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. Changes to the protocol-specified analyses are described in the statistical analysis plan (Appendix 9).

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 (0, 50 cm2 [54 mg], and 75 cm2 [81 mg]). 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 endpoints.

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 clearly outlines the treatment groups, confirming that ARM and TRTxxP are used interchangeably to denote the same treatment assignments.
- 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 is consistent with ADaM standards, which recommend using both planned and actual 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.** This suggests that windowing was indeed applied in the analysis datasets to determine the appropriate analysis visits for subjects.
- 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 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 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	ADSL.ITTFL == 'Y'; ADLB.TRTPN %in% c(0, 81); ADLB.PARAMCD == 'GLUC'; ADLB.!is.na(AVISITN); ADLB1.AVISITN == 20; ADLB1.!is.na(CHG); ADLB1.!is.na(BASE); ADLB1.AVISITN == 0	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 Clinical Data Interchange Standards Consortium (CDISC) compliant Analysis Data Model (ADaM) datasets, facilitating the analysis and submission of data for New Drug and Biologics License Applications to the FDA.
admiraldev	1.3.1	The package provides utility functions for checking data, variables, and conditions in 'admiral' and its extension packages, while also offering additional tools for documentation, testing, and maintenance.
assertthat	0.2.1	This package enhances the functionality of stopifnot() by allowing developers to declare pre- and post-conditions with user-friendly error messages to help users quickly identify any issues in the code.
backports	1.5.0	This package provides backports of functions introduced or modified since R version 3.0.0, allowing users to access these features in older R installations while enabling package developers to selectively import these backports.

Package	Version	Description
base64enc	0.1-3	This package offers flexible tools for encoding and decoding base64 data, improving upon the features of the now-unmaintained base64 package.
bit	4.6.0	This package provides efficient classes and methods for handling boolean and skewed boolean vectors, along with fast integer sorting, set operations, and 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 data handling for large integers, especially for database keys and exact counting operations, while offering methods for coercion and various elementwise and summary functions.
brew	1.0-10	This package provides a templating framework that allows for the integration of text and R code to facilitate report generation, using a syntax similar to that of popular web templating engines.

Package	Version	Description
broom	1.0.8	The Broom package in R provides tools for summarizing and reporting key statistical information about models, allowing users to easily extract model components, overall model statistics, and individual observation details in tidy data format.
cachem	1.1.0	This package provides key-value stores that automatically manage memory by pruning entries based on size constraints or the age of the oldest object to ensure efficient cache management.
callr	3.7.6	This package allows users to conduct computations in an isolated R process, ensuring that the main R session remains unaffected.
cellranger	1.1.0	This package provides helper functions for working with spreadsheets, specifically for managing the A1:D10 style of cell range specification.
checkmate	2.3.2	This package is designed to perform frequent argument checks efficiently, utilizing C to minimize execution time overhead.

Package	Version	Description
cli	3.6.5	This package provides a comprehensive toolkit for creating visually appealing command line interfaces (CLIs) using semantic elements, customizable themes, and various lower-level 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.
commonmark	2.0.0	This package utilizes the 'cmark' reference implementation to convert markdown text into multiple formats such as HTML, LaTeX, and groff man, while also providing an XML representation of the markdown parse tree and supporting GFM extensions like tables and strikethrough text.
cowplot	1.2.0	This R package enhances 'ggplot2' by providing tools for creating publication-quality figures, including themes, plot alignment, complex arrangements, and easy annotation features.

Package	Version	Description
cpp11	0.5.2	The 'cpp11' package provides a C++11 interface to R's C API that aims to enhance safety, conform to R function semantics, and support ALTREP vectors, making it easier to work with R from C++.
crayon	1.5.3	The crayon package provides functionality for colored terminal output in R, supporting ANSI color codes and allowing for easy combination, nesting, and creation of new styles, though it is now superseded by the 'cli' package for new projects.
curl	6.4.0	This package provides bindings to 'libcurl' for performing fully configurable HTTP and FTP requests, allowing responses to be processed in various ways, while also suggesting the more user-friendly 'httr2' package for simplified web client tasks.
datasetjson	0.3.0	This package facilitates the reading, construction, and writing of CDISC Dataset JSON files while ensuring validation against the Dataset JSON schema.
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 to compare two data.frames in R, offering a detailed breakdown of differences and utility functions to help identify the source of discrepancies.
digest	0.6.37	The package provides a function 'digest()' for creating hash digests of various R objects using multiple algorithms, along with an 'hmac()' function for generating hash-based message authentication codes, primarily for easy object comparison rather than cryptographic purposes.
dplyr	1.1.4	This package provides a fast and consistent functionality for efficiently handling data frame-like objects, whether they're stored in memory or in external storage.
emmeans	1.11.2	This package facilitates the computation of estimated marginal means (EMMs) for various types of statistical models, enabling users to conduct contrasts, linear functions of EMMs, and visualize 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 correctly handling non-estimable cases.

Package	Version	Description
evaluate	1.0.4	This package provides tools for parsing and evaluating R expressions, facilitating the recreation of command line behavior in R.
fansi	1.0.6	This package provides R functions for manipulating strings that properly handle ANSI text formatting control sequences.
farver	2.1.2	The 'farver' package enables efficient and fast conversion between different colour spaces and comparisons, enhancing performance over R's built-in colour conversion tools.
fastmap	1.2.0	The package provides efficient implementations of various data structures, including a key-value store, stack, and queue, while preventing memory leakage associated with R's global symbol table through a C++-based approach.
forcats	1.0.0	This package provides tools for reordering and modifying factor levels in R, including features for repositioning levels, ordering them, reversing, shuffling, collapsing rare levels, anonymizing, and manual recoding.
formatters	0.5.11	This package offers a framework for creating and rendering complex tables as ASCII art, along with various formatters to convert values into display-ready strings.

Package	Version	Description
fs	1.6.6	This package provides a cross-platform interface for file system operations, utilizing the 'libuv' C library as its foundation.
generics	0.1.4	The `generics` package in R provides a set of commonly used S3 generics to simplify the creation of methods and reduce potential package dependencies and conflicts.
ggplot2	3.5.2	`ggplot2` is a powerful R package that enables users to create sophisticated 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 facilitates the creation of publication-ready time-to-event (survival) figures using modular functions that integrate seamlessly with 'ggplot2' for customization and enhancement.
glue	1.8.0	This package provides an implementation of interpreted string literals that allows for multiline string formatting, inspired by Python's and Julia's syntax.
gtable	0.3.6	The 'gtable' package in R simplifies the creation and manipulation of complex table layouts by defining a grob class that organizes graphical objects (grobs) within a customizable grid structure.

Package	Version	Description
haven	2.5.5	This package allows users to import foreign statistical file formats into R using the embedded ReadStat C library.
highr	0.11	This package enables syntax highlighting for R source code in LaTeX and HTML formats, with support for other programming languages through the highlight package.
hms	1.1.3	This package provides an S3 class designed for storing and formatting time-of-day values, utilizing the capabilities of the 'difftime' class.
htmltools	0.5.8.1	This package provides tools for generating and outputting HTML content efficiently.
huxtable	5.6.0	This package facilitates the creation of styled tables for data presentation, allowing for seamless export to various formats and easy customization of appearance and layout.
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 data, creating frequency tables, exploring duplicates, and formatting output, all while integrating seamlessly with the tidyverse framework.

Package	Version	Description
jsonlite	2.0.0	The ‘jsonlite’ package in R provides efficient tools for parsing and generating JSON data, making it ideal for statistical applications and web API interactions, while also supporting streaming, validation, and prettification of JSON.
jsonvalidate	1.5.0	This package validates JSON data against specified JSON schemas using the Node libraries ‘is-my-json-valid’ or ‘ajv’, supporting drafts 04, 06, and 07 of the JSON schema.
knitr	1.50	The package provides a versatile tool for dynamically generating reports in R through the use of 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 an advanced graphics package in R designed for creating complex and multi-dimensional data visualizations, heavily inspired by Trellis graphics.
lifecycle	1.0.4	This package facilitates the management of exported functions throughout their life cycle by providing shared conventions, documentation badges, and user-friendly deprecation warnings.

Package	Version	Description
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 objects in R.
magrittr	2.0.3	This package introduces a forward-pipe operator, %>%, that allows for seamless chaining of commands by forwarding values or results into subsequent function calls or expressions.
MASS	7.3-65	The package provides functions and datasets designed to support the textbook "Modern Applied Statistics with S" by Venables and Ripley, facilitating statistical analysis and modeling in R.
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 matrices with numeric, logical, or pattern entries, leveraging underlying libraries such as 'BLAS', 'LAPACK', and 'SuiteSparse'.
memoise	2.0.1	This package provides a mechanism to cache the results of a function, allowing for faster retrieval of previously computed values when called with the same arguments.

Package	Version	Description
metacore	0.2.0	This package creates an immutable container for metadata, enhancing programming efficiency and interoperability within clinical programming workflows.
metatools	0.1.6	This package utilizes metadata information from 'metacore' objects to verify and construct associated metadata columns.
mgcv	1.9-3	This R package provides tools for fitting generalized additive and mixed models, along with various extensions, using methods like restricted marginal likelihood and cross-validation, including support for Bayesian inference and diverse smoothing techniques.
mvtnorm	1.3-3	This package provides functions for computing multivariate normal and t probabilities, quantiles, random variates, densities, and log-likelihoods for multivariate Gaussian models and Gaussian copulas, with support for interval-censored and exact data.
nlme	3.1-168	This package facilitates the fitting and comparison of Gaussian linear and nonlinear mixed-effects models for analyzing complex data structures.

Package	Version	Description
numDeriv	2016.8-1.1	This package provides methods for accurately calculating first and second order numerical derivatives using Richardson's extrapolation, complex step derivatives, and a simple difference method for real scalar and vector-valued functions.
patchwork	1.3.1	The 'patchwork' package enhances the 'ggplot2' plotting system by allowing users to easily combine multiple plots into complex layouts using mathematical operators.
pharmaRTF	0.1.4	This R package provides an enhanced RTF wrapper that enables the inclusion of advanced metadata and features in R tables, catering to regulatory submission requirements such as multiple title levels, footnotes, landscape orientation, and margin control.
pillar	1.11.0	This package offers generics for formatting data columns with a wide array of colors compatible with modern terminal displays, enhancing the visual presentation of information.

Package	Version	Description
pkgbuild	1.4.8	This package provides essential functions for building R packages by locating the necessary compilers across various platforms and configuring the PATH for R to utilize them effectively.
pkgconfig	2.0.3	This package allows users to set configuration options that apply exclusively to individual packages without affecting others.
pkgload	1.4.0	The package streamlines the process of package installation and attachment, facilitating rapid iteration during package development.
prettyunits	1.2.0	This package provides human-readable formatting for various quantities, including time intervals, file sizes, p-values, colors, and numeric values, enhancing the usability and readability of data presentation.
processx	3.8.6	The 'processx' package provides tools for managing and interacting with background system processes in R, including functionalities for checking process status, waiting for completion, retrieving exit statuses, and handling output and error streams non-blockingly.

Package	Version	Description
progress	1.2.3	This R package offers configurable progress bars that display percentage, elapsed time, and estimated completion time in various environments including terminals, Emacs ESS, RStudio, and others, while also providing a C++ API compatible with or without Rcpp.
ps	1.9.1	This package allows users to list, query, and manipulate system processes across Windows, Linux, and macOS operating systems.
purrr	1.1.0	This package provides a comprehensive and consistent toolkit for functional programming in R, enabling users to apply functional programming principles efficiently.
r2rtf	1.1.4	This package facilitates the creation of production-ready Rich Text Format (RTF) tables and figures with a high degree of formatting flexibility.
R6	2.6.1	The package provides a lightweight system for creating reference classes in R, allowing for public and private members, inheritance, and easier use compared to R's built-in reference classes.

Package	Version	Description
RColorBrewer	1.1-3	This R package offers color schemes for maps and graphics, inspired by the designs of Cynthia Brewer, as detailed on the ColorBrewer website.
Rcpp	1.1.0	The 'Rcpp' package enables seamless integration of R and C++ by providing R functions and C++ classes that facilitate the conversion of R data types to C++ equivalents, allowing for enhanced performance and easier integration of third-party libraries.
readr	2.1.5	The 'readr' package in R offers a fast and user-friendly interface for reading rectangular data formats such as CSV, TSV, and fixed-width files, while ensuring robust parsing and error handling for diverse data types.
readxl	1.4.5	This R package provides the ability to import Excel files in both '.xls' and '.xlsx' formats across Windows, Mac, and Linux platforms without requiring external dependencies.
rematch	2.0.0	This package provides a simplified interface for extracting matches and captured groups from regular expressions applied to character vectors, leveraging the functionality of R's `regexpr` function.

Package	Version	Description
renv	1.1.4	'rENV' is a dependency management toolkit for R that enables the creation and management of project-specific libraries, allowing users to save and restore library states for enhanced portability and reproducibility of their projects.
rlang	1.1.6	This package provides a comprehensive toolbox for leveraging base R types and core features, including the condition system and Tidyverse functionalities like tidy evaluation.
roxygen2	7.3.2	The 'roxygen2' package streamlines the process of generating R documentation, NAMESPACE files, and collation fields using specially formatted comments directly within the code, ensuring that documentation remains easily maintainable and up-to-date.
rprojroot	2.1.0	This package provides robust and flexible mechanisms for constructing file paths relative to a project's root directory, identified by specific criteria, to ensure reliable file access within the project structure.

Package	Version	Description
rtables	0.6.13	The ‘rtables’ package in R facilitates the creation of complex, hierarchical reporting tables by enabling multi-level tabulations, flexible data grouping, and contextual summary computations within a user-friendly, pipe-able interface.
scales	1.4.0	This package facilitates the mapping of data to graphical aesthetics, allowing for automatic generation of breaks and labels for axes and legends in visualizations.
snakecase	0.11.1	This package provides a versatile and user-friendly tool for parsing and converting strings into various case formats, such as snake_case and camelCase.
stringi	1.8.7	The `stringi` package provides a comprehensive suite of tools for handling and processing character strings in R, including pattern matching, random string generation, case mapping, and Unicode normalization, all optimized for performance and portability across different locales.
stringr	1.5.1	This package provides a user-friendly set of consistent wrappers around the ‘stringi’ package for efficient string manipulation while ensuring uniform handling of missing values and compatibility between functions.

Package	Version	Description
survival	3.8-3	This R package provides essential tools for survival analysis, including the creation of Surv objects, Kaplan-Meier and Aalen-Johansen curves, Cox proportional hazards models, and parametric accelerated failure time models.
tibble	3.3.0	This package offers a 'tbl_df' class, also known as a tibble, which enhances data frames with more rigorous checks and improved formatting for better usability in R.
tidyr	1.3.1	The 'tidyr' package provides tools for creating tidy data by reshaping datasets, managing hierarchical structures, and handling missing values, ensuring that each column represents a variable, each row an observation, and each cell a single value.
tidyselect	1.2.1	This package provides a backend for implementing select-like functions in R packages, ensuring consistency with other '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 time considerations, and various date-time adjustments and modifications.

Package	Version	Description
Tplyr	1.2.1	This package provides a streamlined tool for manipulating data to facilitate the creation of clinical summaries with an emphasis on traceability.
tzdb	0.5.0	This package provides an up-to-date IANA Time Zone Database and a C++ interface for the 'date' library, facilitating easy handling of dates, date-times, and time zone manipulations in R.
utf8	1.2.6	This package processes and outputs UTF-8 encoded international text, facilitating input validation, normalization, encoding, formatting, and display of Unicode characters.
V8	6.0.4	This R package provides an interface to the V8 JavaScript engine, allowing users to execute JavaScript and WebAssembly code within R.
vctrs	0.6.5	This package introduces new concepts of prototype and size to ensure consistent type coercion and size recycling in R, enhancing the analysis of function interfaces with a focus on type and size stability.

Package	Version	Description
viridisLite	0.4.2	The ‘viridis’ package in R provides color maps that enhance graph readability for individuals with color blindness and are perceptually uniform, featuring bindings for both discrete and continuous color scales in ‘ggplot2’.
vroom	1.6.5	The ‘vroom’ package in R is designed for fast reading and writing of data files, such as CSV and TSV, by employing lazy loading and parallel processing techniques to efficiently handle large datasets.
withr	3.0.2	This package provides a set of functions for safely and temporarily modifying the global state in R while running code, originally derived from the ‘devtools’ package, with minimal dependencies.
xfun	0.52	This package provides a collection of miscellaneous functions that are often utilized in other packages maintained by Yihui Xie.
xml2	1.3.8	This R package provides bindings to ‘libxml2’ for handling XML data through a user-friendly interface that incorporates ‘XPath’ expressions, along with support for XML schema validation.

Package	Version	Description
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, allowing users to read and write YAML files efficiently.
yyjsonr	0.1.21	This R package provides a fast and efficient way to parse, generate, and validate JSON, NDJSON, and GeoJSON data, converting them to and from R objects while supporting standard data types and various data containers.

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)