Note that:

1. All rows are specific to a single device, other than row 10 which is the end of study date (used for censoring)
2. Variable ASEQ is created within this intermediate dataset for the sole purpose of being used as a reference in the time-to-device-event dataset. Notice that row 1 in Figure 6 points to ADDATES sequence number 2, which is the row the describes the device repositioning. Whenever one ADaM dataset is used as input to another ADaM dataset, the variable ASEQ in the predecessor dataset is used to provide traceability.
3. While many BDS variables are used in ADDATES, some required BDS variables are not included, such as PARAM, PARAMCD, and either AVAL or AVALC. As an intermediate dataset not being used directly for analysis, these standard and required BDS variables are not needed.

CONTROLLED TERMINOLOGY FOR CLASS

Define-XML uses controlled terminology for CLASS to describe the structure of every ADaM dataset. At the time of this writing, only 4 choices exist for ADaM dataset class:

1. SUBJECT-LEVEL ANALYSIS DATASET
2. BASIC DATA STRUCTURE
3. OCCURRENCE DATA STRUCTURE
4. ADAM OTHER

Items 1-3 are ADaM structures used in human clinical studies. ADaM datasets that do not fit into one of the first three classes listed are of class “ADAM OTHER”.

It is the intention to add a class of “DEVICE-LEVEL ANALYSIS DATASET”, but until that happens the only choice for an ADDL dataset as described in this document would be “ADAM OTHER”.

For the modified BDS and OCCDS structures described, you could either refer to them as class “ADAM OTHER”, or use “BASIC DATA STRUCTURE” and “OCCURRENCE DATA STRUCTURE”. An issue with using “ADAM OTHER” is that it isn’t very informative, and these datasets as described mostly follow the existing BDS and OCCDS structures. An issue with using the “BASIC DATA STRUCTURE” and “OCCURRENCE DATA STRUCTURE” is that when compliance checks are run based on the current structure requirements, many failures will need an explanation, such as in the conformance section of the Analysis Data Reviewer’s Guide.

Until there are changes in the controlled terminology, you will need to decide what class values make the most sense for your needs.

CONCLUSION

This paper walked through some of the material being developed for a document tentatively titled “ADaM Implementation Guide for Medical Devices (ADaMIG-MD)”. It described a new structure, ADDL, and changes to both BDS and OCCDS to include the device identifier instead of, or in addition to, the unique subject identifier. It also discussed options for handling dataset class until controlled terminology is updated.

Be aware that the dataset structures, variable names, and the examples shown in this paper may change during development or after public review. However, with no current standard that addresses these medical device needs, we hope that the content in this paper can be of help as a starting point.

REFERENCES

All CDISC documents referenced in this paper can be downloaded from https://www.cdisc.org/ or https://wiki.cdisc.org/.

RECOMMENDED READING

- *Analysis Data Model Implementation Guide version 1.1*
- *Study Data Tabulation Model Implementation Guide for Medical Devices (SDTMIG-MD) - Provisional*
- *Prostate Cancer Therapeutic Area User Guide*

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