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

Analysis datasets were derived from SDTM domains collected via electronic Case Report Forms (eCRF) and electronic Data Transfer (eDT) sources as documented in define.xml.

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 are described in the statistical analysis plan.

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 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.

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
ANL01FL	Analysis Flag 01
AVAL	Analysis Value
AVISITN	Analysis Visit (N)
BASE	Baseline Value
BMIBL	Baseline BMI (kg/m^2)
CHG	Change from Baseline
CNSR	Censor
EFFFL	Efficacy Population Flag
HEIGHTBL	Baseline Height (cm)
ITTFL	Intent-To-Treat Population Flag
MMSETOT	MMSE Total
PARAM	Parameter
PARAMCD	Parameter Code
RACE	Race
STUDYID	Study Identifier
TRT01A	Actual Treatment for Period 01
TRT01P	Planned Treatment for Period 01
TRTP	Planned Treatment
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 indicates that subjects were randomized into these treatment groups, confirming the equivalence in meaning between ARM and TRTxxP.
- 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 dual usage of planned and actual treatment variables is consistent with ADaM standards, which recommend including both types of treatment variables for comprehensive analysis.
- Use of ADaMTreatment Grouping Variables in Analysis: Are both planned and actual treatment grouping variables used in analysis? **Yes.** This confirms that both planned and actual treatment grouping variables are indeed used in the analysis of the clinical trial data.

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.** Specifically, the algorithm for "ADADAS.AVISIT" mentions that it is derived based on a windowing algorithm, confirming the use of windowing 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

There are no split datasets in this submission.

5.2 Data Dependencies

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

5.3 Intermediate Datasets

There are no intermediate datasets. All datasets created during processing are included in the final submission.

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.** Therefore, any analysis involving screen failures would need to be conducted separately from the ADaM datasets.
- 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
Subject-Level Analysis Dataset | ADSL	SUBJECT LEVEL ANALYSIS DATASET			X			one record per subject. Screen Failures are excluded.

Dataset Label	Class	Efficacy	Safety	Baseline or other subject characteristics	PK/PD	Primary Objective	Structure
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

Subject-Level Analysis Dataset. one record per subject. Screen Failures are excluded.

Date Imputation Rules:

- **Algorithm to derive ADAE.ASTDT**: AE.AESTDTC, converted to a numeric SAS date. Some events with partial dates are imputed in a conservative manner. If the day component is missing, a value of '01' is used. If both the month and day are missing no imputation is performed as these dates clearly indicate a start prior to the beginning of treatment. There are no events with completely missing start dates.
- **Algorithm to derive ADAE.ASTDTF**: ASTDTF='D' if the day value within the character date is imputed. Note that only day values needed to be imputed for this study.

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); ADLB.PARAMCD == 'GLUC'; ADLB.AVISITN IS NOT NULL; ADLB.AVISITN == 20; ADLB.AVISITN == 0; ADLB.AVISITN == 20 AND ADLB.CHG IS NOT NULL AND ADLB.BASE IS NOT NULL	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

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.EFFFL; ADAS.ITTFL; ADAS.PARAMCD; ADAS.ANL01FL; ADAS.AVAL; ADAS.AVISITN; ADAS.CHG; ADSL.TRTP; ADSL.TRT01P

8.3 Open source R packages

Package	Version	Description
admiral	1.3.0	This R package provides tools for creating CDISC-compliant Analysis Data Model (ADaM) datasets, essential for regulatory submissions to the FDA.
admiraldev	1.3.1	The package provides utility functions for verifying data and variables in 'admiral' and its extension packages, along with additional tools to aid developers in documentation, testing, and maintenance.
assertthat	0.2.1	This R package enhances the functionality of stopifnot() by allowing users to easily specify pre and post conditions for their code, while providing clear and informative error messages when conditions are not met.

Package	Version	Description
backports	1.5.0	This package provides re-implementations of functions introduced or changed since R version 3.0.0, allowing compatibility and selective importing for package developers to support older R installations.
base64enc	0.1-3	This package offers flexible tools for working with base64 encoding, surpassing the capabilities of the outdated base64 package.
bit	4.6.0	This package offers efficient classes and methods for handling boolean and skewed boolean vectors, fast integer sorting and set operations, and foundational tools for range indexing and data compression.
bit64	4.6.0-1	The 'bit64' package provides a way to handle serializable 64-bit signed integers in R, enabling precise management of large integer values, particularly for database keys and exact counting, while offering various methods for conversion and manipulation in data structures.
brew	1.0-10	This package provides a templating framework that combines text and R code for generating reports, using a syntax similar to that of various programming languages' templating systems.

Package	Version	Description
broom	1.0.8	The Broom package in R simplifies the process of summarizing, reporting, and visualizing statistical models by providing functions to extract key information about model components, overall model performance, and individual observations in a tidy format.
cachem	1.1.0	This package provides key-value stores that automatically manage cache size and object age through pruning, ensuring efficiency by adhering to defined constraints.
callr	3.7.6	This package enables computations to be executed in an isolated R process, ensuring that the current R environment remains unaffected.
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 efficient tests and assertions for frequent argument checks, leveraging C for improved performance and reduced execution time overhead.

Package	Version	Description
cli	3.6.5	This package provides a suite of tools for creating visually appealing command line interfaces (CLIs) using semantic elements and customizable themes, along with lower-level elements and support for ANSI colors and text styles.
clipr	0.8.0	This package provides simple utility functions for reading from and writing to the clipboards on Windows, OS X, and X11 systems.
commonmark	2.0.0	This package implements the CommonMark specification for converting markdown text into various formats such as HTML and LaTeX while also providing an XML representation of the markdown parse tree and supporting GitHub Flavored Markdown (GFM) extensions.
cowplot	1.2.0	This R package enhances the creation of publication-quality figures with 'ggplot2' by providing themes, alignment functions, annotation tools, and capabilities to combine plots with images, originally developed for internal use in the Wilke lab.

Package	Version	Description
cpp11	0.5.2	The 'cpp11' package offers a C++11 interface to R's C API, designed to ensure safety against long jumps and exceptions while adhering to standard R function semantics and supporting 'ALTREP' vector interactions.
crayon	1.5.3	The crayon package provides a way to generate colored terminal output using ANSI color codes, supporting features like nesting and custom styles, but is now superseded by the cli package for new projects.
curl	6.4.0	This R package provides bindings to 'libcurl' for executing customizable HTTP/FTP requests and handling responses through various methods, while also suggesting the 'httr2' package for more user-friendly web client capabilities.
datasetjson	0.3.0	This package allows users to read, create, and validate CDISC Dataset JSON files according to the specified schema standards.
desc	1.4.3	This package provides tools for reading, writing, creating, and manipulating DESCRIPTION files, facilitating the management of R packages.

Package	Version	Description
diffdf	1.1.1	This package provides functions for comparing two data frames, offering a detailed breakdown of their differences and utility tools to help identify the source of any discrepancies.
digest	0.6.37	The package provides a function 'digest()' to generate hash digests of various R objects using multiple algorithms, along with an 'hmac()' function for creating hash-based message authentication codes, though it is not intended for cryptographic applications.
dplyr	1.1.4	This package provides a fast and consistent tool for efficiently managing and processing both in-memory and out-of-memory data frame-like objects.
emmeans	1.11.2	This package provides tools to obtain estimated marginal means (EMMs) for various types of models, allowing for the computation of contrasts, trends, and slope comparisons, along with visualization options.
estimability	1.5.1	This package provides tools for assessing the estimability of linear functions of regression coefficients and includes methods to accurately handle non-estimable cases.

Package	Version	Description
evaluate	1.0.4	This package provides tools for parsing and evaluating R commands, facilitating the recreation of command line behavior within R scripts.
fansi	1.0.6	This package provides R users with string manipulation functions that properly handle and account for ANSI text formatting control sequences.
farver	2.1.2	The 'farver' package provides fast and efficient color space conversion and comparisons in R, utilizing C++ for improved performance over traditional methods.
fastmap	1.2.0	The `fastmap` package provides efficient implementations of key-value stores, stacks, and queues in R, utilizing C++ data structures to avoid memory leakage associated with R's global symbol table.
forcats	1.0.0	This package provides tools for reordering and modifying factor levels in R, allowing users to move specified levels to the front, order by first appearance, reverse levels, shuffle randomly, collapse rare levels, anonymize, and manually recode factors.
formatters	0.5.11	This package offers a framework for creating and formatting complex tables as ASCII strings, enabling easy display of structured data in a text-based format.

Package	Version	Description
fs	1.6.6	This package provides a cross-platform interface for performing various file system operations using the 'libuv' C library.
generics	0.1.4	The `generics` package in R offers a set of commonly used S3 generic functions to minimize package dependencies and conflicts.
ggplot2	3.5.2	'ggplot2' is an R package that enables users to create complex and customizable graphics by declaratively mapping data to visual aesthetics based on the principles of the Grammar of Graphics.
ggsurvfit	1.1.0	This package simplifies the creation of publication-ready time-to-event (survival) endpoint figures using modular functions that integrate seamlessly with 'ggplot2' for customization and enhancement.
glue	1.8.0	This package implements interpreted string literals that allow for clear and concise string interpolation, drawing inspiration from Python's and Julia's string formatting methods.
gtable	0.3.6	The 'gtable' package in R provides tools for creating and manipulating grid layouts of graphical objects (grobs), allowing users to easily arrange and combine them for complex visual compositions.

Package	Version	Description
haven	2.5.5	This package facilitates the import of foreign statistical formats into R using the embedded 'ReadStat' C library.
highr	0.11	This package offers syntax highlighting for R source code, supporting LaTeX and HTML output, and extends compatibility to other programming languages through the highlight package.
hms	1.1.3	This package provides an S3 class for representing and formatting time-of-day values, extending the functionality of the existing 'difftime' class in R.
htmltools	0.5.8.1	This package provides tools for generating and outputting HTML content efficiently.
huxtable	5.6.0	This package provides a user-friendly interface for creating and styling tables for data presentation, allowing exports to various formats like HTML, LaTeX, and Word, while offering features like cell spanning and regression table generation.
isoband	0.2.7	This package provides a high-performance C++ implementation for generating contour lines and polygons from regularly spaced elevation data grids.

Package	Version	Description
janitor	2.2.1	The janitor package in R streamlines data cleaning and formatting by enabling users to easily manage column names, generate frequency tables and crosstabs, and identify duplicate records, all while adhering to the tidyverse principles and enhancing user-friendliness for beginners.
jsonlite	2.0.0	The 'jsonlite' package provides efficient tools for parsing, generating, and manipulating JSON data in R, making it particularly useful for statistical data handling and web API interactions.
jsonvalidate	1.5.0	This package validates JSON data against specified JSON schemas using the 'is-my-json-valid' or 'ajv' libraries, supporting drafts 04, 06, and 07 of the JSON schema.
knitr	1.50	This package offers a versatile solution for generating dynamic reports in R by employing Literate Programming techniques.
labeling	0.4.3	This package offers a variety of algorithms for labeling axes in graphical representations.
lattice	0.22-7	Lattice is a high-level data visualization system in R designed for creating complex multi-panel plots and visualizing multivariate data with ease and flexibility.

Package	Version	Description
lifecycle	1.0.4	This package helps manage the life cycle of exported functions by providing shared conventions, documentation badges, and user-friendly deprecation warnings.
lubridate	1.9.4	The 'lubridate' package provides a user-friendly interface for parsing, manipulating, and performing algebraic operations on date-time and time-span data in R.
magrittr	2.0.3	This package introduces a forward-pipe operator, %>%, which facilitates command chaining by forwarding values or expression results into subsequent function calls or expressions, offering flexible right-hand side expression support.
MASS	7.3-65	The package provides functions and datasets that support the content and examples in Venables and Ripley's "Modern Applied Statistics with S" (4th edition), facilitating statistical analysis and modeling in R.

Package	Version	Description
Matrix	1.7-3	This package provides a comprehensive set of classes and efficient methods for handling various types of sparse and dense matrices, including general, symmetric, triangular, and diagonal forms, while supporting numeric, logical, and pattern entries, and leveraging optimized libraries like 'BLAS', 'LAPACK', and 'SuiteSparse'.
memoise	2.0.1	This package allows you to cache the results of a function, enabling faster subsequent calls with the same arguments by returning previously computed values.
metacore	0.2.0	This package provides an immutable container for storing metadata to enhance programming activities and the functionality of other tools within the clinical programming workflow.
metatools	0.1.6	This package utilizes metadata from 'metacore' objects to verify and construct associated metadata columns.
mgcv	1.9-3	This package implements generalized additive (mixed) models with various smoothing parameter estimation methods, supporting advanced features like Bayesian inference and a wide range of smoothers.

Package	Version	Description
mvtnorm	1.3-3	This package provides tools for computing multivariate normal and t probabilities, quantiles, random deviates, densities, and log-likelihoods for multivariate Gaussian models and Gaussian copulae, along with methods for handling interval-censored and exact data.
nlme	3.1-168	This package provides tools for fitting and comparing both Gaussian linear and nonlinear mixed-effects models to analyze complex data structures.
numDeriv	2016.8-1.1	This package provides methods for accurately calculating numerical first and second order derivatives using techniques such as Richardson's extrapolation and complex step differentiation, along with a simpler difference method for quick estimates and cross-checking.
patchwork	1.3.1	The 'patchwork' package for R enhances the 'ggplot2' plotting system by allowing users to easily combine multiple plots into complex layouts using simple mathematical operators.

Package	Version	Description
pharmaRTF	0.1.4	This R package provides an enhanced RTF wrapper that allows for the creation of formatted tables with advanced features and metadata, suitable for regulatory report submissions.
pillar	1.11.0	This package offers generics for formatting data columns with enhanced color options suitable for modern terminal displays.
pkgbuild	1.4.8	This package provides tools for building R packages by locating the necessary compilers and configuring the PATH for proper functionality across different platforms.
pkgconfig	2.0.3	This package allows users to set configuration options specific to individual packages, ensuring that changes apply only to the designated package without affecting others.
pkgload	1.4.0	The package facilitates rapid package development by simulating the installation and attachment process, enabling seamless iteration during development.
prettyunits	1.2.0	This package provides human-readable formatting for various quantities, including time intervals, byte sizes, p-values, and numerical values, making them more intuitive and visually appealing.

Package	Version	Description
processx	3.8.6	The ‘processx’ package provides tools for managing system processes in the background, allowing users to check their status, wait for completion, retrieve exit statuses, terminate processes, and read their standard output and error in a non-blocking manner.
progress	1.2.3	This package offers configurable progress bars for R that display various metrics such as percentage completed, elapsed time, and estimated completion time, and is compatible with multiple environments including terminals, RStudio, and Emacs.
ps	1.9.1	This package provides tools to list, query, and manipulate system processes across Windows, Linux, and macOS platforms.
purrr	1.1.0	This package provides a comprehensive and cohesive set of tools for functional programming in R, enabling efficient and effective management of functions and data manipulation.
r2rtf	1.1.4	This package enables the creation of production-ready Rich Text Format (RTF) tables and figures with flexible formatting options.

Package	Version	Description
R6	2.6.1	The package provides a way to create lightweight R6 classes that utilize reference semantics, allowing for public and private members and supporting inheritance without the complexity of S4 classes or the need for the methods package.
RColorBrewer	1.1-3	This package offers a variety of color schemes for maps and graphics, created by Cynthia Brewer and available at colorbrewer2.org.
Rcpp	1.1.0	The 'Rcpp' package facilitates seamless integration between R and C++ by providing R functions and C++ classes that allow for easy mapping of R data types to their C++ equivalents.
readr	2.1.5	The 'readr' package in R offers a fast and user-friendly approach to reading rectangular data formats such as CSV, TSV, and FWF, with robust parsing capabilities for varying data types and handling unexpected data changes gracefully.
readxl	1.4.5	This R package enables the import of Excel files (.xls and .xlsx) across Windows, Mac, and Linux platforms without requiring external dependencies.

Package	Version	Description
rematch	2.0.0	This package provides a simplified interface for the `regexpr` function, allowing users to easily extract matches and captured groups from regular expressions applied to character vectors.
renv	1.1.4	The 'renv' package for R facilitates project-specific dependency management by enabling users to create and manage local libraries, save their state in a lockfile, and restore libraries for improved project isolation, portability, and reproducibility.
rlang	1.1.6	This package provides a comprehensive toolbox for efficiently working with base types and core R features, including the condition system and key functionalities of the Tidyverse such as tidy evaluation.
roxygen2	7.3.2	The `roxygen2` package simplifies the creation of R package documentation by allowing users to write documentation inline with their code using specially formatted comments.
rprojroot	2.1.0	This package provides robust and flexible methods for constructing file paths relative to a defined project root directory, ensuring reliable access to project-related files.

Package	Version	Description
rtables	0.6.13	The ‘rtables’ package in R offers a flexible framework for creating complex, hierarchical reporting tables that support multi-level tabulations, grouping, and contextual summaries of data.
scales	1.4.0	This package provides tools for mapping data to graphical aesthetics, enabling automatic determination of breaks and labels for axes and legends in visualizations.
snakecase	0.11.1	This package provides a versatile and user-friendly solution for converting and formatting strings into various case styles, including snake and camel case.
stringi	1.8.7	The ‘stringi’ package provides a comprehensive set of tools for manipulating and processing character strings in R, including features for regex pattern searching, string generation, formatting, and Unicode handling, ensuring high performance and portability across different locales.
stringr	1.5.1	This package provides a cohesive and user-friendly interface for string manipulation by wrapping the functionalities of the ‘stringi’ package, ensuring consistency in function usage and handling of edge cases like NA values and zero-length vectors.

Package	Version	Description
survival	3.8-3	This package provides essential tools for survival analysis, including the creation of Surv objects, and techniques such as Kaplan-Meier curves, Aalen-Johansen curves for multi-state models, Cox regression, and parametric accelerated failure time models.
tibble	3.3.0	The package offers a 'tbl_df' class, known as 'tibble', which enhances data frame functionality with stricter validation and improved formatting.
tidyr	1.3.1	The 'tidyr' package provides tools for transforming datasets into tidy formats by facilitating pivoting, nesting, unnesting, and handling of missing values, ultimately aiding in the organization and analysis of data.
tidyselect	1.2.1	This package provides a framework for implementing selection functions that are consistent with the 'tidyverse' syntax, enabling developers to create similar functionalities in their own R packages.

Package	Version	Description
timechange	0.3.0	This R package provides efficient functions for manipulating date-time objects while handling time zones and daylight saving time, allowing for updates, modifications, rounding, and arithmetic operations on date-time components.
Tplyr	1.2.1	This package provides a straightforward tool for streamlining data manipulation tasks essential for generating clinical summaries, with an emphasis on traceability.
tzdb	0.5.0	This package offers an updated copy of the IANA Time Zone Database, providing a C++ interface for the 'date' library to facilitate comprehensive date and time manipulations in R, including time zone adjustments and calendar calculations.
utf8	1.2.6	This package facilitates the processing, validation, normalization, encoding, formatting, and displaying of international text encoded in 'UTF-8' (Unicode).
V8	6.0.4	The package provides an interface to the V8 JavaScript and WebAssembly engine, enabling the execution of JavaScript code from R.

Package	Version	Description
vctrs	0.6.5	This package introduces improved notions of prototype and size for consistent type coercion and size recycling, enhancing analysis of function interfaces through concepts of type- and size-stability.
viridisLite	0.4.2	The 'viridisLite' package provides color maps that enhance graph readability for individuals with color vision deficiencies, ensuring perceptually-uniform colors for both visual display and black-and-white printing, along with support for ggplot2 in R.
vroom	1.6.5	The 'vroom' package is designed for fast reading and writing of data files (such as CSV and TSV) by utilizing a quick indexing step and lazy data loading, allowing only the necessary data to be read.
withr	3.0.2	This package offers a set of functions that allow users to execute code with a temporarily modified global state in a safe manner, originally derived from the 'devtools' package.
xfun	0.52	This package provides a collection of miscellaneous functions that are commonly utilized across various packages maintained by Yihui Xie.

Package	Version	Description
xml2	1.3.8	This R package provides bindings to 'libxml2' for processing XML data with an easy-to-use interface that utilizes 'XPath' expressions, along with capabilities for XML schema validation.
xportr	0.4.3	This package provides tools for creating CDISC-compliant datasets and verifying their adherence to CDISC standards.
yaml	2.3.10	This R package provides an interface to the 'libyaml' library, enabling the parsing and emitting of YAML 1.1 data.
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, while supporting standard R data types and offering configurable handling of NULL and NA values.

9 Appendix

(insert text here or remove this section)

Legacy Data Conversion Plan and Report Appendix

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)