Analysis Data Model Implementation Guide for Non-compartmental Analysis Input Data

Version 1.0 (Final)

Developed by the
CDISC Analysis Data Model Team

Notes to Readers

- This is the final Version 1.1 of the Analysis Data Model Implementation Guide for Non-compartmental Analysis Input Data.
- This implementation guide applies the Analysis Data Model (ADaM) and ADaM Implementation Guide to non-compartmental analysis (NCA) input data.

Revision History

Date	Version
2021-11-29	1.1 Final

See Appendix C for representations and warranties, limitations of liability, and disclaimers.

CONTENTS

1 Introduction

Pharmacokinetics (PK) is the study of the effect of the body on a drug. Different mathematical methods are used to calculate PK parameters that describe, characterize, and quantify this effect. Non-compartmental analysis (NCA) is one class of mathematical methods for studying the level of exposure following administration of a drug and is commonly used to analyze serial drug concentration data from clinical trials by individual subjects.

The purpose of this document is to present the Analysis Data Model (ADaM) Basic Data Structure (BDS) as the specification for the input dataset for NCA. The ADaM Implementation Guide (ADaMIG) for NCA datasets specifies many of the variables needed for calculation of parameters using NCA and provides general naming conventions that can be leveraged for additional variables. This document also provides provides specific guidance for all commonly needed variables and should be viewed as the ADaM BDS class plus additional NCA variables.

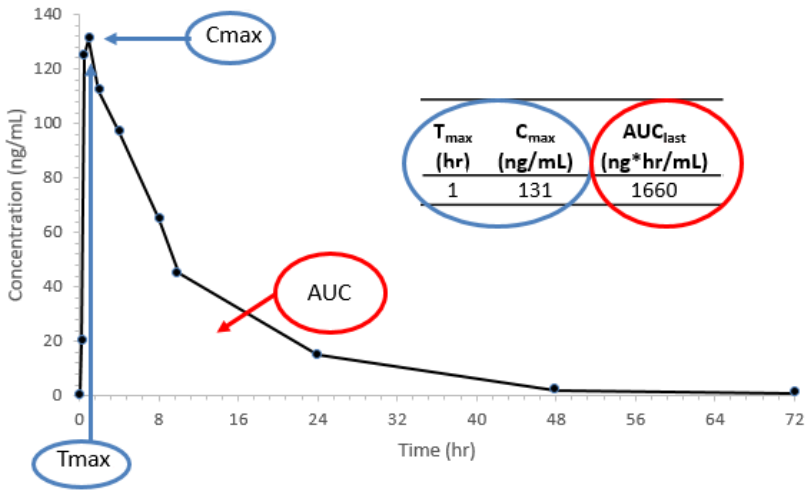
NCA is typically performed using software packages designed to support PK analyses using drug concentration data as one input. In addition, the input data format needs to comprehensively associate subject drug concentrations over time with study drug dosing, support the exclusion of specific records and subjects, and provide other supporting information as needed. The output from NCA (i.e., the PK parameter calculation per subject) is based on the specific dosing regimen, the PK sample collection schedule, and the objective(s) associated with parameter calculations. The PK parameter calculations are typically reported in the SDTM Pharmacokinetics Parameters (PP) domain and not a part of this implementation guide.

The analysis data input for non-compartmental parameter calculation is subject to submission to regulatory bodies; utilization of this standard format also promotes compliance with ADaM standards. It is important to build this dataset based on Study Data Tabulation Model (SDTM) domains and, if applicable, on the other ADaM datasets (e.g., the subject-level analysis dataset, ADSL) that will be submitted. CDISC foundational standards are available at https://www.cdisc.org/standards.

In this document, the ADaM NCA dataset is simply referred to as an ADNCA dataset. It should be noted that this does not imply required naming conventions. The NCA dataset should be named following the ADaM standard naming convention, as described in https://www.cdisc.org/standards/foundational/adam.

2 General Objective of Non-Compartmental Analysis

Figure 2.1. PK Example



Pharmacokinetic (PK) non-compartmental analysis (NCA) is primarily a time-from-event-based analysis that derives multiple parameters from time-concentration profiles for individual subjects. The ADNCA dataset structure is designed to support commonly structured NCAs, including analyses with both discrete time-point measurements (typical for plasma or serum) and measurements from collections over time intervals (typical for urine). The dataset format is developed to support the more common structures for NCA programs but does not prevent additional variables to accommodate more complex variants of or programming for NCA.

The ADNCA dataset structure may be used to create multiple tabular and graphical data presentations as they relate to NCA and PK and pharmacodynamics data review, as well as provide a means to assess event collection compliance where the data collected have a structured chronological sequence. In addition, the ADNCA structure has the potential to be utilized for tabular and graphical data presentation in other PK and pharmacodynamic (PD; the study of the effect of the drug on the body) sparse sampling study designs that do not necessarily require NCA. **The ADaM NCA dataset is not intended to be used for graphical and tabular presentations of results from NCA (e.g., PK parameters such as maximum concentration and area under the curve) that are tabulated in the SDTM Pharmacokinetics Parameters (PP) domain.**

3 Points to Consider in this Document

In reviewing the descriptions of the ADNCA dataset specifications and the examples presented in this document, consider the following:

ADNCA datasets should be "analysis-ready": This means they should contain the variables needed for the intended use of performing non-compartmental analysis (NCA). The ADNCA dataset may be used to create tables, listings, and figures for observed concentration time data, but this is not the primary purpose of the dataset. In addition to required variables such as subject identifiers, treatment variables, and pharmacokinetic (PK) sample variables, some critical variables included in the analysis dataset can be considered "study-specific" as they depend on the specific nature of the disease or indication and the analyses planned in the protocol or statistical analysis plan (SAP). Some variables may be populated by the PK scientist after the NCA is complete as these are meant to document analysis-specific information. It is expected that this approach will be uncommon, but variables where this method may be needed are referenced in the ADNCA metadata.

In addition, ADNCA datasets have the potential to be utilized for general PK analyses where NCA may not necessarily be required, as many of the variables presented in the ADNCA specification are critical to assess PK data for significant sampling or dosing-related deviations prior to generating statistical summaries, tables, figures, and listings. At this time, the datasets used for general PK analyses are based on the application of ADaM standards to the Pharmacokinetics Concentration (PC) domain, to create custom sponsor-defined analysis datasets. The absence of a standard for a PK analysis dataset results in datasets that are not consistent across sponsors. This document provides formal ADaM specification for non-compartmental PK analysis to establish consistency within the field.

Identification of source dataset: When identifying the source dataset for a variable, the immediate predecessor is used (see ADaM, https://www.cdisc.org/standards/foundational/adam). The dosing and subject-level datasets, among others, are common input for many ADNCA variables, if they are available. Dosing datasets may include SDTM exposure domains or a derived exposure dataset utilizing ADaM standards. If the subject-level analysis data (ADSL) is not available or is not a viable option for the purposes of ADNCA generation, use the applicable SDTM variables. Multiple CDISC source datasets may be used to populate ADNCA based on analysis need. Outside of the SDTM PC domain, ADaM sources are expected to be the most common but may not be the only sources used to create this dataset. All data sources used must be submitted to regulatory bodies. The NCA dataset structure can also be leveraged for pharmacodynamics (PD) analysis where the primary dataset source is not PC. In that case it is assumed that the relevant traceability variables and domain references will be included in place of PC.

As an example of identifying the source dataset for a variable, in ADSL the source of the SUBJID variable is identified as DM.SUBJID in the analysis variable metadata. If in the ADNCA dataset AVAL (Analysis Value) is to be supplied from the PC domain and SEX is to be supplied from the demographics domain, then the source is identified as PC.PCSTRESN and DM.SEX, respectively.

- **Rationale for requiring optional ADSL variables in the ADNCA dataset**: It should be noted that select variables in the ADNCA specification are derived from fields listed in ADSL as Optional but which are listed as Required for ADNCA. Permissible ADSL variables required in ADNCA are scientifically necessary to support PK analyses.
- **Ordering of variables**: ADaM (https://www.cdisc.org/standards/foundational/adam) states that the ordering of variables in the analysis dataset should follow a logical ordering (not simply alphabetic). As such, the specifications of the ADNCA dataset are ordered in a way that is sensible to the intended purpose of the dataset, which is to support NCA. Within this document, however, no specific ordering of variables within the illustrated datasets is applied; the tables shown only contain variables relevant to the example. Within this document, the author of each example table applied his or her own logical ordering.

Examples are for illustration only: The examples in this document are intended only 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 and results can be displayed. This document does not cover display formats.

- **Display of metadata and dataset examples for illustration of content only**: Although the metadata elements have been defined in https://www.cdisc.org/standards/foundational/adam, how they are displayed is a function of the mechanism used to display the content. Examples of datasets, formatting, and

presentation styles used in this document are for the purposes of content illustration only, and are not intended to imply any type of display standard or requirement.

- **Examples not meant to be all-inclusive regarding variables**: The examples in this document describe some of the key variables and records that would be included in the ADNCA dataset. They are not intended to illustrate every possible variable that might be included in the analysis dataset, as many variables are dependent on specific study designs.
- **No endorsement of vendors or products**: In an effort to provide illustrations of the ADaM concepts, the examples provided may reference specific programming languages. As with other ADaM documents, references to specific vendor products are examples only and should not be interpreted as an endorsement of these vendors or products.

4 ADaM Metadata

The ADNCA dataset is designed to follow the ADaM BDS. More information about BDS can be found in ADaMIG v1.2 (available at https://www.cdisc.org/standards/foundational/adam).

4.1 Dataset Metadata

Typically, the Analysis Dataset Metadata for an ADNCA dataset is specified as follows:

Table 4.1. Data Structure

Data Structure Name	Data Structure Description	Class of Dataset	SubClass of Dataset	CDISC Notes
ADNCA	Basic Data Structure Non-Compartmental Analysis	BASIC DATA STRUCTURE	NON-COMPARTMENTAL ANALYSIS	Dataset designed to support NCA . Primarily sourced from SDTM PC and supplemented by information from the EX, EC, or other relevant domains.

The Data Structure Name, Data Structure Description, and CDISC Notes are intended to provide information to assist producers in preparing their datasets and are not intended to be metadata submitted in define.xml.

4.1.1 Define.xml Example Dataset Metadata

Table 4.1.1 shows how dataset metadata are specified for NCA. This layout matches Define-XML v2.1 (available at https://www.cdisc.org/standards/data-exchange/define-xml), which includes a methodology for representing SubClass. NCA datasets are of the Class BASIC DATA STRUCTURE, SubClass NON-COMPARTMENTAL ANALYSIS.

Text shown in italics is example content, and can be modified to fit the analysis dataset. All italicized text, including dataset name and description (label), can be modified. In this example, "parameter" refers to analyte, "analysis visit" refers to dose event, and "analysis timepoint" refers to sample.

Table 4.1.1. Define.xml Example Dataset Metadata

Dataset	Description	Class - SubClass	Structure	Purpose	Keys	Documentation	Location
ADNCA	Data for Non-Compartmental Analysis	BASIC DATA STRUCTURE • NON-COMPARTMENTAL ANALYSIS	One record per subject per parameter per analysis visit per analysis timepoint	Analysis	STUDYID, USUBJID, PARAMCD, AVISIT, ATPT	See program...	adnca.xpt

4.2 Variable Metadata

Because NCA data follows the BDS, most of the dataset variables can be found in ADaMIG v1.2, Section 3.3 (available at https://www.cdisc.org/standards/foundational/adam). Standard BDS and subject-level (ADSL) variables that are commonly used in NCA include:

- STUDYID
- USUBJID and SUBJID
- SITEID
- AGE or AAGE, and AGEU
- SEX
- RACE
- TRTP and TRTPN
- TRTA and TRTAN
- DOSEP*, DOSEA*, and DOSEU*
- APERIOD and APERIODC
- AVISIT* and AVISITN
- ADT, ATM, and ADTM
- ASTDT, ASTTM, and ASTDTM
- AENDT, AENTM, and AENDTM
- ATPT and ATPTN
- PARAM, PARAMCD, and PARAMN
- AVAL
- DTYP

*BDS Variables DOSEA, DOSEU, and AVISIT have a different core value for NCA, as described in Table 4.2.2, Standard BDS Variables with Stronger Core for Non-compartmental Analysis.

Additional standard dataset variables specific to NCA are specified in Table 4.2.1, New Standard Non-compartmental Analysis Variables.

Baseline characteristics are commonly needed in NCA, although they are often created in other datasets (e.g., ADSL). For tips for assembling names for these non-standard variables (NSVs), see ADaMIG v1.2, Section 3.1. Common baseline characteristics for NCA include:

- BMIBL (body mass index, BMI, at baseline, associated with the time of reference dosing) and BMIBLU (units)
- HTBL (height at baseline, associated with the time of reference dosing) and HTBLU (units)
- WTBL (weight at baseline, associated with the time of reference dosing) and WTBLU (units)

Note that due to the needs of common analysis tools used for NCA, units for all baseline characteristics are usually stored in a separate variable, rather than as part of the label.

ADaM variables are described here in tabular format. The two rightmost columns, Core and CDISC Notes, provide information about the variables to assist producers in preparing their datasets. These columns are not meant to be metadata submitted in define.xml. The Core column describes whether a variable is required, conditionally required, or permissible. The CDISC Notes column provides more information about the variable. In addition, the Type column specifies whether the variable being described is character or numeric. A richer set of data types (e.g., text, integer, float), described in the Define-XML Specification (available at https://www.cdisc.org/standards/data-exchange/define-xml), should be provided in the metadata by the producer.

Usage of the start and end datetimes in nominal or actual relative time calculation needs to be described in the define.

Table 4.2.1. New Standard Non-compartmental Analysis Variables

Variable Name	Variable Label	Type	Codelist/ Controlled Terms	Core	CDISC Notes
NCAXFL	PK NCA Exclusion Flag	Char	Y	Perm	Flag for exclusion of a record into a PK NCA calculation (Y = exclusion, Null = inclusion)
NCAXFN	PK NCA Exclusion Flag (N)	Num	1	Perm	Numeric flag for exclusion of a record into a PK NCA calculation (1 = exclusion, Null = inclusion). NCAXFN can only be included if NCAXFL is also included.
NCAwXRS	Reason w for PK NCA Exclusion	Char		Perm	This variable is used to explain why the record is not included in the PK NCA.
NCAwXRSN	Reason for PK NCA Exclusion of w (N)	Num		Perm	This variable is used to explain why the record is not included in the PK NCA.
PKSUMXF	PK Summary Exclusion Flag	Char	Y	Perm	Flag for exclusion of a record from a PK summary (1 = exclusion, Null = inclusion)
PKSUMXFN	PK Summary Exclusion Flag (N)	Num	1	Perm	Numeric flag for exclusion of a record from a PK summary (1 = exclusion, Null = inclusion). PKSUMXFN can only be included if PKSUMXFL is also included.
METABFL	Metabolite Flag	Char	Y	Cond	Flag to designate if observations within a subject are associated with a metabolite. Required if parent drug and metabolites are present in the dataset.
COHORT	Subject Cohort	Char		Perm	Relevant to trials where cohorts are defined. This could be another grouping not necessarily associated with ARM.
COHORTN	Subject Cohort (N)	Num		Perm	Numeric representation of the COHORT variable. There must be a one-to-one mapping between COHORT and COHORTN. When COHORT and COHORTN are present, then, on a given record, either both must be populated or both must be null.
ROUTE	Route	Char	(ROUTE)	Perm	Route of treatment delivery. This variable can be a copy of EX.EXROUTE or EC.ECROUTE. May instead be derived from the EX.EXROUTE or EC.ECROUTE.
TRTRINT	Planned Treatment Interval	Num		Perm	Planned time between 2 consecutive treatments in multiple-dose studies (sometimes referred to as "Tau")

Variable Name	Variable Label	Type	Codelist/ Controlled Terms	Core	CDISC Notes
TRTRINTU	Planned Treatment Interval Units	Char	(UNIT)	Perm	Units associated with TRTRINT
DOSPCTDF	Percent Diff. Nominal vs. Actual Dose	Num		Cond	Derived variable using a standard percent difference formula: (100*(DOSEA-DOSEP)/(DOSEP)). DOSPCTDF is required if both DOSEA and DOSEP are populated.
DOSEFRQ	Dose Frequency	Char	(FREQ)	Cond	Usually expressed as the number of repeated administrations of DOSE within a specific time period for multiple dose studies.
ACYCLE	Analysis Cycle	Num		Perm	This is a record-level identifier that reflects cycle and may be of particular importance for studies that examine concentrations in cancer patients. There must be a one-to-one mapping between ACYCLE and ACYCLEC. When ACYCLE and ACYCLEC are present, then, on a given record, either both must be populated or both must be null.
ACYCLEC	Analysis Cycle (C)	Char		Perm	Character representation of the ACYCLE variable. Text characterizing to which analysis cycle the record belongs. This is a record-level identifier that reflects cycle and may be of particular importance for studies that examine concentrations in cancer patients. There must be a one-to-one mapping between ACYCLE and ACYCLEC. When ACYCLE and ACYCLEC are present, then, on a given record, either both must be populated or both must be null.
FANLDT	First Date of Dose for Analyte	Num		Perm	Date of first exposure to treatment associated with PARAM and ANALYTE for a subject in a study where multiple doses have been given. Note that FANLDT may not match TRTSDT or any of TRxxSDT values.
FANLTM	First Time of Dose for Analyte	Num		Perm	Time of first exposure to treatment associated with PARAM and ANALYTE for a subject in a study where multiple doses have been given. If treatment is given over a duration multiple times, this variable will reflect the start time of the first dose.
FANLDTM	First Datetime of Dose for Analyte	Num		Perm	Date and time of first exposure to treatment associated with PARAM and ANALYTE for a subject in a study where multiple doses have been given. If treatment is given over a duration multiple times, this variable will reflect the start date and time of the first dose.
FANLEDT	First End Date of Dose for Analyte	Num		Perm	End date of first exposure to treatment associated with PARAM and ANALYTE for a subject in a study where multiple doses have been given. Note that FANLEDT may not match TRTEDT or any of TRxxEDT values.
FANLETM	First End Time of Dose for Analyte	Num		Perm	End time of first exposure to treatment associated with PARAM and ANALYTE for a subject in a study where multiple doses have been given. If treatment is given over a duration multiple times, this variable will reflect the end time of the first dose.
FANLEDTM	First End Datetime of Dose for Analyte	Num		Perm	End date and time of first exposure to treatment associated with PARAM and ANALYTE for a subject in a study where multiple doses have been given. If treatment is given over a duration multiple times, this variable will reflect the end date and time of the first dose.
PCRFTDT	Reference Date of Dose for Analyte	Num		Req	Date of reference exposure to treatment associated with PARAM and ANALYTE. Based on PC.PCRFTDTC and related to the analyzed profile. If this is a treatment over time, then this is typically the start of the dosing duration.
PCRFTTM	Reference Time of Dose for Analyte	Num		Req	Time of reference exposure to treatment associated with PARAM and ANALYTE. Based on PC.PCRFTDTC and related to the analyzed profile. If this is a treatment over time, then this is typically the start of the dosing duration.
PCRFTDTM	Reference Datetime of Dose for Analyte	Num		Req	Date and time of reference exposure to treatment associated with PARAM and ANALYTE. Based on PC.PCRFTDTC and related to the analyzed profile. If this is a treatment over time, then this is typically the start of the dosing duration.
PCRFEDT	Reference End Date of Dose for Analyte	Num		Cond	The end date of reference exposure to treatment associated with PARAM and ANALYTE. Must be related to the time recorded in PC.PCRFTDTC and to the analyzed profile. If dosing occurs over an interval, this should be populated. If populated, ADOSEDUR and DOSEDURU are required to be filled out.
PCRFETM	Reference End Time of Dose for Analyte	Num		Cond	The end time of the reference exposure to treatment associated with PARAM and ANALYTE. Must be related to the time recorded in PC.PCRFTDTC and to the analyzed profile. If dosing occurs over an interval, this should be populated. If populated, ADOSEDUR and DOSEDURU are required to be filled out.

Variable Name	Variable Label	Type	Codelist/ Controlled Terms	Core	CDISC Notes
PCRFEDTM	Ref. End Datetime of Dose for Analyte	Num		Cond	The end date and time of the reference exposure to treatment associated with PARAM and ANALYTE. Must be related to the time recorded in PC.PCRFTDTC and to the analyzed profile. If dosing occurs over an interval, this should be populated. If populated, ADOSEDUR and DOSEDURU are required to be filled out.
NFRLT	Nom. Rel. Time from Analyte First Dose	Num		Perm	This is the planned elapsed time (for sample point or start of sampling interval) from first exposure to treatment associated with PARAM and ANALYTE. For studies with an extended duration infusion, use the define to document if this is from the start or end of the infusion.
AFRLT	Act. Rel. Time from Analyte First Dose	Num		Perm	This is the actual elapsed time (for sample point or start of sampling interval) from first exposure to treatment associated with PARAM and ANALYTE. Note that this is referring to the first dose available for a particular drug. It is useful in multiple-dosing situations.
NEFRLT	Nom. Rel. End Time from First Dose	Num		Perm	This is the planned elapsed end time of sampling interval from first exposure to study treatment.
AEFRLT	Act. Rel. End Time from First Dose	Num		Perm	This is the actual elapsed end time of sampling interval from first exposure to study treatment.
FRLTU	Rel. Time from First Dose Unit	Char	(PKUNIT)	Perm	This is the unit for all elapsed times from first dose.
NRRLT	Nominal Rel. Time from Ref. Dose	Num		Req	This is the planned elapsed time (for sample point or start of sampling interval) from reference exposure to study treatment.
ARRLT	Actual Rel. Time from Ref. Dose	Num		Req	This is the actual elapsed time (for sample point or start of sampling interval) from reference exposure to study treatment.
MRRLT	Modified Rel. Time from Ref. Dose	Num		Perm	This variable could be used to modify the ARRLT variable based on analysis needs (e.g., setting negative values to zero or having a mix of nominal and actual time based of TMPCTDF).
NERRLT	Nominal Rel. End Time from Ref. Dose	Num		Perm	This is the planned elapsed end time of sampling interval from reference exposure to study treatment.
AERRLT	Actual Rel. End Time from Ref. Dose	Num		Perm	This is the actual elapsed end time of sampling interval from reference exposure to study treatment.
MERRLT	Modified Rel. End Time from Ref. Dose	Num		Perm	This variable could be used to modify the AERRLT variable based on analysis needs (e.g., setting negative values to zero or having a mix of nominal and actual time based on TMPCTDF).
RRLTU	Rel. Time from Ref. Dose Unit	Char	(PKUNIT)	Req	This is the unit for all elapsed times from reference dose.
TMPCTDF	Percent Diff. Nominal vs. Actual Time	Num		Perm	This is the percent difference between nominal and actual time. It is derived by using the standard percent difference formula: 100*(NRRLT - ARRLT)/(NRRLT).
ADOSEDUR	Actual Duration of Treatment Dose	Num		Cond	Total treatment duration, as measured in units given in DOSEDURU, derived from PCRFEDTM-PCRFDTM. This record is generally considered to be associated with an infusion dose and is distinct from TRTDURD, TRTDURM, and TRTDURY, which reference the duration of the entire study rather than the duration of a single treatment event.
NDOSEDUR	Nominal duration of Treatment Dose	Num		Cond	Nominal treatment duration as specified in the protocol, as measured in units given in DOSEDURU. This record is generally considered to be associated with an infusion dose.
DOSEDURU	Duration of Treatment Dose Units	Char	(PKUNIT)	Perm	Units associated with ADOSEDUR and NDOSEDUR. When ADOSEDUR is present, NDOSEDUR and/or DOSEDURU must also be included in the dataset.
AVALU	Analysis Value Unit	Char		Req	Unit for AVAL.
PCSPEC	Specimen Material Type	Char	(SPECTYPE)	Perm	Defines the type of specimen used for a measurement (e.g., SERUM, PLASMA, URINE). This column must be a direct copy of PC.PCSPEC.
PCSTRESC	Character Result/Finding in Std Format	Char		Cond	Character results/findings in a standard format. The purpose of this column is to capture which records are BLQ or LLOQ in the AVAL column. This column must be a direct copy of PC.PCSTRESC.
PCSTRESU	Standard Units	Char	(UNIT)	Cond	Standardized unit associated with AVAL. Units associated with AVAL are needed for clear NCAs. This column must be a direct copy of PC.PCSTRESU.
ALLOQ	Analysis Lower Limit of Quantitation	Num		Cond	Indicates the lower limit of quantitation for an assay. Use if PC.PCLLOQ does not support analysis needs.
PCLLOQ	Lower Limit of Quantitation	Num		Cond	Indicates the lower limit of quantitation for an assay. Must be a direct copy of PC.PCLLOQ.

Variable Name	Variable Label	Type	Codelist/ Controlled Terms	Core	CDISC Notes
VOLUME	Volume Value	Num		Cond	PC.PCSTRESN from a PC volume record. This is the volume related to AVAL. Conditionally required if sample is interval-based collection, such as urine.
VOLUMEU	Volume Value Unit	Char	(UNIT)	Cond	PC.PCSTRESU from a PC volume record. Conditionally required if VOLUME is present.
SPWEIGHT	Specimen Weight Value	Num		Cond	PC.PCSTRESN from a PC specimen weight record, adjustment based on LLOQ rules possible. This is the specimen weight associated with AVAL. Conditionally required if sample is interval based collection, such as a potential non-fluid matrix (e.g., feces).
SPWEIGHU	Specimen Weight Value Unit	Char	(UNIT)	Cond	PC.PCSTRESU from a PC weight record. Conditionally required if SPWEIGHT is present.
PCGRPID	Group ID	Char		Perm	Used to tie together a block of related records in a single domain to support relationships within the domain and between domains. Must be a direct copy of PC.PCGRPID.
PCSEQ	Sequence Number	Num		Cond	PC.PCSEQ associated with AVAL.

Table 4.2.2. Standard BDS Variables with Stronger Core for Non-Compartmental Analysis

The following variables are described in the ADaMIG, but are not required for general BDS use. However, for NCA use, they are required. The only difference between these variables and what is in the ADaMIG is the value for Core.

Variable Name	Variable Label	Type	Codelist/ Controlled Terms	Core	CDISC Notes
DOSEA	Actual Treatment Dose	Num		Req	DOSEA represents the actual treatment dosage associated with the record. This is the actual numeric amount of the dose used for the NCA analysis and may differ from the EX.EXDOSE.
DOSEU	Treatment Dose Units	Char	(UNIT)	Req	The units for DOSEP and DOSEA. It is permissible to use suffixes such as “P” and “A” to record different units for DOSEP and DOSEA, with labels modified accordingly.
AVISIT	Analysis Visit	Char		Req	The analysis visit description; required if an analysis is done by nominal, assigned or analysis visit. AVISIT may contain the visit names as observed (i.e., from SDTM VISIT), derived visit names, time window names, conceptual descriptions (such as Average, Endpoint, etc.), or a combination of any of these. AVISIT is a derived field and does not have to map to VISIT from the SDTM. AVISIT represents the analysis visit of the record, but it does not mean that the record was analyzed. There are often multiple records for the same subject and parameter that have the same value of AVISIT. ANLzzFL and other variables may be needed to identify the records selected for any given analysis. See ADaMIG v1.2, Section 3.3.8, for information about flag variables. AVISIT should be unique for a given analysis visit window. In the event a record does not fall within any predefined analysis time-point window, AVISIT can be populated in any way that the producer chooses to indicate this fact (i.e., blank or “Not Windowed”). The way that AVISIT is calculated, including the variables used in its derivation, should be indicated in the variable metadata for AVISIT. The values and the rules for deriving AVISIT may be different for different parameters within the same dataset. Values of AVISIT are producer-defined and are often directly usable in clinical study report (CSR) displays.

5 Examples

Timing

Example 1: Difference Between AVISIT in ADNCA and "Day" Variables in SDTM

The AVISIT variable in ADNCA is useful for pharmacokinetic (PK) analysis in many situations. For example, it is used as a key variable to extract the concentration-time profiles for different days in multiple-day studies.

When deriving the AVISIT and AVISITN variables from tabulated variables in SDTM domains, the following example shows how the AVISIT variable is different from the PCDY variable in the pharmacokinetic concentrations (PC) domain of SDTM. Similar considerations will apply to VISIT variables in SDTM domains.

The PCDY variable indicates the study day when the sample was taken. This variable is one of the timing variables for the specific observations in the records of the PC domain dataset. This example shows that for the samples taken 24, 36, and 48 hours after dosing, the PCDY variable correctly indicates that these are days 2 and 3 of the study.

However, with respect to the concentration-time profile for PK analysis, the AVISIT variable needs to indicate that these samples are part of the profile that is related to the day 1 dose. So, the AVISIT variable should have a value of "DAY 1" and corresponding AVISITN has the value of "1".

pc.xpt

PCDY	PCTPT	PCRFTDTC
1	PREDOSE	2011-12-26T08:00
1	30MIN	2011-12-26T08:00
1	1H	2011-12-26T08:00
1	2H	2011-12-26T08:00
1	4H	2011-12-26T08:00
1	8H	2011-12-26T08:00
1	12H	2011-12-26T08:00
2	24H	2011-12-26T08:00
2	36H	2011-12-26T08:00
3	48H	2011-12-26T08:00

adnca.xpt

PCRFTDTM	AVISIT	AVISITN
2011-12-26T08:00:00	DAY 1	1
2011-12-26T08:00:00	DAY 1	1
2011-12-26T08:00:00	DAY 1	1
2011-12-26T08:00:00	DAY 1	1
2011-12-26T08:00:00	DAY 1	1
2011-12-26T08:00:00	DAY 1	1
2011-12-26T08:00:00	DAY 1	1
2011-12-26T08:00:00	DAY 1	1
2011-12-26T08:00:00	DAY 1	1
2011-12-26T08:00:00	DAY 1	1

Example 2: Timing and Values for Multiple Oral Dosing

This example shows the nominal and relative times for a multiple oral-dosing trial.

Note that the modified relative time from reference dose (MRRLT) was added for analysis purposes: the negative ARRLT on rows 1 and 8 is assigned zero, as PK software such as Phoenix WNL will only include observations starting from dosing, and not prior to dosing, for parameter estimation.

This table shows the following situation:

Rows 1-7: A pre-dose sample is recorded in row 1 (planned for 15AUG15:09:00, taken at 15AUG15:08:30). For the samples after the initial dose (rows 2-7), the values of the timing variables relative to the first dose (NFRLT and AFRLT) are the same as the values of the timing variables relative to the reference dose (NRRLT and ARRLT).

Rows 8-14: A pre-dose sample (relative to the day 6 dose) is recorded in row 8. For the samples after day 6 pre-dose (rows 9-14), the values of the timing variables relative to the first dose (NFRLT and AFRLT) record the time since administration of the day 1 dose whereas the values of the timing variables (NRRLT and ARRLT) are relative to the day 6 reference dose.

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Row	ATPTREF	ATPT	ADTM	PCRFTDTM	NFRLT	AFRLT	NRRLT	ARRLT	MRRLT	FRLTU	RRLTU	AVAL
1	DAY 1	Predose	15AUG15:08:30	15AUG15:09:00	0.00	-0.50	0.00	-0.50	0.00	h	h	0
2	DAY 1	0.5 H	15AUG15:09:30	15AUG15:09:00	0.50	0.50	0.50	0.50	0.50	h	h	5.168
3	DAY 1	1 H	15AUG15:10:00	15AUG15:09:00	1.00	1.00	1.00	1.00	1.00	h	h	18.020
4	DAY 1	2 H	15AUG15:11:03	15AUG15:09:00	2.00	2.05	2.00	2.05	2.05	h	h	31.580
5	DAY 1	4 H	15AUG15:13:00	15AUG15:09:00	4.00	4.00	4.00	4.00	4.00	h	h	18.500
6	DAY 1	6 H	15AUG15:15:00	15AUG15:09:00	6.00	6.00	6.00	6.00	6.00	h	h	16.700
7	DAY 1	24 H	16AUG15:08:53	15AUG15:09:00	24.00	24.88	24.00	23.88	23.88	h	h	0.656
8	DAY 6	Predose	21AUG15:08:53	21AUG15:09:00	192.00	191.88	0.00	-0.12	0.00	h	h	1.544

Row	ATPTREF	ATPT	ADTM	PCRFTDTM	NFRLT	AFRLT	NRRLT	ARRLT	MRRLT	FRLTU	RRLTU	AVAL
9	DAY 6	0.5 H	21AUG15:09:30	21AUG15:09:00	192.50	192.50	0.50	0.50	0.50	h	h	2.216
10	DAY 6	1 H	21AUG15:10:02	21AUG15:09:00	193.00	193.03	1.00	1.03	1.03	h	h	6.008
11	DAY 6	2 H	21AUG15:11:10	21AUG15:09:00	194.00	194.17	2.00	2.17	2.17	h	h	32.400
12	DAY 6	4 H	21AUG15:13:00	21AUG15:09:00	196.00	196.00	4.00	4.00	4.00	h	h	22.940
13	DAY 6	6 H	21AUG15:15:00	21AUG15:09:00	198.00	198.00	6.00	6.00	6.00	h	h	23.540
14	DAY 6	24 H	22AUG15:08:53	21AUG15:09:00	216.00	215.88	24.00	23.88	23.88	h	h	1.724

Dosing Variables

The following are examples of the different dosing variables that can be used in ADNCA. These variables are available to document specific details of each reference dose, including the planned and actual dose amount and the dosing frequency and interval.

Example 1: Multiple Oral Dosing with Record Inclusion Determined by Actual Dose Received

Row 1: Dosing at day 1. These dosing variables will be present in the ADNCA where the reference treatment is the administration on 12AUG2015.

Row 2: Dosing at day 2. These dosing variables will be present in the ADNCA where the reference treatment is the administration on 13AUG2015. Note that an incomplete dose was taken. Observations linked to this administration can be excluded with the exclusion flags (see Exclusion Flags Example 1, below).

Row 3: Dosing at day 7. These dosing variables will be present in the ADNCA where the reference treatment is the administration on 18AUG2015.

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Row	USUBJID	FANLDTM	PCRFTDTM	DOSETRT	AVISIT	DOSEP	DOSEA	DOSEU	DOSPCTDF	DOSEFRQ	TRTRINT	TRTRINTU
1	001	12AUG15:09:00	12AUG15:09:00	DRUGX	DAY 1	10	10	mg	0	QD	24	h
2	001	12AUG15:09:00	13AUG15:09:00	DRUGX	DAY 2	10	8	mg	20	QD	24	h
3	001	12AUG15:09:00	18AUG15:09:00	DRUGX	DAY 7	10	10	mg	0	QD	24	h

Example 2: Infusion

Row 1: Infusion at day 1. These dosing variables will be present in the ADNCA for subject 001 for every record where the reference treatment is the infusion on 12AUG2015.

Row 2: Infusion at day 1. These dosing variables will be present in the ADNCA for subject 002 for every record where the reference treatment is the infusion on 12AUG2015.

Row 3: Infusion at day 1. These dosing variables will be present in the ADNCA for subject 003 for every record where the reference treatment is the infusion on 12AUG2015. Note that the infusion was stopped after 30 minutes. Observations linked to this infusion can be excluded with the exclusion flags (see Exclusion Flags Example 1, below).

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Row	USUBJID	PCRFTDTM	PCRFEDTM	DOSETRT	AVISIT	DOSEP	DOSEA	DOSEU	DOSPCTDF	DOSEDUR	DOSEDURU
1	001	12AUG15:09:00	12AUG15:10:00	DRUGX	DAY 1	10	10	mg/kg	0	1.00	h
2	002	12AUG15:09:10	12AUG15:10:10	DRUGX	DAY 1	10	10	mg/kg	0	1.00	h
3	003	12AUG15:09:20	12AUG15:09:50	DRUGX	DAY 1	10	5	mg/kg	50	0.50	h

Exclusion Flags

The following are examples of the use of the exclusion flags NCAXFL (for record-level exclusions). The examples show exclusions for reasons that are mainly triggered by considerations around sampling. Other exclusion reasons (e.g., exclusions caused by some violation of dosing requirements) would be referenced accordingly. These variables provide clarity on which intensive PK samples were not included in NCA along with a brief description why, and can be utilized by regulatory agencies during regulatory filings and/or study review.

Example 1: Record-level Exclusions

The table below shows 3 examples for record-level exclusions.

Rows 1-4: These records were included in the analysis.

Row 5: This record for subject CPW-s001 at nominal time 2 hours is excluded because no concentration value is available. The record should still be included in the dataset for traceability reasons and to support consistent reporting. Therefore, NCAXFL is set to "Y" and NCA1XRS is set to "Missing AVAL Value".

Rows 6-12: These records were included in the analysis.

Row 13: This record for subject CPW-s002 at nominal time 4 hours is excluded because the sample was taken outside the time window considered acceptable by the data scientist/analyst. Therefore, NCAXFL is set to "Y" and NCA2XRS set to "Late Sample".

Row 14: This record was included in the analysis.

Rows 15-21: The records for subject CPW-s003 after the dose at time 0 hours are all excluded because the subject vomited too soon after the dose administration. Therefore, NCAXFL is set to "Y" and NCA3XRS set to "Vomiting" for all records for this profile.

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Row	STUDYID	USUBJID	ARRLT	NRRLT	RRLTU	AVAL	PCSTRESU	VOMITFL	VRLT	NCAXFL	NCAXFN	NCA1XRS	NCA2XRS	NCA3XRS
1	CPW	CPW-s001	0	0	h	0	ug/L	Y	0.75					
2	CPW	CPW-s001	0.33333	0.25	h	19.4	ug/L	Y	0.75					
3	CPW	CPW-s001	0.5	0.5	h	118.8	ug/L	Y	0.75					
4	CPW	CPW-s001	1	1	h	115	ug/L	Y	0.75					
5	CPW	CPW-s001	2	2	h		ug/L	Y	0.75	Y	1	Missing AVAL Value		
6	CPW	CPW-s001	4	4	h	91.2	ug/L	Y	0.75					
7	CPW	CPW-s001	8	8	h	67.6	ug/L	Y	0.75					
8	CPW	CPW-s002	0	0	h	0	ug/L							
9	CPW	CPW-s002	0.25	0.25	h	18.4	ug/L							
10	CPW	CPW-s002	0.5	0.5	h	114	ug/L							
11	CPW	CPW-s002	1	1	h	115	ug/L							
12	CPW	CPW-s002	2	2	h	114	ug/L							
13	CPW	CPW-s002	5	4	h	72	ug/L			Y	1		Late Sample	
14	CPW	CPW-s002	8	8	h	59.15	ug/L							
15	CPW	CPW-s003	0	0	h	0	ug/L	Y	0.083333	Y	1			Vomiting
16	CPW	CPW-s003	0.4	0.25	h	19.8	ug/L	Y	0.083333	Y	1			Vomiting
17	CPW	CPW-s003	0.75	0.5	h	126	ug/L	Y	0.083333	Y	1			Vomiting
18	CPW	CPW-s003	1.33333	1	h	131.25	ug/L	Y	0.083333	Y	1			Vomiting
19	CPW	CPW-s003	2	2	h	114	ug/L	Y	0.083333	Y	1			Vomiting
20	CPW	CPW-s003	4	4	h	97.85	ug/L	Y	0.083333	Y	1			Vomiting
21	CPW	CPW-s003	7	8	h	68.25	ug/L	Y	0.083333	Y	1			Vomiting

Example 2: Record-level Exclusion for a Subject

The following table shows an example for record-level exclusion. For an entire subject all subject observations need to be flagged.

Row 1: This record was included in the analysis.

Row 2: This record for subject CPW-s011 at nominal time 0.25 hours is excluded because the sample was taken too late. Therefore, NCAXFL is set to "Y" and NCA1XRS is set to "Late Sample".

Rows 3-14: These records were included in the analysis.

Rows 15-21: All records for subject CPW-s013 are excluded because there are not enough data for PK analysis for day 1. In this particular case, it was also decided not to analyze any of the data for this subject, including the complete profile that is available for day 7. Therefore, NCAXFL is equal to "Y" and NCA2XRS is set to "Incomp. Day 1 Samples".

Rows 22-35: These records were included in the analysis.

Rows 36-42: All records for subject CPW-s013 are excluded because there are not enough data for PK analysis for day 1. In this particular case, it was also decided not to analyze any of the data for this subject, including the complete profile that is available for day 7. Therefore, NCAXFL is equal to "Y" and NCA2XRS is set to "Incomp. Day 1 Samples".

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Row	STUDYID	USUBJID	TRTAN	ARRLT	NRRLT	RRLTU	ATPTREF	AVAL	PCSTRESU	NCAXFL	NCAXFN	NCA1XRS	NCA2XRS
1	CPW	CPW-s011	1	0	0	h	1	0	ug/L				
2	CPW	CPW-s011	1	0.4	0.25	h	1	80.3	ug/L	Y	1	Late Sample	
3	CPW	CPW-s011	1	0.5	0.5	h	1	118.8	ug/L				
4	CPW	CPW-s011	1	1	1	h	1	115	ug/L				
5	CPW	CPW-s011	1	2	2	h	1	132	ug/L				
6	CPW	CPW-s011	1	4	4	h	1	91.2	ug/L				
7	CPW	CPW-s011	1	8	8	h	1	67.6	ug/L				
8	CPW	CPW-s012	1	0	0	h	1	0	ug/L				
9	CPW	CPW-s012	1	0.4	0.25	h	1	19.8	ug/L				
10	CPW	CPW-s012	1	0.75	0.5	h	1	126	ug/L				
11	CPW	CPW-s012	1	1.33333	1	h	1	131.25	ug/L				
12	CPW	CPW-s012	1	2	2	h	1	114	ug/L				
13	CPW	CPW-s012	1	4	4	h	1	97.85	ug/L				
14	CPW	CPW-s012	1	7	8	h	1	68.25	ug/L				
15	CPW	CPW-s013	1	0	0	h	1	0	ug/L	Y	1		Incomp. Day 1 Samples
16	CPW	CPW-s013	1	0.25	0.25	h	1	19.8	ug/L	Y	1		Incomp. Day 1 Samples
17	CPW	CPW-s013	1	0.5	0.5	h	1		ug/L	Y	1		Incomp. Day 1 Samples
18	CPW	CPW-s013	1	1	1	h	1		ug/L	Y	1		Incomp. Day 1 Samples
19	CPW	CPW-s013	1	2	2	h	1		ug/L	Y	1		Incomp. Day 1 Samples
20	CPW	CPW-s013	1	4	4	h	1		ug/L	Y	1		Incomp. Day 1 Samples
21	CPW	CPW-s013	1	7	8	h	1		ug/L	Y	1		Incomp. Day 1 Samples
22	CPW	CPW-s011	1	0	0	h	7	0	ug/L				
23	CPW	CPW-s011	1	0.2	0.25	h	7	28.13	ug/L				
24	CPW	CPW-s011	1	0.5	0.5	h	7	160.38	ug/L				
25	CPW	CPW-s011	1	1	1	h	7	207	ug/L				
26	CPW	CPW-s011	1	2	2	h	7	211.2	ug/L				
27	CPW	CPW-s011	1	4	4	h	7	114	ug/L				
28	CPW	CPW-s011	1	8	8	h	7	74.36	ug/L				
29	CPW	CPW-s012	1	0	0	h	7	0	ug/L				
30	CPW	CPW-s012	1	0.25	0.25	h	7	54.89	ug/L				
31	CPW	CPW-s012	1	0.45	0.5	h	7	69.3	ug/L				
32	CPW	CPW-s012	1	1.33333	1	h	7	108.2813	ug/L				
33	CPW	CPW-s012	1	2	2	h	7	71.25	ug/L				
34	CPW	CPW-s012	1	4	4	h	7	80.72625	ug/L				
35	CPW	CPW-s012	1	7	8	h	7	56.30625	ug/L				
36	CPW	CPW-s013	1	0	0	h	7	0	ug/L	Y	1		Incomp. Day 1 Samples
37	CPW	CPW-s013	1	0.25	0.25	h	7	19.03	ug/L	Y	1		Incomp. Day 1 Samples
38	CPW	CPW-s013	1	0.5	0.5	h	7	166.25	ug/L	Y	1		Incomp. Day 1 Samples
39	CPW	CPW-s013	1	1	1	h	7	163.28	ug/L	Y	1		Incomp. Day 1 Samples
40	CPW	CPW-s013	1	2	2	h	7	159.6	ug/L	Y	1		Incomp. Day 1 Samples
41	CPW	CPW-s013	1	4	4	h	7	137.75	ug/L	Y	1		Incomp. Day 1 Samples
42	CPW	CPW-s013	1	8	8	h	7	89.6	ug/L	Y	1		Incomp. Day 1 Samples

Flags for Recording Meals and Vomiting by Subjects

The ADNCA specification contains variables that allow data scientists to describe that a subject consumed a meal within a defined time window of the dose or that a subject vomited after dose administration. By including this information in the PK analysis dataset, scientists can analyze whether a meal or vomiting has a significant effect on the pharmacokinetic characteristics of a drug. Specific details relating timing of meals, vomit or emesis, or any event that would deem the concentration record unusable should be provided in the define.

Example 1: Handling Meal Data

This table shows how data are represented when certain subjects have a meal within a specified time window.

Rows 1-7: Subject CPW-s001 had a meal before the dose administration. NCAXFL is set to “Y” and NCA1XRS is set to "No Meal".

Rows 8-14: Subject CPW-s002 had no meal. NCAXFL is set blank and NCA1XRS is empty.

Rows 15-21: Subject CPW-s003 had a meal just after the dose administration. NCAXFL is set to “Y” and NCA1XRS is set to "No Meal".

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Row	STUDYID	USUBJID	ARRLT	NRRLT	RRLTU	AVAL	PCSTRESU	NCAXFL	NCA1XRS	DOSEP	DOSEU
1	CPW	CPW-s001	0	0	h	0	ug/L	Y	No Meal	30	mg
2	CPW	CPW-s001	0.33333	0.25	h	19.4	ug/L	Y	No Meal	30	mg
3	CPW	CPW-s001	0.5	0.5	h	118.8	ug/L	Y	No Meal	30	mg
4	CPW	CPW-s001	1	1	h	115	ug/L	Y	No Meal	30	mg
5	CPW	CPW-s001	2	2	h	132	ug/L	Y	No Meal	30	mg
6	CPW	CPW-s001	4	4	h	91.2	ug/L	Y	No Meal	30	mg
7	CPW	CPW-s001	8	8	h	67.6	ug/L	Y	No Meal	30	mg
8	CPW	CPW-s002	0	0	h	0	ug/L			30	mg
9	CPW	CPW-s002	0.25	0.25	h	18.4	ug/L			30	mg
10	CPW	CPW-s002	0.5	0.5	h	114	ug/L			30	mg
11	CPW	CPW-s002	1	1	h	115	ug/L			30	mg
12	CPW	CPW-s002	2	2	h	114	ug/L			30	mg
13	CPW	CPW-s002	5	4	h	72	ug/L			30	mg
14	CPW	CPW-s002	8	8	h	59.15	ug/L			30	mg
15	CPW	CPW-s003	0	0	h	0	ug/L	Y	No Meal	30	mg
16	CPW	CPW-s003	0.4	0.25	h	65	ug/L	Y	No Meal	30	mg
17	CPW	CPW-s003	0.75	0.5	h	126	ug/L	Y	No Meal	30	mg
18	CPW	CPW-s003	1.33333	1	h	131.25	ug/L	Y	No Meal	30	mg
19	CPW	CPW-s003	2	2	h	114	ug/L	Y	No Meal	30	mg
20	CPW	CPW-s003	4	4	h	97.85	ug/L	Y	No Meal	30	mg
21	CPW	CPW-s003	7	8	h	68.25	ug/L	Y	No Meal	30	mg

Example 2: Handling Vomit Data

This table shows how data are represented when certain subjects vomit after drug administration.

Rows 1-7: Subject CPW-s011 did not vomit. NCAXFL and NCA1XRS are empty.

Rows 8-14: Subject CPW-s012 vomited after the dose administration. NCAXFL is set to “Y” and NCA1XRS is set to "Vomit". Note that, at the time of vomiting, most of the drug was already absorbed; only little effect on the PK profile would be expected.

Rows 15-21: Subject CPW-s013 vomited after the dose administration. NCAXFL is set to “Y” and NCA1XRS is set to "Vomit". In this case, most of the drug was not absorbed and the observed drug concentration is significantly lower than expected without vomiting.

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Row	STUDYID	USUBJID	ARRLT	NRRLT	RRLTU	AVAL	PCSTRESU	NCAXFL	NCA1XRS	DOSEP	DOSEU
1	CPW	CPW-s011	0	0	h	0	ug/L			30	mg
2	CPW	CPW-s011	0.33333	0.25	h	19.4	ug/L			30	mg
3	CPW	CPW-s011	0.5	0.5	h	118.8	ug/L			30	mg
4	CPW	CPW-s011	1	1	h	115	ug/L			30	mg
5	CPW	CPW-s011	2	2	h	132	ug/L			30	mg
6	CPW	CPW-s011	4	4	h	91.2	ug/L			30	mg
7	CPW	CPW-s011	8	8	h	67.6	ug/L			30	mg
8	CPW	CPW-s012	0	0	h	0	ug/L	Y	Vomit	30	mg
9	CPW	CPW-s012	0.25	0.25	h	18.4	ug/L	Y	Vomit	30	mg
10	CPW	CPW-s012	0.5	0.5	h	114	ug/L	Y	Vomit	30	mg
11	CPW	CPW-s012	1	1	h	103.5	ug/L	Y	Vomit	30	mg
12	CPW	CPW-s012	2	2	h	102.6	ug/L	Y	Vomit	30	mg
13	CPW	CPW-s012	4.5	4	h	85.5	ug/L	Y	Vomit	30	mg
14	CPW	CPW-s012	8	8	h	53.235	ug/L	Y	Vomit	30	mg
15	CPW	CPW-s013	0	0	h	0	ug/L	Y	Vomit	30	mg
16	CPW	CPW-s013	0.4	0.25	h	49.9	ug/L	Y	Vomit	30	mg
17	CPW	CPW-s013	0.75	0.5	h	63	ug/L	Y	Vomit	30	mg
18	CPW	CPW-s013	1.33333	1	h	65.625	ug/L	Y	Vomit	30	mg
19	CPW	CPW-s013	2	2	h	57	ug/L	Y	Vomit	30	mg
20	CPW	CPW-s013	4	4	h	48.925	ug/L	Y	Vomit	30	mg
21	CPW	CPW-s013	7	8	h	34.125	ug/L	Y	Vomit	30	mg

Urine Data

Example 1: Urine Data

This example shows the nominal and relative start and end times of urine sampling for a multiple oral dosing trial for 1 subject. ARRLT, AERRLT, AVAL, and VOLUME can directly be used in PK software to calculate the urinary PK parameters.

Note that MRRLT can be added for analysis purposes: the negative ARRLT on row 2 and row 6 can be put to zero; PK software such as Phoenix WNL will only include observations starting from dosing, and not prior to dosing, for parameter estimation.

Rows 1-5: These are rows containing urine sampling related to administration on 12AUG2015.

Rows 6-11: These are rows containing urine sampling related to administration on 18AUG2015.

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Row	PARAM	PCRFTDTM	ASTDTM	AENDTM	NRRLT	ARRLT	NERRLT	AERRLT	RRLTU	ATPTREF	ATPT	AVAL	PCSTRESN	PCSTRESU	VOLUME	VOLUMEU
1	Urine Amount (ug)	12AUG15:09:00	11AUG15:08:51	12AUG15:08:50	-24	-24.15	0	-0.17	h	Day 1	-24 to 0 h	0	0	ug/L	2464	mL
2	Urine Amount (ug)	12AUG15:09:00	12AUG15:08:50	12AUG15:13:06	0	-0.17	4	4.1	h	Day 1	0 to 4 h	379940	628	ug/L	605	mL

Row	PARAM	PCRFTDTM	ASTDTM	AENDTM	NRRLT	ARRLT	NERRLT	AERRLT	RRLTU	ATPTREF	ATPT	AVAL	PCSTRESN	PCSTRESU	VOLUME	VOLUMEU
3	Urine Amount (ug)	12AUG15:09:00	12AUG15:13:06	12AUG15:17:05	4	4.1	8	8.08	h	Day 1	4 to 8 h	110143	527	ug/L	209	mL
4	Urine Amount (ug)	12AUG15:09:00	12AUG15:17:05	12AUG15:21:06	8	8.08	12	12.1	h	Day 1	8 to 12 h	63712	362	ug/L	176	mL
5	Urine Amount (ug)	12AUG15:09:00	12AUG15:21:06	18AUG15:08:50	12	12.1	24	23.83	h	Day 1	12 to 24 h	605220	786	ug/L	770	mL
6	Urine Amount (ug)	12AUG15:09:00	18AUG15:08:50	18AUG15:13:05	0	-0.17	4	4.08	h	Day 7	0 to 4 h	328779	729	ug/L	451	mL
7	Urine Amount (ug)	12AUG15:09:00	18AUG15:13:05	18AUG15:17:08	4	4.08	8	8.13	h	Day 7	4 to 8 h	57860	526	ug/L	110	mL
8	Urine Amount (ug)	12AUG15:09:00	18AUG15:17:08	18AUG15:21:10	8	8.13	12	12.17	h	Day 7	8 to 12 h	73568	352	ug/L	209	mL
9	Urine Amount (ug)	12AUG15:09:00	18AUG15:21:10	19AUG15:09:09	12	12.17	24	24.15	h	Day 7	12 to 24 h	780120	788	ug/L	990	mL
10	Urine Amount (ug)	12AUG15:09:00	19AUG15:09:09	20AUG15:09:05	24	24.15	48	48.08	h	Day 7	24 to 48 h	308935	205	ug/L	1507	mL
11	Urine Amount (ug)	12AUG15:09:00	20AUG15:09:05	21AUG15:09:05	48	48.08	72	72.08	h	Day 7	48 to 72 h	152724	156	ug/L	979	mL

Example 2: Urine and Plasma PARAM and PARAMCD Variables

The purpose of the PARAM variable is to completely describe the value found in AVAL and, therefore, it is important that the PARAM value also include information on the units and the specimen type (if applicable). This example shows how the PARAM and PARAMCD variables should be handled when the dataset contains both urine and plasma samples that are both measuring analyte A.

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Row	USUBJID	PARAM	PARAMCD	NRRLT	NERRLT	RRLTU	ATPT	PCSPEC	AVAL	PCSTRESU
1	STD1-56-001	Plasma Analyte A (ug/L)	PANALYTA	0		h	Predose	PLASMA	0	ug/L
2	STD1-56-001	Plasma Analyte A (ug/L)	PANALYTA	0.5		h	0.5 H	PLASMA	115	ug/L
3	STD1-56-001	Plasma Analyte A (ug/L)	PANALYTA	2		h	2 H	PLASMA	1320	ug/L
4	STD1-56-001	Plasma Analyte A (ug/L)	PANALYTA	4		h	4 H	PLASMA	1450	ug/L
5	STD1-56-001	Plasma Analyte A (ug/L)	PANALYTA	8		h	8 H	PLASMA	2119	ug/L
6	STD1-56-001	Plasma Analyte A (ug/L)	PANALYTA	12		h	12 H	PLASMA	2427	ug/L
7	STD1-56-001	Plasma Analyte A (ug/L)	PANALYTA	24		h	24 H	PLASMA	3621	ug/L
8	STD1-56-001	Urine Analyte A (ug/L)	UANALYTA	-4	0	h	-4 H to Predose	URINE	0	ug/L
9	STD1-56-001	Urine Analyte A (ug/L)	UANALYTA	0	4	h	0 to 4 H	URINE	34.5	ug/L
10	STD1-56-001	Urine Analyte A (ug/L)	UANALYTA	4	8	h	4 to 8 H	URINE	84.2	ug/L
11	STD1-56-001	Urine Analyte A (ug/L)	UANALYTA	8	12	h	8 to 12 H	URINE	65.1	ug/L
12	STD1-56-001	Urine Analyte A (ug/L)	UANALYTA	12	24	h	12 to 24 H	URINE	12.5	ug/L
13	STD1-56-001	Plasma Analyte B (ug/L)	PANALYTB	0		h	Predose	PLASMA	0	ug/L
14	STD1-56-001	Plasma Analyte B (ug/L)	PANALYTB	0.5		h	0.5 H	PLASMA	98.1	ug/L
15	STD1-56-001	Plasma Analyte B (ug/L)	PANALYTB	2		h	2 H	PLASMA	118.3	ug/L
16	STD1-56-001	Plasma Analyte B (ug/L)	PANALYTB	4		h	4 H	PLASMA	120.9	ug/L
17	STD1-56-001	Plasma Analyte B (ug/L)	PANALYTB	8		h	8 H	PLASMA	87.4	ug/L

Duplicated Records for Analysis

Example 1: Duplicated Record for Analysis

This example shows how to handle a specific case that can often occur when doing NCA: when 1 record needs to be used in 2 separate ways. This can occur if the last sample for 1 period (or visit) also doubles as the pre-dose sample for the next period (or visit) for the same subject. In this example, baseline values are determined for each analysis visit. The record that will be used in 2 ways (as the 24 hours post-dose record for the DAY 1 analysis visit and as the pre-dose baseline record for the DAY 2 analysis visit) has been duplicated (rows 8-9). The nominal times, actual times, and visit variables have all been altered for this record and the variable DTYPE filled in. Note that the PCSEQ number for the duplicated record is repeated. BASETYPE is needed here because baseline is flagged in each period and needed for analysis. Additionally, BASETYPE is populated to show the specific baseline type associated with each row. Similarly, the dose (PCRFTDTM) associated with row 8 is not the same as that associated with row 9 as the calculation of actual time from reference is determined by the associated baseline dose.

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Row	USUBJID	PCRFTDTM	ADTM	ARRLT	NRRLT	MRRLT	RRLTU	ATPTREF	ATPT	AVAL	PCSTRESU	ABLFL	BASE	BASETYPE	DTYPE	CHG	PCSEQ
1	STD1-56-001	2017-04-03T08:10	2017-04-03T08:05	-0.083	0	0	h	DAY 1	Predose	0	ug/L	Y	0	DAY 1 BASELINE		0	1
2	STD1-56-001	2017-04-03T08:10	2017-04-03T08:41	0.5167	0.5	0.5167	h	DAY 1	0.5 H	383	ug/L		0	DAY 1 BASELINE		383	2
3	STD1-56-001	2017-04-03T08:10	2017-04-03T09:10	1	1	1	h	DAY 1	1 H	533	ug/L		0	DAY 1 BASELINE		533	3
4	STD1-56-001	2017-04-03T08:10	2017-04-03T10:10	2	2	2	h	DAY 1	2 H	455	ug/L		0	DAY 1 BASELINE		455	4
5	STD1-56-001	2017-04-03T08:10	2017-04-03T12:10	4	4	4	h	DAY 1	4 H	443	ug/L		0	DAY 1 BASELINE		443	5
6	STD1-56-001	2017-04-03T08:10	2017-04-03T16:15	8.083	8	8.083	h	DAY 1	8 H	356	ug/L		0	DAY 1 BASELINE		356	6
7	STD1-56-001	2017-04-03T08:10	2017-04-03T20:10	12	12	12	h	DAY 1	12 H	320	ug/L		0	DAY 1 BASELINE		320	7
8	STD1-56-001	2017-04-03T08:10	2017-04-04T08:05	23.917	24	23.917	h	DAY 1	24 H	190	ug/L		0	DAY 1 BASELINE		190	8
9	STD1-56-001	2017-04-04T08:10	2017-04-04T08:05	-0.083	0	0	h	DAY 2	Predose	190	ug/L	Y	190	DAY 2 BASELINE	COPY	0	8
10	STD1-56-001	2017-04-04T08:10	2017-04-04T08:40	0.5	0.5	0.5	h	DAY 2	0.5 H	475	ug/L		190	DAY 2 BASELINE		285	9
11	STD1-56-001	2017-04-04T08:10	2017-04-04T09:10	1	1	1	h	DAY 2	1 H	510	ug/L		190	DAY 2 BASELINE		320	10
12	STD1-56-001	2017-04-04T08:10	2017-04-04T10:10	2	2	2	h	DAY 2	2 H	628	ug/L		190	DAY 2 BASELINE		438	11
13	STD1-56-001	2017-04-04T08:10	2017-04-04T12:25	4.25	4	4.25	h	DAY 2	4 H	532	ug/L		190	DAY 2 BASELINE		342	12
14	STD1-56-001	2017-04-04T08:10	2017-04-04T16:10	8	8	8	h	DAY 2	8 H	487	ug/L		190	DAY 2 BASELINE		297	13
15	STD1-56-001	2017-04-04T08:10	2017-04-04T20:10	12	12	12	h	DAY 2	12 H	332	ug/L		190	DAY 2 BASELINE		142	14
16	STD1-56-001	2017-04-04T08:10	2017-04-05T09:10	25	24	25	h	DAY 2	24 H	200	ug/L		190	DAY 2 BASELINE		10	15

6 Appendices

Appendix A: ADaM ADNCA Standards Development Team

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Appendix B: Glossary and Abbreviations

The following abbreviations and terms are used in this document. Additional definitions can be found in the CDISC Glossary (available at https://www.cdisc.org/standards/glossary).

ADaM	Analysis Data Model
ADaMIG	ADaM Implementation Guide
ADNCA	ADaM NCA (dataset)
ADSL	(ADaM) Subject-Level Analysis (dataset)
Analysis-ready	A dataset that contains all of the variables needed for the specific analysis, so that actual statistical test can be performed without first having to manipulate data
BDS	(ADaM) Basic Data Structure
BMI	Body mass index
CDISC	Clinical Data Interchange Standards Consortium
CSR	Clinical study report
Dataset	A collection of structured data in a single file
Domain	A collection of data points related by a common topic, such as adverse events or demographics
NCA	Non-compartmental analysis
NSV	Non-standard variable
PD	Pharmacodynamics
PK	Pharmacokinetics; the study of the effect of the body on a drug
OCCDS	(ADaM) Structure for Occurrence Data
Occurrence analysis	The counting of subjects with a given record or term. This often includes a structured hierarchy of dictionary coding categories.
Producer	The originator/sender/owner/sponsor of the data.
SAP	Statistical analysis plan
SDTM	Study Data Tabulation Model
SDTMIG	Study Data Tabulation Model Implementation Guide

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