Analysis Data Model (ADaM)
Data Structure for Adverse Event Analysis

Prepared by the

CDISC Analysis Data Model Team

[redacted]

Notes to Readers

This Analysis model uses the principles, structure and standards described in the CDISC Analysis Data Model v2.1 and Implementation Guide v1.0 documents

Revision History

Date	Version	Description
May 10, 2012	1.0	Final.

Note: Please see Appendix A for Representations and Warranties; Limitations of Liability, and Disclaimers.

Contents

1. Introduction

The statistical analysis data structure presented in this document describes the general data structure and content typically found in Analysis Datasets used for common safety analysis of adverse events (AEs). Specifically, this is for analysis consisting of counting subjects with a record or term within a mapped dictionary hierarchy. The data structure is based on the ADaM Analysis Data Model V2.1 (referred to in this document as the ADaM v2.1) [1] and the ADaM Analysis Data Model Implementation Guide (ADaMIG) V1.0 [2].

As presented in the ADaMIG, most analysis methods can be performed using the ADaM Basic Data Structure (BDS) including Parameter (PARAM) and Analysis Value (AVAL). However, analysis of adverse events is one example where data analyzed as described above does not fit well into the BDS structure and are more appropriately analyzed using an SDTM structure with added analysis variables. In particular, for the analysis needs described in this document:

- 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 AE structure presented in this document is built on the nomenclature of the Study Data Tabulation Model Implementation Guide (SDTMIG) V3.1.2, including Amendment 1 to the Study Data Tabulation Model (SDTM) v1.2 and the SDTM Implementation Guide: Human Clinical Trials V3.1.2 [3] standard for collected data, and adds attributes, variables, and data structures required for statistical analyses. The primary SDTM source domain for the AE analysis structure is AE with the corresponding SUPPAE. Many additional variables are added from Subject-Level Analysis Dataset (ADSL).

In this document, the analysis dataset for adverse events (ADAE) is described and required if SDTM AE isn't sufficient to support all AE analysis. The dataset and variable naming conventions and dataset structure described in this document should be followed. The ADAE structure for the standard adverse event safety dataset has at least one record per each AE recorded in SDTM AE domain. However, subjects not analyzed (e.g. screen failures) who have AEs recorded in SDTM AE but not in ADSL do not need to be included in ADAE. Additional rows may be added to have a one record per AE recorded in SDTM AE domain per period/phase per coding path structure if required by the analysis and clearly defined in the dataset and variable metadata. However, this doesn’t exclude a Sponsor from creating additional analysis datasets for AE analysis, even using a different structure if needed for analysis (e.g. time-to-event of adverse events of special interest).

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.

2. Adverse Event Analysis

The safety evaluation of a clinical trial includes the analysis of adverse events. The definition of an adverse event, as presented in International Conference of Harmonization (ICH) E2A [4] guidelines, is

> *Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment.*

Restated, this definition of an adverse event (AE) includes any unfavorable and unintended sign, symptom, or disease that is temporally associated with the use of a medicinal product, regardless of whether the AE is considered to be related to the product.

2.1 Adverse Event Attributes

Important attributes include the level of severity of the AE (Mild, Moderate, or Severe), whether the AE is considered to be related to the study product (Yes or No), and whether the AE is considered serious (Yes or No).

Of particular importance in the analysis of AEs is the definition of 'treatment emergent'. The ICH E9 guidance [5] document defines treatment emergent as an event that emerges during treatment having been absent pre-treatment, or worsens relative to the pre-treatment state. Operationally, classifying AEs as treatment emergent will utilize, in part, the start or worsening date of the AE relating to the trial or treatment start.

Other attributes of AEs include the action taken in response to the event and whether the event led to permanent discontinuation of the investigational product.

2.2 Coding of Adverse Events

Adverse events are recorded in textual or 'verbatim' terms. This verbatim term is a short description of the event and is generally written in free text on the case report form. Verbatim terms are then processed through a coding dictionary so that similar verbatim terms are grouped together by classifying each verbatim term into a hierarchy of medical granularity. Medical Dictionary for Regulatory Activities (MedDRA) [6] has become widely recognized as a global standard for the coding of adverse events. Examples of other coding dictionaries include WHO Adverse Reaction Terminology (WHO-ART), Coding Symbols for a Thesaurus of Adverse Reaction Terms (COSTART), International Classification of Disease (ICD). Each coding dictionary is characterized by classifying each verbatim term into a hierarchy of medical granularity. For example, if a verbatim term was recorded as 'stomach virus', using MedDRA V12.0, this verbatim term would result in a System Organ Class (SOC) of 'Infections and infestations' and a preferred term (PT) of 'Gastroenteritis viral'. The COSTART coding hierarchy would place this event in the 'Body as a Whole' body system, in the 'General' subcategory for this body system, and with the preferred term of 'Flu Syndrome'.

When using coding dictionaries, it is recommended that coding rules and guidelines be developed by the sponsor prior to the classification of adverse events. The objective of these guidelines is to promote medical accuracy and consistency when using the controlled vocabulary of the dictionary. This consistency will be helpful when multiple coded adverse events are combined for two or more clinical studies.

It is also recommended that all levels of terms in the MedDRA hierarchy: System Organ Class (SOC), High Level Group Term (HLGT), High Level Term (HLT), Lowest Level Term (LLT), and Preferred Term (PT) are represented, as these are frequently useful in further analyses of AEs.

In some situations, multiple study reports are created for a single study. For example, an initial study report may be created at the time of the primary analysis for the primary efficacy endpoint. If subjects are followed for safety, a second report may be created years later so that long term safety data can be incorporated. At this time, there may

be a desire to update the coding dictionary so that all events are coded using the most recent version of a dictionary. In this situation, a recommendation is to provide the original coded terms along with the new coded terms so that the implications of the recoding can be more easily investigated.

It should be noted that a more common scenario involving the recoding of adverse events is when events are recoded for an integrated analysis and submitted to a regulatory agency for marketing approval. However, neither the current version of the ADaMIG nor this document fully cover integration of multiple studies. The ADaM and SDS teams are jointly developing a document to address integration of multiple studies. Some of the suggestions included here for handling multiple dictionaries may be revised after this Integration document is released.

2.3 Statistical Analysis

The most frequently used method for the comparison of adverse events between treatment groups is the summarization of the number of subjects who experienced a given adverse event at least once by the dictionary derived term. These counts and related percentages are presented for levels of the MedDRA hierarchy and preferred term. The denominator used for the calculation of the percentages is often determined by a population flag, such as the total number of subjects at risk or total number of subjects exposed to each treatment (e.g. SAFFL='Y'). Note that some subjects exposed to treatment may not have any adverse events, and therefore these subjects would not be represented in the SDTM AE domain and ADaM ADAE analysis dataset. Thus, the values of the denominator usually need to be obtained from ADSL (subject level analysis dataset) rather than directly from ADAE.

This ADaM model primarily discusses the creation of an analysis dataset that is needed for the presentation of frequencies and percents. However, the analysis dataset presented below could be used to conduct more in-depth analysis. For time-to-event analyses, see the ADaM Basic Data Structure for Time to Event Analyses.

3. Points to Consider in this Document

In reviewing the metadata and examples in this document, some of the points to consider are:

- **Ordering of variables:** Within this document, no specific ordering of variables within the illustrated datasets is implied. The ADaM v2.1 [1] states that ideally the ordering of the variables in the analysis dataset follows a logical ordering (not simply alphabetic). The ADaM v2.1 [1] does not provide a specific recommendation for the ordering of the variables. Within this document, the author of each example applied his or her own logical ordering.

- **Identification of source dataset:** When identifying the source dataset for a variable, the immediate predecessor is used, as described in the ADaM v2.1 [1]. For example, in ADSL the source is identified as DM.SUBJID in the analysis variable metadata. When SUBJID is used in ADAE, the source is identified as ADSL.SUBJID.

- **Analysis-ready:** ADAE should be "analysis-ready," meaning it should contain all of the variables needed for the specific analysis, so that the analysis can be replicated by performing the actual statistical test without first having to manipulate data. Analysis-ready does not mean that a formatted display can be generated in a single statistical procedure. ADAE adheres to this principle as unique subject counts can be obtained by running a standard statistical procedure (e.g., SAS PROC, S-PLUS function, etc.) and denominators can be derived from ADSL.

- **Examples are for illustration only:** Note that the examples in this document are only intended as illustrations and should not be viewed as a statement of the standards themselves. In addition, the examples are intended to illustrate content and not appearance; it is understood that there are many different ways that data can be displayed. This document does not cover display formats.

- **Display of metadata for illustration of content only:** Though the metadata elements have been defined in the ADaM v2.1 [1], how the metadata are displayed is a function of the mechanism used to display the content. The presentation formats used in this document are for the purposes of illustration of content only, and are not intended to imply any type of display standard or requirement.

- **Analysis results metadata:** Analysis results metadata have not been included for any examples in this document. As stated in the ADaM v2.1 [1], analysis results metadata are not required. However, best practice is that they be provided to assist the reviewer by identifying the critical analyses, providing links between results, documentation, and datasets, and documenting the analyses performed.

- **Examples not meant to be all inclusive regarding variables:** The examples describe some of the key variables and records that would be included in the dataset. It is not intended to illustrate every possible variable that might be included in the analysis dataset; for example core variables required for subgroup analyses are not included in all the illustrations.

- **Source/Derivation Column:** The algorithms provided in the Source/Derivation column are for illustration purposes only and are not intended to imply universally accepted definitions or derivations of variables. Algorithms are producer-defined and dependent on trial and analysis design.

- **No endorsement of vendors or products:** As with other ADaM documents, references to specific vendor products are examples only and therefore should not be interpreted as an endorsement of these vendors or products.

4. ADaM Metadata

Typically, the Analysis Dataset Metadata are specified as follows:

Table 4.1 Example of ADaM ADAE Dataset Metadata[1]

Dataset Name	Dataset Description	Dataset Location	Dataset Structure	Key Variables of Dataset	Class of Dataset	Documentation
ADAE	Adverse Event Analysis Dataset	pathname/analysis/datasets/adae.xpt	one record per subject per each AE recorded in SDTM AE domain (optional: per coding path, per Analysis Period and/or Phase)	USUBJID, AEDECOD, AESEQ, (optional: AEBODSYS, APHASE, APERIODC) *Depending on study design and analyses, additional variables such as key flags may be needed*	ADAE*	ADAE.SAS *Example: Dictionary used is MedDRA V11.1*

* Note: Class of dataset may change in a future version as the ADaM team develops a general occurrence model document

4.1 ADAE Variables and Variable Metadata

As stated earlier, the AE data structure is not BDS. There is no PARAM nor AVAL, for example. However, some of the variables described for the BDS structure in the ADaMIG version 1 [2] can be used in the AE structure, as shown below.

The more standardized variables commonly occurring in an ADaM AE analysis dataset (ADAE) are described here in tabular format. In general, include all SDTM AE and SUPPAE domain variables needed for analysis or traceability. Additional study or therapeutic specific variables may be added as needed but should follow the standard variable naming conventions described in the ADaMIG version 1 [2]. A variable should not use the prefix AE unless it is either (1) coming from the SDTM AE or SUPPAE domain or (2) the numeric version of the SDTM variable. In general, the analysis version of an SDTM variable is named by replacing the "AE" prefix with an "A" for analysis. Choose variable names with care to prevent unintended conflicts with standard names.

[1] The display presentation of the metadata should be determined between the sponsor and the recipient. The example is only intended to illustrate content and not appearance.

As described in the ADaM v2.1 [1], the two rightmost columns of metadata ("Core" and "CDISC Notes") provide information about the variables to assist users in preparing their datasets. These columns are not meant to be metadata. The "Core" column, as defined in the ADaMIG version 1 [2], describes whether a variable is required (Req), conditionally required (Cond), or permissible (Perm). The "CDISC Notes" column provides more information about the variable. In addition, the "Type" column is being used to define whether the variable is character (Char) or numeric value (Num). More specific information will be provided in metadata.

4.1.1 ADSL Variables

Merge any ADSL variables needed for analysis or reference.

Be aware that population indicator flags may not be appropriate to include in ADAE because only subjects with an SDTM AE record would have an ADAE record. For this reason, it is recommended that population indicators and denominator counts for percentages be derived from ADSL and not from ADAE.

4.1.2 Identifier Variables

Include the identifier variables from SDTM:

Table 4.1.2.1 Identifier Variables

ADAE – Adverse Event Analysis Dataset					
Variable Name	**Variable Label**	**Type**	**Code List / Controlled Terms**	**Core**	**CDISC Notes**
STUDYID	Study Identifier	Char		Req	AE.STUDYID
USUBJID	Unique Subject Identifier	Char		Req	AE.USUBJID
SUBJID	Subject Identifier for the Study	Char		Perm	ADSL.SUBJID
SITEID	Study Site Identifier	Char		Perm	ADSL.SITEID
AESEQ	Sequence Number	Num		Req	AE.AESEQ Required for traceability back to SDTM AE.

4.1.3 Dictionary Coding Variables

Dictionary coding variables provided in SDTM, typically MedDRA, should be included as needed for analysis, review, or traceability. It is recommended but not required that all levels of terms in the MedDRA hierarchy [System Organ Class (SOC), High Level Group Term (HLGT), High Level Term (HLT), Lowest Level Term (LLT), and Preferred Term (PT)] are represented, as these are frequently useful in further analyses of AEs. If other coding variables are included in SDTM and pertinent for analysis, these should be included in ADaM. For any public versioned dictionary, including MedDRA, the metadata for each coding variable should include both the name and version of the dictionary.

Table 4.1.3.1 Dictionary Coding Variables for MedDRA

ADAE – Adverse Event Analysis Dataset					
Variable Name	**Variable Label**	**Type**	**Code List / Controlled Terms**	**Core**	**CDISC Notes**
AETERM	Reported Term for the Adverse Event	Char		Req	AE.AETERM

ADAE – Adverse Event Analysis Dataset					
Variable Name	**Variable Label**	**Type**	**Code List / Controlled Terms**	**Core**	**CDISC Notes**
AEDECOD	Dictionary-Derived Term	Char	MedDRA	Req	AE.AEDECOD This is typically one of the primary variables used in an AE analysis and would be brought in from the SDTM AE domain. Equivalent to the Preferred Term (PT in MedDRA). As mentioned above, all other SDTM AE and SUPPAE domain variables needed for analysis or traceability should also be included. Include the dictionary version in the variable metadata.
AEBODSYS	Body System or Organ Class	Char	MedDRA	Req	AE.AEBODSYS This is typically one of the primary variables used by the Sponsor in an AE analysis and would be brought in from the SDTM AE domain. As mentioned above, all other SDTM AE and SUPPAE domain variables needed for analysis or traceability should also be included. Include the dictionary version in the variable metadata.
AEBDSYCD	Body System or Organ Class Code	Num	MedDRA	Perm	AE.AEBDSYCD This would be copied from the SDTM AE domain or supplemental qualifier dataset. Include the dictionary version in the variable metadata.
AELLT	Lowest Level Term	Char	MedDRA	Cond	AE.AELLT This would be copied from the SDTM AE domain or supplemental qualifier dataset. Include the dictionary version in the variable metadata. Conditional on whether used for analysis.
AELLTCD	Lowest Level Term Code	Num	MedDRA	Perm	AE.AELLTCD This would be copied from the SDTM AE domain or supplemental qualifier dataset. Include the dictionary version in the variable metadata.
AEPTCD	Preferred Term Code	Num	MedDRA	Perm	AE.AEPTCD This would be copied from the SDTM AE domain or supplemental qualifier dataset. Include the dictionary version in the variable metadata.

ADAE – Adverse Event Analysis Dataset					
Variable Name	**Variable Label**	**Type**	**Code List / Controlled Terms**	**Core**	**CDISC Notes**
AEHLT	High Level Term	Char	MedDRA	Cond	AE.AEHLT This would be copied from the SDTM AE domain or supplemental qualifier dataset. Include the dictionary version in the variable metadata. Conditional on whether used for analysis.
AEHLTCD	High Level Term Code	Num	MedDRA	Perm	AE.AEHLTCD This would be copied from the SDTM AE domain or supplemental qualifier dataset. Include the dictionary version in the variable metadata.
AEHLGT	High Level Group Term	Char	MedDRA	Cond	AE.AEHLGT This would be copied from the SDTM AE domain or supplemental qualifier dataset. Include the dictionary version in the variable metadata. Conditional on whether used for analysis.
AEHLTGCD	High Level Group Term Code	Num	MedDRA	Perm	AE.AEHLGTCD This would be copied from the SDTM AE domain or supplemental qualifier dataset. Include the dictionary version in the variable metadata.
AESOC	Primary System Organ Class	Char	MedDRA	Cond	AE.AESOC This would be copied from the SDTM AE domain or supplemental qualifier dataset. Include the dictionary version in the variable metadata. Conditional on whether a secondary SOC was used for the primary analysis. See Amendment 1 to SDTM [3].
AESOCCD	Primary System Organ Class Code	Num	MedDRA	Perm	AE.AESOCCD This would be copied from the SDTM AE domain or supplemental qualifier dataset. Include the dictionary version in the variable metadata.

4.1.4 Timing Variables

Timing variables are copied from SDTM and derived within ADaM. Included below are the common timing variables. If other timing variables are collected in SDTM and pertinent for analysis, these should be included in ADaM. Additional timing variables, such as those for analysis period or phase, can be included. For more details on timing variables, see the BDS structure in the ADaMIG version 1 [2].

Table 4.1.4.1 Timing Variables

ADAE – Adverse Event Analysis Dataset					
Variable Name	**Variable Label**	**Type**	**Code List / Controlled Terms**	**Core**	**CDISC Notes**
AESTDTC	Start Date/Time of Adverse Event	Char	ISO 8601	Perm	Copied from AE.AESTDTC
ASTDT	Analysis Start Date	Num		Cond	Created from converting AE.AESTDTC from character ISO8601 format to numeric date format, applying imputation rules as specified in the SAP or metadata. Conditional on whether start date is pertinent for study and AE.AESTDTC is populated in SDTM.
ASTDTM	Analysis Start Date/Time	Num		Cond	Created from converting AE.AESTDTC from character ISO8601 format to numeric date-time format, applying imputation rules as specified in the SAP or metadata. Conditional on whether start date-time is pertinent for study and AE.AESTDTC with time is populated in SDTM.
ASTDTF	Analysis Start Date Imputation Flag	Char	(DATEFL)	Cond	Created during conversion of AE.AESTDTC from character to numeric. Imputation flags are described in the ADaMIG V1.0 [2] General Timing Variable Convention #6. Conditional on whether any imputation is done for the start date.
ASTTMF	Analysis Start Time Imputation Flag	Char	(TIMEFL)	Cond	Created during conversion of AE.AESTDTC from character to numeric. Imputation flags are described in the ADaMIG V1.0 [2] General Timing Variable Convention #6. Conditional on whether any imputation is done for the start time.

ADAE – Adverse Event Analysis Dataset					
Variable Name	**Variable Label**	**Type**	**Code List / Controlled Terms**	**Core**	**CDISC Notes**
AEENDTC	End Date/Time of Adverse Event	Char	ISO 8601	Perm	Copied from AE.AEENDTC
AENDT	Analysis End Date	Num		Cond	Created from converting AE.AEENDTC from character ISO8601 format to numeric date format, applying imputation rules as specified in the SAP or metadata. Conditional on whether end date is pertinent for study and AE.AEENDTC is populated in SDTM.
AENDTM	Analysis End Date/Time	Num		Cond	Created from converting AE.AEENDTC from character ISO8601 format to numeric date-time format, applying imputation rules as specified in the SAP or metadata. Conditional on whether end date-time is pertinent for study and AE.AEENDTC with time is populated in SDTM.
AENDTF	Analysis End Date Imputation Flag	Char	(DATEFL)	Cond	Created during conversion of AE.AEENDTC from character to numeric. Imputation flags are described in the ADaMIG V1.0 [2] General Timing Variable Convention #6. Conditional on whether any imputation is done for the end date.
AENTMF	Analysis End Time Imputation Flag	Char	(TIMEFL)	Cond	Created during conversion of AE.AEENDTC from character to numeric. Imputation flags are described in the ADaMIG V1.0 [2] General Timing Variable Convention #6. Conditional on whether any imputation is done for the end time.
ASTDY	Analysis Start Relative Day	Num		Cond	Example derivation: ASTDT – ADSL.TRTSDT + 1 if ASTDT ≥ TRTSDT, else ASTDT – ADSL.TRTSDT if ASTDT < TRTSDT This variable may instead be copied from AESTDY. Conditional on whether analysis start relative day is pertinent to the study.

ADAE – Adverse Event Analysis Dataset					
Variable Name	**Variable Label**	**Type**	**Code List / Controlled Terms**	**Core**	**CDISC Notes**
AESTDY	Study Day of Start of Adverse Event	Num		Perm	AE.AESTDY ASTDY may differ from AESTDY due to date imputation and the option in ADaM to use a reference date other than SDTM's RFSTDTC. Including AE.AESTDY in addition to ASTDY adds traceability.
AENDY	Analysis End Relative Day	Num		Perm	Example derivation: AENDT – ADSL.TRTSDT + 1 if AENDT ≥ TRTSDT, else AENDT – ADSL.TRTSDT if AENDT < TRTSDT This variable may instead be copied from AEENDY.
AEENDY	Study Day of End of Adverse Event	Num		Perm	AE.AEENDY AENDY may differ from AEENDY due to date imputation and the option in ADaM to use a reference date other than SDTM's RFSTDTC. Including AE.AEENDY in addition to AENDY adds traceability.
ADURN	AE Duration (N)	Num		Perm	Derive from ASTDT (or ASTDTM) and AENDT (or AENDTM)
ADURU	AE Duration Units	Char		Cond	Conditional on whether ADURN is included.
AEDUR	Duration of Adverse Event	Char	ISO 8601	Perm	AE.AEDUR Because AEDUR is a collected field and ADURN is derived, the values will often differ. Including AEDUR in addition to ADURN can add traceability.
APERIOD	Period	Num		Perm	The numeric value characterizing the period to which the record belongs.
APERIODC	Period (C)	Char		Perm	Text characterizing to which period the record belongs. One-to-one map to APERIOD.

ADAE – Adverse Event Analysis Dataset					
Variable Name	**Variable Label**	**Type**	**Code List / Controlled Terms**	**Core**	**CDISC Notes**
APHASE	Phase	Char		Perm	Example derivation: If ASTDT<ADSL.TRTSDT, then APHASE='RUN-IN' Else if ASTDT > ADSL.TRTEDT + x days then APHASE='FOLLOW-UP', Else APHASE='TREATMENT'. The number x is defined by the sponsor, should be consistent with the Treatment Emergent Analysis Flag (TRTEMFL) variable described below and often incorporates the known half-life of the drug.

Values in parenthesis are the names of CDISC Controlled Terminology codelists.

4.1.5 Indicator Variables

Indicator variables can be copied from SDTM or derived within ADaM. If indicator variables other than those shown here are included in SDTM and pertinent for analysis, these should be copied to ADaM. If other indicator analysis variables are needed for analysis, these can also be added.

Table 4.1.5.1 Indicator Variables

ADAE – Adverse Event Analysis Dataset					
Variable Name	**Variable Label**	**Type**	**Code List / Controlled Terms**	**Core**	**CDISC Notes**
TRTEMFL	Treatment Emergent Analysis Flag	Char	Y	Cond	Example derivation: If ADSL.TRTSDT≤ASTDT≤ADSL.TRTEDT + x days then TRTEMFL='Y' The number x is defined by the sponsor and often incorporates the known half-life of the drug. Variable TRTEMFL is to be used for any analysis of treatment-emergent AEs. This variable is conditional on whether the concept of treatment emergent is a key feature of the AE analyses.

ADAE – Adverse Event Analysis Dataset					
Variable Name	**Variable Label**	**Type**	**Code List / Controlled Terms**	**Core**	**CDISC Notes**
AETRTEM	Treatment Emergent Flag	Char	(NY)	Perm	SUPPAE.QVAL where QNAM='AETRTEM'. See the SDTMIG version 3.1.2 [3] for more information. TRTEMFL may differ from AETRTEM due to different definitions, date imputation, and other analysis rules. Including AETRTEM in addition to TRTEMFL will add traceability.
ANLzzFL	Analysis Record Flag zz	Char	Y	Cond	The ANLzzFL flag is useful in many circumstances; an example is when there is more than one coding path included for analysis, in which case separate analysis flags could be used to denote primary coding path or the records used for analysis from each coding path. See the ADaMIG version 1 [2] for more information on this flag variable. This variable is conditional on whether analysis records flags are needed for analysis.
PREFL	Pre-treatment Flag	Char	Y	Cond	Example derivation: If ASTDT < ADSL.TRTSDT then PREFL='Y' This variable is conditional on whether the concept of pre-treatment AEs is a feature of the study and whether used for analysis.
FUPFL	Follow-up Flag	Char	Y	Cond	Example derivation: If ASTDT > ADSL.TRTEDT then FUPFL='Y' This variable is conditional on whether the concept of follow-up AEs is a feature of the study and whether used for analysis.

Values in parenthesis are the names of CDISC Controlled Terminology codelists.

4.1.6 Occurrence Flag Variables

Occurrence flags can be used to prepare data for analysis. They are typically created by sorting the data in the required order and then flagging the first treatment emergent record. The more common occurrence flags for MedDRA and a structure for additional flags are show below:

Table 4.1.6.1 Occurrence Flag Variables

ADAE – Adverse Event Analysis Dataset					
Variable Name	**Variable Label**	**Type**	**Code List / Controlled Terms**	**Core**	**CDISC Notes**
AOCCFL	1st Occurrence of Any AE Flag	Char	Y	Perm	Example derivation: Sort the data in the required order and flag the first treatment emergent record for each subject.
AOCCSFL	1st Occurrence of SOC Flag	Char	Y	Perm	Example derivation: Sort the data in the required order and flag the first treatment emergent record for each body system for each subject.
AOCCPFL	1st Occurrence of Preferred Term Flag	Char	Y	Perm	Example derivation: Sort the data in the required order and flag the first treatment emergent record for each preferred term for each subject.
AOCCIFL	1st Max Sev./Int. Occurrence Flag	Char	Y	Perm	Example derivation: Sort the data in the required order and flag the first treatment emergent record for maximum severity for each subject.
AOCCSIFL	1st Max Sev./Int. Occur Within SOC Flag	Char	Y	Perm	Example derivation: Sort the data in the required order and flag the first treatment emergent record for maximum severity within body system for each subject.
AOCCPIFL	1st Max Sev./Int. Occur Within PT Flag	Char	Y	Perm	Example derivation: Sort the data in the required order and flag the first treatment emergent record for maximum severity within preferred term for each subject.
AOCCzzFL	1st Occurrence of ….	Char	Y	Perm	Additional flag variables as needed for analysis. Derivation rules for these flags need to be described in the metadata.

4.1.7 Treatment/Dose Variables

The treatment variable used for analysis must be included. Typically this would be TRTP, TRTA, TRTxxP, or TRTxxA. See the ADaMIG version 1 [2] for more details on these variables. Additional dosing variables may also be included.

Table 4.1.7.1 Treatment Variables

ADAE – Adverse Event Analysis Dataset					
Variable Name	**Variable Label**	**Type**	**Code List / Controlled Terms**	**Core**	**CDISC Notes**
DOSEAEON	Study Drug Dose at AE Onset	Num		Perm	Study drug dose a subject took when adverse event occurred. Example derivation: Obtained from EX.EXDOSE where AESTDTC falls between the values of EX.EXSTDTC and EX.EXENDTC
DOSAEONU	Study Drug Dose at AE Onset Units	Char		Cond	Conditional on whether DOSEAEON is included.
DOSECUM	Cumulative Study Drug Dose	Num		Perm	Cumulative study drug dose at the start of the AE.
DOSECUMU	Cumulative Study Drug Dose Units	Char		Cond	Conditional on whether DOSECUM is included.

4.1.8 Descriptive Variables

Variables that describe the adverse event, including severity, relationship, and toxicity grade, are often used in analysis. If the analysis version of the variable differs from the version in SDTM, additional variables must be added using the conventions below and described in Section 4.1 . Below are some common descriptive variables that are often included in ADAE. Any other SDTM variables should be included as appropriate (e.g. AEOUT, AESDTH, etc.).

Table 4.1.8.1 Descriptive Variables

ADAE – Adverse Event Analysis Dataset					
Variable Name	**Variable Label**	**Type**	**Code List / Controlled Terms**	**Core**	**CDISC Notes**
AESER	Serious Event	Char	(NY)	Req	AE.AESER
AESEV	Severity/Intensity	Char	(AESEV)	Perm	AE.AESEV
AESEVN	Severity/Intensity (N)	Num	1, 2, 3	Perm	Code AE.AESEV to numeric Low intensity should correspond to low value

ADAE – Adverse Event Analysis Dataset					
Variable Name	**Variable Label**	**Type**	**Code List / Controlled Terms**	**Core**	**CDISC Notes**
ASEV	Analysis Severity/Intensity	Char	*	Perm	Apply imputation rules for missing severity of adverse events as specified in the SAP or metadata. May change case of text, such as from all uppercase in AESEV to mixed case in ASEV.
ASEVN	Analysis Severity/Intensity (N)	Num	1, 2, 3	Perm	Code ASEV to numeric Low intensity should correspond to low value
SEVGRy	Pooled Severity Group y	Char	*	Perm	Pooled grouping of AE Severity for analysis (e.g. mild/moderate or severe).
SEVGRyN	Pooled Severity Group y (N)	Num	*	Perm	Code SEVGRy to numeric Low intensity should correspond to low value
AEREL	Causality	Char	*	Perm	AE.AEREL
AERELN	Causality (N)	Num	*	Perm	Code AE.AEREL to numeric Low relation should correspond to low value
AREL	Analysis Causality	Char	*	Perm	Apply imputation rules for missing causality of study drug as specified in the SAP or metadata. May change case of text, such as from all uppercase in AEREL to mixed case in AREL.
ARELN	Analysis Causality (N)	Num	*	Perm	Code AREL to numeric
RELGRy	Pooled Causality Group y	Char	*	Perm	Pooled grouping of causality of study drug for analysis (e.g. related, Not related).
RELGRyN	Pooled Causality Group y (N)	Num	*	Perm	Code of RELGRy to numeric Low intensity should correspond to low value
AETOXGR	Standard Toxicity Grade	Char	*	Perm	AE.AETOXGR
AETOXGRN	Standard Toxicity Grade (N)	Num	*	Perm	Code AETOXGR to numeric Low toxicity should correspond to low value
ATOXGR	Analysis Toxicity Grade	Char	*	Perm	Toxicity grade for analysis. May be based on AETOXGR or an imputed or assigned value. May change case of text, such as from all uppercase in AETOXGR to mixed case in ATOXGR.

ADAE – Adverse Event Analysis Dataset					
Variable Name	**Variable Label**	**Type**	**Code List / Controlled Terms**	**Core**	**CDISC Notes**
ATOXGRN	Analysis Toxicity Grade (N)	Num	*	Perm	Code ATOXGR to numeric Low toxicity should correspond to low value
TOXGGRy	Pooled Toxicity Grade Group y	Char	*	Perm	Pooled grouping of toxicity grade for analysis.
TOXGGRyN	Pooled Toxicity Grade y (N)	Num	*	Perm	Code of TOXGGRy to numeric Low toxicity should correspond to low value
AEACN	Action Taken with Study Treatment	Char	(ACN)	Perm	AE.AEACN

* Indicates variable may be subject to sponsor-defined controlled terminology. Values in parenthesis are the names of CDISC Controlled Terminology codelists.

4.1.9 MedDRA Query Variables

Standardized MedDRA Queries (SMQs) are becoming increasingly common in clinical trial safety evaluations, particularly when known or suspected safety issues are associated with experimental compounds. In addition, Customized Queries (CQs) are often used to modify an SMQ or identify AEs of special interest through grouping of MedDRA terms. The following variables are used to identify SMQs and CQs, where the 'zz' indicates a number starting with 01 for each SMQ or CQ of interest. This ordering can be based on importance or some other sponsor-defined criteria. It is recommended that the ordering be consistent across studies within a development program, but it is recognized that there may be situations where this is not possible or practical.

Table 4.1.9.1 Standardized MedDRA Query Variables

ADAE – Adverse Event Analysis Dataset					
Variable Name	**Variable Label**	**Type**	**Code List / Controlled Terms**	**Core**	**CDISC Notes**
SMQzzNAM	SMQ zz Name	Char		Cond	The standardized MedDRA query's name. Would be blank for terms that are not in the SMQ. Therefore this variable could be blank if none of the terms within the SMQ are present in the dataset. Conditional on whether SMQ analysis is done.

ADAE – Adverse Event Analysis Dataset					
Variable Name	**Variable Label**	**Type**	**Code List / Controlled Terms**	**Core**	**CDISC Notes**
SMQzzCD	SMQ zz Code	Num		Perm	The standardized MedDRA queries number code.
SMQzzSC	SMQ zz Scope	Char	BROAD, NARROW	Cond	The search strategy for SMQs can be narrow or broad. The preferred terms that are narrow in scope have high specificity for identifying events of interest while the broad terms have high sensitivity. By definition, all narrow terms are also considered within the broad score. Therefore, to summarize all broad terms, terms with either narrow OR broad would be considered. Will be null for terms that do not meet the criteria. Conditional on whether SMQ analysis is done.
SMQzzSCN	SMQ zz Scope (N)	Num	1, 2	Perm	Will be null for terms that do not meet the criteria.
CQzzNAM	Customized Query zz Name	Char		Cond	The customized query (CQ) name or name of the AE of special interest category based on a grouping of MedDRA terms. Would be blank for terms that are not in the CQ. Conditional on whether CQ analysis is done. Examples: “DERMATOLOGICAL EVENTS”, “CARDIAC EVENTS”, “IARS (INFUSION ASSOCIATED REACTIONS)”

4.1.10 Original or Prior Coding Variables

The suite of variables used for the primary analysis are described in section 4.1.2. Variables described here are those from original (or prior) analyses, and not used directly for analysis from this data set.

Keeping multiple sets of mapping variables is not common, but there are a couple instances where it might be helpful:

- When a study is mapped to one version of MedDRA or other mapping dictionary for an interim analysis and another for final analysis
- When studies using different version of MedDRA or other mapping dictionary are pooled together for an integrated analysis

The variables described below provide traceability to original (or prior) analysis(es). The suffix “y” represents an integer [1-9] corresponding to a previous version. Include the dictionary name and version as part of the metadata for each variable.

These variable names at this time are recommendations only. There is an ADaM sub-team currently working on integration, and this group may create different naming conventions for that type of analysis.

Table 4.1.10.1 Original or Prior MedDRA Coding Variables

ADAE – Adverse Event Analysis Dataset					
Variable Name	**Variable Label**	**Type**	**Code List / Controlled Terms**	**Core**	**CDISC Notes**
DECDORGy	PT in Original Dictionary y	Char	MedDRA	Perm	Original preferred term coding of AE.AETERM using MedDRA or other dictionary version X.X.
BDSYORGy	SOC in Original Dictionary y	Char	MedDRA	Perm	Original body system coding of AE.AETERM using MedDRA or other dictionary version X.X.
HLGTORGy	HLGT in Original Dictionary y	Char	MedDRA	Perm	Original HLGT coding of AE.AETERM using MedDRA or other dictionary version X.X.
HLTORGy	HLT in Original Dictionary y	Char	MedDRA	Perm	Original HLT coding of AE.AETERM using MedDRA or other dictionary version X.X.
LLTORGy	LLT in Original Dictionary y	Char	MedDRA	Perm	Original LLT coding of AE.AETERM using MedDRA or other dictionary version X.X.
LLTNORGy	LLT Code in Original Dictionary y	Char	MedDRA	Perm	Original LLT code of AE.AETERM using MedDRA or other dictionary version X.X.

4.2 Other Metadata

Because the AE structure does not use parameters, there is no need for Parameter Value-Level Metadata.

The other type of ADaM metadata is the Analysis Results Metadata, which may be included for analysis of AEs. (see ADaM v2.1 [1] for more details).

5. Example 1: Analysis of Treatment Emergent Adverse Events

The basic summary of adverse event frequencies described in section 12.2.2 (and located in section 14.3.1) of ICH Guideline E3 [7] report should be used to display frequencies in treatment and control groups.

This example displays a simple summary of all treatment emergent adverse events. The example is based on a two treatment parallel design study. The display summarizes (1) the number of subjects in each treatment group in whom any adverse event was experienced and (2) the rate of occurrence in each treatment group.

5.1 Analysis Display Example Layout

Table 5.1.1 Example of Summary of Treatment Emergent Adverse Events[2]

Table 14.2.7.1

Summary of Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Analysis Population: Safety

SYSTEM ORGAN CLASS **Preferred Term**	**Treatment A** **(N = xxx)** **n (%)**	**Treatment B** **(N = xxx)** **n (%)**
Number of subjects reporting at least one adverse event	x (x.x)	x (x.x)
BLOOD AND LYMPHATIC SYSTEM DISORDERS		
At least one event	x (x.x)	x (x.x)
Anaemia	x (x.x)	x (x.x)
…	x (x.x)	x (x.x)
CARDIAC DISORDERS		
At least one event	x (x.x)	x (x.x)
Angina pectoris	x (x.x)	x (x.x)
Coronary artery disease	x (x.x)	x (x.x)
Ventricular tachycardia	x (x.x)	x (x.x)
Myocardial infarction	x (x.x)	x (x.x)
Ventricular fibrillation	x (x.x)	x (x.x)
…	x (x.x)	x (x.x)
<Other SOCs and PTs>		

Page 1 of x

N = Safety subjects, i.e., subjects who received at least one dose of study drug
n = Number of subjects reporting at least one treatment emergent adverse event
% = n / N * 100
Adverse events are presented by descending frequency within Treatment B
System organ classes and preferred terms are coded using MedDRA version x.x.

[2] The style of the display of the results of an analysis will be determined by the sponsor. The example is intended to illustrate content not appearance.

5.2 Sample ADAE Variable Metadata

Table 5.2.1 Example of ADAE Variable Metadata

Dataset Name	Variable Name	Variable Label	Variable Type	Display Format	Codelist / Controlled Terms	Source / Derivation
ADAE	STUDYID	Study Identifier	text	$3		AE.STUDYID
ADAE	USUBJID	Unique Subject Identifier	text	$11		AE.USUBJID
ADAE	AESEQ	Sequence Number	integer	3.0		AE.AESEQ
ADAE	AETERM	Reported Term for the Adverse Event	text	$200		AE.AETERM
ADAE	AEDECOD	Dictionary-Derived Term	text	$200	MedDRA	AE.AEDECOD MedDRA Version 11.1
ADAE	AEBODSYS	Body System or Organ Class	text	$200	MedDRA	AE.AEBODSYS MedDRA Version 11.1
ADAE	TRTEMFL	Treatment Emergent Analysis Flag	text	$1	Y	If ADSL.TRTSDT <= ASTDT<=(ADSL.TRTEDT +14) then TRTEMFL='Y'
ADAE	PREFL	Pre-treatment Flag	text	$1	Y	If ASTDT < ADSL.TRTSDT then PREFL='Y'
ADAE	FUPFL	Follow-up Flag	text	$1	Y	If ASTDT > ADSL.TRTEDT+14 then FUPFL='Y'
ADAE	AESTDTC	Start Date/Time of Adverse Event	text	$10		AE.AESTDTC
ADAE	ASTDT	Analysis Start Date	integer	yymmdd10.		<Sponsor will insert derivation here>
ADAE	ASTDTF	Analysis Start Date Imputation Flag	text	$1	(DATEFL)	If start date is completely missing or missing the year then ASTDTF='Y' Else if start date has month missing then ASTDTF='M' Else if start date has day missing then ASTDTF='D'
ADAE	AEENDTC	End Date/Time of Adverse Event	text	$10		AE.AEENDTC
ADAE	AENDT	Analysis End Date	integer	yymmdd10.		<Sponsor will insert derivation here>

Dataset Name	Variable Name	Variable Label	Variable Type	Display Format	Codelist / Controlled Terms	Source / Derivation
ADAE	AENDTF	Analysis End Date Imputation Flag	text	$1	(DATEFL)	If end date is completely missing or missing the year then AENDTF='Y' Else if end date has month missing then AENDTF='M' Else if end date has day missing then AENDTF='D'
ADAE	AESER	Serious Event	text	$1	(YN)	AE.AESER
ADAE	APHASE	Phase	text	$15	PRE-TREATMENT TREATMENT FOLLOW-UP	If ASTDT<ADSL.TRTSDT, then APHASE='PRE-TREATMENT' Else if ASTDT > ADSL.TRTEDT + 14 days then APHASE='FOLLOW-UP', Else APHASE='TREATMENT'
ADAE	AESEV	Severity/Intensity	text	$25	(AESEV)	AE.AESEV
ADAE	ASEV	Analysis Severity/Intensity	text	$25	Mild Moderate Severe	If AE.AESEV='MILD' then ASEV='Mild' Else if AE.AESEV='MODERATE' then ASEV='Moderate' Else if AE.AESEV is equal to 'SEVERE' or Severity/Intensity is missing then ASEV='Severe'
ADAE	ASEVN	Analysis Severity/Intensity (N)	integer	1.0	1, 2, 3	Map ASEV to ASEVN in the following manner: 'Mild' = 1 'Moderate' = 2 'Severe' = 3
ADAE	AEREL	Causality	text	$25	NOT RELATED UNLIKELY RELATED POSSIBLY RELATED PROBABLY RELATED DEFINITELY RELATED	AE.AEREL
ADAE	RELGR1	Pooled Causality Group 1	text	$25	Not Related Related	If AE.AEREL is equal to 'NOT RELATED' or 'UNLIKELY RELATED' then RELGR1='Not Related' Else if AE.AEREL is equal to 'POSSIBLY RELATED' or 'PROBABLY RELATED' or 'DEFINITELY RELATED' or Causality is missing then RELGR1='Related'

Dataset Name	Variable Name	Variable Label	Variable Type	Display Format	Codelist / Controlled Terms	Source / Derivation
ADAE	RELGR1N	Pooled Causality Group 1 (N)	integer	1.0	0, 1	Map RELGR1 to RELGR1N in the following manner: 'Not Related' = 0 'Related' = 1
ADAE	SAFFL	Safety Population Flag	text	$1	Y,N	ADSL.SAFFL
ADAE	AOCCFL	1st Occurrence of Any AE Flag	text	$1	Y	Subset ADAE to Treatment Emergent Adverse Events (TRTEMFL='Y') Sort by Subject (USUBJID), Analysis Start Date (ASTDT), and Sequence Number (AESEQ) and flag the first record (set AOCCFL='Y') within each Subject
ADAE	AOCCSFL	1st Occurrence of SOC Flag	text	$1	Y	Subset ADAE to Treatment Emergent Adverse Events (TRTEMFL='Y') Sort by Subject (USUBJID), System Organ Class (AEBODSYS), Analysis Start Date (ASTDT), and Sequence Number (AESEQ) and flag the first record (set AOCCSFL ='Y') within each Subject and SOC
ADAE	AOCCPFL	1st Occurrence of Preferred Term Flag	text	$1	Y	Subset ADAE to Treatment Emergent Adverse Events (TRTEMFL='Y') Sort by Subject (USUBJID), System Organ Class (AEBODSYS), Preferred Term (AEDECOD) Analysis Start Date (ASTDT), and Sequence Number (AESEQ) and flag the first record (set AOCCPFL ='Y') within each Subject, SOC, and PT
ADAE	TRTA	Actual Treatment	text	$6	Drug A Drug B	ADSL.TRT01A
ADAE	TRTAN	Actual Treatment (N)	integer	1.0	1, 2	ADSL.TRT01AN Drug A = 1 Drug B = 2
ADAE	TRTSDT	Date of First Exposure to Treatment	integer	yymmdd10.		ADSL.TRTSDT
ADAE	TRTEDT	Date of Last Exposure to Treatment	integer	yymmdd10.		ADSL.TRTEDT
ADAE	AGE	Age	integer	3.0		ADSL.AGE

Dataset Name	Variable Name	Variable Label	Variable Type	Display Format	Codelist / Controlled Terms	Source / Derivation
ADAE	AGEGR1	Pooled Age Group 1	text	$4	<65, >=65	ADSL. AGEGR1
ADAE	SEX	Sex	text	$1	(SEX)	ADSL.SEX
ADAE	RACE	Race	text	$41	(RACE)	ADSL.RACE

5.3 Sample ADAE Data

Table 5.3.1 is an illustration of the adverse events analysis dataset (ADAE) defined above. The ADAE dataset illustrated in this example was designed to support some standard subsets and/or classifications of treatment emergent adverse events including seriousness, severity, and relationship to study drug. The example describes some of the key variables and records that would be included in the dataset.

Key points to note in the example are:

1. The producer of the dataset chose to use record level actual treatment variable (TRTA) populated with the same value across all rows in the dataset rather than subject level treatment variable (TRT01A). For a parallel design either TRTA or TRT01A could be used as the actual treatment identifier. The producer interpreted TRTA as the treatment associated with the record for analysis display purposes and populated the pre-treatment records with treatment even though subjects had not yet received treatment at that time.

2. Variables such as AESEQ, AETERM, and AESTDTC are copied in from SDTM AE domain to provide data point traceability.

3. Variables such as AEBODSYS, AEDECOD, AESER, AESEV, and AEREL are copied in from the SDTM AE domain for analysis purposes.

4. ASTDT is the AE timing variable used for analysis. Other timing variables such as AENDT/ASTDTF/AENDTF/ AESTDTC/AEENDTC/TRTSDT/TRTEDT are supportive variables for metadata traceability.

5. The addition of ASEV and RELGR1 allow for the imputation of missing severity and grouping and imputation of Relationship to Study Drug as specified in the Statistical Analysis Plan.

6. The Occurrence Flags (AOCCzzFL) are permissible. The main purpose of these flags is to facilitate data point traceability between records in the dataset and unique counts in the summary displays. In addition if a Time to Event (TTE) Analysis is built off of Adverse Events, the flags provide a crucial link between the summary records in the TTE BDS and the source of the records in ADAE. If the producer of the ADAE dataset has standard programs in place to summarize unique counts of events then they may chose not to create these flags.

7. The core variables of AGE, AGEGR1, SEX, and RACE are included in ADAE to facilitate subgroup analyses.

Table 5.3.1 Sample ADAE Data

Row	STUDYID	USUBJID	AESEQ	AETERM	AEDECOD	AEBODSYS	TRTEMFL	PREFL	FUPFL
1	XYZ	XYZ-001-001	1	HEADACHE	Headache	Nervous system disorders		Y	
2	XYZ	XYZ-001-001	2	CHRONIC BACK PAIN	Back pain	Musculoskeletal and connective tissue disorders		Y	
3	XYZ	XYZ-001-001	3	NOSE BLEEDING RIGHT NOSTRIL	Epistaxis	Respiratory, thoracic and mediastinal disorders		Y	
4	XYZ	XYZ-001-001	4	PROBLEMS OF HYPOTENSION	Hypotension	Vascular disorders	Y		
5	XYZ	XYZ-001-001	5	HEADACHE	Headache	Nervous system disorders	Y		
6	XYZ	XYZ-001-001	6	HEADACHE	Headache	Nervous system disorders	Y		
7	XYZ	XYZ-001-001	7	LOOSE STOOL	Diarrhoea	Gastrointestinal disorders	Y		
8	XYZ	XYZ-001-001	8	ABDOMINAL DISCOMFORT	Abdominal discomfort	Gastrointestinal disorders	Y		
9	XYZ	XYZ-001-001	9	DIARRHEA	Diarrhoea	Gastrointestinal disorders	Y		
10	XYZ	XYZ-001-001	10	ABDOMINAL FULLNESS DUE TO GAS	Abdominal distension	Gastrointestinal disorders	Y		
11	XYZ	XYZ-001-001	11	NAUSEA (INTERMITTENT)	Nausea	Gastrointestinal disorders	Y		
12	XYZ	XYZ-001-001	12	WEAKNESS	Asthenia	General disorders and administration site conditions	Y		
13	XYZ	XYZ-001-001	13	HEADACHE	Headache	Nervous system disorders	Y		
14	XYZ	XYZ-001-001	14	HEADACHE	Headache	Nervous system disorders	Y		
15	XYZ	XYZ-001-001	15	HYPOTENSIVE	Hypotension	Vascular disorders	Y		
16	XYZ	XYZ-001-001	16	HEADACHE	Headache	Nervous system disorders			Y

Row	AESTDTC	ASTDT	ASTDTF	AEENDTC	AENDT	AENDTF	AESER	APHASE	AESEV	ASEV	ASEVN
1	2006-01	2006-01-01	D	2006-01-22	2006-01-22		N	PRE-TREATMENT	MILD	Mild	1
2	2006-01-21	2006-01-21		2006-01-28	2006-01-28		N	PRE-TREATMENT	MODERATE	Moderate	2
3	2006-01-22	2006-01-22		2006-01-22	2006-01-22		N	PRE-TREATMENT	MILD	Mild	1
4		2006-01-23	Y		2006-05-15	Y	N	TREATMENT	MILD	Mild	1

Row	AESTDTC	ASTDT	ASTDTF	AEENDTC	AENDT	AENDTF	AESER	APHASE	AESEV	ASEV	ASEVN
5	2006-01-24	2006-01-24		2006-01	2006-01-31	D	N	TREATMENT	MODERATE	Moderate	2
6	2006-02	2006-02-01	D	2006-02-05	2006-02-05		N	TREATMENT	SEVERE	Severe	3
7	2006-03-05	2006-03-05		2006-03-06	2006-03-06		N	TREATMENT		Severe	3
8	2006-03-05	2006-03-05		2006	2006-05-15	M	N	TREATMENT	MODERATE	Moderate	2
9	2006-03-17	2006-03-17		2006-03-18	2006-03-18		N	TREATMENT	MODERATE	Moderate	2
10	2006-03-17	2006-03-17		2006-03-19	2006-03-19		N	TREATMENT	MILD	Mild	1
11	2006-04-20	2006-04-20		2006-04-22	2006-04-22		N	TREATMENT	MILD	Mild	1
12	2006-05-17	2006-05-17		2006-05-20	2006-05-20		N	TREATMENT	MILD	Mild	1
13	2006-05-20	2006-05-20		2006-05-22	2006-05-22		N	TREATMENT	MILD	Mild	1
14	2006-05-23	2006-05-23		2006-06-27	2006-06-27		N	TREATMENT	MILD	Mild	1
15	2006-05-21	2006-05-21		2006-05-25	2006-05-25		Y	TREATMENT	SEVERE	Severe	3
16	2006-06-01	2006-06-01		2006-06-01	2006-06-01		N	FOLLOW-UP	MILD	Mild	1

Row	AEREL	RELGR1	RELGR1N	SAFFL	AOCCFL	AOCCSFL	AOCCPFL	TRTA	TRTAN	TRTSDT	TRTEDT
1	NOT RELATED	Not Related	0	Y				Drug A	1	2006-01-23	2006-05-15
2	NOT RELATED	Not Related	0	Y				Drug A	1	2006-01-23	2006-05-15
3	NOT RELATED	Not Related	0	Y				Drug A	1	2006-01-23	2006-05-15
4	POSSIBLY RELATED	Related	1	Y	Y	Y	Y	Drug A	1	2006-01-23	2006-05-15
5	PROBABLY RELATED	Related	1	Y		Y	Y	Drug A	1	2006-01-23	2006-05-15
6	PROBABLY RELATED	Related	1	Y				Drug A	1	2006-01-23	2006-05-15
7	DEFINITELY RELATED	Related	1	Y		Y	Y	Drug A	1	2006-01-23	2006-05-15
8	DEFINITELY RELATED	Related	1	Y			Y	Drug A	1	2006-01-23	2006-05-15
9	DEFINITELY RELATED	Related	1	Y				Drug A	1	2006-01-23	2006-05-15
10	DEFINITELY RELATED	Related	1	Y			Y	Drug A	1	2006-01-23	2006-05-15
11	PROBABLY RELATED	Related	1	Y			Y	Drug A	1	2006-01-23	2006-05-15
12	POSSIBLY RELATED	Related	1	Y		Y	Y	Drug A	1	2006-01-23	2006-05-15
13	UNLIKELY RELATED	Not Related	0	Y				Drug A	1	2006-01-23	2006-05-15

Row	AEREL	RELGR1	RELGR1N	SAFFL	AOCCFL	AOCCSFL	AOCCPFL	TRTA	TRTAN	TRTSDT	TRTEDT
14	UNLIKELY RELATED	Not Related	0	Y				Drug A	1	2006-01-23	2006-05-15
15	UNLIKELY RELATED	Not Related	0	Y				Drug A	1	2006-01-23	2006-05-15
16	UNLIKELY RELATED	Not Related	0	Y				Drug A	1	2006-01-23	2006-05-15

Row	AGE	AGEGR1	SEX	RACE
1	54	<65	M	ASIAN
2	54	<65	M	ASIAN
3	54	<65	M	ASIAN
4	54	<65	M	ASIAN
5	54	<65	M	ASIAN
6	54	<65	M	ASIAN
7	54	<65	M	ASIAN
8	54	<65	M	ASIAN
9	54	<65	M	ASIAN
10	54	<65	M	ASIAN
11	54	<65	M	ASIAN
12	54	<65	M	ASIAN
13	54	<65	M	ASIAN
14	54	<65	M	ASIAN
15	54	<65	M	ASIAN
16	54	<65	M	ASIAN

6. Example 2: Analysis of Hemorrhages (SMQ) among Treatment Emergent Adverse Events by Sex

This example demonstrates how to incorporate SMQs into an AE analysis data set. In this example, an SMQ for hemorrhages is being used. This particular SMQ is hierarchical with only narrow-scope terms, including terms referring to different types of hemorrhage, hematoma, bleeding, etc. (for a full description of SMQs one may refer to the Maintenance and Support Services Organization (MSSO's) Introductory Guide for Standardized MedDRA Queries [8]).

Key points to note in the example are:

1. The exact name of the SMQ being used in this example is "Haemorrhages (SMQ)". This precise terminology is used throughout the example.
2. As mentioned above, this particular SMQ contains only narrow scope terms. However, in order to illustrate best practice, the scope is also specified when a reference is made to the SMQ. Although redundant in this particular case, it is important to show which scope is being used when providing SMQ-based summaries since the scope can often have a profound effect on the percent of subjects who meet certain SMQ criteria.

6.1 Analysis Display Example Layouts

Table 6.1.1 Example of Summary of Haemorrhages (SMQ) (Narrow Scope) Adverse Events by Sex and Actual Treatment Group[3]

Table 14.2.7.3

Summary of Haemorrhages (SMQ) (Narrow Scope) Adverse Events by Sex and Actual Treatment Group

Analysis Population: Safety

Preferred Term	Treatment Group n (%)			
	B (N=447)		A (N=455)	
	Females (N=281)	Males (N=166)	Females (N=297)	Males (N=158)
Any Haemorrhages (SMQ) (Narrow Scope) Event	36 (12.8)	48 (28.9)	26 (8.8)	31 (19.6)
Cerebral haemorrhage	11 (3.9)	15 (9.0)	6 (2.0)	13 (8.2)
Conjunctival haemorrhage	0	1 (0.6)	0	0
Ecchymosis	1 (0.4)	0	0	0
Epistaxis	0	1 (0.6)	0	0
Extradural haematoma	1 (0.4)	0	1 (0.3)	1 (0.6)
Gastrointestinal haemorrhage	10 (3.6)	4 (2.4)	8 (2.7)	6 (3.8)
Haematuria	1 (0.4)	2 (1.2)	0	3 (1.9)
Haemoptysis	1 (0.4)	1 (0.6)	0	0
Haemorrhage	1 (0.4)	2 (1.2)	0	0
Infusion site haemorrhage	1 (0.4)	4 (2.4)	2 (0.7)	2 (1.3)
Melaena	0	0	0	1 (0.6)
Petechiae	0	1 (0.6)	0	0
Subarachnoid haemorrhage	14 (5.0)	24 (14.5)	12 (4.0)	11 (7.0)
Subdural haematoma	2 (0.7)	2 (1.2)	0	0

[3] The style of the display of the results of an analysis will be determined by the sponsor. The example is intended to illustrate content not appearance.

Figure 14.2.7.1
Mosaic Plot of Hemorrhagic (SMQ) Preferred Terms by Sex and Actual Treatment Group
Analysis Population: Safety

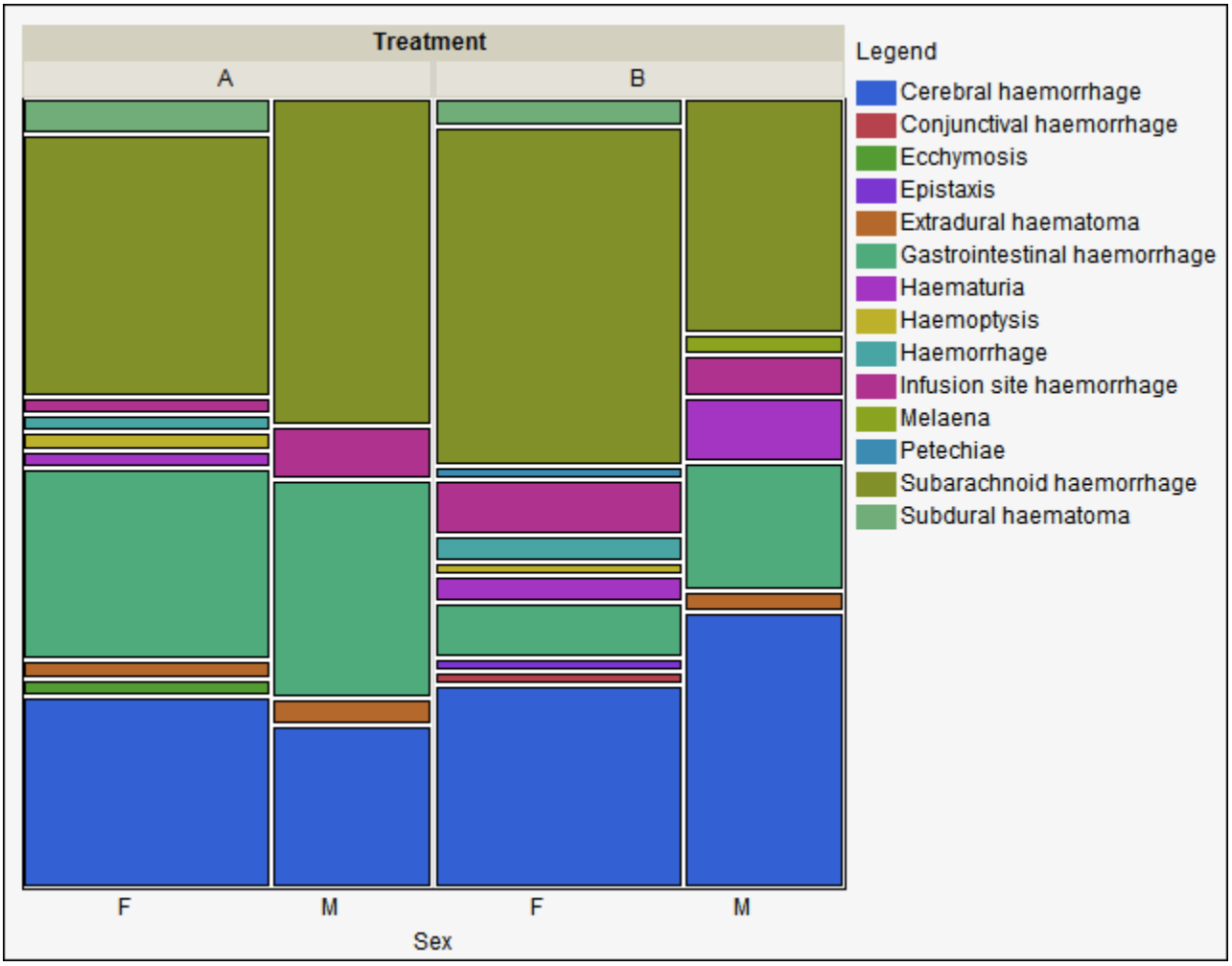

Figure 6.1.1 Example of Mosaic Plot of Haemorrhages (SMQ) (Narrow Scope) Preferred Terms by Sex and Actual Treatment Group[4]

[4] The style of the display of the results of an analysis will be determined by the sponsor. The example is intended to illustrate content not appearance.

Figure 14.2.7.2

Hemorrhagic (SMQ) Preferred Terms Sorted by Relative Risk

Analysis Population: Safety Population

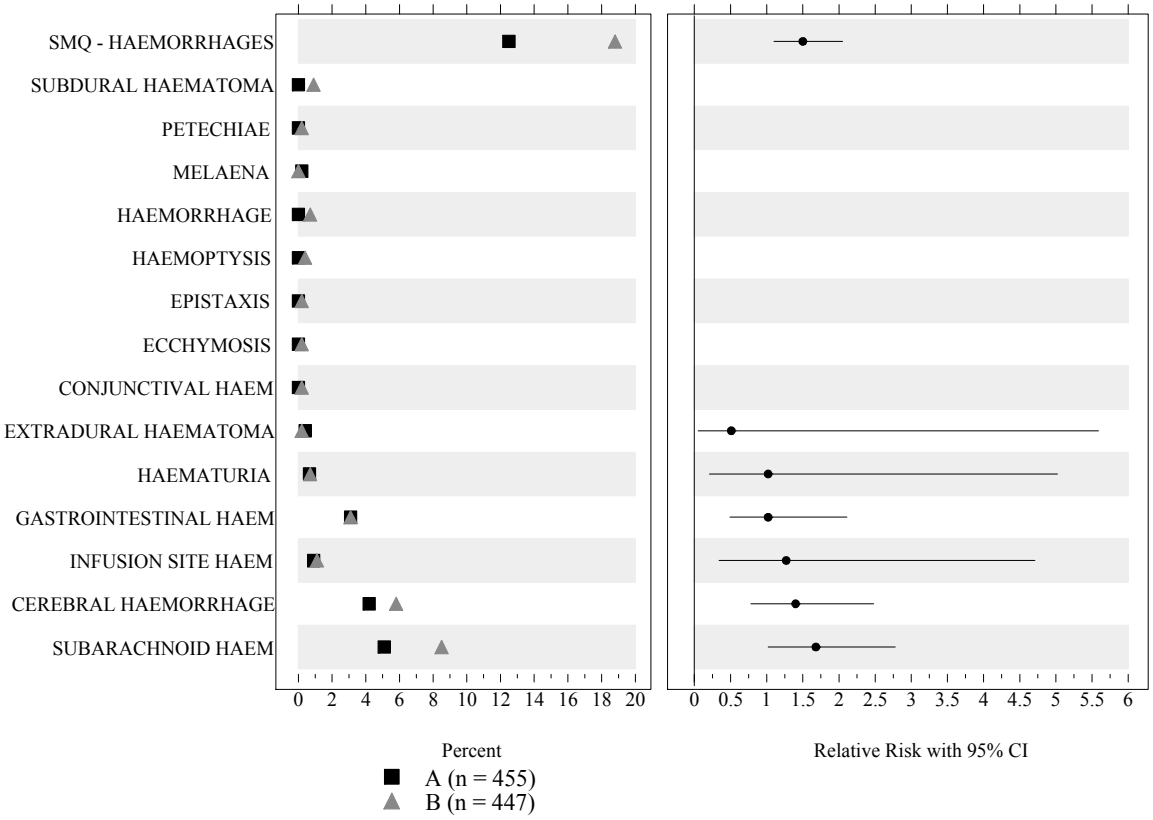

Figure 6.1.2 Example of Haemorrhages (SMQ) (Narrow Scope) Preferred Terms Sorted by Relative Risk[5]

[5] The style of the display of the results of an analysis will be determined by the sponsor. The example is intended to illustrate content not appearance.

6.2 Sample ADAE Variable Metadata

In Table 6.2.1 below, four variables relate to our primary SMQ of interest (hemorrhage terms), SMQ01CD, SMQ01NAM SMQ01SC, and SMQ01SCN. The '01' indicates that this is the first SMQ and subsequent SMQs or subSMQs would be sequenced accordingly. Note that this ordering can be based on importance or some other sponsor-defined criteria. The first two of these variables, SMQ01CD and SMQ01NAM contain the numeric code and name for the SMQ from the MedDRA dictionary. The next two variables, SMQ01SC and SMQ01SCN, are character and numeric variables, respectively, that indicate not only whether or not the given AE meets the criteria for the given SMQ, but also whether the term meets the SMQ's broad or narrow scope (the 'SC' suffix is for "scope").

Table 6.2.1 Example of ADAE Variable Metadata

Dataset Name	Variable Name	Variable Label	Variable Type	Display Format	Codelist / Controlled Terms	Source / Derivation
ADAE	USUBJID	Unique Subject Identifier	Text	$6		ADSL.USUBJID
ADAE	AETERM	Reported Term for the Adverse Event	Text	$200		AE.AETERM
ADAE	AEDECOD	Dictionary-Derived Term	Text	$200	MedDRA	AE.AEDECOD
ADAE	AEBODSYS	Body System or Organ Class	Text	$200	MedDRA	AE.AEBODSYS
ADAE	ASTDT	Analysis Start Date	Integer	yymmdd10.		<Sponsor will insert derivation here>
ADAE	AEPTCD	Preferred Term Code	integer	8.0		AE.AEPTCD
ADAE	SMQ01CD	SMQ 01 Code	integer	8.0		SMQ01CD=20000039 if the AEPTCD is included in this SMQ.
ADAE	SMQ01NAM	SMQ 01 Name	Text	$200		SMQ01NAM='Haemorrhage terms (excl laboratory terms) (SMQ)' if the AEPTCD is included in this SMQ.
ADAE	SMQ01SC	SMQ 01 Scope	Text	$6	BROAD, NARROW	For this given SMQ, all scopes are Narrow.

Dataset Name	Variable Name	Variable Label	Variable Type	Display Format	Codelist / Controlled Terms	Source / Derivation
ADAE	SMQ01SCN	SMQ 01 Scope (N)	integer	1.0	1, 2	Map SMQ01SC to SMQ01SCN in the following manner: Broad = 1 Narrow = 2.

6.3 Sample ADAE Data

Table 6.3.1: Sample ADAE Data Showing SMQ Variables

Row	USUBJID	AETERM	AEDECOD	AEBODSYS	ASTDT	AEPTCD	SMQ01CD	SMQ01NAM	SMQ01SC	SMQ01SCN
1	0092017	SCLERAL BLEED RIGHT EYE	Scleral haemorrhage	Eye disorders	2009-06-09	10050508	20000039	Haemorrhage terms (excl laboratory terms) (SMQ)	NARROW	2
2	0112012	BRUISING OF LEFT UPPER ARM	Contusion	Injury, poisoning and procedural complications	2008-08-27	10050584	20000039	Haemorrhage terms (excl laboratory terms) (SMQ)	NARROW	2
3	0112012	BRUISING TO LEFT WRIST	Contusion	Injury, poisoning and procedural complications	2007-08-22	10050584	20000039	Haemorrhage terms (excl laboratory terms) (SMQ)	NARROW	2
4	0112013	NAUSEA	Nausea	Gastrointestinal disorders	2010-06-16	10028813				
5	0112014	NOSE BLEEDING	Epistaxis	Respiratory, thoracic and mediastinal disorders	2009-11-22	10015090	20000039	Haemorrhage terms (excl laboratory terms) (SMQ)	NARROW	2

Row	USUBJID	AETERM	AEDECOD	AEBODSYS	ASTDT	AEPTCD	SMQ01CD	SMQ01NAM	SMQ01SC	SMQ01SCN
6	0122006	EPISTAXIS	Epistaxis	Respiratory, thoracic and mediastinal disorders	2009-11-06	10015090	20000039	Haemorrhage terms (excl laboratory terms) (SMQ)	NARROW	2

7. Example 3: Analysis of Peripheral Sensory Neuropathy (PSN) Adverse Events by Severity and Cumulative Dose Exposure

Some institutions and organizations use standardized coding guidelines for reporting of adverse events. Examples of such standardized scales are [NCI (National Cancer Institute) and ACTG (Antiviral therapeutic area)]. These scales may be based upon variables as collected on AE CRFs, such as a grading scheme based upon severity [AESEV/AESEVN]. Other guidelines may be so objective that some variables, for example, drug relatedness [AEREL/AERELN] are not captured.

In this example the adverse event analysis dataset is used to summarize the frequency of peripheral sensory neuropathy (PSN) by cumulative dose exposure in an oncology study. In this study PSN was reported on the CRF at each cycle and at each 6-month follow-up visit, using the National Cancer Institute Common Toxicity Criteria (NCI CTC) version 4.03 [9] Peripheral sensory neuropathy (MedDRA v12.0 Code = 10034620):

- Grade 0 = None;
- Grade 1 = Asymptomatic; loss of deep tendon reflexes or paresthesia;
- Grade 2 = Moderate symptoms; limiting instrumental ADL;
- Grade 3 = Severe symptoms; limiting self care ADL;
- Grade 4 = Life-threatening consequences; urgent intervention indicated;
- Grade 5 = Death.

As a result of using this means of reporting, the PSN events reported in this module were all coded to ‘paresthesia’.

7.1 Analysis Display Example Layout

Table 7.1.1 Example of Summary of Cumulative Dose Quartiles to First Onset for PSN by Severity Grade[6]

Table 14.2.7.4

Summary of cumulative dose quartiles to first onset for PSN by severity grade

Analysis population: Intent-to-treat

Cumulative dose	Number of patients Exposed	PSN grade			
		Number (%) of patients with grade ≥ 1	Number (%) of patients with grade ≥ 2	Number (%) of patients with grade ≥ 3	Number (%) of patients with grade 4 or 5
Total number of patients with PSN		x (x.x)	x (x.x)	x (x.x)	x (x.x)
1st quartile (3 cycles)	N	x (x.x)	x (x.x)	x (x.x)	x (x.x)
2nd quartile (6 cycles)	N	x (x.x)	x (x.x)	x (x.x)	x (x.x)
3rd quartile (9 cycles)	N	x (x.x)	x (x.x)	x (x.x)	x (x.x)
4th quartile (12 cycles)	N	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Median cumulative dose to first onset (mg/m^2)		X	X	X	X

[6] The style of the display of the results of an analysis will be determined by the sponsor. The example is intended to illustrate content not appearance.

7.2 Sample ADAE Variable Metadata

Table 7.2.1: Sample ADAE Variable Metadata for selected variables

Dataset Name	Variable Name	Variable Label	Variable Type	Display Format	Codelist / Controlled Terms	Source / Derivation
ADAE	USUBJID	Unique Subject Identifier	Text	$7		ADSL.USUBJID
ADAE	ITTFL	Intent-to-Treat Population Flag	Text	$1	Y,N	ADSL.ITTFL
ADAE	AEDECOD	Dictionary-Derived Term	Text	$200	MedDRA	AE.AEDECOD
ADAE	AETOXGR	Standard Toxicity Grade	Text	$25	1, 2, 3, 4, 5	AE.AETOXGR
ADAE	AETOXGRN	Standard Toxicity Grade (N)	integer	1.0	1, 2, 3, 4, 5	Code AE.AETOXGR to numeric
ADAE	DOSECUM	Cumulative Study Drug Dose	Float	6.2		Total all values of EX.EXDOSE for the subject up to the start of the AE.
ADAE	DOSECUMU	Cumulative Study Drug Dose Units	Text	$2	mg	EX.EXDOSU
ADAE	DOSCMGR1	Cumulative Dose Group 1	integer	$12	Quartile 1 Quartile 2 Quartile 3 Quartile 4	Missing if DOSECUM=0, else DOSCMGR1 = Quartile 1 if DOSECUM is in the 1st Quartile, Quartile 2 if in the 2nd Quartile, Quartile 3 if in the 3rd Quartile and Quartile 4 if in the 4th Quartile.

7.3 Sample ADAE Data

Key points to note in the example are:

1. This is a simple example to only illustrate the cumulative dose variables that can be added to ADAE. It does not include additional variables that would also be needed for analysis like a flag to indicate the first occurrence for PSN.
2. Row 3 and 7 include two patients who had no dose of study drug at the time of PSN and would not be included in the table.

Table 7.3.1: Sample ADAE Data Showing Cumulative Dose Variables

Row	USUBJID	ITTFL	AEDECOD	AETOXGR	AETOXGRN	DOSECUM	DOSECUMU	DOSCMGR1
1	101-002	Y	PARESTHESIA	3	3	247.06	mg	Quartile 1
2	101-003	Y	PARESTHESIA	2	2	674.02	mg	Quartile 3
3	101-005	Y	PARESTHESIA	1	1	0	mg	
4	101-006	Y	PARESTHESIA	2	2	900.00	mg	Quartile 4
5	101-008	Y	PARESTHESIA	4	4	493.30	mg	Quartile 2
6	101-010	Y	PARESTHESIA	3	3	894.29	mg	Quartile 4
7	101-012	Y	PARESTHESIA	1	1	0	mg	

8. Example 4: Analysis of Treatment Emergent Adverse Events in a Cross-over Interaction Study

This example is a phase I, open-label, three periods cross-over study. Subjects are treated for 7 days within each period with a 7-day wash-out between periods. In each period, subjects are to receive one of 3 treatments (A, B, or A + B combined) in order of the sequence they are randomized to. Treatment emergent AEs were defined as AEs that occurred or worsened from the start of the treatment period through 72 hours after the end of the treatment period. Non-treatment emergent AEs were those that occurred before the first treatment period or more than 72 hours after the end of the treatment period until the start of the next treatment period. Post-treatment emergent AEs were those that occurred more than 72 hours after the last treatment period.

8.1 Analysis Display Example Layout

Table 8.1.1 Example of Summary of Treatment Emergent AEs by System Organ Class and Preferred Term and Treatment Group[7]

Table 14.2.7.5
Summary of Treatment Emergent AEs by System Organ Class and Preferred Term and Treatment Group
Analysis Population: Safety

	Treatment A (N = xxx)		Treatment B (N = xxx)		Treatment A + B (N = xxx)	
SYSTEM ORGAN CLASS **Preferred Term**	**n (%)**	**No. of events**	**n (%)**	**No. of events**	**n (%)**	**No. of events**
Any TEAE	x (x.x)	x	x (x.x)	x	x (x.x)	x
GASTROINTESTINAL DISORDER	x (x.x)	x	x (x.x)	x	x (x.x)	x
Nausea	x (x.x)	x	x (x.x)	x	x (x.x)	x
Constipation	x (x.x)	x	x (x.x)	x	x (x.x)	x
Vomiting	x (x.x)	x	x (x.x)	x	x (x.x)	x
Diarrhoea	x (x.x)	x	x (x.x)	x	x (x.x)	x
INFECTIONS AND INFESTATIONS	x (x.x)	x	x (x.x)	x	x (x.x)	x
Pharyngitis	x (x.x)	x	x (x.x)	x	x (x.x)	x
NERVOUS SYSTEM DISORDERS	x (x.x)	x	x (x.x)	x	x (x.x)	x
Headache	x (x.x)	x	x (x.x)	x	x (x.x)	x
Dizziness	x (x.x)	x	x (x.x)	x	x (x.x)	x
Syncope	x (x.x)	x	x (x.x)	x	x (x.x)	x
<Other SOCs and PTs>						

TEAE = treatment emergent adverse event
N = Safety subjects, i.e., subjects who received at least one dose of study drug in that particular period
n = Number of subjects reporting at least one treatment emergent adverse event
% = n / N * 100
Adverse events are presented by descending frequency of SOC and PT within SOC within Treatment A+B
System organ classes and preferred terms are coded using MedDRA version x.x.

[7] The style of the display of the results of an analysis will be determined by the sponsor. The example is intended to illustrate content not appearance.

8.2 Sample ADAE Variable Metadata

Table 8.2.1: Sample ADAE Variable Metadata for selected variables

Dataset Name	Variable Name	Variable Label	Variable Type	Display Format	Codelist / Controlled Terms	Source / Derivation
ADAE	USUBJID	Unique Subject Identifier	Text	$7		ADSL.USUBJID
ADAE	TRTA	Actual Treatment	Text	$13	Treatment A Treatment B Treatment A+B	ADSL.TRT01A if in the 1st period, ADSL.TRT02A if in the 2nd period, or ADSL.TRT03A if in the 3rd period
ADAE	TRTAN	Actual Treatment (N)	Integer	1.0	1, 2, 3	Code TRTA to numeric. Treatment A = 1 Treatment B = 2 Treatment A+B = 3
ADAE	SAFFL	Safety Population Flag	Text	$1	Y,N	ADSL.SAFFL
ADAE	AEBODSYS	Body System or Organ Class	Text	$200	MedDRA	AE.AEBODSYS
ADAE	AEDECOD	Dictionary-Derived Term	Text	$200	MedDRA	AE.AEDECOD
ADAE	ASTDTM	Analysis Start Date/Time	Integer	Datetime.		Converting AE.AESTDTC from character ISO8601 format to numeric date format, applying sponsor defined imputation rules.
ADAE	ASTDTF	Analysis Start Date Imputation Flag	text	$1	(DATEFL)	The level of imputation done for the start date (D if day was imputed, M if month was imputed, or Y if year was imputed).
ADAE	ASTTMF	Analysis Start Time Imputation Flag	text	$1	(TIMEFL)	The level of imputation done for the start time (H if hour was imputed, M if minutes were imputed).

Dataset Name	Variable Name	Variable Label	Variable Type	Display Format	Codelist / Controlled Terms	Source / Derivation
ADAE	TRTEMFL	Treatment Emergent Analysis Flag	Text	$1	Y	If ADSL.TR01SDTM LE ASTDTM LE (ADSL.TR01EDTM+72 hours) or ADSL.TR02SDTM LE ASTDTM LE (ADSL.TR02EDTM+72 hours) or ADSL.TR03SDTM LE ASTDTM LE (ADSL.TR03EDTM+72 hours) then TRTEMFL=Y
ADAE	PREFL	Pre-treatment Flag	Text	$1	Y	If TRTEMFL ^='Y' and FUPFL^='Y' then PREFL='Y'
ADAE	FUPFL	Follow-up Flag	Text	$1	Y	if ASTDTM GT (ADSL.TR03EDTM+72 hours) then FUPFL='Y'
ADAE	ASTDY	Analysis Start Relative Day	Integer	3.0		Date portion of ASTDTM- date portion of ADSL.TRT01SDTM+1 day if date portion of ASTDTM is on or after date portion of TRT01SDTM, else date portion of ASTDTM- date portion of ADSL.TR01SDTM if date portion of ASTDTM precedes date portion of TR01SDTM
ADAE	EPOCH	Epoch	Text	$200	RUN-IN, FIRST TREATMENT, FIRST WASHOUT, SECOND TREATMENT, SECOND WASHOUT, THIRD TREATMENT, THIRD WASHOUT, FOLLOW-UP	AE.EPOCH

Dataset Name	Variable Name	Variable Label	Variable Type	Display Format	Codelist / Controlled Terms	Source / Derivation
ADAE	APHASE	Phase	Text	$50	RUN-IN, FIRST TREATMENT, FIRST WASHOUT, SECOND TREATMENT, SECOND WASHOUT, THIRD TREATMENT, THIRD WASHOUT, FOLLOW-UP	If AESDTM < ADSL.TR01SDTM then APHASE='RUN-IN', else if ADSL.TR01SDTM LE AESDTM LE (ADSL.TR01EDTM+72 hours) then APHASE ='FIRST TREATMENT', else if (ADSL.TR01EDTM+72 hours) < AESDTM < ADSL.TR02SDTM then APHASE ='FIRST WASHOUT', etc.
ADAE	APERIOD	Period	Integer	1.0	1, 2, 3	If TR01SDTM LE ASTDTM LE (TR01EDTM+72 hours) then APERIOD=1, else if TR02SDTM LE ASTDTM LE (TR02EDTM+72 hours) then APERIOD=2, else if TR03SDTM LE ASTDTM LE (TR03EDTM+72 hours) then APERIOD=3
ADAE	APERIODC	Period (C)	Text	$50	PERIOD 01, PERIOD 02, PERIOD 03	If APERIOD=1 then APERIODC='PERIOD 01', else if APERIOD=2 then APERIODC='PERIOD 02', else if APERIOD=03 then APERIODC='PERIOD 03'
ADAE	TR01SDTM	Datetime of First Exposure in Period 01	Integer	Datetime.		ADSL.TR01SDTM
ADAE	TR01EDTM	Datetime of Last Exposure in Period 01	Integer	Datetime.		ADSL.TR01EDTM
ADAE	TR02SDTM	Datetime of First Exposure in Period 02	Integer	Datetime.		ADSL.TR02SDTM
ADAE	TR02EDTM	Datetime of Last Exposure in Period 02	Integer	Datetime.		ADSL.TR02EDTM
ADAE	TR03SDTM	Datetime of First Exposure in Period 03	Integer	Datetime.		ADSL.TR03SDTM

Dataset Name	Variable Name	Variable Label	Variable Type	Display Format	Codelist / Controlled Terms	Source / Derivation
ADAE	TR03EDTM	Datetime of Last Exposure in Period 03	Integer	Datetime.		ADSL.TR03EDTM

8.3 Sample ADAE Data

Table 8.3.1 is an illustration of the adverse events analysis dataset (ADAE) defined above.

Key points to note in the example are:

1. The SDTM variable EPOCH was kept for traceability and to illustrate the differences between this variable and APHASE and APERIOD.
2. Treatment start and end datetimes for each period were kept and used to calculate APERIOD and TRTEMFL. Another option would have been to use ADSL variables relating to period start and end datetimes (APxxSDTM and APxxEDTM). However, if different periods for efficacy and safety were defined this latter option wouldn't work.
3. The producer of the dataset chose to populate APERIOD as an analysis period where the wash-out and follow-up period were not populated for APERIOD. The same applied for the record level actual treatment variable (TRTA) which was left missing for records not associated with a treatment. However, this is left up to the sponsor.
4. Row 5 indicates an AE that occurs in the follow-up EPOCH, is post-treatment emergent and not related to any analysis period or treatment.
5. Row 8 indicates an AE that occurs in the follow-up EPOCH but within the third treatment phase and analysis period and associated with treatment A+B.

Table 8.3: Sample ADAE Data

Row	USUBJID	TRTA	TRTAN	SAFFL	AEBODSYS	AEDECOD	ASTDTM	ASTDTF	ASTTMF	TRTEMFL	PREFL	FUPFL
1	101-001	A	1	Y	GASTROINTESTINAL DISORDERS	VOMITING	05MAY08:16:00:00		M	Y		
2	101-001	B	2	Y	INFECTIONS AND INFESTATIONS	PHARYNGITIS	16MAY08:06:42:00			Y		
3	101-001	A+B	3	Y	NERVOUS SYSTEM DISORDERS	HEADACHE	01JUN08:15:30:00			Y		
4	101-001	A+B	3	Y	NERVOUS SYSTEM DISORDERS	CONSTIPATION	02JUN08:07:15:00			Y		
5	101-001			Y	INFECTIONS AND INFESTATIONS	ORAL HERPES	07JUN08:08:00:00					Y
6	101-002			Y	VASCULAR DISORDERS	HYPOTENSION	25MAY08:13:20:00				Y	
7	101-002	A+B	3	Y	NERVOUS SYSTEM DISORDERS	HEADACHE	27MAY08:22:10:00			Y		
8	101-002	A+B	3	Y	NERVOUS SYSTEM DISORDERS	HEADACHE	02JUN08:22:10:00			Y		

Row	ASTDY	EPOCH	APHASE	APERIOD	APERIODC	TR01SDTM	TR01EDTM	TR02SDTM
1	5	FIRST TREATMENT	FIRST TREATMENT	1	PERIOD 01	01MAY08:10:05:00	07MAY08:09:10:10	15MAY08:08:15:00
2	16	SECOND TREATMENT	SECOND TREATMENT	2	PERIOD 02	01MAY08:10:05:00	07MAY08:09:10:00	15MAY08:08:15:00
3	32	THIRD TREATMENT	THIRD TREATMENT	3	PERIOD 03	01MAY08:10:05:00	07MAY08:09:10:00	15MAY08:08:15:00
4	33	THIRD TREATMENT	THIRD TREATMENT	3	PERIOD 03	01MAY08:10:05:00	07MAY08:09:10:00	15MAY08:08:15:00
5	38	FOLLOW-UP	FOLLOW-UP			01MAY08:10:05:00	07MAY08:09:10:00	15MAY08:08:15:00
6	26	SECOND WASHOUT	SECOND WASHOUT			30APR08:12:05:00	06MAY08:08:32:00	14MAY08:11:55:00
7	28	THIRD TREATMENT	THIRD TREATMENT	3	PERIOD 03	30APR08:12:05:00	06MAY08:08:32:00	14MAY08:11:55:00
8	34	FOLLOW-UP	THIRD TREATMENT	3	PERIOD 03	30APR08:12:05:00	06MAY08:08:32:00	14MAY08:11:55:00

Row	TR02EDTM	TR03SDTM	TR03EDTM
1	21MAY08:10:30:00	20MAY08:13:50:00	03JUN08:07:20:00
2	21MAY08:10:30:00	29MAY08:13:50:00	03JUN08:07:20:00
3	21MAY08:10:30:00	29MAY08:13:50:00	03JUN08:07:20:00

Row	TR02EDTM	TR03SDTM	TR03EDTM
4	21MAY08:10:30:00	29MAY08:13:50:00	03JUN08:07:20:00
5	21MAY08:10:30:00	29MAY08:13:50:00	03JUN08:07:20:00
6	20MAY08:08:10:00	26MAY08:15:40:00	01JUN08:09:13:00
7	20MAY08:08:10:00	26MAY08:15:40:00	01JUN08:09:13:00
8	20MAY08:08:10:00	26MAY08:15:40:00	01JUN08:09:13:00

9. References

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   http://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03_2010-06-14.xls

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