Analysis Data Reviewer's Guide

Sponsor Name; Study Protocol Number; ADRG Template Version ccyy-mm-dd

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1 Introduction

1.1 Purpose

This document provides context for the analysis datasets and terminology that benefit from additional explanation beyond the Data Definition document (define.xml)for an invididual study. In addition, this document provides a summary of ADaM conformance findings.

1.2 Acronyms

Acronym	Translation
aCRF	Annotated Case Report Form
ADaM	Analysis Dataset Model
ADRG	Analysis Data Reviewer's Guide
eCRF	Electronic Case Report Form
eDT	Electronic Data Transfer (e.g. central lab data, ECG vendor data, PK data, etc.)
IG	Implementation Guide
NA	Not Applicable
SDTM	Study Data Tabulation Model
TAUG	Therapeutic Area User Guide

2 Dataset Standards

Standard or Dictionary	Versions Used
SDTM	SDTM Implementation Guide Version 3.1.2 ; SDTM Version 1.2
Medical Events Dictionary	MedDRA version 8.0
Define-XML	Define version 1.0.0

2.1 Source Data Used for Analysis Dataset Creation

(insert your text here)

Include the following text if applicable: Please refer to the Legacy Data Conversion Plan and Report Appendix for additional details.

3 Protocol Description

3.1 Protocol Number and Title

Protocol Number: CDISCPILOT01

Protocol Title: Safety and Efficacy of the Xanomeline Transdermal Therapeutic System (TTS) in Patients with Mild to Moderate Alzheimer's Disease

Protocol Versions:

The protocol was amended 3 times. For the first 2 amendments, changes were made to the ambulatory ECG assessments. Changes to the protocol-specified analyses included omission of secondary or sensitivity analyses, omission of some efficacy endpoints, omission of some safety endpoints, and the inclusion of additional types of analyses.

3.2 Protocol Designin Relation to ADaM Concepts

3.2.1 Protocol Objective

The primary objectives of this study were to determine if there is a statistically significant relationship between the change in both the ADAS-Cog (11) and CIBIC+ scores, and drug dose, and to document the safety profile of the xanomeline TTS.

3.2.2 Protocol Methodology

This was a prospective, randomized, multi-center, double-blind, placebo-controlled, parallel-group study. Subjects were randomized equally to placebo, xanomeline low dose, or xanomeline high dose. Subjects applied 2 patches daily and were followed for a total of 26 weeks.

3.2.3 Number of Subjects Planned in Total and by Group

300 subjects total (100 subjects in each of 3 groups)

3.2.4 Study Design Schema

The study design included three treatment groups: placebo, xanomeline low dose (54 mg), and xanomeline high dose (81 mg). The treatment duration was 26 weeks, with assessments at various time points including Weeks 8, 16, and 24 for efficacy and safety evaluations.

4 Analysis Considerations Related to Multiple Analysis Datasets

4.1 Core Variables

Core variables are those that are represented across all/most analysis datasets.

Variable Name	Variable Description
AGE	Age
AGEGR1	Pooled Age Group 1
AVAL	Analysis Value
AVISITN	Analysis Visit (N)
BASE	Baseline Value
BMIBL	Baseline BMI (kg/m^2)
CHG	Change from Baseline
CNSR	Censor
HEIGHTBL	Baseline Height (cm)
MMSETOT	MMSE Total
PARAM	Parameter
PARAMCD	Parameter Code
RACE	Race
STUDYID	Study Identifier
TRT01A	Actual Treatment for Period 01
TRTPN	Planned Treatment (N)
USUBJID	Unique Subject Identifier
WEIGHTBL	Baseline Weight (kg)

4.2 Treatment Variables

- ARM versus TRTxxP: Are the values of ARM equivalent in meaning to values of TRTxxP? **Yes.** The study design specifies that subjects are randomized into these treatment groups, confirming that ARM and TRTxxP values correspond to the same treatment categories.
- ACTARM versus TRTxxA: If TRTxxA is used, then are the values of ACTARM equivalent in meaning to values of TRTxxA?
- Use of ADaM Treatment Variables in Analysis: Are both planned and actual treatment variables used in analysis? **Yes.** This confirms that both planned and actual treatment variables are incorporated into the analysis of the clinical trial data.
- Use of ADaMTreatment Grouping Variables in Analysis: Are both planned and actual treatment grouping variables used in analysis? **Yes.** This dual usage allows for a

comprehensive comparison between the intended treatment allocations and the actual treatments received by participants.

4.3 Subject Issues that Require Special Analysis Rules

(insert your text hereor indicate that there were no subject issues to be documented)

4.4 Use of Visit Windowing, Unscheduled Visits, and Record Selection

- Was windowing used in one or more analysis datasets? **Yes.** The specific mention of the windowing algorithm in the methods section confirms its application in the analysis datasets.
- Were unscheduled visits used in any analyses?
- Additional Content of Interest <See ADRG Completion Guidelines foradditional content of interest, and includetext here or remove this text >.

4.5 Imputation/Derivation Methods

- If date imputation was performed, were there rules that were used in multiple analysis datasets?
- Additional Content of Interest <See ADRG Completion Guidelines foradditional content of interest, and include text here or remove this text >.

5 Analysis Data Creation and Processing Issues

5.1 Split Datasets

(insert your textortablehereor indicate there are no split datasets)

dataset name	depend on the following datasets

5.2 Data Dependencies

dataset name	depend on the following datasets
ADADAS	
ADAE	ADSL
ADLBC	ADSL
ADSL	
ADTTE	ADAE, ADSL

5.3 Intermediate Datasets

(insert your text hereor indicate there are no intermediate datasets)

6 Analysis Dataset Descriptions

6.1 Overview

- Are data for screen failures, including data for run-in screening (for example, SDTM values of ARMCD='SCRNFAIL', or 'NOTASSGN') included in ADaM datasets? **No.** This exclusion is a standard practice in clinical trial analysis to focus on subjects who were randomized and received treatment.
- Are data taken from an ongoing study?
- Do the analysis datasets support all protocol-and statistical analysis plan-specified objectives?
- Include all objectives listed in the protocol or SAP which are not supported in the analysis datasets and the reason for their absence.

Additional Content of Interest

(See ADRG Completion Guidelines for additional content of interest, and includetext here or remove this text).

6.2 Analysis Datasets

Dataset

Dataset Label	Class	Efficacy	Safety	Baseline or other subject characteristics	PK/PD	Primary Objective	Structure
ADAS-Cog Analysis | ADADAS	BASIC DATA STRUCTURE	X					one record per subject per parameter per analysis visit per analysis date
Adverse Events Analysis Dataset | ADAE	ADAM OTHER		X				one record per subject per adverse event
Analysis Dataset Lab Blood Chemistry | ADLBC	BASIC DATA STRUCTURE	X	X				one record per subject per parameter per analysis visit

Dataset Label	Class	Efficacy	Safety	Baseline or other subject characteristics	PK/PD	Primary Objective	Structure
Subject-Level Analysis Dataset | ADSL	SUBJECT LEVEL ANALYSIS DATASET			X			one record per subject. Screen Failures are excluded.
AE Time To 1st Derm. Event Analysis | ADTTE	BASIC DATA STRUCTURE		X				one record per subject per parameter

6.2.1 ADSL – Subject Level Analysis Dataset

(insert your text here)

(insert date imputation rules if applicable)

6.2.2 Dataset – Dataset Label

(A new section is required for each dataset that is hyperlinked in the inventory table. This section should be copied to create a new section for each dataset. The text in the section header above must be edited to match the dataset name and label.

7 Data Conformance Summary

7.1 Conformance Inputs

Specify the software name and version for the analysis datasets

(Text here)

Specify the version of the validation rules (i.e. CDISC, FDA) for the analysis datasets

(Text here)

Specify the software name and version for the define.xml

(Text here)

Specify the version of the validation rules (i.e. CDISC, FDA) for the define.xml

(Text here)

Provide any additionalcompliance evaluation information:

(Text here)

7.2 Issues Summary

(insert your text here and/or use following table)

Dataset	Diagnostic Message	Severity	Count	Explanation

8 Submission of Programs

All programs for analysis datasets and primary and secondary efficacy resultsaresubmitted. They were all createdon a platformusing.The internal reference date used to create dates in ADaM datasets is.

8.1 ADaM Programs

Program Name	Output	Dataset Description
adadas	adadas.rds	ADAS-Cog Analysis
adae	adae.rds	Adverse Events Analysis Dataset
adlbc	adlbc.rds	Analysis Dataset Lab Blood Chemistry
adsl	adsl.rds	Subject-Level Analysis Dataset
adtte	adtte.rds	AE Time To 1st Derm. Event Analysis

8.2 Analysis Output Programs

r_file	outputs	filters	variables
tlf-demographic.r	tlf-demographic-pilot5.out	ADSL.STUDYID == 'CDISCPILOT01'; ADSL.ITTFL == 'Y'	ADSL.AGE; ADSL.AGEGR1; ADSL.RACE; ADSL.HEIGHTBL; ADSL.WEIGHTBL; ADSL.BMIBL; ADSL.MMSETOT
tlf-efficacy.r	tlf-efficacy-pilot5.rtf	ADLB.TRTPN IN (0, 81) AND ADLB.PARAMCD == 'GLUC' AND NOT ISNA(ADLB.AVISITN); ADLB.AVISITN == 20; ADLB.AVISITN == 0; ADLB.AVISITN == 20 AND NOT ISNA(ADLB.CHG) AND NOT ISNA(ADLB.BASE)	ADSL.STUDYID; ADSL.USUBJID; ADLB.BASE; ADLB.TRTPN; ADLB.PARAMCD; ADLB.AVISITN; ADLB.CHG; ADLB.AVAL
tlf-kmplot.r	pdf/tlf-kmplot-pilot5.pdf	ADSL.SAFFL == 'Y'; ADSL.STUDYID == 'CDISCPILOT01'; ADTEE.PARAMCD == 'TTDE'; ADTEE.STUDYID == 'CDISCPILOT01'	ADSL.STUDYID; ADSL.USUBJID; ADSL.TRT01A; ADTE.PARAMCD; ADTE.AVAL; ADTE.CNSR; ADTE.PARAM

r_file	outputs	filters	variables
tlf-primary.r	tlf-primary-pilot5.rtf	ADAS.EFFFL == 'Y'; ADAS.ITTFL == 'Y'; ADAS.PARAMCD == 'ACTOT'; ADAS.ANL01FL == 'Y'; ADSL.EFFFL == 'Y'; ADSL.ITTFL == 'Y'	ADAS.AVAL; ADAS.CHg

8.3 Open source R packages

Package	Version	Description
admiral	1.3.0	This R package provides tools for programming Clinical Data Interchange Standards Consortium (CDISC) compliant Analysis Data Model (ADaM) datasets, facilitating the derivation of analysis datasets required for New Drug or Biologics License Applications to the FDA.
admiraldev	1.3.1	The package provides utility functions for checking data, variables, and conditions used in the 'admiral' and its extension packages, along with helper tools for documentation, testing, and maintenance.

Package	Version	Description
assertthat	0.2.1	This package enhances the functionality of stopifnot() by allowing developers to easily declare pre and post conditions for their code, while providing user-friendly error messages when those conditions are not met.
backports	1.5.0	This package provides re-implementations of functions introduced or changed since R v3.0.0, allowing for conditional exports that enable compatibility with older R versions while utilizing new features when available.
base64enc	0.1-3	This package offers flexible tools for handling base64 encoding, surpassing the capabilities of the now-abandoned base64 package.
bit	4.6.0	This package offers efficient classes and methods for handling boolean and skewed boolean vectors, along with fast integer sorting, unique detection, and set operations, while also providing foundational tools for range indexing and data compression.

Package	Version	Description
bit64	4.6.0-1	The ‘bit64’ package in R provides support for 64-bit signed integers, allowing for precise handling of large integers, such as database keys, with various coercion methods and compatibility in data structures like vectors and data frames.
brew	1.0-10	This package provides a templating framework that allows users to combine R code and text for effective report generation, using a syntax similar to popular web templating languages.
broom	1.0.8	The Broom package in R streamlines the summarization and reporting of statistical models by providing functions that extract key information, including model coefficients, overall fit statistics, and observation-level details, into tidy tibbles for easier analysis and visualization.
cachem	1.1.0	This package provides key-value stores that automatically manage memory by pruning objects based on size limits or age constraints, ensuring efficient cache management.
callr	3.7.6	This package enables users to execute computations in an isolated R process, ensuring that the current R environment remains unaffected.

Package	Version	Description
cellranger	1.1.0	This package provides helper functions for working with spreadsheets, specifically focusing on the "A1:D10" style of cell range specification.
checkmate	2.3.2	This package provides tools for performing efficient and frequent argument checks, with a significant portion implemented in C to enhance performance and reduce execution time overhead.
cli	3.6.5	This package provides a collection of tools for creating visually appealing command line interfaces (CLIs) with support for styling elements, custom themes, and various ANSI colors and text styles.
clipr	0.8.0	This package provides simple utility functions for reading from and writing to the clipboard across Windows, OS X, and X11 systems.
commonmark	2.0.0	This package provides a comprehensive Markdown parser that converts Markdown text into various formats such as HTML and LaTeX, while also offering an XML representation of the parse tree and support for GitHub Flavored Markdown (GFM) extensions.

Package	Version	Description
cowplot	1.2.0	This R package enhances 'ggplot2' by providing tools for creating publication-quality figures, including themes, alignment and arrangement functions for complex layouts, and features for annotating plots and integrating images.
cpp11	0.5.2	The 'cpp11' package offers a safe, C++11 interface to R's C API, ensuring compatibility with R's function semantics and supporting ALTREP vectors while protecting against long jumps and exceptions.
crayon	1.5.3	The crayon package provides colored terminal output with ANSI color and highlight codes, allowing for customizable and nested styles in R projects.
curl	6.4.0	This package provides bindings to 'libcurl' for making customizable HTTP/FTP requests with options for processing responses in memory, on disk, or through streaming, making it suitable for users with familiarity in 'libcurl'.
datasetjson	0.3.0	This package allows users to read, construct, and write CDISC Dataset JSON files while ensuring validation against the Dataset JSON schema.

Package	Version	Description
desc	1.4.3	This package provides tools for reading, writing, creating, and manipulating DESCRIPTION files for R packages, enabling efficient package management and development.
diffdf	1.1.1	This package provides functions to compare two data.frames, offering a detailed analysis of their differences and utility functions to identify sources of discrepancies.
digest	0.6.37	This package provides functions to create hash digests of arbitrary R objects using various algorithms, enabling easy comparison of R language objects and the generation of hash-based message authentication codes, but it is not intended for cryptographic purposes.
dplyr	1.1.4	This package provides a fast and reliable tool for efficiently handling data frame-like objects, whether they are stored in memory or in an external storage system.
emmeans	1.11.2	This package facilitates the calculation of estimated marginal means (EMMs) for various types of statistical models, enabling users to perform contrasts, trends, and slope comparisons, along with providing visualizations and displays of the results.

Package	Version	Description
estimability	1.5.1	This package offers tools for assessing the estimability of linear functions of regression coefficients and includes methods for handling non-estimable cases appropriately.
evaluate	1.0.4	This package provides parsing and evaluation tools that simplify the recreation of command line behavior in R.
fansi	1.0.6	This package provides R functions for string manipulation that accurately handle ANSI text formatting control sequences.
farver	2.1.2	The 'farver' package provides efficient and fast functions for converting and comparing colors across different color spaces, leveraging C++ implementations for enhanced performance.
fastmap	1.2.0	Fastmap provides efficient data structures for key-value storage, stack, and queue in R, while avoiding memory leaks associated with the global symbol table by utilizing C++ implementations.
forcats	1.0.0	This package provides tools for reordering factor levels, modifying them, and handling rare levels through features like moving specified levels to the front, ordering by appearance, reversing, shuffling, collapsing, anonymizing, and recoding.

Package	Version	Description
formatters	0.5.11	This package offers a framework for generating complex ASCII tables and includes formatters for converting values into display-ready strings.
fs	1.6.6	This package provides a cross-platform interface for file system operations, leveraging the 'libuv' C library for enhanced performance and compatibility.
generics	0.1.4	The generics package in R provides a set of commonly used S3 generics to minimize package dependencies and conflicts.
ggplot2	3.5.2	`ggplot2` is an R package that allows users to create complex and customizable graphics by declaratively mapping data variables to aesthetic elements based on the principles of the Grammar of Graphics.
ggsurvfit	1.1.0	This R package facilitates the creation of publication-ready survival endpoint figures by providing modular functions that integrate seamlessly with 'ggplot2' for customizable data visualization.
glue	1.8.0	This package provides an implementation of interpreted string literals that allows for multiline string formatting and interpolation, drawing inspiration from Python and Julia's string handling features.

Package	Version	Description
gtable	0.3.6	The ‘gtable’ package in R provides tools for creating, manipulating, and combining grid-based graphical objects (grobs) in a flexible and structured manner, allowing for complex table-like layouts in visualizations.
haven	2.5.5	This R package allows users to import various foreign statistical file formats into R by leveraging the embedded ReadStat C library.
highr	0.11	This package provides syntax highlighting for R source code, supporting output in LaTeX and HTML, and integrates with Andre Simon’s highlight package for additional language support.
hms	1.1.3	This package implements an S3 class for handling and formatting time-of-day values using the ‘difftime’ class in R.
htmltools	0.5.8.1	This package provides tools for generating and outputting HTML content, facilitating the creation and manipulation of web-based documents.

Package	Version	Description
huxtable	5.6.0	This package creates styled tables for data presentation that can be exported to various formats such as HTML, LaTeX, RTF, Word, Excel, PowerPoint, typst, SVG, and PNG, featuring a user-friendly interface for customizing aesthetics and layouts, with additional functions for generating regression tables.
isoband	0.2.7	This package provides a fast C++ implementation for generating contour lines (isolines) and contour polygons (isobands) from regularly spaced elevation data grids.
janitor	2.2.1	The janitor package in R streamlines data cleaning and formatting by providing functions for standardizing data frame column names, generating frequency tables, and identifying duplicate records, all while maintaining compatibility with the tidyverse and enhancing usability for beginner to intermediate users.
jsonlite	2.0.0	The 'jsonlite' package provides efficient tools for parsing, generating, and manipulating JSON data in R, making it ideal for statistical data processing and web API interaction.

Package	Version	Description
jsonvalidate	1.5.0	This package validates JSON data against a JSON schema using the 'is-my-json-valid' or 'ajv' libraries, supporting Drafts 04, 06, and 07 of JSON schema.
knitr	1.50	The package offers a versatile solution for generating dynamic reports in R by utilizing Literate Programming techniques.
labeling	0.4.3	This package offers various algorithms for labeling axes in graphical plots.
lattice	0.22-7	Lattice is a high-level data visualization system in R that offers powerful and flexible tools for creating multivariate graphics, inspired by Trellis graphics.
lifecycle	1.0.4	This package simplifies the management of exported functions by providing conventions for life cycle tracking, documentation badges, and user-friendly deprecation warnings.
lubridate	1.9.4	The 'lubridate' package in R simplifies working with date and time data by providing user-friendly functions for parsing, extracting components, and performing algebraic manipulations on date-time objects.

Package	Version	Description
magrittr	2.0.3	This package introduces a forward-pipe operator, %>%, that allows for the seamless chaining of commands by forwarding values or expression results into subsequent function calls, enhancing code readability and flexibility.
MASS	7.3-65	This package provides functions and datasets that support the applications and methodologies presented in Venables and Ripley's "Modern Applied Statistics with S" (4th edition, 2002).
Matrix	1.7-3	This package provides a comprehensive hierarchy of sparse and dense matrix classes, supporting various types of matrices and efficient operations through integration with BLAS, LAPACK, and SuiteSparse libraries.
memoise	2.0.1	This package allows you to cache the results of a function, enabling faster retrieval of previously computed values when the function is called again with the same arguments.
metacore	0.2.0	This package provides an immutable container for managing metadata, thereby enhancing the programming capabilities and functionalities within clinical programming workflows.

Package	Version	Description
metatools	0.1.6	The package utilizes metadata stored in 'metacore' objects to validate and construct associated metadata columns.
mgcv	1.9-3	This R package provides tools for fitting generalized additive (mixed) models with various smoothing techniques and parameter estimation methods, supporting Bayesian inference and offering a wide range of distributions beyond the exponential family.
mvtnorm	1.3-3	This package provides tools for computing probabilities, quantiles, random deviates, and densities for multivariate normal and t distributions, and includes functionality for log-likelihood estimation and score functions for multivariate Gaussian models and copulas based on Cholesky factors, accommodating both interval-censored and exact data.
nlme	3.1-168	This package provides tools for fitting and comparing Gaussian linear and nonlinear mixed-effects models, facilitating the analysis of hierarchical and grouped data structures.

Package	Version	Description
numDeriv	2016.8-1.1	This package offers methods for calculating accurate numerical first and second order derivatives using techniques such as Richardson's extrapolation and complex step differentiation, while also providing a simpler difference method for quick approximations and validation.
patchwork	1.3.1	The 'patchwork' package in R enhances the 'ggplot2' plotting system by enabling users to easily combine multiple plots into a single, complex layout using mathematical operators.
pharmaRTF	0.1.4	This R package provides an enhanced RTF wrapper for creating regulatory-compliant tables with features like multiple title levels, footnotes, landscape orientation, and customizable margins, which are not typically available in standard table packages like 'Huxtable' or 'GT'.
pillar	1.11.0	This package offers 'pillar' and 'colonnade' generics for formatting data columns with a diverse array of colors suitable for modern terminal displays.
pkgbuild	1.4.8	This package provides essential functions for building R packages by locating the necessary compilers and configuring the PATH for various platforms.

Package	Version	Description
pkgconfig	2.0.3	This package allows users to set configuration options specific to individual packages, ensuring that changes only affect the designated package without impacting others.
pkgload	1.4.0	The package facilitates rapid development by simulating the installation and attachment of R packages, enabling continuous iteration during the development process.
prettyunits	1.2.0	This package provides a user-friendly way to format various quantities such as time intervals, byte sizes, p-values, and colors into more readable representations.
processx	3.8.6	The package provides tools for managing system processes in the background, including monitoring their statuses, handling their input/output, and controlling their execution.
progress	1.2.3	This package offers configurable progress bars that display percentage, elapsed time, and estimated completion time, compatible with various terminal environments and providing a C++ API for enhanced functionality.
ps	1.9.1	This package allows users to list, query, and manipulate all system processes across Windows, Linux, and macOS operating systems.

Package	Version	Description
purrr	1.1.0	This R package provides a comprehensive and cohesive set of tools for functional programming.
r2rtf	1.1.4	This package enables users to create production-ready Rich Text Format (RTF) tables and figures with flexible formatting options.
R6	2.6.1	The package enables the creation of lightweight R6 classes with reference semantics, allowing for public and private members, inheritance, and does not rely on S4 or the methods package.
RColorBrewer	1.1-3	This package provides a variety of color schemes for maps and graphics, inspired by designs from Cynthia Brewer, which can be accessed through the ColorBrewer website.
Rcpp	1.1.0	The 'Rcpp' package facilitates the integration of R and C++ by allowing seamless interoperability between R data types and C++ classes, enabling efficient coding and the incorporation of third-party libraries.
readr	2.1.5	The 'readr' package provides a fast and user-friendly interface for reading rectangular data formats such as CSV, TSV, and fixed-width files, while ensuring robust parsing capabilities for diverse data types.

Package	Version	Description
readxl	1.4.5	This R package enables users to import Excel files (.xls and .xlsx) seamlessly across different operating systems, leveraging embedded libraries for efficient reading.
rematch	2.0.0	This package provides a convenient wrapper around the 'regexpr' function to extract matches and captured groups from regular expressions applied to character vectors.
renv	1.1.4	The 'renv' package is a dependency management toolkit for R that allows users to create and manage project-specific R libraries, save their state in a lockfile, and restore the library as needed to enhance project isolation, portability, and reproducibility.
rlang	1.1.6	This package provides a toolbox for manipulating base types, utilizing core R features, and leveraging the principles of tidy evaluation from the Tidyverse.
roxygen2	7.3.2	The 'roxygen2' package facilitates the generation of R documentation, 'NAMESPACE' files, and collation fields by using specially formatted comments directly within the code, ensuring that documentation remains current and synchronized with code changes.

Package	Version	Description
rprojroot	2.1.0	This package provides robust, reliable, and flexible methods for constructing file paths relative to a specified project root directory, which is identified by the presence of specific files.
rtables	0.6.13	The 'rtables' package provides a framework for creating complex hierarchical tabulations and reporting tables from data, allowing for advanced structuring, grouping, and summary computations within a customizable interface.
scales	1.4.0	This package facilitates the mapping of data to visual aesthetics by offering tools for automatically generating breaks and labels for axes and legends in graphical representations.
snakecase	0.11.1	This package provides a versatile and user-friendly tool for parsing and converting strings into various cases, such as snake_case and camelCase, among others.
stringi	1.8.7	The 'stringi' package provides a comprehensive set of tools for efficient text processing, including pattern searching, random string generation, case mapping, and Unicode handling, making it suitable for various natural language processing tasks.

Package	Version	Description
stringr	1.5.1	This R package provides a user-friendly set of consistent wrappers around the 'stringi' package, streamlining string manipulation tasks while ensuring uniform handling of NA values and zero-length vectors.
survival	3.8-3	This R package provides essential tools for survival analysis, including the creation of Surv objects, Kaplan-Meier and Aalen-Johansen curve calculations, Cox regression models, and parametric accelerated failure time models.
tibble	3.3.0	The package provides a 'tbl_df' class, known as a 'tibble', that offers enhanced data frame functionality with stricter data checking and improved formatting.
tidyr	1.3.1	The 'tidyr' package provides tools for creating tidy data by reshaping datasets, managing hierarchies, extracting values, and handling missing information to ensure each column represents a variable, each row an observation, and each cell a single value.

Package	Version	Description
tidyselect	1.2.1	This package provides a backend for implementing select-like functions in a way that aligns with the selection interfaces used across the 'tidyverse' ecosystem, making it easier for developers to create consistent and intuitive data selection methods in their own packages.
timechange	0.3.0	This package provides efficient tools for manipulating date-time objects, including time-zone management, daylight saving adjustments, and date-time component modifications.
Tplyr	1.2.1	This package provides a streamlined tool for simplifying data manipulation tasks required to generate clinical summaries with a focus on traceability.
tzdb	0.5.0	This package offers an updated copy of the IANA Time Zone Database along with a C++ interface for the 'date' library, facilitating date and time functionalities in R, including support for time zone adjustments and calendar calculations.
utf8	1.2.6	This package provides functionalities to process, validate, normalize, encode, format, and display UTF-8 encoded international text (Unicode).

Package	Version	Description
V8	6.0.4	The package provides an R interface to the V8 JavaScript engine, allowing users to execute JavaScript and WebAssembly code directly within R.
vctrs	0.6.5	This package introduces concepts of prototype and size to enhance type-coercion and size-recycling mechanisms, promoting type- and size-stability for better function interface analysis.
viridisLite	0.4.2	The 'viridis' package provides color maps designed to enhance graph readability for individuals with color blindness and ensures perceptual uniformity in both color and black-and-white formats, along with support for use in 'ggplot2'.
vroom	1.6.5	The 'vroom' package is designed for fast reading and writing of data files, such as CSV and TSV, by using efficient indexing and lazy loading to minimize memory usage.
withr	3.0.2	This package provides a set of functions to execute code with a safely and temporarily modified global state, originally derived from the 'devtools' package, while maintaining minimal dependencies.

Package	Version	Description
xfun	0.52	The package provides a collection of miscellaneous functions that are commonly utilized in other packages maintained by Yihui Xie.
xml2	1.3.8	This package provides bindings to 'libxml2' for XML data manipulation using a simplified interface based on XPath expressions, along with support for XML schema validation and XSLT transformations through an additional package.
xportr	0.4.3	This package provides tools for constructing CDISC compliant datasets and verifying their adherence to CDISC standards.
yaml	2.3.10	This package provides an interface to the 'libyaml' library for parsing and emitting YAML 1.1 data in R.
yyjsonr	0.1.21	This R package provides a fast parser, generator, and validator for converting JSON, NDJSON, and GeoJSON data to and from R objects, supporting various standard data types and structures.

9 Appendix

(insert text here or remove this section)

10 Purpose

The purpose of this appendix is to document thetraceability ofkeyoutput analysis results with ADaM when the analysis results were generated using a legacy process.

Because of transformations required during ADaM conversion, some of the terms, categories and data formats used in the tabulation data have been translated into CDISC standard formats in the ADaM data. This appendix identifies differences between the legacyanalysisand ADaM data, and explains how ADaM represents the equivalent data.

11 Conversion Data Flow

The legacy data was converted to SDTM/ADaMas described in the following data flow diagram.

Rationale:

(Text here)

12 Converted Data Summary

12.1 Issues Encountered and Resolved

- (Text and/or table here)
- (Text and/or table here) # Traceability Data Flow

The legacy data traceability from collection to submission is described in the following data flow diagram.

13 Outstanding Issues

- (Text and/or table here)
- (Text and/or table here)