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Using the ADaM ADAE Structure for non-AE Data

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ABSTRACT

The final and official ADaM ADAE structure titled "Analysis Data Model (ADaM) Data Structure for Adverse Event Analysis" was developed as an appendix to the ADaM v2.1 to allow simple production of standard Adverse Event tables.

An ADaM sub-team is expanding this structure to cover other data analyzed in a similar fashion, such as Concomitant Medications. The basic premise is that data with the same analysis needs as the standard adverse events tables can and should use this structure.

This presentation, by members of that ADaM sub-team, describes the AE analysis need and shows how to apply it for other data, such as Concomitant Medications, Medical History, and even Laboratory Events. Examples of ADaM SAS® data sets and useful SAS program code are included.

INTRODUCTION

In May of 2012, the ADaM document titled "Analysis Data Model (ADaM) Data Structure for Adverse Event Analysis" (referred to within this paper as the "ADAE document") was finalized by the ADaM team and posted to the Clinical Data Interchange Standards Consortium (CDISC) website. It is an appendix to the ADaM document version 2.1 and the ADaM Implementation Guide (IG) version 1.0, focused specifically on reporting needs for Adverse Event (AE) data. The introduction section of the ADAE document explains the reasons why the BDS structure is not used for typical AE analyses, specifically:

- There is no need for AVAL or AVALC. Occurrences are counted in analysis, and there are typically one or more records for each occurrence.
- A dictionary is used for coding the occurrence, and it includes a well-structured hierarchy of categories and terminology. Mapping this hierarchy to BDS variables PARAM and generic *CAT variables would lose the structure and meaning of the dictionary.
- Dictionary content is typically not modified for analysis purposes. In other words, there is no need for analysis versions of the dictionary hierarchy.

The ADAE document also states:

Adverse events are just one example of data that can use the structure described within this document. An ADaM sub-team is working to expand this to other data where there is no need for an analysis variable or parameter as would be seen in a BDS structure because records are simply counted for analysis. Example data for these types of analyses are concomitant medications and medical history.

This referenced document, which will expand the AE structure to these other types of data, is still not yet available even in draft form. In the interim, how can we apply the AE document to meet our Concomitant Medications and Medical History analysis needs?

ANALYSIS NEEDS

First, let's be sure we understand our analysis needs.

As described in the ADAE document introduction (and copied above to this paper's introduction), there are some specific reasons why the BDS structure doesn't meet the needs of the typical AE analyses. Basically, we'd use this ADAE structure when data is being summarized based on a well-defined hierarchy of categories and terminology, without the need of an AVAL or AVALC, and without the need to modify the hierarchy for analysis.

It is the analysis need that drives the dataset structure.

Concomitant Medications and Medical History data are often also summarized based on a well-defined hierarchy of categories and terminology, without the need of an AVAL or AVALC, and without the need to modify the hierarchy for

analysis. Thus, when we have these same analysis needs as described in the ADAE document, it makes sense to use an ADAE-like structure than a BDS structure.

CODING DICTIONARY

For Adverse Events, the coding dictionary Medical Dictionary for Regulatory Activities (MedDRA) is used. The Study Data Tabulation Model (SDTM) data, pre-cursor to all ADaM data, contains mapping variables in the AE domain for versions 3.1.3 and later, though in SDTM versions prior to 1.3 some variables are found instead in SUPPAE.

When Medical History terms are mapped to a coding dictionary, MedDRA is also typically used. Thus the same coding variables see in the SDTM AE dataset (and potentially SUPPAE) would be found in the SDTM MH dataset (and SUPPMH) when it is mapped for use in summary tables.

Concomitant Medications, on the other hand, are usually mapped to the World Health Organization Drug Dictionary (WHODD). It is also a hierarchy structure, but is used to map medications rather than events. When Concomitant Medications are mapped for use in summary tables, the SDTM CM dataset will contain these mapping variables.

Thus incoming data from SDTM, be it AE, CM, or MH (and potentially SUPPAE, SUPPCM, or SUPPMH), will contain the hierarchy structure variables that are to be used in analysis.

LABORATORY EVENTS

Many central laboratories now provide their data with the National Cancer Institute Common Toxicity Criteria (NCI-CTC) coding included. When mapped to the LB domain in SDTM, we find this information recorded in the variables LBTOXGR (toxicity grade value using a standard toxicity scale) and LBTOX (Description of toxicity quantified by LBTOXGR).

LBTOX can thus be thought of as an event contained within the laboratory data. These laboratory events are easily mapped to a standard dictionary, such as MedDRA. It's worth noting that the mapping of laboratory data to the MedDRA terminology may or may not be done in SDTM; if it isn't done in SDTM, it would then be part of the derivation of the analysis dataset. Once MedDRA hierarchy categories are added to laboratory data, they can be used to produce laboratory event tables, similar to adverse event tables.

DATASET STRUCTURE

AE STRUCTURE

The ADAE document states in the introduction that "The ADAE structure for the standard adverse event safety dataset has at least one record per each AE recorded in SDTM AE domain." The only exception is for subjects who aren't analyzed, have no records in ADSL, yet have records in the SDTM AE domain.

There may, however, be more rows in the ADAE structure than were in the SDTM AE domain. As the ADAE document explains, this could happen when events are to be analyzed using both primary and secondary coding paths. Another reason rows may need to be added is when an event record falls into more than one analysis period and will be reported in each.

In the more general case, the ADAE structure will have the same number of rows as the corresponding AE domain. We might think of the ADAE structure as being created by the following steps:

- Take all records of AE, and all variables needed for analysis or traceability
- Transpose SUPPAE and merge useful variables
- Merge appropriate variables from ADSL
- Derive any additional variables needed for ADAE

APPLYING TO CONCOMITANT MEDICATIONS AND MEDICAL HISTORY

To apply this general rule to Concomitant Medications or Medical History, we can replace the AE above with either CM or MH. This give us:

- Take all records of AE/CM/MH, and all variables needed for analysis or traceability
- Transpose SUPPAE/SUPPCM/SUPPMH and merge useful variables
- Merge appropriate variables from ADSL
- Derive any additional variables needed for ADAE/ADCM/ADMH.

APPLYING TO LABORATORY EVENTS

The NCI-CTC applies to only a subset of the suite of laboratory tests typically collected, and only to those meeting the defined criteria specified in the hierarchy. This means that unlike AE data, just a subset of rows in the LB domain would contain the hierarchy category variables for use in creating summary tables.

Instead of keeping the large number of laboratory data rows with missing hierarchy category variables, it's worth considering creating a separate laboratory analysis dataset, just for laboratory event analyses. This means that there would likely be two laboratory analysis datasets:

- One for traditional laboratory analyses, such as change from baseline or shift tables
- One for laboratory event analyses, with a dictionary hierarchy applied

DERIVING NEW VARIABLES

Although many of the variables that comprise the ADAE dataset are those copied directly from the SDTM AE domain, there are some derived variables. For example:

ADAE TIMING VARIABLES

There are often imputation rules for partial or completely missing dates, and these imputed dates are used to derive corresponding study day variables. Common ADAE timing variables in ADAE are:

Variable Name	Variable Label	Type	Notes
ASTDT	Analysis Start Date	Num	Numeric version of AESTDTC. May be imputed.
ASTDTF	Analysis Start Date Imputation Flag	Char	Used when imputing ASTDT from a partial or fully missing AESTDTC, following imputation rules
ASTDY	Analysis Start Day	Num	Usually derived from ASTDT and a reference date from ADSL
AENDT	Analysis End Date	Num	Numeric version of AEENDTC. May be imputed.
AENDTF	Analysis End Date Imputation Flag	Char	Used when imputing ASTDT from a partial or fully missing AEENDTC, following imputation rules
AENDY	Analysis End Day	Num	Usually derived from AENDT and a reference date from ADSL

Table 1. Timing Variables from ADAE

APPLYING TIMING VARIABLES TO OTHER DATA

These same variables from **Table 1. Timing Variables from ADAE** could also apply to Concomitant Medications and Medical History data. With just a few modifications to make them more generic, we would have something like:

Variable Name	Variable Label	Type	Notes
ASTDT	Analysis Start Date	Num	Numeric version of CMSTDTC/MHSTDTC. May be imputed.
ASTDTF	Analysis Start Date Imputation Flag	Char	Used when imputing ASTDT from a partial or fully missing CMSTDTC/MHSTDTC, following imputation rules
ASTDY	Analysis Start Day	Num	Usually derived from ASTDT and a reference date from ADSL
AENDT	Analysis End Date	Num	Numeric version of CMENDTC/MHENDTC. May be imputed.

Variable Name	Variable Label	Type	Notes
AENDTF	Analysis End Date Imputation Flag	Char	Used when imputing ASTDT from a partial or fully missing CMENDTC/MHENDTC, following imputation rules
AENDY	Analysis End Day	Num	Usually derived from AENDT and a reference date from ADSL

Table 2. Possible Timing Variables for Medical History and Concomitant Medications

Laboratory data doesn't contain a start and end date, but instead just a collection date. Rather than the variables described in **Table 2. Possible Timing Variables for Medical History and Concomitant Medications**, we'd have:

Variable Name	Variable Label	Type	Notes
ADT	Analysis Date	Num	Numeric version of LBDTC. May be imputed.
ADTF	Analysis Date Imputation Flag	Char	Used when imputing ADT from a partial or fully missing LBDTC, following imputation rules
ADY	Analysis Day	Num	Usually derived from ADT and a reference date from ADSL

Table 3. Possible Timing Variables for Lab Events

ADAE FLAG VARIABLES

Flags are often used to show which records are to be used in analysis. Common flags needed in ADAE analyses are:

Variable Name	Variable Label	Type	Notes
ANLzzFL	Analysis Record Flag zz	Char	As in BDS, this flag denotes whether the row will be included in a specific analysis.
TRTEMFL	Treatment Emergent Analysis Flag	Char	Usually derived by comparing analysis start date and end dates with study reference dates found in ADSL
PREFL	Pre-treatment Flag	Char	Usually derived by comparing ASTDT with a study reference start date found in ADSL
FUPFL	Follow-up Flag	Char	Usually derived by comparing ASTDT with a study reference end date found in ADSL

Table 4. ADAE Flag Variables

APPLYING FLAG VARIABLES TO OTHER DATA

The variable TRTEMFL in **Table 4. ADAE Flag Variables** doesn't apply to Concomitant Medications, Medical History, or Laboratory data. The remaining Adverse Event variables, however, apply to each of these other types of data, with no modifications.

Concomitant Medications and Laboratory analyses may require an additional flag variable that shows whether a medication was taken or laboratory event happened while on study drug. A potential variable to capture this information could be as described below:

Variable Name	Variable Label	Type	Notes
ONTRTFL	On-Treatment Flag	Char	Usually derived by comparing either ASTDT and AENDT or ADT with study reference dates found in ADSL

Table 5. Possible Flag Variable for non-AE data

METADATA

Between the ADaM IG and AE Appendix documents, there are currently 3 official ADaM structure classes: ADSL, BDS, and ADAE. When creating dataset metadata, we use the appropriate structure name for the dataset class attribute. If we create a dataset structure other than these, we must use the dataset class attribute of OTHER.

This means that for any other hierarchical occurrence data we will need to identify the class as a structure of OTHER.

CONCOMITANT MEDICATIONS EXAMPLE

We will now walk through an example application of this idea for a Concomitant Medication analysis table. This is only an example, and your analysis needs may differ and thus require different data.

ANALYSIS OUTPUT NEED

Here is an example of a standard Concomitant Medication table layout. It is similar in structure to a standard Adverse Event table, where it is organized by different levels of a hierarchical dictionary, and we're simply counting unique subjects within each hierarchical category.

Table 1
Concomitant Medications Initiated Day -7 through Follow-up
Treated Subjects

	Group 1 (n=nn)	Group 2 (n=nn)
- Any Medication Use -	nn (xx.x%)	nn (xx.x%)
ADRENERGICS/SYMPATHOMIMETICS		
-- Overall -	nn (xx.x%)	nn (xx.x%)
EPINEPHRINE	nn (xx.x%)	nn (xx.x%)
OXYMETAZOLINE	nn (xx.x%)	nn (xx.x%)
XYLOMETAZOLINE	nn (xx.x%)	nn (xx.x%)
PSEUDOEPHEDRINE	nn (xx.x%)	nn (xx.x%)
ANGIOTENSIN-II RECEPTOR ANTAGONISTS		
- Overall -	nn (xx.x%)	nn (xx.x%)
LOSARTAN	nn (xx.x%)	nn (xx.x%)
IRBESARTAN	nn (xx.x%)	nn (xx.x%)
VALSARTAN	nn (xx.x%)	nn (xx.x%)
…		

**Multiple uses of a specific medication for a subject are counted once in the frequency for the medication. Likewise, multiple uses within a specific medication class for a subject are counted once in the frequency for the medication class. Includes concomitant medications initiated 7 days prior to the first dose of study medication and continued after the subjects enrollment.*

Figure 1: Example Concomitant Medication Table

EXAMPLE CONCOMITANT MEDICATION INPUT DATA

Below are some example input datasets with content that is needed to produce the output in **Figure 1: Example Concomitant Medication Table**. Note that these are not full datasets, but rather a subset of variables and

observations just to demonstrate the concept. Only one subject is shown, and only a few concomitant medications for that subject.

USUBJID	CMSEQ	CMTRT	CMDECOD	CMCLAS	CMSTDTC	CMENDTC
BP3304-A01	1	SUDAFED	PSEUDOEPHEDRIN E HYDROCHLORIDE	ADRENERGICS/SY MPATHOMIMETICS	2009-06-27	
BP3304-A01	2	SUPRARENIN	ADRENALIN	ADRENERGICS/SY MPATHOMIMETICS	2009-06-27	2009-12-18
BP3304-A01	3	OXYMETAZOLIN	OXYMETAZOLINE	DIHYDROPYRIDINE DERIVATIVES	2009-08-18	2009-10-31

Table 6. Example CM source data

USUBJID	RDOMAIN	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL
BP3304-A01	CM	CMSEQ	1	PREFCODE	Preferred Term Code	PSEUDOEPHEDRINE HYDROCHLORIDE
BP3304-A01	CM	CMSEQ	2	PREFCODE	Preferred Term Code	EPINEPHRINE
BP3304-A01	CM	CMSEQ	3	PREFCODE	Preferred Term Code	OXYMETAZOLINE

Table 7. Example SUPPCM source data

USUBJID	MITTFL	ARMCD	TRT01P	TRTSDT	TRTEDT
BP3304-A01	Y	A	100 MG BP3304	6/30/2009	1/11/2010

Table 8. Example ADSL source data

EXAMPLE CONCOMITANT MEDICATION ANALYSIS DATASET CODE

Here is some example code that could used to produce the analysis dataset from the input datasets shown above in **Table 6. Example CM source data**, **Table 7. Example SUPPCM source data**, and **Table 8. Example ADSL source data**.

```
/* Get the suppqual dataset, convert seq number to numeric */
data _supp;
 set <sdtm library>.suppcm;
  cmseq=input(idvarval,best.);
run;

proc sort data= _supp;
   by rdomain usubjid idvar  cmseq;
run;

/* get suppqual ready for merging */
proc transpose data=_supp out=_trn(drop=idvar: _:);
  by rdomain usubjid idvar  cmseq;
  id qnam;
  var qval;
  idlabel qlabel;
run;

proc sort data=<SDTM library>.CM out=CM;
 by  usubjid cmseq;
run;
```

```
/*  create the SDTM plus version of domain CM */
data cmplus;
 merge cm _trn;
 by  usubjid cmseq;
run;

/*  prepare to merge the necessary variables from ADSL */
proc sort data= =<ADaM library>.adsl out=adsl;
   by usubjid;
run;

/*  create timing variables. If SDTM provides incomplete dates
     must use date imputation rules and populate corresponding flags  */
data adcm;
  merge cmplus(in=a) adsl;
  by usubjid;
  if a;

  /*  for complete dates */
  ASTDT=input(CMSTDTC,ND8601DA.);
  AENDT=input(CMENDTC,ND8601DA.);

  /*  for incomplete dates */
  ASTDT  = < some imputation rule>;
  ASTDTF = < must be populated>;
  AENDT  = < some imputation rule>;
  AENDTF = < must be populated>;

  ASTDY  = ASTDT - TRTSDT + ( ASTDT>= TRTSDT);
  AENDY  = AENDT - TRTSDT + ( ASTDT>= TRTSDT);

  If ( ASTDT >= TRTSDT - 7 ) then ANL01FL  = 'Y' ;
run;
```

The code needed to produce the analysis table from the analysis dataset should be very similar to the code used to produce an AE table from the AE analysis dataset, so it is not shown here.

LABORATORY EVENTS EXAMPLE 1

ANALYSIS OUTPUT NEED

Here is an example of a Laboratory Events table layout, summarized by two levels of hierarchy (MedDRA System Organ Class and Preferred Term), and also broken down by grade. It is also similar to an standard Adverse Event table, since it summarizes records using a hierarchical dictionary, and counts unique subjects within each category.

Table 3
Clinical Laboratory Events by NCI-CTCAE Grade
Number of Subjects (%) by Body System and MedDRA Term
Safety-Evaluable Subjects

MedDRA System Organ Class/ Preferred Term	NCI CTCAE Grade	Group 1 (n=nn)	Group 2 (n=nn)
Any Instance			
Total	Total	nn (xx.x%)	nn (xx.x%)
	4	nn (xx.x%)	nn (xx.x%)
	3	nn (xx.x%)	nn (xx.x%)
	2	nn (xx.x%)	nn (xx.x%)
	1	nn (xx.x%)	nn (xx.x%)
Blood and Lymphatic System Disorders			
Total	Total	nn (xx.x%)	nn (xx.x%)
	4	nn (xx.x%)	nn (xx.x%)
	3	nn (xx.x%)	nn (xx.x%)
	2	nn (xx.x%)	nn (xx.x%)
	1	nn (xx.x%)	nn (xx.x%)
Hypoalbuminemia	Total	nn (xx.x%)	nn (xx.x%)
	4	nn (xx.x%)	nn (xx.x%)
	3	nn (xx.x%)	nn (xx.x%)
	2	nn (xx.x%)	nn (xx.x%)
	1	nn (xx.x%)	nn (xx.x%)
Leukocytosis	Total	nn (xx.x%)	nn (xx.x%)
	4	nn (xx.x%)	nn (xx.x%)
	3	nn (xx.x%)	nn (xx.x%)
	2	nn (xx.x%)	nn (xx.x%)
Investigations		nn (xx.x%)	nn (xx.x%)
Total	Total	nn (xx.x%)	nn (xx.x%)
	4	nn (xx.x%)	nn (xx.x%)
	3	nn (xx.x%)	nn (xx.x%)
	2	nn (xx.x%)	nn (xx.x%)
	1	nn (xx.x%)	nn (xx.x%)
Alkaline phosphatase increased	Total	nn (x.x%)	nn (x.x%)
	4	nn (x.x%)	nn (x.x%)
	3	nn (x.x%)	nn (x.x%)
	2	nn (x.x%)	nn (x.x%)
	1	nn (x.x%)	nn (x.x%)
…			

Notes: Multiple occurrences of a specific laboratory event for a subject were counted once at the highest NCI-CTCAE grade (version 4).

Figure 2. Laboratory Events Table with Hierarchy

EXAMPLE LABORATORY EVENTS INPUT DATA

Here are example input datasets with content that is needed to produce the output shown above in **Figure 2. Laboratory Events Table with Hierarchy**. Note that these are not full datasets, but rather a subset of variables and observations just to demonstrate the concept. Only one subject is shown, and only a few laboratory results for that subject.

	STUDYID	DOMAIN	USUBJID	LBSEQ	LBTESTCD	LBTEST	LBSPEC	LBCAT
1	BP3304	LB	BP3304-A01	1	ALB	Albumin	BLOOD	CHEMISTRY
2	BP3304	LB	BP3304-A01	67	GLUC	Glucose	BLOOD	CHEMISTRY
3	BP3304	LB	BP3304-A01	71	SODIUM	Sodium	BLOOD	CHEMISTRY
4	BP3304	LB	BP3304-A01	87	ALB	Albumin	BLOOD	CHEMISTRY
5	BP3304	LB	BP3304-A01	88	ALP	Alkaline Phosphatase	BLOOD	CHEMISTRY

	LBSTRESN	LBSTRESU	LBSTNRLO	LBSTNRHI	LBNRIND	TOXICITY	LBTOXGR
1	34	g/L	36	51	LOW	Hypoalbuminemia	1
2	7.7714	mmol/L	3.60	5.49	HIGH	Hyperglycemia	1
3	132	mmol/L	136	145	LOW	Hyponatremia	1
4	25	g/L	36	51	LOW	Hypoalbuminemia	2
5	125	U/L	40	115	HIGH	Alkaline phosphatase increased	1

Table 9. Example LB source data

USUBJID	RDOMAIN	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL
BP3304-A01	LB	LBSEQ	1	LLT	Low Level Term Code	10020943
BP3304-A01	LB	LBSEQ	1	SOC	System Organ Class	Metabolism and nutrition disorders
BP3304-A01	LB	LBSEQ	67	LLT	Low Level Term Code	10020639
BP3304-A01	LB	LBSEQ	67	SOC	System Organ Class	Metabolism and nutrition disorders
BP3304-A01	LB	LBSEQ	71	LLT	Low Level Term Code	10021038
BP3304-A01	LB	LBSEQ	71	SOC	System Organ Class	Metabolism and nutrition disorders
BP3304-A01	LB	LBSEQ	87	LLT	Low Level Term Code	10020943
BP3304-A01	LB	LBSEQ	87	SOC	System Organ Class	Metabolism and nutrition disorders
BP3304-A01	LB	LBSEQ	88	LLT	Low Level Term Code	10001675

USUBJID	RDOMAIN	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL
BP3304-A01	LB	LBSEQ	88	SOC	System Organ Class	Investigations

Table 10. Example SUPPLB source data

USUBJID	SAFFL	ARMCD	TRT01P	TRTSDT	TRTEDT
BP3304-A01	Y	A	100 MG BP3304	6/30/2009	1/11/2010

Table 11. Example ADSL source data

EXAMPLE LABORATORY EVENTS ANALYSIS DATASET CODE

The code below, that we could use to create a laboratory events analysis dataset, is suspiciously similar to the concomitant medications analysis data code above. This will produce our analysis dataset.

```
/* Get the suppqual dataset, convert seq number to numeric */
data _supp;
 set <sdtm library>.supplb;
  lbseq=input(idvarval,best.);
run;

proc sort data= _supp;
   by rdomain usubjid idvar  lbseq;
run;

/* get suppqual ready for merging */
proc transpose data=_supp out=_trn(drop=idvar: _:);
  by rdomain usubjid idvar  lbseq;
  id qnam;
  var qval;
  idlabel qlabel;
run;

proc sort data=<SDTM library>.LB out=LB;
 by  usubjid lbseq;
run;

/*  create the SDTM plus version of domain LB */
data lbplus;
 merge lb _trn;
 by  usubjid lbseq;
run;

/*  prepare to merge the necessary variables from ADSL */
proc sort data= =<ADaM library>.adsl out=adsl;
   by usubjid;
run;

/*  Add ADSL variables  */
data adlbtox;
  merge lbplus(in=a) adsl;
  by usubjid;
  if a;
run;

/* Now to set the analysis flags.  Only the worse term and toxicity
   grade per subject post-baseline are to be counted */
proc sort data=adlbtox;
  by llt descending lbtoxgr usubjid;
run;
```

```
data adlbtox;
  set adlbtox;
    by soc llt descending lbtoxgr usubjid;
      if first.usubjid then anl01fl='Y';
run;
```

EXAMPLE LABORATORY EVENTS ANALYSIS DATASET

The resulting analysis dataset below would then be used to produce **Figure 2. Laboratory Events Table with Hierarchy**.

	STUDYID	USUBJID	LBSEQ	LBTESTCD	LBTEST	LBSPEC	LBSTRESN	LBSTRESU	LBSTNRHI
1	BP3304	BP3304-A01	88	ALP	Alkaline Phosphatase	BLOOD	125	U/L	115
2	BP3304	BP3304-A01	67	GLUC	Glucose	BLOOD	7.7714	mmol/L	5.49549
3	BP3304	BP3304-A01	87	ALB	Albumin	BLOOD	25	g/L	51
4	BP3304	BP3304-A01	1	ALB	Albumin	BLOOD	34	g/L	51
5	BP3304	BP3304-A01	71	SODIUM	Sodium	BLOOD	132	mmol/L	145

	LBNRIND	TOXICITY	LBTOXGR	SAFFL	TRT01P	TRT01PN	TRTSDT	TRTEDT	ANL01FL
1	HIGH	Alkaline phosphatase increased	1	Y	100 MG BP3304	1	6/30/2009	1/11/2010	Y
2	HIGH	Hyperglycemia	1	Y	100 MG BP3304	1	6/30/2009	1/11/2010	Y
3	LOW	Hypoalbuminemia	2	Y	100 MG BP3304	1	6/30/2009	1/11/2010	Y
4	LOW	Hypoalbuminemia	1	Y	100 MG BP3304	1	6/30/2009	1/11/2010	Y
5	LOW	Hyponatremia	1	Y	100 MG BP3304	1	6/30/2009	1/11/2010	Y

Table 12. Example lab event analysis dataset

LABORATORY EVENTS EXAMPLE 1

ANALYSIS OUTPUT NEED

Here is an example of another possible Laboratory Events table layout:

Table 3
Laboratory Events by Highest NCI CTCAE Grade for Laboratory Variables
Safety-Evaluable Patients

					NCI CTCAE Grade			
Variable	Grade	Treatment	n	Total	4	3	2	1
Absolute neutrophil count	Low	Group 1	nnn	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)
		Group 2	nnn	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)
Alkaline phosphatase	High	Group 1	nnn	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)
…								

NCI CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events, version 3.
A laboratory event occurred if the NCI CTCAE grade for a post-baseline laboratory measurement increased from baseline. Baseline was the patient's last observation prior to the initiation of study drug. Abnormalities in patients with missing baseline values were included.
n = the number of patients with post-baseline values for the laboratory variable and treatment group.

Figure 3. Laboratory Events Table by Grade and Test

Note that unlike the first Laboratory Events table in **Figure 2. Laboratory Events Table with Hierarchy**, this table does not make use of the hierarchy. For this reason, the Adverse Event structure would not apply. In fact, the BDS structure would work very well for this analysis! Decisions for analysis datasets are made based on analysis needs and not type of data, and some data can appear in more than one analysis dataset.

CONCLUSION

Much of the data structure useful for analysis of Concomitant Medications, Medical History, and even Laboratory Events data can be drawn from the ADAE document.

For Concomitant Medications and Medical History, we typically have exactly the same number of rows in the analysis dataset as we did in the SDTM dataset. The content of the dataset is basically data from the incoming SDTM domain plus its SUPPQUAL data, variables from ADSL, and a few derived variables.

For Laboratory events, the analysis dataset is typically a subset of rows from the SDTM dataset. Here we keep only the laboratory tests have mappings to a dictionary term.

With a few modifications, we can use derived variables from ADAE for these other structures. Keep in mind that we can't use the metadata class of ADAE for anything other than adverse event data, so we must instead use the class of OTHER for these structures.

Only apply the structure from the ADAE document to create data that meets a similar analysis need. Specifically, the data needs a hierarchical dictionary, and counts are determined by summing the unique subjects in each level of the hierarchy.

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RECOMMENDED READING

- MSSO. Introductory Guide MedDRA Version 14.0. Download from http://www.who.int/medical_devices/innovation/MedDRAintroguide_version14_0_March2011.pdf. Note: this document does not address the latest version of MedDRA but provides an introduction to MedDRA principles.

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