ADaM Structure for Occurrence Data (OCCDS)

Version 1.0

Prepared by the

CDISC Analysis Data Model Team

Notes to Readers

This Analysis model uses the principles, structures and standards described in the CDISC Analysis Data Model Version 2.1 and Implementation Guide v1.1 documents.

Revision History

Date	Version	Summary of Changes
2016-02-12	1.0	Released version reflecting all changes identified during finalization of referenced document ADaMIG v1.1.
2015-06-01	1.0	Provisional release reflecting all changes and corrections identified during comment period.
2014-03-25	1.0 Draft	Draft version released for public comment

See Appendix C for Representations and Warranties, Limitations of Liability, and Disclaimers.

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1 Introduction

1.1 Purpose

The statistical analysis data structure presented in this document describes the general data structure and content typically found in occurrence analysis. Occurrence analysis is the counting of subjects with a given record or term, and often includes a structured hierarchy of dictionary coding categories. Examples of data that fit into this structure include those used for typical analysis of Adverse Events, Concomitant Medications, and Medical History. The structure is based on the ADaM Analysis Data Model V2.1 [1] and the ADaM Analysis Data Model Implementation Guide (ADaMIG) V1.1 [2].

This document is based on the document titled "Analysis Data Model (ADaM) Data Structure for Adverse Event Analysis" released by the CDISC ADaM team on May 10, 2012. It replaces this earlier document, making it more generic and applicable to analysis of more than just adverse event data.

The table shows a summary of differences between the two documents:

Table 1.1.1: Differences between Data Structures

	Data Structure for Adverse Events Analysis	**Data Structure for Occurrence Data**
Applications	Only adverse events	Adverse events plus other types of data
ADaM version	ADaM v 2.1, ADaMIG v1.0	ADaM v 2.1, ADaMIG v1.1
SDTM version	SDTM v1.2, SDTMIG v3.1.2	SDTM v 1.4, SDTMIG v3.2
Dataset metadata class	ADAE	OCCURRENCE DATA STRUCTURE
ANLzzFL label	"Analysis Record Flag zz"	"Analysis Flag zz"
AOCCFL label	"1st Occurrence of Any AE Flag"	"1st Occurrence within Subject Flag"
Study Drug Dose at Onset	Variable name "DOSEAEON" and label "Study Drug at AE Onset"	Variable name "DOSEON" and label "Treatment Dose at Record Start"
Treatment Dose Units	Separate variables named "DOSAEONU" and "DOSECUMU"	Variable name "DOSEU" and label "Treatment Dose Units"
Cumulative Actual Treatment Dose	Variable name "DOSECUM" and label "Cumulative Study Drug Dose"	Variable name "DOSCUMA" and label "Cumulative Actual Treatment Dose"
Original or Prior Coding Variables	Use of "y" suffix to represent prior version	Use of "w" suffix to represent prior version

As presented in the ADaMIG, many analysis methods can be performed using the ADaM Basic Data Structure (BDS) including Parameter (PARAM) and Analysis Value (AVAL). However, data analyzed as described above do not fit well into the BDS structure and are more appropriately analyzed using an SDTM structure with added analysis variables. Specifically, the data and analysis described in this document must meet these criteria:

- There is no need for AVAL or AVALC. Occurrences are counted in analysis, and there are typically one or more records for each occurrence assessment.
- A dictionary is often used for coding the occurrence and typically includes a well-structured hierarchy of categories and terminology. Re-mapping this hierarchy to BDS variables PARAM and generic *CAT variables would lose the structure and meaning of the dictionary. Per the Study Data Tabulation Model Implementation Guide (SDTMIG) V3.2 [3], a dictionary is expected for Adverse Events and Concomitant Medications, and recommended for Medical History. Although not as common, Clinical Events, Procedures, and Substance Use may also be coded. (Data for a particular study that could have been coded but wasn't should use this structure because analysis results are similar, and this will allow analysis programming to work the same way – for example, Medical History data might be coded in one study, not coded in another, yet the analysis tables look very similar.)
- The data content is typically not modified for analysis purposes. In other words, there is no need for analysis versions of the variables that hold the dictionary hierarchy or category terms.

This does not mean that all categorical data are appropriate for OCCDS. More standard categorical data that would never be mapped to a hierarchical dictionary, such as questionnaire responses, fit nicely in BDS and should not use OCCDS.

Typically, findings data fit nicely into BDS, while events and interventions fit nicely into OCCDS. However, this is not always the case: Exposure data, from an interventions SDTM structure, is quite often analyzed in BDS because that analysis isn't simply counting records, though there could be an OCCDS intermediate dataset used to help derive those BDS summary parameters. In all cases, it's the combination of input data and analysis needs that determines the dataset structure required.

The structure presented in this document is built on the nomenclature of the SDTMIG V3.2 [3] standard for collected data, and adds attributes, variables, and data structures required for statistical analyses. The primary source domain for the structure is the SDTM domain plus the corresponding Supplemental Qualifier dataset. Many additional variables are added from Subject-Level Analysis Dataset (ADSL).

In this document, the analysis datasets described are required when SDTM data aren't sufficient to support all analyses. Whether an analysis dataset is needed is left up to the producer (see ADaM Analysis Data Model V2.1 Section 4.1.1). If an analysis dataset is needed, and it meets the criteria listed above, it should use OCCDS.

The dataset and variable naming conventions and the dataset structure described in this document should be followed.

The structure for the occurrence analysis dataset is usually one record per each record in the corresponding SDTM domain. Examples of when the number of records in the analysis dataset would not match the number in SDTM include:

- SDTM data contain screen failures but screen failures are not analyzed. In this case, the screen failure records are not needed in the analysis dataset.
- The topic, such as an adverse event or concomitant medication, spans several treatment periods and needs to be counted in each. Based on the analysis need, a separate row might be required for each treatment period spanned and analyzed.
- An adverse event needs to be analyzed along multiple coding paths. In this case, a row would be needed for each coding path analyzed. An alternate solution, if multiple coding paths are not needed together, would be to put records for each coding path into a separate analysis dataset.

This doesn't exclude a producer from creating additional datasets for other analyses, or even using a different structure if needed for analysis (e.g. time-to-event of adverse events of special interest).

1.2 Points to Consider When Interpreting 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 applied. 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 their own logical ordering. Though there is not an across-example consistency of ordering of variables, within an example the ordering of the variables within the illustrated analysis dataset matches the order of the variables as presented in the associated metadata.
- **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 the occurrence analysis dataset, the source is identified as ADSL.SUBJID.
- **Analysis-ready:** The occurrence analysis dataset 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. For typical occurrence analyses, unique subject counts are derived by running a standard statistical procedure (e.g., SAS PROC, S-PLUS function, etc.) on the occurrence analysis dataset, while denominator counts 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. Additionally, the metadata examples just include the metadata necessary to understand the respective example datasets. Refer to Define-XML v2.0 [11] for additional information (e.g., variable length and origin) required when building a valid define.xml file according to the Define-XML v2.0 standard.
- **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 consumer 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. They are 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 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.

1.3 Conventions Used in this Document

Throughout this document the terms “producer” and “consumer” are used to refer to the originator/sender/owner/sponsor of the data and the user/reviewer/recipient of the data, respectively. These terms are used to simplify the document, and are not intended to imply that these examples only apply to analysis datasets in the context of electronic submissions to regulatory agencies.

2 Data Analysis and Coding

2.1 Statistical Analysis

The most frequently used method for the comparison between treatment groups of data in this structure is the summarization of the number of subjects with at least one occurrence of a term. These counts and related percentages are presented at different levels of the dictionary hierarchy, when the hierarchy exists. 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 number of subjects exposed to treatment. Note that some subjects in the population may not have any records, and therefore these subjects would not be represented in the SDTM domain nor the corresponding OCCDS analysis dataset. Thus, the denominators usually need to be obtained from ADSL (subject level analysis dataset) rather than directly from the occurrence analysis dataset.

This ADaM model primarily discusses the creation of an analysis dataset that is needed for the presentation of frequencies and percentages. However, the analysis datasets presented here could be used to construct more in-depth analysis dataset, even in a different structure. For time-to-event analyses, see the ADaM Basic Data Structure for Time to Event Analyses appendix.

2.2 Dictionary Coding

Data are often collected in textual or 'verbatim' content, a short description of an event or intervention generally written in free text on the case report form. Verbatim content is then processed through a coding dictionary so that similar verbatim content is grouped together by classifying them into a hierarchy of medical granularity.

Medical Dictionary for Regulatory Activities (MedDRA) [4] 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) [5] and International Classification of Disease (ICD) [6], and Coding Symbols for a Thesaurus of Adverse Reaction Terms (COSTART) [7] which was replaced by MedDRA but can still be found in older studies.

The coding dictionary is characterized by classifying each verbatim into a hierarchy of medical granularity. For example, if the verbatim content recorded was 'stomach virus', 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'. Using MedDRA V12.0, this verbatim content would result in a System Organ Class (SOC) of 'Infections and infestations' and a preferred term (PT) of 'Gastroenteritis viral'.

When using coding dictionaries, it is recommended that coding rules and guidelines be developed by the producer prior to the classification of terminology. The process of coding verbatim terms with a dictionary is outside the scope of this document. The objective of coding guidelines is to promote medical accuracy and consistency when using the controlled vocabulary of the dictionary. This consistency will support a variety of downstream analysis needs, such as when events need to be recoded to integrate data from two or more clinical studies.

2.2.1 Recoding of Occurrence Data

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 content is 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 occurrence data is when data 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 covers integration of multiple studies. The ADaM team is 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 Adverse Events

The safety evaluation of a clinical trial includes the analysis of adverse events, and that analysis is typically done using this data structure. The definition of an adverse event, as presented in International Conference of Harmonization (ICH) E2A [8] 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.*

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 [9] 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 important attributes of AEs include the action taken in response to the event and whether the event led to permanent discontinuation of the investigational product.

2.4 Concomitant Medications Data

Concomitant medications data can be coded to a hierarchy such as WHO Drug and summarized by medication and/or ingredient within class.

2.5 Pre-specified Data

In some cases, data can be gathered on a case report form that contains a pre-specified category and a checkbox to indicate whether or not the subject had this event, condition, or treatment. This information is stored in these variables as described in the SDTMIG. --PRESP is used to indicate that the term is a pre-specified one, and --OCCUR is either Y or N to indicate whether the subject did or did not have the event, condition, or treatment. --TERM or --TRT will have a known and finite set of values, so these values may be adequate to use as a summarization category. Often these pre-specified terms are grouped into categories at collection using the --CAT and --SCAT variables, creating additional levels of summarization categories. In this situation, data are analyzed by variables such as --TERM, --TRT, --CAT and --SCAT, and dictionary coding might not be necessary. For example, medical history and clinical events data are often captured in this way.

Note that this pre-specified data option does not work well for Adverse Events because the Study Data Tabulation Model Implementation Guide (SDTMIG) V3.2 [3] does not permit the use of variable AEOCCUR. In other words, all records in SDTM AE must correspond to an actual occurrence of the event.

2.6 Combining Spontaneous and Pre-specified Occurrences

It is technically feasible to apply the same coding dictionary to both collected and pre-specified data and combine these data for analysis. Whether or not to do so is a statistical judgment that should be carefully considered and described in programming specifications. A pre-specified question on a case report form makes it more likely to receive data, and would therefore increase the frequency in a summary. In deciding whether to pool pre-specified and spontaneous data, the statistician should consider the way data were gathered and weigh the possibility of over-reporting pre-specified data. The statistician should also carefully consider and describe the correct denominator for percentages.

If data are pooled in this way, take care that non-occurring data (--OCCUR=N) are properly excluded from the analysis.

2.7 Other Data

Other similar data, with or without coding hierarchy, can be summarized similarly. An example of summarizing without a coding hierarchy can be seen in the example in Section 11.

Some examples of other data that can also be summarized using OCCDS include:

- Clinical Events, when collected by category and not mapped to a dictionary, but summarized in a similar way as Adverse Events.
- Protocol violations, when summarized by counting subjects with violations within each category.
- Laboratory data containing National Cancer Institute Common Toxicity Criteria (NCI-CTC) [10] information that has been coded with MedDRA and summarized as laboratory events. When these events are summarized like adverse events, an extension of the adverse event examples that are shown in this document can be used.

In all cases, OCCDS should be used when a summary of the hierarchy is done, counting the number of subjects at each level of the hierarchy. Alternately, BDS should be used for counting when there isn't a hierarchy, when the terms are counted rather than the subjects, and when variables such as AVAL and PARAM are appropriate to include.

3 ADaM Metadata

As described in the ADaM Analysis Data Model V2.1 [1], variables that are copied from SDTM must have the same variable name, label, values, and meaning as in SDTM. Because the Occurrence Data Structure (OCCDS) can be used for adverse events, concomitant medications, and other occurrence data, metadata shown in this section reference different SDTM domains. For clarity, the following conventions are used:

- When referring to the 2-letter prefix in variable names, the standard convention is to use "--", as described in the Study Data Tabulation Model v1.4 [3].
- The "--" convention was intended for variable names, not domain names, and "--" is difficult to read in the documentation for SDTM domain names. This document uses the convention of "XX" to represent a domain name, as was done in the Analysis Data Model (ADaM) Examples in Commonly Used Statistical Analysis Methods appendix document.
- Variable labels that differ depending on SDTM domain are shown with the SDTM observation class label followed by an asterisk (*), referencing a note at the end of the table.

Take care when creating actual metadata to replace "--", "XX", and generic variable labels with the actual 2-letter domain code and label from SDTM.

3.1 Dataset Metadata

Typically, the following Analysis Dataset Metadata is specified as follows:

Table 3.1.1 Example of ADaM OCCDS Dataset Metadata*****,

Dataset Name	Dataset Description	Dataset Location	Dataset Structure	Key Variables of Dataset	Class of Dataset	Documentation
ADXXXXXX	<Dataset label>	adxxxxxx.xpt	one record per record in SDTM domain (optional: per coding path, per Analysis Period and/or Phase)†	*List variables, such as USUBJID, --SEQ*	OCCURRENCE DATA STRUCTURE	*Example: Dictionary used is MedDRA V11.1*

3.2 ADaM Variables and Variable Metadata

As stated earlier, OCCDS is different from BDS. There is no PARAM nor AVAL, for example. However, some of the variables described for BDS in the ADaM Implementation Guide version 1.1 [2] can be used in OCCDS, as shown below.

The more standardized variables commonly occurring in an ADaM OCCDS are described here in tabular format. In general, include all variables from the SDTM dataset and corresponding supplemental qualifiers that are needed for analysis or traceability. For traceability when copying variables from SUPPQUAL, it is recommended to use variable names that exactly match the corresponding SUPPQUAL.QNAM values. Additional study or therapeutic specific variables may be added as needed but should follow the standard variable naming conventions described in the ADaM Implementation Guide version 1.1 [2]. For example, variables with the 2-letter SDTM prefix are most commonly those that are copied from the SDTM or transposed SUPPQUAL dataset, or the numeric version of the SDTM variable, but not analysis versions of SDTM variables. Choose variable names with care to prevent unintended conflicts with standard names.

* The display presentation of the metadata should be determined between the producer and the consumer. The example is only intended to illustrate content and not appearance.
† See discussion near the end of the Introduction section of this document for examples of when the analysis data structure might not be one record per record in SDTM domain

As described in the ADaM Analysis Data Model 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 ADaM Implementation Guide version 1.1 [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.

3.2.1 ADSL Variables

Merge any ADSL variables needed for analysis or reference.

Be aware that only subjects with an SDTM record would have an analysis record. For this reason, it is recommended that population indicators and denominator counts for percentages be derived from ADSL and not from the occurrence analysis dataset.

3.2.2 Identifier Variables

Include the identifier variables from SDTM:

Table 3.2.2.1 OCCDS Identifier Variables

Variable Name	Variable Label	Type	Code List / Controlled Terms	Core	CDISC Notes
STUDYID	Study Identifier	Char		Req	XX.STUDYID
USUBJID	Unique Subject Identifier	Char		Req	XX.USUBJID
SUBJID	Subject Identifier for the Study	Char		Perm	ADSL.SUBJID
SITEID	Study Site Identifier	Char		Perm	ADSL.SITEID
--SEQ	Sequence Number	Num		Req*	XX.--SEQ This would be copied from the SDTM domain XX. This may be missing for derived rows. Required for traceability back to SDTM.

**Note that the only sequence number option shown is --SEQ, because it is unlikely that multiple SDTM domains would be used as input to a single OCCDS dataset.*

3.2.3 Dictionary Coding and Categorization Variables

Dictionary coding and categorization variables provided in SDTM should be included as needed for analysis, review, or traceability. Variables shown below are the common coding variables. If other coding variables are included in SDTM and pertinent for analysis, these should be included in ADaM using a similar naming convention as shown below. For any public versioned dictionary, the metadata for each coding variable should include both the name and version of the dictionary.

Common Dictionary Coding Variables for MedDRA

MedDRA coding is typically used for AEs and Medical History. Copy to the analysis dataset the needed MedDRA terms and codes from SDTM. It is recommended but not required that all levels of terms for the primary path 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)] be included, especially in the AE analysis dataset, as these are frequently useful in further analyses of events.

Table 3.2.3.1 MedDRA Dictionary Coding Variables

Variable Name	Variable Label	Type	Codelist / Controlled Terms	Core	CDISC Notes
--TERM	Reported Term*	Char		Req	XX.--TERM This would be copied from the SDTM domain XX.
--DECOD	Dictionary-Derived Term	Char	MedDRA	Cond	XX.--DECOD This would be copied from the SDTM domain XX. It is typically one of the primary variables used in an analysis and would be brought in from the SDTM domain. Equivalent to the Preferred Term (PT in MedDRA). As mentioned above, all other SDTM domain variables and supplemental qualifiers needed for analysis or traceability should also be included. Include the dictionary version in the metadata. Conditional on whether coded and used for analysis. Required for Adverse Event data.
--BODSYS	Body System or Organ Class	Char	MedDRA	Cond	XX.--BODSYS This would be copied from the SDTM domain XX. It is typically one of the primary variables used in an analysis and would be brought in from the SDTM domain. As mentioned above, all other SDTM domain variables and supplemental qualifiers needed for analysis or traceability should also be included. Include the dictionary version in the metadata. Conditional on whether coded and used for analysis. Required for Adverse Event data.
--BDSYCD	Body System or Organ Class Code	Num	MedDRA	Perm	XX.--BDSYCD This would be copied from the SDTM domain XX or supplemental qualifier dataset. Include the dictionary version in the metadata.
--LLT	Lowest Level Term	Char	MedDRA	Cond	XX.-- LLT This would be copied from the SDTM domain XX or supplemental qualifier dataset. Include the dictionary version in the metadata. Conditional on whether coded and used for analysis.
--LLTCD	Lowest Level Term Code	Num	MedDRA	Perm	XX.--LLTCD This would be copied from the SDTM domain XX or supplemental qualifier dataset. Include the dictionary version in the metadata.
--PTCD	Preferred Term Code	Num	MedDRA	Perm	XX.--PTCD This would be copied from the SDTM domain XX or supplemental qualifier dataset. Include the dictionary version in the metadata.
--HLT	High Level Term	Char	MedDRA	Cond	XX.--HLT This would be copied from the SDTM domain XX or supplemental qualifier dataset. Include the dictionary version in the metadata. Conditional on whether used for analysis.
--HLTCD	High Level Term Code	Num	MedDRA	Perm	XX.--HLTCD This would be copied from the SDTM domain XX or supplemental qualifier dataset. Include the dictionary version in the metadata.
--HLGT	High Level Group Term	Char	MedDRA	Cond	XX.--HLGT This would be copied from the SDTM domain XX or supplemental qualifier dataset. Include the dictionary version in the metadata. Conditional on whether used for analysis.

Variable Name	Variable Label	Type	Codelist / Controlled Terms	Core	CDISC Notes
--HLGTCD	High Level Group Term Code	Num	MedDRA	Perm	XX.--HLGTCD This would be copied from the SDTM domain XX or supplemental qualifier dataset. Include the dictionary version in the metadata.
--SOC	Primary System Organ Class	Char	MedDRA	Cond	XX.--SOC This would be copied from the SDTM domain XX or supplemental qualifier dataset. Include the dictionary version in the metadata. Conditional on whether a secondary SOC was used for analysis.
--SOCCD	Primary System Organ Class Code	Num	MedDRA	Perm	XX.--SOCCD This would be copied from the SDTM domain XX or supplemental qualifier dataset. Include the dictionary version in the metadata.

** This variable label differs depending on the SDTM domain. See Study Data Tabulation Model V1.4 and Study Data Tabulation Model Implementation Guide (SDTMIG) V3.2 [3] for details.*

NOTE: MedDRA allows for secondary paths for Lower Level Terms. One may be required to report on secondary paths along with primary paths. Please see section 8for an example layout for one possible way to handle this analysis need.

Common Dictionary Coding Variables for WHO Drug

WHO Drug coding is typically used for Concomitant Medications. Copy to the analysis dataset the needed WHO Drug terms and codes from SDTM CM and SUPPCM. The variables shown in this table 3.2.3.2 are intended for a single WHO Drug coding path.

Table 3.2.3.2 WHO Drug Dictionary Coding Variables

Variable Name	Variable Label	Type	Codelist / Controlled Terms	Core	CDISC Notes
CMTRT	Reported Name of Drug, Med, or Therapy	Char		Req	CM.CMTRT
CMDECOD	Standardized Medication Name	Char	WHO Drug	Cond	CM.CMDECOD This is typically one of the primary variables used in CM analysis and would be copied from the SDTM CM domain. Include the dictionary version in the variable metadata. Conditional on whether coded and used for analysis.
CMCLAS	Medication Class	Char		Perm	CM.CMCLAS Include the dictionary version in the metadata.
CMCLASCD	Medication Class Code	Char		Perm	CM.CMCLASCD Include the dictionary version in the metadata.
ATCy	ATC Level y Text	Char	WHO Drug	Cond	Corresponds to the ATC Level Text for WHO Drug Conditional, based on analysis at multiple levels (y)
ATCyCD	ATC Level y Code	Char	WHO Drug	Cond	Corresponds to the ATC Level Code for WHO Drug Conditional, based on analysis at multiple levels (y)

Other Categorization Variables

When categories are used for the intended analysis, instead of or in addition to MedDRA or WHO Drug, these generic categorization variables are commonly used:

Table 3.2.3.3 Other Categorization Variables

Variable Name	Variable Label	Type	Codelist / Controlled Terms	Core	CDISC Notes
--CAT	Category*	Char		Perm	XX.--CAT This would be copied from the SDTM domain XX.
--SCAT	Subcategory*	Char		Perm	XX.--SCAT This would be copied from the SDTM domain XX.
ACATy	Analysis Category y	Char		Perm	Category used in analysis. May be derived from --CAT and/or --SCAT. Examples include records of special interest like prohibited medications, concomitant medications taken during an infusion reaction, growth factors, antimicrobial medications, and other such categories not defined elsewhere or present in SDTM domains.

** This variable label differs depending on the SDTM domain. See Study Data Tabulation Model V1.4 and Study Data Tabulation Model Implementation Guide (SDTMIG) V3.2 [3] for details.*

3.2.4 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 ADaM Implementation Guide version 1.1 [2].

Table 3.2.4.1 Timing Variables

Variable Name	Variable Label	Type	Codelist / Controlled Terms	Core	CDISC Notes
--STDTC	Start Date/Time of Observation*	Char	ISO 8601	Perm	Copied from XX.--STDTC This would be copied from the SDTM domain XX.
ASTDT	Analysis Start Date	Num		Cond	Created from converting XX.--STDTC 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 is populated in SDTM.
ASTTM	Analysis Start Time	Num		Cond	Created from converting XX.--STDTC from character ISO8601 format to numeric time format, applying imputation rules as specified in the SAP or metadata. Conditional on whether start time is pertinent for study and is populated in SDTM.
ASTDTM	Analysis Start Date/Time	Num		Cond	Created from converting XX.--STDTC 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 is populated in SDTM.
ASTDTF	Analysis Start Date Imputation Flag	Char	(DATEFL)	Cond	Created during conversion of XX.--STDTC from character to numeric. Imputation flags are described in the ADaM Analysis Data Model Implementation Guide (ADaMIG) V1.1 [2] General Timing Variable Conventions. Conditional on whether any imputation is done for the start date.
ASTTMF	Analysis Start Time Imputation Flag	Char	(TIMEFL)	Cond	Created during conversion of XX.--STDTC from character to numeric. Imputation flags are described in the ADaM Analysis Data Model Implementation Guide (ADaMIG) V1.1 [2] General Timing Variable Conventions. Conditional on whether any imputation is done for the start time.

Variable Name	Variable Label	Type	Codelist / Controlled Terms	Core	CDISC Notes
--ENDTC	End Date/Time of Observation*	Char	ISO 8601	Cond	Copied from XX.--ENDTC This would be copied from the SDTM domain XX. Conditional on whether end date is pertinent for study and is populated in SDTM.
AENDT	Analysis End Date	Num		Cond	Created from converting XX.--ENDTC 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 is populated in SDTM.
AENTM	Analysis End Time	Num		Cond	Created from converting XX.--ENDTC from character ISO8601 format to numeric time format, applying imputation rules as specified in the SAP or metadata. Conditional on whether end time is pertinent for study and is populated in SDTM.
AENDTM	Analysis End Date/Time	Num		Cond	Created from converting XX.--ENDTC 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 is populated in SDTM.
AENDTF	Analysis End Date Imputation Flag	Char	(DATEFL)	Cond	Created during conversion of XX.--ENDTC from character to numeric. Imputation flags are described in the ADaM Analysis Data Model Implementation Guide (ADaMIG) V1.1 [2] General Timing Variable Conventions. Conditional on whether any imputation is done for the end date.
AENTMF	Analysis End Time Imputation Flag	Char	(TIMEFL)	Cond	Created during conversion of XX.--ENDTC from character to numeric. Imputation flags are described in the ADaM Analysis Data Model Implementation Guide (ADaMIG) V1.1 [2] General Timing Variable Conventions. 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 --STDY. Conditional on whether analysis start relative day is pertinent to the study.
--STDY	Study Day of Start of Observation*	Num		Perm	XX.--STDY This would be copied from the SDTM domain XX. ASTDY may differ from --STDY due to date imputation and the option in ADaM to use a reference date other than SDTM's RFSTDTC. Including XX.--STDY 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 --ENDY.
--ENDY	Study Day of End of Observation*	Num		Perm	XX.--ENDY This would be copied from the SDTM domain XX. AENDY may differ from --ENDY due to date imputation and the option in ADaM to use a reference date other than SDTM's RFSTDTC. Including XX.--ENDY in addition to AENDY adds traceability.
ADURN	Analysis Duration (N)	Num		Perm	Derive from ASTDT (or ASTDTM) and AENDT (or AENDTM).
ADURU	Analysis Duration Units	Char	(UNIT)	Cond	Conditional on whether ADURN is included and units are not included in the label of ADURN.
--DUR	Duration of XX	Char	ISO 8601	Perm	XX.--DUR

Variable Name	Variable Label	Type	Codelist / Controlled Terms	Core	CDISC Notes
					This would be copied from the SDTM domain XX. Because --DUR is a collected field and ADURN is derived, the values will often differ. Including XX.--DUR in addition to ADURN adds traceability.
APERIOD	Period	Num		Perm	APERIOD is a record-level timing variable that represents the analysis period within the study associated with the record for analysis purposes. The value of APERIOD (if populated) must be one of the xx values found in the ADSL TRTxxP variables. See the ADaM Implementation Guide version 1.1 [2] for more information on this variable.
APERIODC	Period (C)	Char		Perm	Text characterizing to which period the record belongs. One-to-one map to APERIOD.
APHASE	Phase	Char		Perm	APHASE is a categorization of timing within a study, for example a higher-level categorization of APERIOD or an analysis epoch. For example, APHASE could describe spans of time for SCREENING, ON TREATMENT, and FOLLOW-UP. See the ADaM Implementation Guide version 1.1 [2] for more information on this variable.

** This variable label differs depending on the SDTM domain. See Study Data Tabulation Model V1.4 and Study Data Tabulation Model Implementation Guide (SDTMIG) V3.2 [3] for details.*
Code Lists in parenthesis are the names of CDISC Controlled Terminology.

3.2.5 Indicator Variables

Some indicator variables can be copied from SDTM, while others are 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 3.2.5.1 SDTM Indicator Variables

Variable Name	Variable Label	Type	Codelist / Controlled Terms	Core	CDISC Notes
--OCCUR	XX Occurrence	Char	(NY)	Cond	Copied from XX.--OCCUR This would be copied from the SDTM domain XX. Conditional on whether this content is pertinent for analysis and is populated in SDTM.
--PRESP	XX Pre-Specified	Char	(NY)	Cond	Copied from XX.--PRESP This would be copied from the SDTM domain XX. Conditional on whether this content is pertinent for analysis and is populated in SDTM.

Code lists in parenthesis are the names of CDISC Controlled Terminology.

Table 3.2.5.2 OCCDS Indicator Variables

Variable Name	Variable Label	Type	Codelist / Controlled Terms	Core	CDISC Notes
ANLzzFL	Analysis 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 ADaM Implementation Guide version 1.1 [2] for more information on this flag variable. This variable is conditional on whether analysis records flags are needed for analysis.

With Adverse Events and Concomitant Medications, typically indicator flags are also assigned based on the timing of the analysis record in relation to the study. Below are some common indicator flags for these types of data.

Table 3.2.5.3 Adverse Events Indicator Variables

Variable Name	Variable Label	Type	Code List / Controlled Terms	Core	CDISC Notes
TRTEMFL	Treatment Emergent Analysis Flag	Char	Y	Cond	Treatment emergent flag as defined for analysis. 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. Example derivation: If ADSL.TRTSDT≤ASTDT≤ADSL.TRTEDT + x days then TRTEMFL='Y' The number x is defined by the producer and often incorporates the known half-life of the drug. It should be consistent with variable APHASE (described above) if APHASE is also used.
AETRTEM	Treatment Emergent Flag	Char	(NY)	Perm	Treatment emergent flag from SDTM, if available. See the SDTMIG version 3.2 [3] for more information. Derivation: SUPPAE.QVAL where QNAM='AETRTEM'. TRTEMFL may differ from AETRTEM due to different definitions, date imputation and other analysis rules. Including AETRTEM in addition to TRTEMFL will add traceability.

Code lists in parenthesis are the names of CDISC Controlled Terminology.

Table 3.2.5.4 Concomitant Medications Indicator Variables

Variable Name	Variable Label	Type	Code List / Controlled Terms	Core	CDISC Notes
ONTRTFL	On Treatment Record Flag	Char	Y	Cond	Character indicator of whether the observation occurred while the subject was on treatment. Example derivation: If ADSL.TRTSDT <= ASTDT <= ADSL.TRTEDT then ONTRTFL = 'Y' This variable is conditional on whether the concept of on-treatment is a feature of the study and used in analysis.

Table 3.2.5.5 Adverse Events and Concomitant Medications Indicator Variables

Variable Name	Variable Label	Type	Code List / Controlled Terms	Core	CDISC Notes
PREFL	Pre-treatment Flag	Char	Y	Cond	Character indicator of whether the observation occurred before the subject started treatment. Example derivation: If ASTDT < ADSL.TRTSDT then PREFL='Y' This variable is conditional on whether the concept of pre-treatment is a feature of the study and used in analysis.
FUPFL	Follow-up Flag	Char	Y	Cond	Character indicator of whether the observation occurred while the subject was on follow-up. Example derivation: If ASTDT > ADSL.TRTEDT then FUPFL='Y' This variable is conditional on whether the concept of follow-up is a feature of the study and used in analysis.

3.2.6 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 use of the word "first" in this section doesn't necessarily mean chronological, though that is an option. The more common occurrence flags and a structure for additional flags are shown below:

Table 3.2.6.1 OCCDS Occurrence Flag Variables

Variable Name	Variable Label	Type	Codelist / Controlled Terms	Core	CDISC Notes
AOCCFL	1st Occurrence within Subject Flag	Char	Y	Perm	Character indicator for the first occurrence of any event/intervention/finding within the subject. Example derivation: Sort the data in the required order and flag the first treatment emergent record for each subject.
AOCCPFL	1st Occurrence of Preferred Term Flag	Char	Y	Perm	Character indicator for the first occurrence of the preferred term within the subject. Example derivation: Sort the data in the required order and flag the first treatment emergent record for each --DECOD for each subject.
AOCCIFL	1st Max Sev./Int. Occurrence Flag	Char	Y	Perm	Character indicator for the first occurrence of the event/intervention/finding with the maximum severity/intensity within the subject. Example derivation: Sort the data in the required order and flag the first treatment emergent record for maximum severity for each subject.
AOCCPIFL	1st Max Sev./Int. Occur Within PT Flag	Char	Y	Perm	Character indicator for the first occurrence of the maximum severity/intensity within the subject and preferred term. 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.

Table 3.2.6.2 MedDRA Occurrence Flag Variables

Variable Name	Variable Label	Type	Codelist / Controlled Terms	Core	CDISC Notes
AOCCSFL	1st Occurrence of SOC Flag	Char	Y	Perm	Character indicator for the first occurrence of the system organ class within the subject. Example derivation: Sort the data in the required order and flag the first treatment emergent record for each body system for each subject.
AOCCSIFL	1st Max Sev./Int. Occur Within SOC Flag	Char	Y	Perm	Character indicator for the first occurrence of the maximum severity/intensity within the subject and system organ class. 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.

3.2.7 Treatment/Dose Variables

The treatment variable used for analysis must be included. Typically this would be TRTP, TRTA, TRTxxP, or TRTxxA. See the ADaM Implementation Guide version 1.1 [2] for more details on these variables. Additional dosing variables may also be included.

Table 3.2.7.1 Treatment/Dose Variables

Variable Name	Variable Label	Type	Codelist / Controlled Terms	Core	CDISC Notes
DOSEON	Treatment Dose at Record Start	Num		Perm	Dose received at the point in time of the record start date. Example derivation: Obtained from EX.EXDOSE where --STDTC falls between the values of EX.EXSTDTC and EX.EXENDTC
DOSCUMA	Cumulative Actual Treatment Dose	Num		Perm	Cumulative actual study drug dosage at the point in time of the record start date.
DOSEU	Treatment Dose Units	Char	(UNIT)	Cond	Conditional on whether DOSEON and/or DOSCUMA are included.

3.2.8 Descriptive Variables

Variables that describe the record are often used in analysis. Include these and any other SDTM variables if 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 3.2.

Shown here are some common descriptive variables that are often included in ADAE. Any other SDTM variables should be included as appropriate (e.g. AEOUT, AESDTH).

Table 3.2.8.1 Adverse Event Descriptive Variables

Variable Name	Variable Label	Type	Codelist / 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
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

Variable Name	Variable Label	Type	Codelist / Controlled Terms	Core	CDISC Notes
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 relation 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.
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 producer-defined controlled terminology.*
Code Lists in parenthesis are the names of CDISC Controlled Terminology.

Medical History data typically does not contain descriptive variables. If needed for analysis, use variables as shown above for Adverse Events, replacing the prefix “AE” with “MH”.

Shown here are some common descriptive variables that are often included in ADCM. Any other SDTM variables should be included as appropriate.

Table 3.2.8.2 Concomitant Medications Descriptive Variables

Variable Name	Variable Label	Type	Code List / Controlled Terms	Core	CDISC Notes
CMSTAT	Completion Status	Char		Perm	CM.CMSTAT
CMINDC	Indication	Char		Perm	CM.CMINDC
CMDOSE	Dose per Administration	Num		Perm	CM.CMDOSE
CMDOSFRM	Dose Form	Char		Perm	CM.CMDOSFRM
CMDOSRGM	Intended Dose Regimen	Char		Perm	CM.CMDOSRGM
CMROUTE	Route of Administration	Char		Perm	CM.CMROUTE

3.2.9 Standardized MedDRA Query Variables

Standardized MedDRA Queries (SMQs) [13] are becoming increasingly common in clinical trial safety evaluations, particularly when known or suspected safety issues are associated with experimental compounds. In addition, Customized MedDRA Queries (CMQs) are often used to modify an SMQ or identify Adverse

Event or Medical History records of special interest. The following variables are used to identify SMQs and CMQs, 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 producer-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 3.2.9.1 Standardized MedDRA Query Variables

Variable Name	Variable Label	Type	Codelist / Controlled Terms	Core	CDISC Notes
SMQzzNAM	SMQ zz Name	Char		Cond	The standardized MedDRA queries name. Would be blank for terms that are not in the SMQ. Therefore this variable could be blank for all records if no terms within the study were included in the SMQ. Conditional on whether SMQ analysis is done.
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 scope. 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 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)"

3.2.10 Original or Prior Coding Variables

The suite of variables used for the primary analysis is described in section 3.2.3. 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 a mapping dictionary for an interim analysis and another for final analysis
- When studies using different version of a mapping dictionary are pooled together for an integrated analysis

The variables described below provide traceability to original (or prior) analysis(es). The suffix "w" 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 3.2.10.1 Original or Prior MedDRA Coding Variables

Variable Name	Variable Label	Type	Codelist / Controlled Terms	Core	CDISC Notes
DECDORGw	PT in Original Dictionary w	Char	MedDRAw*	Perm	Original preferred term coding of XX.--TERM using MedDRA or other dictionary version X.X.
BDSYORGw	SOC in Original Dictionary w	Char	MedDRAw*	Perm	Original body system coding of XX.--TERM using MedDRA or other dictionary version X.X.
HLGTORGw	HLGT in Original Dictionary w	Char	MedDRAw*	Perm	Original HLGT coding of XX.--TERM using MedDRA or other dictionary version X.X
HLTORGw	HLT in Original Dictionary w	Char	MedDRAw*	Perm	Original HLT coding of XX.--TERM using MedDRA or other dictionary version X.X.
LLTORGw	LLT in Original Dictionary w	Char	MedDRAw*	Perm	Original LLT coding of XX.--TERM using MedDRA or other dictionary version X.X.
LLTNORGw	LLT Code in Original Dictionary w	Char	MedDRAw*	Perm	Original LLT code of XX.--TERM using MedDRA or other dictionary version X.X.

** For each version of an external dictionary, a different reference name must be used. The individual reference names will point to a dedicated section in the data definition file where all external dictionaries used in the analysis are listed, including dictionary name and version.*

Table 3.2.10.2 Original or Prior WHO Drug Coding Variables

Variable Name	Variable Label	Type	Code List / Controlled Terms	Core	CDISC Notes
DECDORGw	Standardized Med Name in Orig Dict w	Char	WHODRUGy*	Perm	Original standardized medication name of CM.CMTRT using WHO Drug version X.X
CLASORGw	Medication Class in Orig Dictionary w	Char	WHODRUGy*	Perm	Original medication class of CM.CMTRT using WHO Drug version X.X
CLCDORGw	Medication Class Code in Orig Dict w	Char	WHODRUGy*	Perm	Original medication class code of CM.CMTRT using WHO Drug version X.X
ATyCORGw	ATC Level y Code in Orig Dictionary w	Char	WHODRUGw*	Perm	Original ATC Level y code of CM.CMTRT using WHO Drug version X.X
ATyTORGw	ATC Level y Text in Orig Dictionary w	Char	WHODRUGw*	Perm	Original ATC Level y text of CM.CMTRT using WHO Drug version X.X

** For each version of an external dictionary, a different reference name must be used. The individual reference names will point to a dedicated section in the data definition file where all external dictionaries used in the analysis are listed, including dictionary name and version.*

3.3 Other Metadata

Because OCCDS does not use parameters, there is typically no need for Value Level Metadata.

The other type of ADaM metadata which may be included is the Analysis Results Metadata. The CDISC Analysis Results Metadata Version 1.0 for Define-XML Version 2 [14] has examples of how to represent Analysis Results Metadata.

4 Example 1: Analysis of Treatment Emergent Adverse Event

The basic summary of adverse event frequencies described in section 12.2.2 (and located in section 14.3.1) of ICH Guideline E3 [12] 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 the adverse event occurred and (2) the rate of occurrence in each treatment group.

4.1 Analysis Display Example Layout

Table 4.1.1 Example of Summary of Treatment Emergent Adverse Events*

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)
…	x (x.x)	x (x.x)
<Other SOCs and PTs>		

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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.

* The style of the display of the results of an analysis will be determined by the producer. The example is intended to illustrate content not appearance.

4.2 Sample ADaM Variable Metadata

This example describes an adverse events ADaM dataset named ADAE. ADAE is not a required dataset name.

Table 4.2.1 Example of ADaM Variable Metadata

Dataset Name	Variable Name	Variable Label	Variable Type	Codelist / Controlled Terms	Source / Derivation
ADAE	STUDYID	Study Identifier	text		AE.STUDYID
ADAE	USUBJID	Unique Subject Identifier	text		AE.USUBJID
ADAE	AESEQ	Sequence Number	integer		AE.AESEQ
ADAE	AETERM	Reported Term for the Adverse Event	text		AE.AETERM
ADAE	AEDECOD	Dictionary-Derived Term	text	MedDRA	AE.AEDECOD MedDRA Version 11.1
ADAE	AEBODSYS	Body System or Organ Class	text	MedDRA	AE.AEBODSYS MedDRA Version 11.1
ADAE	TRTEMFL	Treatment Emergent Analysis Flag	text	Y	If ADSL.TRTSDT <= ASTDT<=(ADSL.TRTEDT +14) then TRTEMFL='Y'
ADAE	PREFL	Pre-treatment Flag	text	Y	If ASTDT < ADSL.TRTSDT then PREFL='Y'
ADAE	FUPFL	Follow-up Flag	text	Y	If ASTDT > ADSL.TRTEDT+14 then FUPFL='Y'
ADAE	AESTDTC	Start Date/Time of Adverse Event	date	ISO 8601	AE.AESTDTC
ADAE	ASTDT	Analysis Start Date	integer		<Producer will insert derivation here>
ADAE	ASTDTF	Analysis Start Date Imputation Flag	text	D, M, Y	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	date	ISO 8601	AE.AEENDTC
ADAE	AENDT	Analysis End Date	integer		<Producer will insert derivation here>
ADAE	AENDTF	Analysis End Date Imputation Flag	text	D, M, Y	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	Y, N	AE.AESER
ADAE	APHASE	Phase	text	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	MILD, MODERATE, SEVERE	AE.AESEV
ADAE	ASEV	Analysis Severity/Intensity	text	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'

Dataset Name	Variable Name	Variable Label	Variable Type	Codelist / Controlled Terms	Source / Derivation
ADAE	ASEVN	Analysis Severity/Intensity (N)	integer	1, 2, 3	Map ASEV to ASEVN in the following manner: 'Mild' = 1 'Moderate' = 2 'Severe' = 3
ADAE	AEREL	Causality	text	NOT RELATED, UNLIKELY RELATED, POSSIBLY RELATED, PROBABLY RELATED, DEFINITELY RELATED	AE.AEREL
ADAE	RELGR1	Pooled Causality Group 1	text	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'
ADAE	RELGR1N	Pooled Causality Group 1 (N)	integer	0, 1	Map RELGR1 to RELGR1N in the following manner: 'Not Related' = 0 'Related' = 1
ADAE	SAFFL	Safety Population Flag	text	Y,N	ADSL.SAFFL
ADAE	AOCCFL	1st Occurrence within Subject Flag	text	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	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	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	Drug A, Drug B	ADSL.TRT01A
ADAE	TRTAN	Actual Treatment (N)	integer	1, 2	ADSL.TRT01AN Drug A = 1 Drug B = 2
ADAE	TRTSDT	Date of First Exposure to Treatment	integer		ADSL.TRTSDT
ADAE	TRTEDT	Date of Last Exposure to Treatment	integer		ADSL.TRTEDT
ADAE	AGE	Age	integer		ADSL.AGE
ADAE	AGEGR1	Pooled Age Group 1	text	<65, >=65	ADSL. AGEGR1
ADAE	SEX	Sex	text	M, F	ADSL.SEX
ADAE	RACE	Race	text	BLACK OR AFRICAN AMERICAN, AMERICAN	ADSL.RACE

Dataset Name	Variable Name	Variable Label	Variable Type	Codelist / Controlled Terms	Source / Derivation
				INDIAN OR ALASKA NATIVE, ASIAN, NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER, WHITE	

4.3 Sample ADaM Data

Table 4.3.1 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 (AOCC*FL) 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.
7. The core variables of AGE, AGEGR1, SEX, and RACE are included in ADAE to facilitate subgroup analyses.

Table 4.3.1 Sample ADaM 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		

Row	STUDYID	USUBJID	AESEQ	AETERM	AEDECOD	AEBODSYS	TRTEMFL	PREFL	FUPFL
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	AEREL
1 (cont)	2006-01	01JAN2006	D	2006-01-22	22JAN2006		N	PRE-TREATMENT	MILD	Mild	1	NOT RELATED
2 (cont)	2006-01-21	21JAN2006		2006-01-28	28JAN2006		N	PRE-TREATMENT	MODERATE	Moderate	2	NOT RELATED
3 (cont)	2006-01-22	22JAN2006		2006-01-22	22JAN2006		N	PRE-TREATMENT	MILD	Mild	1	NOT RELATED
4 (cont)		23JAN2006	Y		15MAY2006	Y	N	TREATMENT	MILD	Mild	1	POSSIBLY RELATED
5 (cont)	2006-01-24	24JAN2006		2006-01	31JAN2006	D	N	TREATMENT	MODERATE	Moderate	2	PROBABLY RELATED
6 (cont)	2006-02	01FEB2006	D	2006-02-05	05FEB2006		N	TREATMENT	SEVERE	Severe	3	PROBABLY RELATED
7 (cont)	2006-03-05	05MAR2006		2006-03-06	06MAR2006		N	TREATMENT		Severe	3	DEFINITELY RELATED
8 (cont)	2006-03-05	05MAR2006		2006	15MAY2006	M	N	TREATMENT	MODERATE	Moderate	2	DEFINITELY RELATED
9 (cont)	2006-03-17	17MAR2006		2006-03-18	18MAR2006		N	TREATMENT	MODERATE	Moderate	2	DEFINITELY RELATED
10 (cont)	2006-03-17	17MAR2006		2006-03-19	19MAR2006		N	TREATMENT	MILD	Mild	1	DEFINITELY RELATED
11 (cont)	2006-04-20	20APR2006		2006-04-22	22APR2006		N	TREATMENT	MILD	Mild	1	PROBABLY RELATED
12 (cont)	2006-05-17	17MAY2006		2006-05-20	20MAY2006		N	TREATMENT	MILD	Mild	1	POSSIBLY RELATED
13 (cont)	2006-05-20	20MAY2006		2006-05-22	22MAY2006		N	TREATMENT	MILD	Mild	1	UNLIKELY RELATED
14 (cont)	2006-05-23	23MAY2006		2006-06-27	27JUN2006		N	TREATMENT	MILD	Mild	1	UNLIKELY RELATED
15 (cont)	2006-05-21	27MAY2006		2006-05-25	29MAY2006		Y	TREATMENT	SEVERE	Severe	3	UNLIKELY RELATED
16 (cont)	2006-06-01	01JUN2006		2006-06-01	01JUN2006		N	FOLLOW-UP	MILD	Mild	1	UNLIKELY RELATED

** Variables ending in suffix DTC are character date/time fields in the ISO8601 format. Variables ending in DT are numeric dates, here shown using SAS date format date9. Other numeric date formats can be used, but care should be taken with newer date formats which might not be understood by all statistical packages*

Row	RELGR1	RELGR1N	SAFFL	AOCCFL	AOCCSFL	AOCCPFL	TRTA	TRTAN	TRTSDT*	TRTEDT*	AGE	AGEGR1	SEX	RACE
1 (cont)	Not Related	0	Y				Drug A	1	23JAN2006	15MAY2006	54	<65	M	ASIAN
2 (cont)	Not Related	0	Y				Drug A	1	23JAN2006	15MAY2006	54	<65	M	ASIAN
3 (cont)	Not Related	0	Y				Drug A	1	23JAN2006	15MAY2006	54	<65	M	ASIAN
4 (cont)	Related	1	Y	Y	Y	Y	Drug A	1	23JAN2006	15MAY2006	54	<65	M	ASIAN
5 (cont)	Related	1	Y		Y	Y	Drug A	1	23JAN 2006	15MAY 2006	54	<65	M	ASIAN
6 (cont)	Related	1	Y				Drug A	1	23JAN 2006	15MAY 2006	54	<65	M	ASIAN
7 (cont)	Related	1	Y		Y	Y	Drug A	1	23JAN 2006	15MAY 2006	54	<65	M	ASIAN
8 (cont)	Related	1	Y			Y	Drug A	1	23JAN 2006	15MAY 2006	54	<65	M	ASIAN
9 (cont)	Related	1	Y				Drug A	1	23JAN 2006	15MAY 2006	54	<65	M	ASIAN
10 (cont)	Related	1	Y			Y	Drug A	1	23JAN 2006	15MAY 2006	54	<65	M	ASIAN
11 (cont)	Related	1	Y			Y	Drug A	1	23JAN 2006	15MAY 2006	54	<65	M	ASIAN
12 (cont)	Related	1	Y		Y	Y	Drug A	1	23JAN 2006	15MAY 2006	54	<65	M	ASIAN
13 (cont)	Not Related	0	Y				Drug A	1	23JAN 2006	15MAY 2006	54	<65	M	ASIAN
14 (cont)	Not Related	0	Y				Drug A	1	23JAN 2006	15MAY 2006	54	<65	M	ASIAN
15 (cont)	Not Related	0	Y				Drug A	1	23JAN 2006	15MAY 2006	54	<65	M	ASIAN
16 (cont)	Not Related	0	Y				Drug A	1	23JAN 2006	15MAY 2006	54	<65	M	ASIAN

** Variables ending in DT are numeric dates, here shown using SAS date format date9. Other numeric date formats can be used, but care should be taken with newer date formats which might not be understood by all statistical packages.*

5 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 [13].)

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.

5.1 Analysis Display Example Layouts

Table 5.1.1 Example of Summary of Haemorrhages (SMQ) (Narrow Scope) Adverse Events by Sex and Actual Treatment Group*

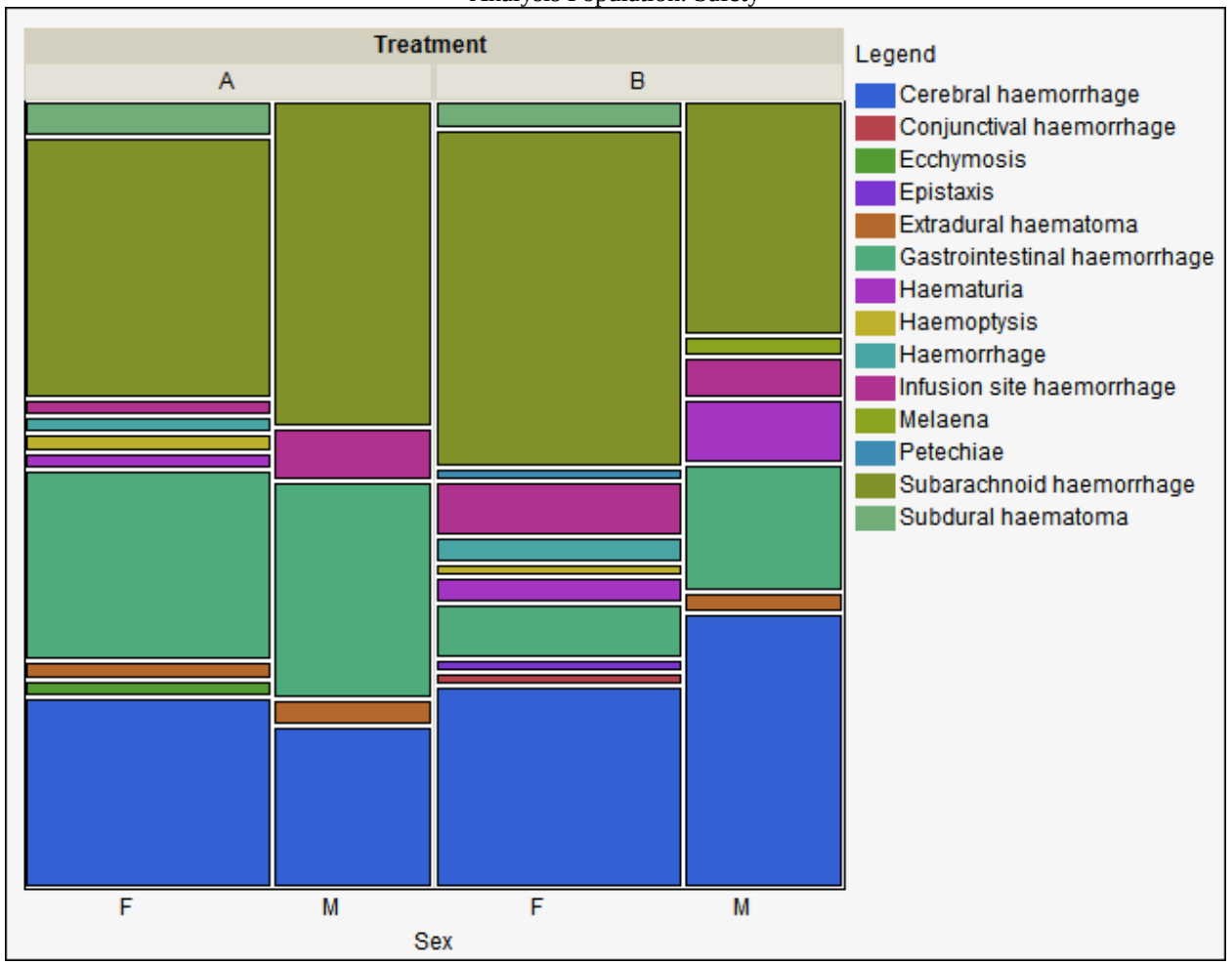
Table 14.2.7.3
Summary of Haemorrhages (SMQ) (Narrow Scope) Adverse Events by Sex and Actual Treatment Group
Analysis Population: Safety

	Gender n (%)			
	Females		Males	
Preferred Term	B (N=281)	A (N=166)	B (N=297)	A (N=158)
Any Haemorrhages (SMQ) (Narrow Scope) Event	36 (8.0)	48 (10.5)	26 (8.8)	31 (19.6)
Cerebral haemorrhage	11 (2.4)	15 (3.3)	6 (2.0)	13 (8.2)
Conjunctival haemorrhage	0	1 (0.2)	0	0
Ecchymosis	1 (0.2)	0	0	0
Epistaxis	0	1 (0.2)	0	0
Extradural haematoma	1 (0.2)	0	1 (0.3)	1 (0.6)
Gastrointestinal haemorrhage	10 (2.2)	4 (0.9)	8 (2.7)	6 (3.8)
Haematuria	1 (0.2)	2 (0.4)	0	3 (1.9)
Haemoptysis	1 (0.2)	1 (0.2)	0	0
Haemorrhage	1 (0.2)	2 (0.4)	0	0
Infusion site haemorrhage	1 (0.2)	4 (0.9)	2 (0.7)	2 (1.3)
Melaena	0	0	0	1 (0.6)
Petechiae	0	1 (0.2)	0	0
Subarachnoid haemorrhage	14 (3.1)	24 (5.3)	12 (4.0)	11 (7.0)
Subdural haematoma	2 (0.4)	2 (0.4)	0	0

* The style of the display of the results of an analysis will be determined by the producer. The example is intended to illustrate content not appearance.

Figure 5.1.1 Example of Mosaic Plot of Haemorrhages (SMQ) (Narrow Scope) Preferred Terms by Sex and Actual Treatment Group*

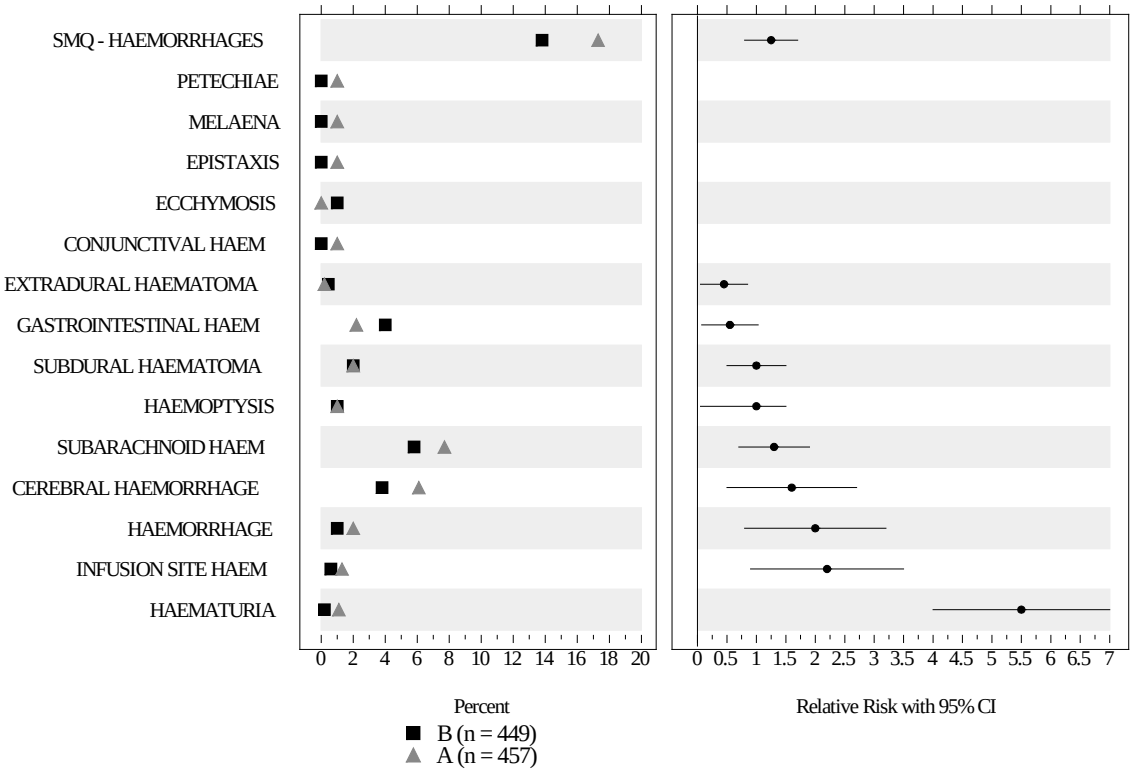
Figure 14.2.7.1
Mosaic Plot of Hemorrhagic (SMQ) Preferred Terms by Sex and Actual Treatment Group
Analysis Population: Safety



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

Figure 5.1.2 Example of Haemorrhages (SMQ) (Narrow Scope) Preferred Terms Sorted by Relative Risk*

Figure 14.2.7.2
Hemorrhagic (SMQ) Preferred Terms Sorted by Relative Risk
Analysis Population: Safety Population



5.2 Sample ADaM Variable Metadata

This example describes an adverse events ADaM dataset named ADAE. ADAE is not a required dataset name. In Table 5.2.1 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 producer-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").

* The style of the display of the results of an analysis will be determined by the producer. The example is intended to illustrate content not appearance.

Table 5.2.1 Example of ADaM Variable Metadata

Dataset Name	Variable Name	Variable Label	Variable Type	Codelist / Controlled Terms	Source / Derivation
ADAE	USUBJID	Unique Subject Identifier	text		ADSL.USUBJID
ADAE	AETERM	Reported Term for the Adverse Event	text		AE.AETERM
ADAE	AEDECOD	Dictionary-Derived Term	text	MedDRA	AE.AEDECOD
ADAE	AEBODSYS	Body System or Organ Class	text	MedDRA	AE.AEBODSYS
ADAE	ASTDT	Analysis Start Date	integer		<Producer will insert derivation here>
ADAE	AEPTCD	Preferred Term Code	integer		AE.AEPTCD
ADAE	SMQ01CD	SMQ 01 Code	integer		SMQ01CD=20000039 if the AEPTCD is included in this SMQ.
ADAE	SMQ01NAM	SMQ 01 Name	text		SMQ01NAM='Haemorrhage terms (excl. laboratory terms) (SMQ)' if the AEPTCD is included in this SMQ.
ADAE	SMQ01SC	SMQ 01 Scope	text	BROAD, NARROW	For this given SMQ, all scopes are Narrow.
ADAE	SMQ01SCN	SMQ 01 Scope (N)	integer	1, 2	Map SMQ01SC to SMQ01SCN in the following manner: Broad = 1 Narrow = 2

5.3 Sample ADaM Data

Table 5.3.1: Sample ADaM 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	09JUN2009	10050508	20000039	Haemorrhage terms (excl laboratory terms) (SMQ)	NARROW	2
2	0112012	BRUISING OF LEFT UPPER ARM	Contusion	Injury, poisoning and procedural complications	27AUG2008	10050584	20000039	Haemorrhage terms (excl laboratory terms) (SMQ)	NARROW	2
3	0112012	BRUISING TO LEFT WRIST	Contusion	Injury, poisoning and procedural complications	22AUG2007	10050584	20000039	Haemorrhage terms (excl laboratory terms) (SMQ)	NARROW	2
4	0112013	NAUSEA	Nausea	Gastrointestinal disorders	16JUN2010	10028813				
5	0112014	NOSE BLEEDING	Epistaxis	Respiratory, thoracic and mediastinal disorders	22NOV2009	10015090	20000039	Haemorrhage terms (excl laboratory terms) (SMQ)	NARROW	2
6	0122006	EPISTAXIS	Epistaxis	Respiratory, thoracic and mediastinal disorders	06NOV2009	10015090	20000039	Haemorrhage terms (excl laboratory terms) (SMQ)	NARROW	2

** Variables ending in DT are numeric dates, here shown using SAS date format date9. Other numeric date formats can be used, but care should be taken with newer date formats which might not be understood by all statistical packages.*

6 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/ARELN] 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 [10] 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'.

6.1 Analysis Display Example Layout

Table 6.1.1 Example of Summary of Cumulative Dose Quartiles to First Onset for PSN by Severity Grade*

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

* The style of the display of the results of an analysis will be determined by the producer. The example is intended to illustrate content not appearance.

6.2 Sample ADaM Variable Metadata

This example describes an adverse events ADaM dataset named ADAE. ADAE is not a required dataset name.

Table 6.2.1: Sample ADaM Variable Metadata for selected variables

Dataset Name	Variable Name	Variable Label	Variable Type	Codelist / Controlled Terms	Source / Derivation
ADAE	USUBJID	Unique Subject Identifier	text		ADSL.USUBJID
ADAE	ITTFL	Intent-to-Treat Population Flag	text	Y,N	ADSL.ITTFL
ADAE	AEDECOD	Dictionary-Derived Term	text	MedDRA	AE.AEDECOD
ADAE	AETOXGR	Standard Toxicity Grade	text	1, 2, 3, 4, 5	AE.AETOXGR
ADAE	AETOXGRN	Standard Toxicity Grade (N)	integer	1, 2, 3, 4, 5	Code AE.AETOXGR to numeric
ADAE	DOSCUMA	Cumulative Actual Treatment Dose	float		Total all values of EX.EXDOSE for the subject up to the start of the AE.
ADAE	DOSEU	Treatment Dose Units	text	mg	EX.EXDOSEU
ADAE	DOSCMGR1	Cumulative Dose Group 1	text	Quartile 1, Quartile 2, Quartile 3, Quartile 4	Missing if DOSCUMA=0, else DOSCMGR1 = Quartile 1 if DOSCUMA 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.

6.3 Sample ADaM Data

Key points to note in the example are:

1. Variable DOSCMGR1 is not a standard variable. It has been added for analysis purposes and uses the naming conventions from the ADaMIG.
2. 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.
3. 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 6.3.1: Sample ADaM Data Showing Cumulative Dose Variables

Row	USUBJID	ITTFL	AEDECOD	AETOXGR	AETOXGRN	DOSCUMA	DOSEU	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	

7 Example 4: Analysis of Treatment Emergent Adverse Events in a Cross-Over Interaction Study

This example is a phase I, open-label, three period 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.

In addition to standard cross-over analysis, this example also includes analysis using both a primary and a secondary coding path.

7.1 Analysis Display Example Layout

Table 7.1.1 Example of Summary of Treatment Emergent AEs by System Organ Class and Preferred Term and Treatment Group*

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.

* The style of the display of the results of an analysis will be determined by the producer. The example is intended to illustrate content not appearance.

7.2 Sample ADaM Variable Metadata

This example describes an adverse events ADaM dataset named ADAE. ADAE is not a required dataset name.

Table 7.2.1: Sample ADaM Variable Metadata for selected variables

Dataset Name	Variable Name	Variable Label	Variable Type	Codelist / Controlled Terms	Source / Derivation
ADAE	USUBJID	Unique Subject Identifier	text		ADSL.USUBJID
ADAE	TRTA	Actual Treatment	text	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	integer	1, 2, 3	Code TRTA to numeric. Treatment A = 1 Treatment B = 2 Treatment A+B = 3
ADAE	SAFFL	Safety Population Flag	text	Y,N	ADSL.SAFFL
ADAE	AEBODSYS	Body System or Organ Class	text	MedDRA	AE.AEBODSYS
ADAE	AEDECOD	Dictionary-Derived Term	text	MedDRA	AE.AEDECOD
ADAE	ASTDTM	Analysis Start Date/Time	integer		Converting AE.AESTDTC from character ISO8601 format to numeric date format, applying producer defined imputation rules.
ADAE	ASTDTF	Analysis Start Date Imputation Flag	text	D, M, Y	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	M, H	The level of imputation done for the start time (H if hour was imputed, M if minutes were imputed).
ADAE	TRTEMFL	Treatment Emergent Analysis Flag	text	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	Y	If TRTEMFL ^=’Y’ and FUPFL^=’Y’ then PREFL=’Y’
ADAE	FUPFL	Follow-up Flag	text	Y	if ASTDTM GT (ADSL.TR03EDTM+72 hours) then FUPFL=’Y’
ADAE	ASTDY	Analysis Start Relative Day	integer		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	RUN-IN, FIRST TREATMENT, FIRST WASHOUT, SECOND TREATMENT, SECOND WASHOUT, THIRD TREATMENT, FOLLOW-UP	AE.EPOCH
ADAE	APHASE	Phase	text	RUN-IN, FIRST TREATMENT, FIRST WASHOUT, SECOND	If AESDTM < ADSL.TR01SDTM then APHASE=’RUN-IN’, else ifADSL.TR01SDTM LE AESDTM LE(ADSL.TR01EDTM+72 hours)

Dataset Name	Variable Name	Variable Label	Variable Type	Codelist / Controlled Terms	Source / Derivation
				TREATMENT, SECOND WASHOUT, THIRD TREATMENT, FOLLOW-UP	then APHASE =’FIRST TREATMENT’, else if(ADSL.TR01EDTM+72 hours) < AESDTM< ADSL.TR02SDTM then APHASE=’FIRST WASHOUT’, etc.
ADAE	APERIOD	Period	integer	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	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		ADSL.TR01SDTM
ADAE	TR01EDTM	Datetime of Last Exposure in Period 01	integer		ADSL.TR01EDTM
ADAE	TR02SDTM	Datetime of First Exposure in Period 02	integer		ADSL.TR02SDTM
ADAE	TR02EDTM	Datetime of Last Exposure in Period 02	integer		ADSL.TR02EDTM
ADAE	TR03SDTM	Datetime of First Exposure in Period 03	integer		ADSL.TR03SDTM
ADAE	TR03EDTM	Datetime of Last Exposure in Period 03	integer		ADSL.TR03EDTM

7.3 Sample ADaM Data

Table 7.3.1 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 producer.
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 7.3.1: Sample ADaM Data

Row	USUBJID	TRTA	TRTAN	SAFFL	AEBODSYS	AEDECOD	ASTDTM*	ASTDTF	ASTTMF	TRTEMFL	PREFL	FUPFL	ASTDY	EPOCH
1	101-001	A	1	Y	GASTROINTESTINAL DISORDERS	VOMITING	05MAY08:16:00:00		M	Y			5	FIRST TREATMENT
2	101-001	B	2	Y	INFECTIONS AND INFESTATIONS	PHARYNGITIS	16MAY08:06:42:00			Y			16	SECOND TREATMENT
3	101-001	A+B	3	Y	NERVOUS SYSTEM DISORDERS	HEADACHE	01JUN08:15:30:00			Y			32	THIRD TREATMENT
4	101-001	A+B	3	Y	NERVOUS SYSTEM DISORDERS	CONSTIPATION	02JUN08:07:15:00			Y			33	THIRD TREATMENT
5	101-001			Y	INFECTIONS AND INFESTATIONS	ORAL HERPES	07JUN08:08:00:00					Y	38	FOLLOW-UP
6	101-002			Y	VASCULAR DISORDERS	HYPOTENSION	25MAY08:13:20:00				Y		26	SECOND WASHOUT
7	101-002	A+B	3	Y	NERVOUS SYSTEM DISORDERS	HEADACHE	27MAY08:22:10:00			Y			28	THIRD TREATMENT
8	101-002	A+B	3	Y	NERVOUS SYSTEM DISORDERS	HEADACHE	02JUN08:22:10:00			Y			34	FOLLOW-UP

** Variables ending in DTM are numeric datetimes, here shown using SAS format datetime16. Other numeric datetime formats can be used, but care should be taken with newer formats which might not be understood by all statistical packages.*

Row	APHASE	APERIOD	APERIODC	TR01SDTM*	TR01EDTM*	TR02SDTM*	TR02EDTM*	TR03SDTM*	TR03EDTM*
1 (cont)	FIRST TREATMENT	1	PERIOD 01	01MAY08:10:05:00	07MAY08:09:10:10	15MAY08:08:15:00	21MAY08:10:30:00	20MAY08:13:50:00	03JUN08:07:20:00
2 (cont)	SECOND TREATMENT	2	PERIOD 02	01MAY08:10:05:00	07MAY08:09:10:00	15MAY08:08:15:00	21MAY08:10:30:00	29MAY08:13:50:00	03JUN08:07:20:00
3 (cont)	THIRD TREATMENT	3	PERIOD 03	01MAY08:10:05:00	07MAY08:09:10:00	15MAY08:08:15:00	21MAY08:10:30:00	29MAY08:13:50:00	03JUN08:07:20:00
4 (cont)	THIRD TREATMENT	3	PERIOD 03	01MAY08:10:05:00	07MAY08:09:10:00	15MAY08:08:15:00	21MAY08:10:30:00	29MAY08:13:50:00	03JUN08:07:20:00
5 (cont)	FOLLOW-UP			01MAY08:10:05:00	07MAY08:09:10:00	15MAY08:08:15:00	21MAY08:10:30:00	29MAY08:13:50:00	03JUN08:07:20:00
6 (cont)	SECOND WASHOUT			30APR08:12:05:00	06MAY08:08:32:00	14MAY08:11:55:00	20MAY08:08:10:00	26MAY08:15:40:00	01JUN08:09:13:00
7 (cont)	THIRD TREATMENT	3	PERIOD 03	30APR08:12:05:00	06MAY08:08:32:00	14MAY08:11:55:00	20MAY08:08:10:00	26MAY08:15:40:00	01JUN08:09:13:00
8 (cont)	THIRD TREATMENT	3	PERIOD 03	30APR08:12:05:00	06MAY08:08:32:00	14MAY08:11:55:00	20MAY08:08:10:00	26MAY08:15:40:00	01JUN08:09:13:00

** Variables ending in DTM are numeric datetimes, here shown using SAS format datetime16. Other numeric datetime formats can be used, but care should be taken with newer formats which might not be understood by all statistical packages.*

8 Example 5: MedDRA Secondary Path

In MedDRA, a collected term can be mapped along more than one path, as shown in the diagram below.

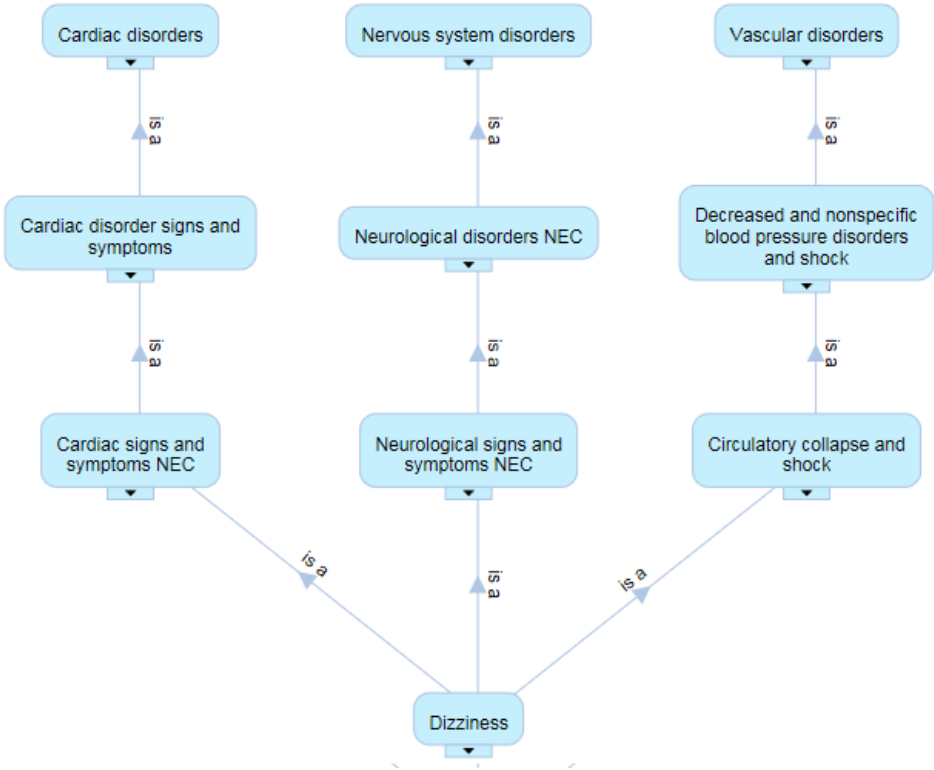
Whenever more than one path is possible, there is always a primary coding path plus one or more secondary paths. When a secondary path will be used for analysis, SDTMIG version 3.2 allows for capture of both a primary and secondary System Organ Class (SOC), as described in the CDISC Notes column for these variables:

- **AEBODSYS**: "Dictionary derived. Body system or organ class used by the sponsor from the coding dictionary (e.g., MedDRA). When using a multi-axial dictionary such as MedDRA, this should contain the SOC used for the sponsor's analyses and summary tables which may not necessarily be the primary SOC."
- **AESOC**: "Dictionary-derived text description of the primary System Organ Class. Will be the same as AEBODSYS if the primary SOC was used for analysis."

As with other SDTM variables, these are typically copied from SDTM to ADaM and used directly in the occurrence analysis.
This section describes different ways to handle multiple coding paths and gives an example on how to create a single analysis dataset with two different coding paths.

Typically adverse event analysis includes only the primary coding path. However, some indications also perform analysis on the secondary path. For example in study of brain cancer, a headache might need to be analyzed according to a secondary path that attributes this to the cancer. This is why SDTM has the option of including two different paths.

Figure 8.1: Possible MedDRA Coding Paths for term "Dizziness" [15]



When a secondary path is used, often the analysis need is:

- One set of tables showing primary path, such as shown in section 4, using AESOC for analysis.
- Another separate set of tables showing secondary path, similar to what is shown in section 4 but using AEBODSYS for analysis.

For this type of analysis need, analysis can be made straightforward by creating one dataset for the primary path tables, and a separate dataset for the secondary path tables. The remainder of this section describes an analysis need beyond this, where both primary and secondary analyses are performed on the same table.

8.1 Analysis Display Example

The analysis need is to produce the following table:

Table 8.1.1: Example Analysis Display*

Table 14.2.8.3
Treatment Emergent AEs by Primary and Secondary SOCs, Preferred Term
(Population: Safety Subjects)

System Organ Class Preferred Term	Placebo (n=xxx)		Drug X (n=xxx)	
	Primary SOC n (%)	Primary + Secondary SOC n (%)	Primary SOC n (%)	Primary + Secondary SOC n (%)
CARDIAC DISORDERS	0 (x.x)	0 (x.x)	0 (x.x)	1 (x.x)
Dizziness [2]	0 (x.x)	0 (x.x)	0 (x.x)	1 (x.x)
ENDOCRINE DISORDERS	0 (x.x)	1 (x.x)	2 (x.x)	2 (x.x)
Autoimmune thyroiditis [1]	0 (x.x)	0 (x.x)	1 (x.x)	1 (x.x)
Thyroid atrophy[1]	0 (x.x)	1 (x.x)	1 (x.x)	1 (x.x)
NERVOUS SYSTEM DISORDERS	2 (x.x)	2 (x.x)	1 (x.x)	1 (x.x)
Dizziness [1]	2 (x.x)	2 (x.x)	1 (x.x)	1 (x.x)
VASCULAR DISORDERS	0 (x.x)	1 (x.x)	0 (x.x)	0 (x.x)
Dizziness [2]	0 (x.x)	1 (x.x)	0 (x.x)	0 (x.x)

SOC = System Organ Class;
[1] Preferred term comes from primary system organ class path
[2] Preferred term comes from secondary system organ class path

8.2 Sample SDTM AE Data

As described above in the introduction to this section, both SDTM variables AEBODSYS and AESOC are included in the SDTM AE data, and each represents a different coding path used for analysis. In table 8.2.1 below, notice that AEBODSYS and AESOC are the same on some rows but different on others. When only a primary path is to be used, the values of AEBODSYS and AESOC are the same. When a secondary path is to be used, AEBODSYS and AESOC are different. For the purpose of this example we see that the AE Dizziness was coded to different MedDRA coding paths in different subjects based on further information available.

Table 8.2.1: Sample SDTM AE data for selected variables

Row	STUDYID	USUBJID	AESEQ	AEDECOD	AEBODSYS	AESTDTC	AESOC
1	XYZ	XYZ-1-001	1	Autoimmune thyroiditis	Endocrine disorders	2008-05-13	Endocrine disorders
2	XYZ	XYZ-1-001	2	Dizziness	Cardiac disorders	2008-06-13	Nervous system disorders
3	XYZ	XYZ-2-002	1	Dizziness	Vascular disorders	2008-09-13	Nervous system disorders
4	XYZ	XYZ-3-003	1	Thyroid atrophy	Endocrine disorders	2008-09-13	Endocrine disorders
5	XYZ	XYZ-4-004	1	Dizziness	Nervous system disorders	2008-09-09	Nervous system disorders

* The style of the display of the results of an analysis will be determined by the producer. The example is intended to illustrate content not appearance.

8.3 Sample ADaM Data

As mentioned earlier in this section, a typical way to analyze adverse event data with multiple paths is to split the different coding paths into separate analysis datasets. Each analysis dataset would contain the records from the SDTM AE dataset, but one dataset would use AEBODSYS for analysis and the other would use AESOC. Dataset metadata, including dataset labels and documentation, would explain the different datasets and their individual analysis purposes.

In this case, the data were kept in a single analysis dataset, with rows for each coding path, as shown in table 8.3.1, to facilitate analysis for the table shown in table 8.1.1.

Key points to note in the example are:

1. The analysis record flag variables can be used to differentiate between primary path and secondary path records. In this example, ANL01FL is used to identify the primary coding path and ANL02FL is used to identify the secondary coding path.
2. Row 2 and 3 represent a single adverse event of Dizziness from SDTM. It was coded to two system organ classes: Nervous system disorders (primary SOC) and Cardiac disorders (original coding). Both rows in ADAE have the same value of AESEQ.
3. Rows 4 and 5 represent a single adverse event of Dizziness. It was coded to two system organ classes: Nervous system disorders (primary SOC) and Vascular disorders (original coding). Both rows in ADAE have the same value of AESEQ.
4. Rows 6-7 use only one path, so no additional records are necessary.
5. AEBODSYS and AESOC are unchanged from SDTM. New variable ASOC is added as an analysis version of the body system to facilitate the analysis. ASOC is not a required name.
6. The purpose of this example is not to state how MedDRA secondary paths are to be handled, only to provide an example.

Table 8.3.1: Sample ADaM ADAE data for selected variables

Row	USUBJID	TRTA	AESEQ	AEDECOD	AEBODSYS	AESOC	ASOC	ANL01FL	ANL02FL
1	XYZ-1-001	Drug X	1	Autoimmune thyroiditis	Endocrine disorders	Endocrine disorders	Endocrine disorders	Y	
2	XYZ-1-001	Drug X	2	Dizziness	Cardiac disorders	Nervous system disorders	Cardiac disorders		Y
3	XYZ-1-001	Drug X	2	Dizziness	Cardiac disorders	Nervous system disorders	Nervous system disorders	Y	
4	XYZ-2-002	Placebo	1	Dizziness	Vascular disorders	Nervous system disorders	Vascular disorders		Y
5	XYZ-2-002	Placebo	1	Dizziness	Vascular disorders	Nervous system disorders	Nervous system disorders	Y	
6	XYZ-3-003	Drug X	1	Thyroid atrophy	Endocrine disorders	Endocrine disorders	Endocrine disorders	Y	
7	XYZ-4-004	Placebo	1	Dizziness	Nervous system disorders	Nervous system disorders	Nervous system disorders	Y	

9 Example 6: Analysis of Concomitant Medications

This example displays a simple summary of all concomitant medications. The example is based on a two treatment parallel design study. The display summarizes (1) the number of patients in each treatment group who took a concomitant medication and (2) the rate of occurrence in each treatment group. In this example, analysis results metadata have not been included. As stated in the ADaMIG, analysis results metadata are not needed or even advisable for every analysis included in a clinical study report or submission.

9.1 Analysis Display Example Layout

Table 9.1.1 Example of Summary of Concomitant Medications*

Table 14.1.5
Summary of Concomitant Medications by Medication Class and Preferred Term
Analysis Population: Safety

Medication Class/Preferred Term	Treatment A (N=4)	Treatment B (N=5)	Total (N=9)
Any Concomitant Medication	4 (100.0%)	4 (80.0%)	8 (88.9%)
ANALGESICS	2 (50.0%)	2 (40.0%)	4 (44.4%)
PARACETAMOL	2 (50.0%)	2 (40.0%)	4 (44.4%)
ANTIBACTERIALS FOR SYSTEMIC USE	1 (25.0%)	1 (20.0%)	2 (22.2%)
AMOXICILLIN	1 (25.0%)	1 (20.0%)	2 (22.2%)
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	1 (25.0%)	2 (40.0%)	3 (33.3%)
IBUPROFEN	1 (25.0%)	2 (40.0%)	3 (33.3%)
DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	0	2 (40.0%)	2 (22.2%)
MONTELUKAST	0	1 (20.0%)	1 (11.1%)
SALBUTAMOL	0	2 (40.0%)	2 (22.2%)
NASAL PREPARATIONS	2 (50.0%)	0	2 (22.2%)
FLUTICASONE PROPIONATE	2 (50.0%)	0	2 (22.2%)
PSYCHOANALEPTICS	1 (25.0%)	0	1 (11.1%)
SERTRALIN	1 (25.0%)	0	1 (11.1%)

* The style of the display of the results of an analysis will be determined by the producer. The example is intended to illustrate content not appearance.

9.2 Sample ADaM Variable Metadata

This example describes an adverse events ADaM dataset named ADCM. ADCM is not a required dataset name.

Table 9.2.1 Example of ADaM Variable Metadata

Dataset Name	Variable Name	Variable Label	Variable Type	Codelist / Controlled Terms	Source / Derivation
ADCM	STUDYID	Study Identifier	text		CM.STUDYID
ADCM	USUBJID	Unique Subject Identifier	text		CM.USUBJID
ADCM	CMSEQ	Sequence Number	integer		CM.CMSEQ
ADCM	CMTRT	Reported Name of Drug, Med or Therapy	text		CM.CMTRT
ADCM	CMMODIFY	Modified Reported Name	text		CM.CMMODIFY
ADCM	CMDECOD	Standardized Medication Name	text	WHODRUG	CM.CMDECOD WHO Drug Dictionary March 2012
ADCM	ATC1CD	ATC Level 1 Code	text	WHODRUG	ATC Level 1 Code WHO Drug Dictionary March 2012
ADCM	ATC2CD	ATC Level 2 Code	text	WHODRUG	ATC Level 2 Code WHO Drug Dictionary March 2012
ADCM	ATC3CD	ATC Level 3 Code	text	WHODRUG	ATC Level 3 Code WHO Drug Dictionary March 2012
ADCM	ATC1	ATC Level 1 Text	text	WHODRUG	ATC Level 1 Text WHO Drug Dictionary March 2012
ADCM	ATC2	ATC Level 2 Text	text	WHODRUG	ATC Level 2 Text WHO Drug Dictionary March 2012
ADCM	ATC3	ATC Level 3 Text	text	WHODRUG	ATC Level 3 Text WHO Drug Dictionary March 2012
ADCM	AOCCFL	1st Occurrence within Subject Flag	text	Y	<Producer will insert derivation here>
ADCM	AOCC01FL	First Occurrence of ATC Level 1 Flag	text	Y	<Producer will insert derivation here>
ADCM	AOCC02FL	First Occurrence of ATC Level 2 Flag	text	Y	<Producer will insert derivation here>
ADCM	AOCC03FL	First Occurrence of ATC Level 3 Flag	text	Y	<Producer will insert derivation here>
ADCM	AOCCPFL	1st Occurrence of Preferred Term Flag	text	Y	<Producer will insert derivation here>
ADCM	CMINDC	Indication	text		CM.CMINDC
ADCM	CMDOSFRM	Dose Form	text	TABLET	CM.CMDOSFRM
ADCM	CMDOSE	Dose per Administration	text		CM.CMDOSE
ADCM	CMDOSU	Dose Units	text	mg	CM.CMDOSU
ADCM	CMDOSFRQ	Dosing Frequency Per Interval	text	ONCE, PRN, QD, QID	CM.CMDOSFRQ
ADCM	CMROUTE	Route of Administration	text	ORAL	CM.CMROUTE
ADCM	CMSTDTC	Start Date/Time of Medication	date	ISO 8601	CM.CMSTDTC
ADCM	ASTDT	Analysis Start Date	integer	date9.	<Producer will insert derivation here>
ADCM	ASTDTF	Analysis Start Date Imputation Flag	text	D, M, Y	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'
ADCM	CMENDTC	End Date/Time of Medication	date	ISO 8601	CM.CMENDTC

Dataset Name	Variable Name	Variable Label	Variable Type	Codelist / Controlled Terms	Source / Derivation
ADCM	AENDT	Analysis End Date	integer	date9.	<Producer will insert derivation here>
ADCM	AENDTF	Analysis End Date Imputation Flag	text	D, M, Y	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'
ADCM	CMENRF	End Relative to Reference Period	text	ONGOING	CM.CMENRF
ADCM	ONTRTFL	On-Treatment Flag	text	Y	<Producer will insert derivation here>
ADCM	PREFL	Pre-treatment Flag	text	Y	<Producer will insert derivation here>
ADCM	SAFFL	Safety Population Flag	text	Y,N	ADSL.SAFFL
ADCM	TRTA	Actual Treatment	text	Drug A, Drug B	ADSL.TRT01A
ADCM	TRTAN	Actual Treatment (N)	integer	1, 2	ADSL.TRT01AN Drug A = 1 Drug B = 2
ADCM	TRTSDT	Date of First Exposure to Treatment	integer	date9.	ADSL.TRTSDT
ADCM	TRTEDT	Date of Last Exposure to Treatment	integer	date9.	ADSL.TRTEDT
ADCM	AGE	Age	integer		ADSL.AGE
ADCM	AGEGR1	Pooled Age Group 1	text	<65, >=65	ADSL. AGEGR1
ADCM	SEX	Sex	text	M, F	ADSL.SEX
ADCM	RACE	Race	text	ASIAN	ADSL.RACE

9.3 Sample ADaM Data

Table 9.3.1 is an illustration of the concomitant medications analysis dataset (ADCM) defined above. The ADCM dataset illustrated in this example was designed to support some standard subsets and/or classifications of concomitant medications. 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 the record level actual treatment variable (TRTA) populated with the same value across all rows in the dataset rather than the 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 baseline records with treatment even though subjects had not yet received treatment at that time.
2. Variables such as CMSEQ, CMTRT, and CMSTDTC are copied in from SDTM CM domain to provide data point traceability.
3. Variables such as CMDECOD are copied in from the SDTM CM domain for analysis purposes.
4. ASTDT and AENDT are the CM timing variables used for analysis. Other timing variables such as ASTDTF/AENDTF/ CMSTDTC/CMENDTC/TRTSDT/TRTEDT are supportive variables for metadata traceability.
5. The Occurrence Flags (AOCCFL, AOCCPFL, AOCC01FL, AOCC02FL, AOCC03FL) are permissible, and not required. 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 Analysis is built off of Concomitant Medications, the flags provide a crucial link between the summary records in the TTE BDS and the source of the records in ADCM.
6. The core variables of AGE, AGEGR1, SEX, and RACE are included in ADCM to facilitate subgroup analyses.

Table 9.3.1 Sample ADCM Data

Row	STUDYID	USUBJID	CMSEQ	CMTRT	CMMODIFY	CMDECOD	ATC1CD	ATC1	ATC2CD
1	ABC	ABC-001	1	TYLENOL	TYLENOL	PARACETAMOL	N	NERVOUS SYSTEM	N02
2	ABC	ABC-001	2	TYLENOL	TYLENOL	PARACETAMOL	N	NERVOUS SYSTEM	N02
3	ABC	ABC-001	3	TYLENOL	TYLENOL	PARACETAMOL	N	NERVOUS SYSTEM	N02
4	ABC	ABC-001	4	TYLENOL	TYLENOL	PARACETAMOL	N	NERVOUS SYSTEM	N02
5	ABC	ABC-001	5	CONTAC MS	CONTAC MS	CONTAC MS	N	NERVOUS SYSTEM	N02
6	ABC	ABC-001	6	FLONASE	FLONASE	FLUTICASONE PROPIONATE	R	RESPIRATORY SYSTEM	R01
7	ABC	ABC-002	1	ROBITUSSIN COUGH	ROBITUSSIN	NOVAHISTINE DMX	R	RESPIRATORY SYSTEM	R05
8	ABC	ABC-002	2	MOTRIN	MOTRIN	IBUPROFEN	M	MUSCULO-SKELETAL SYSTEM	M01
9	ABC	ABC-002	3	IBUPROFEN	IBUPROFEN	IBUPROFEN	M	MUSCULO-SKELETAL SYSTEM	M01
10	ABC	ABC-003	1	ZOLLOFT	ZOLOFT	SERTRALIN	N	NERVOUS SYSTEM	N06

Row	ATC2	ATC3CD	ATC3	AOCCFL	AOCCPFL
1 (cont)	ANALGESICS	N02B	OTHER ANALGESICS AND ANTIPYRETICS	Y	Y
2 (cont)	ANALGESICS	N02B	OTHER ANALGESICS AND ANTIPYRETICS		
3 (cont)	ANALGESICS	N02B	OTHER ANALGESICS AND ANTIPYRETICS		
4 (cont)	ANALGESICS	N02B	OTHER ANALGESICS AND ANTIPYRETICS		
5 (cont)	ANALGESICS	N02B	OTHER ANALGESICS AND ANTIPYRETICS		Y
6 (cont)	NASAL PREPARATIONS	R01A	DECONGESTANTS AND OTHER NASAL PREPARATIONS FOR TOP		Y
7 (cont)	COUGH AND COLD PREPARATIONS	R05FA	COUGH SUPPRESSANTS AND EXPECTORANTS, COMBINATIONS		Y
8 (cont)	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	M01A	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-S		Y
9 (cont)	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	M01A	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-S		
10 (cont)	PSYCHOANALEPTICS	N06A	ANTIDEPRESSANTS		Y

Row	AOCC01FL	AOCC02FL	AOCC03FL	CMINDC	CMDOSFRM	CMDOSE	CMDOSU	CMDOSFRQ	CMROUTE	CMSTDTC*	ASTDT*	CMENDTC*
1 (cont)	Y	Y	Y	HEADACHE	TABLET	100	mg	ONCE	ORAL	2011-01-02	02Jan2011	2011-01-02
2 (cont)				HEADACHE	TABLET	100	mg	ONCE	ORAL	2011-01-04	04Jan2011	2011-01-04
3 (cont)				HEADACHE	TABLET	100	mg	ONCE	ORAL	2011-01-10	10Jan2011	2011-01-10
4 (cont)				HEADACHE	TABLET	100	mg	ONCE	ORAL	2011-01-15	15Jan2011	2011-01-15
5 (cont)				COLD	TABLET	200	mg	ONCE	ORAL	2011-01-17	17Jan2011	2011-01-17
6 (cont)	Y	Y	Y	COUGH	TABLET	50	mg	QD	ORAL	2009-02-01	01Feb2009	
7 (cont)		Y	Y	INFECTION	SUSPENSION	500	mg	QID	ORAL	2011-03-01	01Mar2011	2011-03-15
8 (cont)	Y	Y	Y	LEG PAIN	TABLET	500	mg	PRN	ORAL	2011-05-14	14May2011	2011-06-01
9 (cont)				ARTHRITIS	TABLET	250	mg	QD	ORAL	2011-06-10	10Jun2011	
10 (cont)	Y	Y	Y	ANXIETY	TABLET	50	mg	QD	ORAL	2001-03		

** Variables ending in suffix DTC are character date/time fields in the ISO8601 format. Variables ending in DT are numeric dates, here shown using SAS date format date9. Other numeric date formats can be used, but care should be taken with newer date formats which might not be understood by all statistical packages.*

Row	AENDT*	CMENRF	ONTRTFL	PREFL	SAFFL	TRTA	TRTAN	TRTSDT*	TRTEDT*	AGE	AGEGR1	SEX	RACE
1 (cont)	02Jan2011			Y	Y	Drug A	1	23JAN2011	15MAY2011	54	<65	M	ASIAN
2 (cont)	04Jan2011			Y	Y	Drug A	1	23JAN2011	15MAY2011	54	<65	M	ASIAN
3 (cont)	10Jan2011			Y	Y	Drug A	1	23JAN2011	15MAY2011	54	<65	M	ASIAN
4 (cont)	15Jan2011			Y	Y	Drug A	1	23JAN 2011	15MAY2011	54	<65	M	ASIAN
5 (cont)	17Jan2011			Y	Y	Drug A	1	23JAN2011	15MAY2011	54	<65	M	ASIAN
6 (cont)		ONGOING	Y	Y	Y	Drug A	1	23JAN2011	15MAY2011	54	<65	M	ASIAN
7 (cont)	15Mar2011			Y	Y	Drug B	2	10MAY2011	25NOV201	54	<65	M	ASIAN

Row	AENDT*	CMENRF	ONTRTFL	PREFL	SAFFL	TRTA	TRTAN	TRTSDT*	TRTEDT*	AGE	AGEGR1	SEX	RACE
8 (cont)	01Jun2011		Y		Y	Drug B	2	10MAY2011	25NOV2011	54	<65	M	ASIAN
9 (cont)		ONGOING	Y		Y	Drug B	2	10MAY2011	25NOV2011	54	<65	M	ASIAN
10 (cont)		ONGOING	Y	Y	Y	Drug A	1	16JUN2011	03JAN2012	54	<65	M	ASIAN

** Variables ending in DT are numeric dates, here shown using SAS date format date9. Other numeric date formats can be used, but care should be taken with newer date formats which might not be understood by all statistical packages.*

10 Example 7: Analysis of Medical History Mapped to MedDRA

The basic summary of medical history frequencies described in section 12.2.2 (and located in section 14.3.1) of ICH Guideline E3 [12] report should be used to display frequencies in treatment and control groups.

This example displays a simple summary of all spontaneously reported medical history. The example is based on a two treatment parallel design study. The display summarizes (1) the number of subjects in each treatment group who had a given medical history event and (2) the rate of occurrence in each treatment group.

10.1 Analysis Display Example Layout

Table 10.1.1 Example of Summary of Medical History*

Summary of General Medical History Events Safety Population			
HISTORY CATEGORY **Body System** **Event**	**Active Drug (N=4)**	**Placebo (N=5)**	**Total (N=9)**
Any Medical History	3 (75.0%)	3 (60.0%)	6 (66.7%)
GASTROINTESTINAL	1 (25.0%)	0	1 (11.1%)
Gastrointestinal disorders	1 (25.0%)	0	1 (11.1%)
Abdominal pain	1 (25.0%)	0	1 (11.1%)
Gastroesophageal reflux disease	1 (25.0%)	0	1 (11.1%)
Nausea	1 (25.0%)	0	1 (11.1%)
HEMATOLOGICAL/LYMPHATIC	1 (25.0%)	0	1 (11.1%)
Blood and lymphatic system disorders	1 (25.0%)	0	1 (11.1%)
Anaemia	1 (25.0%)	0	1 (11.1%)
RESPIRATORY	3 (75.0%)	3 (60.0%)	6 (66.7%)
Immune system disorders	2 (50.0%)	3 (60.0%)	5 (55.6%)
Seasonal allergy	2 (50.0%)	3 (60.0%)	5 (55.6%)
Infections and infestations	1 (25.0%)	2 (40.0%)	3 (33.3%)
Upper respiratory tract infection	1 (25.0%)	2 (40.0%)	3 (33.3%)
Respiratory, thoracic and mediastinal disorders	1 (25.0%)	3 (60.0%)	4 (44.4%)
Asthma	1 (25.0%)	0	1 (11.1%)
Dyspnoea	0	3 (60.0%)	3 (33.3%)

* The style of the display of the results of an analysis will be determined by the producer. The example is intended to illustrate content not appearance.

The count and percent of unique subjects per classification group may be based on any of the classification variables. In this table, the count and percent of unique subjects is summarized by the variables MHSCAT, MHBODSYS, and MHDECOD. The table also summarizes the number of subjects who had any medical history event (e.g. the row 'Any Medical History'). The denominator counts (shown here in the (N=) in the column headings) are taken from the ADSL dataset and are based on the count of subjects in the population in the population of interest. Note that not all subjects in the population of interest will necessarily have data in the medical history file.

This presentation is analogous to the logic typically used for Adverse Events summaries.

10.2 Sample ADaM Variable Metadata

This example describes an adverse events ADaM dataset named ADMH. ADMH is not a required dataset name.

Table 10.2.1 Example of ADaM Variable Metadata

Dataset Name	Variable Name	Variable Label	Variable Type	Codelist / Controlled Terms	Source / Derivation
ADCM	STUDYID	Study Identifier	text		MH.STUDYID
ADMH	USUBJID	Unique Subject Identifier	text		MH.USUBJID
ADMH	MHSEQ	Sequence Number	integer		MH.MHSEQ
ADMH	MHCAT	Category for Medical History	text		MH.MHCAT
ADMH	MHSCAT	Sub Category for Medical History	text		MH.MHSCAT
ADMH	MHDECOD	Dictionary-Derived Term	text		MH.MHDECOD
ADMH	MHBODSYS	Body System or Organ Class	text		MH.MHBODSYS
ADMH	MHTERM	Reported Term for the Medical History	text		MH.MHTERM
ADMH	MHSTDTC	Start Date/Time of Medication	datetime	ISO 8601	MH.MHSTDTC
ADMH	ASTDT	Analysis Start Date	integer		From MH.MHSTDTC, converted to SAS Date. Any derivations to derive partial start dates are applied here and listed in comments.
ADMH	ASTTM	Analysis Start Time	integer		From MH.MHSTDTC, converted to SAS Time.
ADMH	ASTDTM	Analysis Start Date/Time	integer		From MH.MHSTDTC, converted to SAS Datetime.
ADMH	MHENDTC	End Date/Time of Medication	datetime	ISO 8601	MH.MHENDTC
ADMH	AENDT	Analysis End Date	integer		From MH.MHENDTC, converted to SAS Date. Any derivations to derive partial start dates are applied here and listed in comments.
ADMH	AENTM	Analysis End Time	integer		From MH.MHENDTC, converted to SAS Time.
ADMH	AENDTM	Analysis End Date/Time	integer		From MH.MHENDTC, converter to SAS Datetime.
ADMH	MHENRF	End Relative to Reference Period	text		MH.MHENRF

10.3 Sample ADaM Data

Table 10.3.1 is an illustration of the Medical History analysis dataset (ADMH) defined above. The ADMH dataset illustrated in this example was designed to support some standard subsets and/or classifications of Medical Histories. The example describes key variables and records that would be included in the dataset.

The example data are assumed to be gathered on a case report form that contains a set of defined categories. A subject may or may not have had any significant medical history in any of the categories on the form. There is a record in the medical history file for each symptom or condition listed on the form; subjects with no recorded medical history may not appear in this file. The MHCAT variable indicates the type of CRF page the data were gathered on, and MHSCAT indicates the CRF category. MHTERM is the symptom term that was recorded; MHDECOD and MHBODSYS are taken from matching the text in MHTERM with a coding dictionary (in this case MedDRA). The date variables indicate the beginning and end timing of the medical history event.

Key points to note in the example are:

1. Variables such as MHSTDTC and MHENDTC are copied in from SDTM MH domain to provide data point traceability.
2. Variables such as MHSCAT, MHDECOD, and MHBODSYS are copied in from the SDTM MH domain for analysis purposes.
3. ASTDT and AENDT are the timing variables used for analysis. Another timing variable MHENRF is a supportive variable for metadata traceability.
4. This is a simple example to only illustrate variables that are relevant to ADMH. It does not include all variables that could be needed for analysis or all indicated in metadata in table 10.2.1. For example, it does not include variables like severity of the History event.
5. For this analysis, the subject level treatment variable (TRT01A or TRT01P, not shown) would be appropriate. Record-level treatment variables would not be needed since the data are gathered prior to start of study treatment.
6. The TRTEMFL (treatment emergent flag), ONTRTFL (on-treatment flag), FUPFL (follow-up flag) and PREFL (pre-treatment flag) are not included in this analysis file because this dataset will only be used for baseline summaries. (Note that these variables could be defined if there was an analysis purpose that called for them). Similarly, the Occurrence Flags are permissible but not required unless needed for a specific analysis purpose.
7. Core variables (such as AGE, RACE, and SEX) would typically be added to the dataset but are not shown in this example.

Table 10.3.1 Sample Medical History Data for Spontaneously Reported Events

Row	USUBJID	MHTERM	MHDECOD	MHBODSYS	MHCAT	MHSCAT	MHSTDTC*	ASTDT*	MHENDTC*	AENDT*	MHENRF
1	ABC-001	ANEMIA	Anaemia	Blood and lymphatic system disorders	MEDICAL HISTORY	HEMATOLOGICAL/ LYMPHATIC	2010-02-01	01FEB2010			ONGOING
2	ABC-001	GERD	Gastroesophageal reflux disease	Gastrointestinal disorders	MEDICAL HISTORY	GASTROINTESTINAL	2011-01-04	04JAN2011	2011-01-04	04JAN2011	
3	ABC-001	NAUSEA	Nausea	Gastrointestinal disorders	MEDICAL HISTORY	GASTROINTESTINAL	2011-01-10	10JAN2011	2011-01-10	10JAN2011	
4	ABC-001	SPLEEN PAIN	Abdominal pain	Gastrointestinal disorders	MEDICAL HISTORY	GASTROINTESTINAL	2011-01-15	15JAN2011	2011-01-15	15JAN2011	
5	ABC-001	ASTHMA	Asthma	Respiratory, thoracic and mediastinal disorders	MEDICAL HISTORY	RESPIRATORY	2011-01-17	17JAN2011	2011-01-17	17JAN2011	
6	ABC-002	SEASONAL ALLERGIES	Seasonal allergy	Immune system disorders	MEDICAL HISTORY	RESPIRATORY	2011-05-14	14MAY2011	2011-06-01	01JUN2011	

** Variables ending in suffix DTC are character date/time fields in the ISO8601 format. Variables ending in DT are numeric dates, here shown using SAS date format date9. Other numeric date formats can be used, but care should be taken with newer date formats which might not be understood by all statistical packages.*

11 Example 8: Analysis of Medical History Pre-specified Events

In the example data shown below, the data are gathered on a case report form that contains a pre-specified category (in this case diabetes history), including a checkbox to indicate whether or not the subject had this condition. Diabetes history is not coded.

Analysis of the number of subjects with and without pre-specified events is an option for medical history. This option does not have a counterpart in adverse events analysis, because the AE domain does not allow for the collection of pre-specified events with AEOCCUR of N.

11.1 Analysis Display Example Layout

The data are analyzed here by counting the number of unique subjects per treatment group, MHCAT, MHTERM, and MHOCCUR. The values of MHOCCUR are formatted from Y and N to more readable values (e.g., 'Y=Reported History') for presentation. For the examples below, we assume that the ADMH file is merged with ADSL to ensure that all safety subjects are identified. However, there may be some safety subjects in ADSL who do not occur in ADMH. (This situation can occur due to missing CRF data).

Table 11.1.1 Example of Summary of Medical History*

Summary of Diabetes History Events
Safety Population

Diabetes History Category	Active Drug (N=4)	Placebo (N=4)	Total (N=8)
DIABETES HISTORY			
DIABETES MELLITUS[1]			
N=No History	3 (75.0%)	2 (100.0%)	5 (83.3%)
Y=Reported History	1 (25.0%)	0	1 (16.7%)
Diabetes History Not Available[1]	0	2	2

[1] Population counts in the column header include all subjects in the safety population. Percentages are based on the number of safety subjects in each treatment group for whom diabetes history data are available. The 'No Reported History' counts are based on subjects with the 'No' box checked on Medical History CRF page xxx.

The choice of denominator will be based on statistical judgment and should be clearly described in the programming specifications. The choice of denominator should also be clearly identified somewhere on the report (for instance, in the title or footnotes).

In the example above, we based the denominator on only the subjects in the population of interest who have records in ADMH with MHCAT = 'DIABETES HISTORY'.

An alternative analysis would be to base the denominator on the number of subjects in the population (typically defined by the number of subjects with appropriate population flags in ADSL).

* The style of the display of the results of an analysis will be determined by the producer. The example is intended to illustrate content, not appearance.

Table 11.1.2 Alternate Example of Summary of Medical History*

Summary of Diabetes History Events Safety Population			
Diabetes History Category	**Active Drug (N=4)**	**Placebo (N=4)**	**Total (N=8)**
DIABETES HISTORY			
DIABETES MELLITUS			
N=No Reported History	3 (75.0%)	2 (50.0%)	5 (62.5%)
Y=Reported History	1 (25.0%)	0 (0.0%)	1 (12.5%)
Unknown[1]	0 (0.0%)	2 (50.0%)	2 (25.0%)
[1] Population counts in the column header include all subjects in the safety population. Percentages are based on the number of safety subjects in each treatment group, whether they had diabetes history data or not. The 'Unknown' counts are based on subjects who did not have a Medical History CRF page xxx.			

11.2 Sample ADaM Variable Metadata

This example describes an adverse events ADaM dataset named ADMH. ADMH is not a required dataset name.

Table 11.2.1 Sample ADaM Variable Metadata

Variable Name	Variable Label	Variable Type	Codelist / Controlled Terms	Source / Derivation
STUDYID	Study Identifier	text		MH.STUDYID
USUBJID	Unique Subject Identifier	text		MH.USUBJID
MHSEQ	Sequence Number	integer		MH.MHSEQ
MHCAT	Category for Medical History	text		MH.MHCAT
MHTERM	Reported Term for the Medical History	text		MH.MHTERM
MHSTDTC	Start Date/Time of Medical History Event	datetime	ISO8601	MH.MHSTDTC
ASTDT	Analysis Start Date	integer		From MHSTDTC, converted to SAS Date. Any derivations to derive partial start dates are applied here and listed in comments.
ASTTM	Analysis Start Time	integer		From MH.MHSTDTC, converted to SAS Time.
ASTDTM	Analysis Start Date/Time	integer		From MH.MHSTDTC, converted to SAS Datetime.
MHENDTC	End Date/Time of Medical History Event	datetime	ISO8601	MH.MHENDTC
AENDT	Analysis End Date	integer		From MHENDTC, converted to SAS Date. Any derivations to derive partial start dates are applied here and listed in comments.
AENTM	Analysis End Time	integer		From MHENDTC, converted to SAS Time.
AENDTM	Analysis End Date/Time	integer		From MHENDTC, converted to SAS Datetime.
MHPRESP	Medical History Event Pre-Specified	text	N,Y	MH.MHPRESP Is Med Hx event from pre-specified CRF page

* The style of the display of the results of an analysis will be determined by the producer. The example is intended to illustrate content, not appearance.

Variable Name	Variable Label	Variable Type	Codelist / Controlled Terms	Source / Derivation
MHOCCUR	Medical History Occurrence	text	N,Y	MH.MHOCCUR Did subject have the event, Y or N
MHENRTPT	End Relative to Reference Time Point	text	ONGOING	MH.MHENRTPT
MHENTPT	End Reference Time Point	text	SCREENING	MH.MHENTPT

11.3 Sample ADaM Data

Table 11.3.1 is an illustration of the Medical History (Pre-Specified Events) analysis dataset (ADMH) defined above. The ADMH dataset illustrated in this example was designed to support some standard subsets and/or classifications of Medical Histories. The example describes key variables and records that would be included in the dataset.

Key points to note in the example are:

1. This is a simple example to only illustrate the ADMH Pre-Specified Events. It does not include all variables that could also be needed for analysis or all indicated in Metadata.
2. The dataset is prepared to support analysis of pre-specified events by populating the variables MHCAT, MHTERM, MHPRESP, and MHOCCUR.
3. The MHCAT variable indicates the type of CRF page the data were gathered on, and MHPRESP is Y to indicate that the term is a pre-specified one. MHOCCUR is either Y or N to indicate whether the subject did or did not have the event.
4. MHTERM is the symptom term. Since the MHTERM variable for pre-specified events will have a known and finite set of values, these values are used here as a summarization category.
5. In this example, MHDECOD and MHBODSYS are not used. Instead MHCAT is used to categorize the data.
6. The date variables indicate the beginning and end timing of the medical history event (if any). It is null on records that do not indicate an event.

Table 11.3.1 Sample Medical History Data for Pre-specified Events

Row	USUBJID	MHSEQ	MHTERM	MHCAT	MHPRESP	MHOCCUR	MHSTDTC*	MHENDTC*	MHENRTPT	MHENTPT
1	ABC-001	6	DIABETES MELLITUS	DIABETES HISTORY	Y	N				
2	ABC-002	1	DIABETES MELLITUS	DIABETES HISTORY	Y	N				
3	ABC-003	1	DIABETES MELLITUS	DIABETES HISTORY	Y	Y	2001-03		ONGOING	SCREENING
4	ABC-004	3	DIABETES MELLITUS	DIABETES HISTORY	Y	N				
5	ABC-005	4	DIABETES MELLITUS	DIABETES HISTORY	Y	N				
6	ABC-006	6	DIABETES MELLITUS	DIABETES HISTORY	Y	N				
7	ABC-007	5	DIABETES MELLITUS	DIABETES HISTORY	Y	N				
8	ABC-008	6	DIABETES MELLITUS	DIABETES HISTORY	Y	N				
9	ABC-009	1	DIABETES MELLITUS	DIABETES HISTORY	Y	N				

** Variables ending in suffix DTC are character date/time fields in the ISO8601 format.*

Appendices

Appendix A: References

1. Analysis Data Model (ADaM) version 2.1
   http://www.cdisc.org/adam
2. Analysis Data Model (ADaM) Implementation Guide version 1.1
   http://www.cdisc.org/adam
3. Study Data Tabulation Model Implementation Guide (SDTMIG) V3.2 and the SDTM document V1.4
   http://www.cdisc.org/sdtm
4. Medical Dictionary for Regulatory Activities (MedDRA)
   http://www.meddramsso.com/
5. World Health Organization Adverse Reaction Terminology (WHO-ART)
   http://www.umc-products.com/DynPage.aspx?id=73589&mn1=1107&mn2=1664
6. International Classification of Diseases (ICD)
   http://www.who.int/classifications/icd/en/
7. Coding Symbols for a Thesaurus of Adverse Reaction Terms (COSTART)
   http://www.nlm.nih.gov/research/umls/sourcereleasedocs/current/CST/
   Note: This coding system has been replaced by MedDRA at US FDA.
8. International Conference of Harmonization E2A "Clinical Safety Data Management: Definitions and Standards for Expedited Reporting"
   http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E2A/Step4/E2A_Guideline.pdf
9. International Conference of Harmonization E9 "Statistical Principles for Clinical Trials"
   http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E9/Step4/E9_Guideline.pdf
10. National Cancer Institute Common Toxicity (NCI CTC) version 4.03
    http://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03_2010-06-14.xls
11. CDISC Define-XML Specification 2.0
    http://www.cdisc.org/define-xml
12. International Conference of Harmonization E3 "Structure and Content of Clinical Study Reports"
    http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E3/Step4/E3_Guideline.pdf
13. Standardised MedDRA Queries (SMQs)
    http://www.meddramsso.com/subscriber_smq.asp
14. CDISC Analysis Results Metadata Specification Version 1.0 for Define-XML Version 2
    http://www.cdisc.org/
15. The National Center for Biomedical Ontology Bioportal
    http://bioportal.bioontology.org/ontologies/MEDDRA?p=classes&conceptid=root

Appendix B: Revision History

This section lists all changes in the OCCDS document from Provisional version 1.0 to Final version 1.0.

Category/Section	Type	Description
Section 3.2.5 Indicator Variables	Update	Removed the word "Record" from the label of variable ANLzzFL to make it consistent with ADaMIG v1.1.

Appendix C: Representations and Warranties, Limitations of Liability, and Disclaimers

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