Analysis Data Reviewer's Guide

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Study CDISCPILOT01

ADRG Template Version ccyy-mm-dd

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. Other changes in the study conduct are not described in this study report due to the nature of this CDISC Pilot Project.

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 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 equivalence of ARM and TRTxxP is standard in clinical trial datasets, where ARM provides a descriptive label and TRTxxP provides a numeric representation of the same treatment groups.
- 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 allows for a comprehensive analysis of treatment effects based on both the intended and actual treatment assignments.

- 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.** 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 aligns with standard practices in clinical trial data analysis where screen failures are typically excluded from analysis datasets 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
Subject Level Analysis Dataset	ADSL			X			One observation per subject

6.2.1 5.2.1ADSL – Subject Level Analysis Dataset

(insert your text here)

(insert date imputation rules if applicable)

6.2.2 5.2.xDataset – 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	Macro Used

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	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.AVAL; ADAS.CHG

8.3 Open source R packages

Package	Version	Description
admiral	1.3.0	This R package provides tools for creating and managing Clinical Data Interchange Standards Consortium (CDISC) compliant Analysis Data Model (ADaM) datasets, essential for submitting New Drug or Biologics License Applications to the FDA.
admiraldev	1.3.1	The package provides utility functions for checking data, variables, and conditions in the 'admiral' framework, along with tools to assist developers in maintaining documentation and testing for 'admiral' and its extension packages.
assertthat	0.2.1	This package extends the functionality of `stopifnot()` by allowing users to declare pre- and post-conditions for their code, while providing informative error messages to help identify issues.
backports	1.5.0	This package provides re-implemented functions from R version 3.0.0 and later, allowing developers to utilize new features while maintaining compatibility with older R installations through conditional exports.
base64enc	0.1-3	This package offers flexible tools for handling base64 encoding in R, providing an enhanced alternative to the deprecated base64 package.

Package	Version	Description
bit	4.6.0	This package offers efficient classes and methods for handling boolean and skewed boolean vectors, as well as fast operations for sorting and manipulating integer sets, along with foundational tools for range indexing and data compression.
bit64	4.6.0-1	The 'bit64' package provides support for 64-bit signed integers in R, enabling precise handling of large integer values useful for database keys and exact counting, with specialized methods for coercion and various operations while being compatible with vectors, matrices, arrays, and data frames.
brew	1.0-10	This package provides a templating framework that facilitates the integration of text and R code for generating reports, utilizing a syntax akin to popular web templating languages.
broom	1.0.8	The Broom package in R simplifies the reporting and visualization of statistical models by providing functions to summarize model components, overall model statistics, and individual observation metrics within tidy tibbles.

Package	Version	Description
cachem	1.1.0	This package provides key-value stores that automatically manage memory by pruning objects based on specified size limits or age constraints.
callr	3.7.6	This package allows users to execute computations in a separate R process, ensuring that the current R session remains unaffected.
cellranger	1.1.0	This package provides helper functions for working with spreadsheets, specifically for handling cell range specifications in the “A1:D10” format.
checkmate	2.3.2	This package provides efficient argument checking through tests and assertions, utilizing C for optimal performance and minimal execution time overhead.
cli	3.6.5	This package provides a suite of tools for creating visually appealing command line interfaces (CLIs) using semantic elements, customizable themes, and lower-level CLI components, while supporting 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 environments.

Package	Version	Description
commonmark	2.0.0	This package utilizes the 'cmark' implementation to convert CommonMark markdown text into multiple 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 provides tools for creating publication-quality figures with ggplot2, including themes, alignment functions, and annotation capabilities, originally developed for internal use in the Wilke lab.
cpp11	0.5.2	The 'cpp11' package offers a safe and modern C++11 interface to R's C API, enhancing compatibility with R's semantics while supporting features like ALTREP vectors.
crayon	1.5.3	The crayon package provides colored terminal output for R, supporting ANSI color codes and allowing for easy combination, nesting, and creation of new styles, but is now superseded by the cli package for new projects.

Package	Version	Description
curl	6.4.0	This package provides bindings to 'libcurl' for making fully configurable HTTP/FTP requests, allowing responses to be processed in various ways including memory, disk, or streaming.
datasetjson	0.3.0	This package enables the reading, construction, and writing of CDISC Dataset JSON files while ensuring compliance with the associated Dataset JSON schema for clinical data interchange.
desc	1.4.3	This package provides tools for reading, writing, creating, and manipulating DESCRIPTION files, specifically designed for packages that handle other packages.
diffdf	1.1.1	This package provides functions to compare two data frames, highlighting differences and offering utilities to help diagnose discrepancies.
digest	0.6.37	This R package provides a function to create hash digests of assorted R objects using various algorithms, enabling easy comparison of objects and includes functionality for generating hash-based message authentication codes.

Package	Version	Description
dplyr	1.1.4	This package provides a fast and consistent tool for efficiently handling data frame-like objects, both in-memory and out-of-memory.
emmeans	1.11.2	This package facilitates the calculation of estimated marginal means (EMMs) for various statistical models, allowing users to compute contrasts, visualize results, and explore trends and comparisons of slopes.
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 correctly.
evaluate	1.0.4	This package provides parsing and evaluation tools that simplify the recreation of command line behaviors in R.
fansi	1.0.6	This package provides R string manipulation functions that accurately handle ANSI text formatting control sequences, ensuring proper text processing and representation.
farver	2.1.2	The 'farver' package provides efficient and fast color space conversion and comparison functionalities, implemented in C++, offering improvements over base R's `convertColor` function.

Package	Version	Description
fastmap	1.2.0	Fastmap is an R package that provides efficient data structures, such as key-value stores, stacks, and queues, while avoiding memory leakage issues associated with using environments for key-value storage.
forcats	1.0.0	This package provides helpers for reordering, modifying, and managing factor levels in R, allowing users to rearrange levels, collapse rare categories, anonymize data, and recode factors efficiently.
formatters	0.5.11	This package offers a framework for rendering complex tables into ASCII format, along with various formatters to convert values into display-ready strings.
fs	1.6.6	This package provides a cross-platform interface for performing file system operations, leveraging the capabilities of the 'libuv' C library.
generics	0.1.4	The `generics` package in R establishes a collection of commonly used S3 generics to minimize package dependencies and conflicts.
ggplot2	3.5.2	`ggplot2` is an R package that enables users to create complex graphics by declaratively mapping data variables to visual aesthetics, following the principles of the Grammar of Graphics.

Package	Version	Description
ggsurvfit	1.1.0	This package simplifies the creation of publication-ready survival endpoint figures by providing modular functions that integrate seamlessly with 'ggplot2' for customization and enhancement.
glue	1.8.0	This package provides an implementation of interpreted string literals, allowing for easy string interpolation and multi-line string capabilities, inspired by features from Python and Julia.
gtable	0.3.6	The 'gtable' package provides tools for creating and manipulating tables of graphical objects ('grobs') in R, allowing users to define grid layouts and easily combine and arrange these objects into complex visual compositions.
haven	2.5.5	The package facilitates the import of foreign statistical data formats into R using the embedded 'ReadStat' C library.
highr	0.11	This package offers syntax highlighting for R source code, supporting outputs in LaTeX and HTML, and can also highlight other programming languages through the use of the highlight package.

Package	Version	Description
hms	1.1.3	This package provides an S3 class for managing and formatting time-of-day values, utilizing the 'difftime' class for accurate time representation.
htmltools	0.5.8.1	This package provides tools for generating and outputting HTML content.
huxtable	5.6.0	This package creates customizable styled tables for data presentation, allowing export to various formats such as HTML, LaTeX, and Word, while offering features for manipulating cell styles, borders, and number formatting.
isoband	0.2.7	This package provides a fast C++ implementation for generating contour lines and polygons from regularly spaced elevation data grids.
janitor	2.2.1	The janitor package in R provides user-friendly functions for cleaning and formatting data frames, generating frequency tables and cross-tabulations, and identifying duplicate records, all while adhering to the tidyverse principles.
jsonlite	2.0.0	The 'jsonlite' package in R is a fast and efficient tool for parsing and generating JSON data, specifically designed for statistical applications and web API interactions, while also providing functionality for streaming, validating, and prettifying JSON.

Package	Version	Description
jsonvalidate	1.5.0	This package validates JSON data against JSON schemas using the Node.js libraries 'is-my-json-valid' or 'ajv', supporting drafts 04, 06, and 07 of JSON schema.
knitr	1.50	This package offers a versatile solution for generating dynamic reports in R by utilizing Literate Programming techniques.
labeling	0.4.3	This package offers a variety of algorithms for generating axis labels in graphical representations.
lattice	0.22-7	Lattice is a high-level data visualization system in R that focuses on multivariate data, offering both standard and flexible graphics capabilities inspired by Trellis graphics.
lifecycle	1.0.4	This package facilitates the management of exported functions by implementing shared conventions, documentation badges, and user-friendly deprecation warnings throughout their life cycle.
lubridate	1.9.4	The 'lubridate' package provides fast and user-friendly tools for parsing, manipulating, and performing algebraic operations on date-time and time-span objects in R, with a consistent syntax for easy usage.

Package	Version	Description
magrittr	2.0.3	This package introduces a forward-pipe operator, %>%, that allows for the chaining of commands by passing the result of an expression directly into the next function call, offering flexible support for various right-hand side expressions.
MASS	7.3-65	This R package provides functions and datasets that support the applications and concepts presented in the book “Modern Applied Statistics with S” by Venables and Ripley.
Matrix	1.7-3	This package provides a comprehensive hierarchy of sparse and dense matrix classes, along with efficient methods for matrix operations, leveraging optimized libraries like ‘BLAS’, ‘LAPACK’, and ‘SuiteSparse’.
memoise	2.0.1	This package caches the results of a function, allowing it to return previously computed values when called with the same arguments, thereby improving efficiency.
metacore	0.2.0	This package provides an immutable container that holds metadata to enhance programming activities and improve the functionality of other packages within the clinical programming workflow.

Package	Version	Description
metatools	0.1.6	This package utilizes metadata information from 'metacore' objects to verify and construct associated metadata columns.
mgcv	1.9-3	This package provides tools for fitting generalized additive (mixed) models and extensions, facilitating multiple smoothing parameter estimation and Bayesian inference, with support for various smoothers and distributions beyond the exponential family.
mvtnorm	1.3-3	This package provides tools for computing multivariate normal and t probabilities, quantiles, random deviates, and densities, along with log-likelihoods and score functions for multivariate Gaussian models and Gaussian copulae, specifically tailored for interval-censored and exact data.
nlme	3.1-168	The package enables users to fit and compare both Gaussian linear and nonlinear mixed-effects models for statistical analysis.

Package	Version	Description
numDeriv	2016.8-1.1	This package provides methods for calculating accurate numerical first and second order derivatives using techniques such as Richardson's extrapolation and complex step derivatives, along with a simpler difference method for quick calculations and cross-checking.
patchwork	1.3.1	The 'patchwork' package enhances the 'ggplot2' API by enabling the flexible composition and arrangement of multiple plots using intuitive mathematical operators.
pharmaRTF	0.1.4	This R package provides an enhanced RTF wrapper that allows users to export tables from existing R packages like 'Huxtable' or 'GT' while adding essential metadata and features for regulatory reports, such as multiple title levels, footnotes, landscape orientation, and customizable margins.
pillar	1.11.0	This package offers generics for formatting data columns with a wide array of colors suitable for modern terminal displays.
pkgbuild	1.4.8	This package offers functions for building R packages by locating necessary compilers across different platforms and configuring the PATH accordingly.

Package	Version	Description
pkgconfig	2.0.3	This package allows users to set configuration options that apply only to individual packages, ensuring that changes do not affect other packages.
pkgload	1.4.0	This package simulates the installation and attachment process of a package, facilitating rapid iteration during package development as a core feature of the 'devtools' package.
prettyunits	1.2.0	This package provides human-readable formatting for various quantities, including time intervals, byte sizes, p-values, colors, and general numerical representations.
processx	3.8.6	The 'processx' package provides tools for managing system processes in the background, allowing users to check the status, wait for completion, retrieve exit statuses, terminate processes, and read their standard output and error through non-blocking connections.

Package	Version	Description
progress	1.2.3	This package provides configurable progress bars for R applications, displaying information such as percentage completed, elapsed time, and estimated completion time, and is compatible with various environments including terminals, Emacs ESS, RStudio, Windows Rgui, and macOS R.app.
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.
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 R6 package provides a framework for creating lightweight reference classes in R that support public and private members, inheritance, and are simpler to use compared to R's S4 reference classes.
RColorBrewer	1.1-3	This package offers color schemes for maps and other graphics, created by Cynthia Brewer, as detailed on the ColorBrewer website.

Package	Version	Description
Rcpp	1.1.0	The 'Rcpp' package facilitates seamless integration of R and C++ by allowing R functions to interface with C++ classes, enabling efficient data type mapping and enhancing performance for new code and third-party library integration.
readr	2.1.5	The 'readr' package in R is designed to efficiently and accurately read rectangular data formats such as CSV, TSV, and FWF, while offering robust parsing capabilities to handle various data structures.
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.
rematch	2.0.0	This package provides a simplified interface to the `regexpr` function for extracting matches and captured groups from regular expressions applied to character vectors.
renv	1.1.4	`renv` is an R package that provides a toolkit for managing project-specific R libraries, enabling users to isolate, save, and restore package dependencies to enhance reproducibility and portability.

Package	Version	Description
rlang	1.1.6	This package provides a comprehensive set of tools for handling base types, leveraging core R features such as the condition system, and integrating essential 'Tidyverse' functionalities, particularly for tidy evaluation.
roxygen2	7.3.2	The 'roxygen2' package provides a streamlined way to generate R documentation, 'NAMESPACE' files, and collation fields using specially formatted comments directly in the code, facilitating easier maintenance and updates.
rprojroot	2.1.0	This package provides robust and flexible methods for constructing file paths relative to a project's root directory, which is identified by specific criteria, such as the presence of a designated regular file.
rtables	0.6.13	The 'rtables' package in R facilitates the creation of complex, hierarchical reporting tables by allowing users to declare multi-level tabulations and apply them to data with a flexible and convenient interface.
scales	1.4.0	This package facilitates the mapping of data to graphical aesthetics by offering tools for automatically generating breaks and labels for axes and legends.

Package	Version	Description
snakecase	0.11.1	This package provides a straightforward and adaptable solution for parsing and converting strings into various case formats, such as snake case and camel case, among others.
stringi	1.8.7	The 'stringi' package offers a comprehensive suite of tools for efficient manipulation and processing of character strings in R, including pattern searching, random string generation, case mapping, Unicode operations, and more, all while ensuring portability across different locales and platforms.
stringr	1.5.1	This package provides a user-friendly and consistent interface to the 'stringi' package for string manipulation in R, ensuring uniform handling of arguments, NA values, and seamless integration between functions.
survival	3.8-3	This R package provides essential survival analysis tools, including the creation of Surv objects, Kaplan-Meier and Aalen-Johansen curves, Cox regression models, and parametric accelerated failure time models.

Package	Version	Description
tibble	3.3.0	The package offers a 'tbl_df' class, known as a tibble, which provides enhanced data frame functionality with stricter validation and improved formatting for better data handling in R.
tidyr	1.3.1	The 'tidyr' package in R provides tools for creating tidy data by reshaping datasets, managing nested structures, extracting values from strings, and handling missing values.
tidyselect	1.2.1	This package provides a backend for implementing select-like functions in your own R packages, ensuring consistency with the 'tidyverse' selection interfaces.
timechange	0.3.0	This package provides efficient tools for manipulating date-time objects with features for time-zone management, daylight saving adjustments, and various date-time modifications such as rounding and component updating.
Tplyr	1.2.1	This package simplifies data manipulation for generating clinical summaries with a focus on traceability.

Package	Version	Description
tzdb	0.5.0	This package offers an updated IANA Time Zone Database along with a C++ interface for the 'date' library, facilitating comprehensive date and time manipulation in R, including time zone adjustments and calendar-specific calculations.
utf8	1.2.6	This package provides tools for processing, validating, normalizing, encoding, formatting, and displaying UTF-8 encoded international text using Unicode.
V8	6.0.4	This R package provides an interface to the V8 JavaScript engine, enabling users to execute JavaScript and WebAssembly code within R.
vctrs	0.6.5	This package provides tools for consistent type coercion and size recycling by introducing new notions of prototype and size, enhancing the analysis of function interfaces through type- and size-stability.
viridisLite	0.4.2	The 'viridisLite' package provides color maps that enhance graph readability for individuals with color blindness and are perceptually uniform for both color and black-and-white printing, along with offering bindings for use in 'ggplot2'.

Package	Version	Description
vroom	1.6.5	The 'vroom' package in R is designed for fast reading and writing of data files (such as CSV, TSV, and FWF) by utilizing an initial indexing step and lazy loading, allowing for efficient data processing with minimal resource usage.
withr	3.0.2	This package offers a collection of functions designed to safely and temporarily modify the global state in R, allowing users to run code with these modifications without affecting the overall environment.
xfun	0.52	This 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 processing XML data through a consistent interface that utilizes 'XPath' expressions, along with support for XML schema validation.
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 implements the 'libyaml' YAML 1.1 parser and emitter for R, enabling the reading and writing of YAML data conveniently.

Package	Version	Description
yyjsonr	0.1.21	This R package provides a fast parser, generator, and validator for converting between JSON, NDJSON, GeoJSON, and R objects, supporting standard data types and offering specialized handling for 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)