

Analysis Data Reviewer's Guide

Study CDISCPilot01

ADRG Template Version ccyy-mm-dd

Introduction

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 individual study. In addition, this document provides a summary of ADaM conformance findings.

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

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

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.

Protocol Description

Protocol Number and Title

Protocol Number: CDISCPilot01

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

Protocol Versions:

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

Protocol Designin Relation to ADaM Concepts

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]), and to document the safety profile of the xanomeline TTS.

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.

Number of Subjects Planned in Total and by Group

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

Study Design Schema

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

Analysis Considerations Related to Multiple Analysis Datasets

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

Variable Name	Variable Description
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)

Treatment Variables

- ARM versus TRTxnP Are the values of ARM equivalent in meaning to values of TRTxnP? (insert additional text here or a mapping table or a figure)
- ACTARM versus TRTxnA If TRTxnA is used, then are the values of ACTARM equivalent in meaning to values of TRTxnA? (insert additional text here or a mapping table or a figure)
- Use of ADaM Treatment Variables in Analysis Are both planned and actual treatment variables used in analysis? (insert additional text here or a mapping table or a figure)
- Use of ADaMTreatment Grouping Variables in Analysis Are both planned and actual treatment grouping variables used in analysis? (insert additional text here or a mapping table or a figure)

Subject Issues that Require Special Analysis Rules

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

Use of Visit Windowing, Unscheduled Visits, and Record Selection

- Was windowing used in one or more analysis datasets? (insert additional text here)
- Were unscheduled visits used in any analyses? (insert additional text here)
- Additional Content of Interest <SeeADRG Completion Guidelines for additional content of interest, and include text here or remove this text>.

Imputation/Derivation Methods

- If date imputation was performed, were there rules that were used in multiple analysis datasets? (insert additional text here)
- Additional Content of Interest <SeeADRG Completion Guidelines for additional content of interest, and include text here or remove this text >.

Analysis Data Creation and Processing Issues

Split Datasets

(insert your text or table here or indicate there are no split datasets)

Data Dependencies

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

Intermediate Datasets

(insert your text here or indicate there are no intermediate datasets)

Analysis Dataset Descriptions

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?
- Are data taken from an ongoing study?
- Do the analysis datasets support all protocol-and statistical analysis plan-specified objectives? (insert additional text here)

- 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).

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

5.2.1ADSL – Subject Level Analysis Dataset

(insert your text here)

(insert date imputation rules if applicable)

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.

Note that the header numbering in this section is NOT automatic. The header number for each dataset must be manually edited.)

Data Conformance Summary

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 additional compliance evaluation information:

(Text here)

Issues Summary

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

Dataset	Diagnostic Message	Severity	Count	Explanation

Submission of Programs

All programs for analysis datasets and primary and secondary efficacy results are submitted. They were all created on a platform using The internal reference date used to create dates in ADaM datasets is.

ADaM Programs

Program Name	Output	Macro Used

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		ADLB.TRTPN IN (0, 81) AND ADLB.PARAMCD == 'GLUC' AND NOT ISNA(ADLB.AVISITN); ADLB.AVISITN == 20; ADLB.AVISITN == 0; ADLB.AVISITN == 20 AND NOT ISNA(ADLB.CHG) AND NOT ISNA(ADLB.BASE)	ADSL.STUDYID; ADSL.USUBJID; ADLB.BASE; ADLB.TRTPN; ADLB.PARAMCD; ADLB.AVISITN; ADLB.CHG; ADLB.AVAL
tlf-kmplot.r	pdf/tlf-kmplot-pilot5.pdf	ADSL.SAFFL == 'Y'; ADSL.STUDYID == 'CDISCPILOT01'; ADTEE.PARAMCD == 'TTDE'; ADTEE.STUDYID == 'CDISCPILOT01'	ADSL.STUDYID; ADSL.USUBJID; ADSL.TRT01A; ADTEE.AVAL; ADTEE.CNSR; ADTEE.PARAM; ADTEE.PARAMCD

r_file	outputs	filters	variables
tlf-primary.r	tlf-primary-pilot5.rtf	ADAS.EFFFL == 'Y'; ADAS.ITTFL == 'Y'; ADAS.PARAMCD == 'ACTOT'; ADAS.ANL01FL == 'Y'; ADSL.EFFFL == 'Y'; ADSL.ITTFL == 'Y'	ADAS.EFFFL; ADAS.ITTFL; ADAS.PARAMCD; ADAS.ANL01FL; ADAS.AVAL; ADAS.AVISITN; ADAS.CHG; ADSL.TRTP; ADSL.TRT01P

Open source R packages

Package	Version	Description
admiral	1.3.0	This R package provides tools for programming Clinical Data Interchange Standards Consortium (CDISC) compliant Analysis Data Model (ADaM) datasets, essential for regulatory submissions to the FDA.
admiraldev	1.3.1	The package provides utility functions for checking data, variables, and conditions used in ‘admiral’ and its extension packages, along with additional tools for documentation, testing, and maintenance assistance for developers.
assertthat	0.2.1	This package enhances the functionality of stopifnot() by allowing users to easily define pre and post conditions for their code, while providing clear and user-friendly error messages when those conditions are not met.

Package	Version	Description
backports	1.5.0	This package provides re-implementations of functions introduced or modified since R version 3.0.0 as backports, allowing developers to selectively use new functionality while maintaining compatibility with older R installations.
base64enc	0.1-3	This package offers flexible tools for handling base64 encoding, surpassing the capabilities of the now-unmaintained base64 package.
bit	4.6.0	This package provides efficient methods for handling boolean and skewed boolean vectors, performing fast integer sorting and set operations, and includes foundational tools for range indexing and chunked processing.
bit64	4.6.0-1	The ‘bit64’ package provides support for 64-bit signed integers in R, enabling precise handling of large numbers, particularly for database keys and exact counting, while ensuring compatibility with various data structures and methods.
brew	1.0-10	This package implements a templating framework that allows users to seamlessly integrate text and R code for generating reports, using a syntax similar to various popular templating languages.

Package	Version	Description
broom	1.0.8	The broom package in R streamlines the summarization of statistical models by providing functions that extract model components, overall fit metrics, and individual observation details, making it easier to report results and create visualizations from multiple models.
cachem	1.1.0	This package provides key-value store functionality with automatic pruning capabilities, allowing users to impose constraints on total size and the age of the oldest object while automatically managing cache contents.
callr	3.7.6	This package allows users to perform computations 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 for handling cell range specifications in the “A1:D10” format.
checkmate	2.3.2	This package provides tools for efficiently performing frequent argument checks, with a significant portion of its code implemented in C to ensure minimal impact on execution time.

Package	Version	Description
cli	3.6.5	This package provides a comprehensive suite of tools for creating visually appealing command line interfaces (CLIs) using semantic elements, custom theming, and ANSI color support, along with lower level CLI components.
clipr	0.8.0	This package provides simple utility functions for reading from and writing to the clipboard across Windows, OS X, and X11 systems.
commonmark	2.0.0	This package provides a CommonMark-compliant Markdown parser that converts Markdown text into various formats such as HTML, LaTeX, and groff man, while also exposing the parse tree in XML and supporting GitHub Flavored Markdown (GFM) extensions like tables and strikethrough.
cowplot	1.2.0	This package enhances the creation of publication-quality figures using ‘ggplot2’ by providing themes, alignment and arrangement functions, and annotation tools, originally developed for internal use in the Wilke lab.
cpp11	0.5.2	The ‘cpp11’ package offers a C++11 interface to R’s C API, ensuring safety against long jumps and exceptions while conforming to R function semantics and supporting ‘ALTREP’ vectors.

Package	Version	Description
crayon	1.5.3	The crayon package provides colored terminal output with ANSI support, allowing for customizable styles and highlighting, and is intended for use in R projects, though it is now superseded by the ‘cli’ package.
curl	6.4.0	This package provides bindings to ‘libcurl’ for performing fully configurable HTTP/FTP requests, enabling users to process responses in various ways, including in memory, on disk, or through streaming.
datasetjson	0.3.0	This package enables users to read, build, and export CDISC Dataset JSON files while ensuring compliance with the Dataset JSON schema for validation purposes.
desc	1.4.3	This package provides tools to read, write, create, and manipulate DESCRIPTION files, facilitating the management of R packages.
diffdf	1.1.1	This package provides functions to compare two data.frames, delivering a comprehensive analysis of their differences and offering utilities to identify the sources of discrepancies.

Package	Version	Description
digest	0.6.37	This R package provides a function <code>digest()</code> for generating hash digests of various R objects using multiple algorithms, facilitating easy comparison of objects, along with an <code>hmac()</code> function for creating hash-based message authentication codes, while not intended for cryptographic use.
dplyr	1.1.4	This package provides a rapid and reliable framework for efficiently handling data frames and similar objects, capable of processing data both in-memory and out-of-memory.
emmeans	1.11.2	The package enables the estimation of marginal means for various models, facilitating contrasts, trends, and slope comparisons, while providing visualization tools for these analyses.
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.
evaluate	1.0.4	This package provides tools for parsing and evaluating R expressions, enabling users to replicate command line behaviors within their R scripts.

Package	Version	Description
fansi	1.0.6	This package provides functions for string manipulation in R that specifically handle ANSI text formatting control sequences, ensuring accurate processing of styled text.
farver	2.1.2	The ‘farver’ package facilitates fast color space conversion and comparisons in R, offering efficient functionalities for working with various color representations, implemented in C++ for improved performance over traditional methods.
fastmap	1.2.0	Fastmap provides an efficient implementation of key-value stores, stacks, and queues in R, utilizing C++ data structures to prevent memory leakage associated with traditional environments.
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 order, shuffle randomly, collapse rare levels, anonymize, and manually recode levels.
formatters	0.5.11	This package offers tools for creating and formatting complex ASCII tables, 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 that leverages the ‘libuv’ C library for enhanced performance and consistency.
generics	0.1.4	The “generics” package in R offers a set 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 to visual aesthetics based on the principles outlined in “The Grammar of Graphics.”
ggsurvfit	1.1.0	This package facilitates the creation of publication-ready time-to-event (survival) endpoint figures using modular functions that seamlessly integrate with ‘ggplot2’ for customization and enhancement.
glue	1.8.0	This package provides an implementation of interpreted string literals, allowing for easy embedding of expressions and multiline text, modeled after features from Python and Julia.
grid	4.1.0	The ‘grid’ package provides tools for creating and manipulating complex layouts of graphical objects (grobs) in a grid format, enabling the construction of intricate visual compositions.

Package	Version	Description
haven	2.5.5	The package allows users to import foreign statistical data 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, and also supports other programming languages through the highlight package.
hms	1.1.3	This package implements an S3 class designed for storing and formatting time-of-day values, utilizing the capabilities of the ‘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, with options for exporting to various formats such as HTML, LaTeX, and Word, while also supporting advanced features like cell spanning and regression table generation.
isoband	0.2.7	This package provides a fast C++ implementation for generating contour lines (isolines) and contour polygons (isobands) from regularly spaced elevation data grids.

Package	Version	Description
janitor	2.2.1	The janitor package in R provides user-friendly functions for formatting data frame column names, generating frequency tables and crosstabs, exploring duplicate records, and producing well-formatted tabulation results, all while adhering to the tidyverse principles.
jsonlite	2.0.0	The ‘jsonlite’ package provides a fast and flexible framework for parsing and generating JSON data in R, making it particularly useful for statistical applications 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 tool for generating dynamic reports in R using Literate Programming techniques.
labeling	0.4.3	This package offers a variety of algorithms for generating and formatting axis labels in R visualizations.
lattice	0.22-7	Lattice is a high-level data visualization system in R that excels in creating complex, multivariate graphics inspired by Trellis graphics, while balancing ease of use with flexibility for diverse visualization needs.

Package	Version	Description
lifecycle	1.0.4	This package simplifies the management of exported functions by providing conventions, documentation badges, and user-friendly deprecation warnings throughout their life cycle.
lubridate	1.9.4	The ‘lubridate’ package provides user-friendly functions for parsing, manipulating, and performing algebraic operations on date-time and time-span objects, with a consistent and memorable syntax.
magrittr	2.0.3	This package introduces a forward-pipe operator, <code>%>%</code> , which facilitates command chaining by passing values or expression results directly into subsequent function calls or expressions.
MASS	7.3-65	The package provides functions and datasets that support the concepts and methods presented in the book “Modern Applied Statistics with S” by Venables and Ripley, facilitating statistical analysis and modeling.
Matrix	1.7-3	This package provides a comprehensive suite of classes for sparse and dense matrices—including general, symmetric, triangular, and diagonal types—with efficient methods for manipulation and operations, leveraging low-level libraries like ‘BLAS’, ‘LAPACK’, and ‘SuiteSparse’.

Package	Version	Description
memoise	2.0.1	The package provides functionality to cache the results of a function, enabling it to return previously computed values when called again with the same arguments.
metacore	0.2.0	This package provides an immutable container for holding metadata, enhancing programming activities and supporting the functionality of other packages within the clinical programming workflow.
metatools	0.1.6	This package utilizes metadata information from ‘metacore’ objects to validate and construct associated metadata columns.
mgcv	1.9-3	This package provides tools for fitting generalized additive (mixed) models and their extensions, enabling multiple smoothing parameter estimation, Bayesian inference, and support for various distributions and smoothers.
mvtnorm	1.3-3	This R package provides tools for computing probabilities, quantiles, random deviates, and densities for multivariate normal and t distributions, as well as log-likelihood functions for multivariate Gaussian models and copulas, supporting both interval-censored and exact data.

Package	Version	Description
nlme	3.1-168	This package facilitates the fitting and comparison of both Gaussian linear and nonlinear mixed-effects models for statistical analysis.
numDeriv	2016.8-1.1	This R package provides various methods for accurately calculating first and second order numerical derivatives, utilizing techniques such as Richardson's extrapolation and complex step derivatives, along with a simpler difference method for quick cross-checks.
patchwork	1.3.1	The 'patchwork' package extends the 'ggplot2' API to facilitate the complex composition of multiple plots through the use of mathematical operators, enabling users to easily combine and arrange plots in various layouts.
pharmaRTF	0.1.4	This R package provides an enhanced wrapper for generating RTF documents with advanced formatting capabilities, including multiple title levels, footnotes, and customizable layout options, specifically designed for regulatory submission reports created with existing R table packages like 'Huxtable' or 'GT'.

Package	Version	Description
pillar	1.11.0	This package offers generics for formatting data columns with a comprehensive array of colors, enhancing the visual appeal in modern terminal environments.
pkgbuild	1.4.8	This package provides essential functions for building R packages by locating the necessary compilers for various platforms and configuring the system PATH accordingly.
pkgconfig	2.0.3	This package allows users to set configuration options specifically for individual packages, ensuring that these options only affect the specified package without impacting others.
pkgload	1.4.0	The package facilitates the simulation of installing and attaching R packages, enabling efficient development and rapid iteration within the ‘devtools’ framework.
prettyunits	1.2.0	This package provides a user-friendly way to format and present various quantities, including time intervals, bytes, p-values, colors, and numerical values, in a more human-readable format.

Package	Version	Description
processsx	3.8.6	The ‘processsx’ package provides tools to manage and interact with system processes in the background, allowing users to check their status, wait for completion, retrieve exit statuses, terminate processes, and handle their standard output and error streams.
progress	1.2.3	This package provides customizable progress bars for R that display percentage, elapsed time, and estimated completion time, functioning across various platforms and integrating with a C++ API.
ps	1.9.1	This package allows users to list, query, and manipulate all system processes across Windows, Linux, and macOS platforms.
purrr	1.1.0	This package provides a comprehensive and cohesive suite of tools for functional programming in R, enabling users to efficiently apply functional paradigms to their data processing and analysis tasks.
r2rtf	1.1.4	This package allows users to create production-ready Rich Text Format (RTF) tables and figures with flexible formatting options.

Package	Version	Description
R6	2.6.1	The package facilitates the creation of lightweight R6 classes, which feature reference semantics, support for public and private members, and inheritance, without the complexity of S4 classes.
RColorBrewer	1.1-3	This R package provides color schemes for maps and other graphics, designed by Cynthia Brewer, to enhance visual representation and readability.
Rcpp	1.1.0	The ‘Rcpp’ package enables seamless integration between R and C++ by providing R functions and C++ classes that allow for efficient data type mapping and the utilization of third-party libraries.
readr	2.1.5	The ‘readr’ package in R offers a fast and user-friendly approach to reading and parsing various rectangular data formats, such as CSV, TSV, and fixed-width files, with robust handling of unexpected data variations.
readxl	1.4.5	This R package facilitates the import of both ‘.xls’ and ‘.xlsx’ Excel files across Windows, Mac, and Linux platforms, utilizing embedded libraries for seamless data access.

Package	Version	Description
rematch	2.0.0	This R package provides a simplified interface for extracting matches and captured groups from regular expressions applied to character vectors.
renv	1.1.4	renv is an R package that facilitates dependency management by allowing users to create and manage project-local libraries, save their state to a lockfile, and restore libraries for enhanced project isolation, portability, and reproducibility.
rlang	1.1.6	This package provides tools for working with base types, core R features such as the condition system, and key ‘Tidyverse’ functionalities including tidy evaluation.
roxygen2	7.3.2	The package automates the generation of Rd documentation, NAMESPACE files, and collation fields in R by using specially formatted comments within the code, streamlining the documentation process and keeping it aligned with code changes.
rprojroot	2.1.0	This package provides a system for managing file paths relative to a project’s root directory, ensuring robust and flexible file access based on specific criteria.

Package	Version	Description
rtables	0.6.13	The ‘rtables’ package in R facilitates the creation of complex multi-level reporting tables by modeling the tabulation process as hierarchical, tree-like structures, allowing for intricate grouping, splitting, and summary computations within the tables.
scales	1.4.0	This package provides tools for mapping data to graphical aesthetics, including automatic determination of axis and legend breaks and labels.
snakecase	0.11.1	This package provides a user-friendly tool for parsing and converting strings into various formats such as snake case and camel case.
stringi	1.8.7	The ‘stringi’ package provides a comprehensive set of fast and portable tools for string manipulation and processing, including pattern searching, random string generation, and Unicode handling, enhancing functionality across various locales and platforms.
stringr	1.5.1	This package provides a user-friendly interface with consistent functionality for string manipulation, leveraging the capabilities of the ‘stringi’ package while effectively handling ‘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, estimation of Kaplan-Meier and Aalen-Johansen curves, and implementation of Cox and parametric accelerated failure time models.
tibble	3.3.0	This package offers a ‘tbl_df’ class, known as a ‘tibble’, which enhances data frame functionality with stricter validation and improved formatting.
tidyverse	1.3.1	The ‘tidyverse’ package in R provides tools for creating tidy data by reshaping and organizing datasets, including functionalities for pivoting, nesting, unnesting, and handling missing values.
tidyselect	1.2.1	This package provides a backend for implementing select-like functions in R, ensuring consistent behavior with other ‘tidyverse’ selection interfaces.
timechange	0.3.0	This R package provides efficient tools for manipulating date-time objects, including time-zone adjustments, daylight saving time considerations, and various date-time component modifications.
Tplyr	1.2.1	This package streamlines data manipulation for generating clinical summaries with an emphasis on traceability.

Package	Version	Description
tzdb	0.5.0	This package provides an updated Time Zone Database from the IANA, along with a C++ interface for advanced date and date-time handling, facilitating easier integration for R packages.
utf8	1.2.6	This package provides tools for processing, validating, normalizing, encoding, formatting, and displaying UTF-8 encoded international text (Unicode).
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 offers tools for consistent type coercion and size recycling by introducing new concepts of prototype and size, which are linked to type- and size-stability for analyzing function interfaces.
viridisLite	0.4.2	The ‘viridisLite’ package provides color maps that enhance graph readability for individuals with color blindness and are perceptually uniform, along with ‘ggplot2’ bindings for both discrete and continuous color scales.

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, utilizing lazy loading to optimize performance by only reading the data that is needed.
withr	3.0.2	This package provides a collection of functions that allow users to safely and temporarily modify the global state of R code execution.
xfun	0.52	This package provides a collection of miscellaneous functions that are commonly utilized in various other packages maintained by Yihui Xie.
xml2	1.3.8	This package provides bindings to ‘libxml2’ for handling XML data through a user-friendly interface based on ‘XPath’ expressions, while also supporting XML schema validation.
xportr	0.4.3	This package provides tools for constructing CDISC-compliant datasets and verifying their compliance with CDISC standards.
yaml	2.3.10	This package provides an interface to the ‘libyaml’ YAML 1.1 parser and emitter for R, allowing users to easily read and write YAML files.

Package	Version	Description
yyjsonr	0.1.21	This package provides a fast JSON parser, generator, and validator that converts JSON, NDJSON, and GeoJSON data to and from R objects, supporting standard R data types while handling NULL and NA values.

Appendix

(insert text here or remove this section)

Legacy Data Conversion Plan and Report Appendix

Purpose

The purpose of this appendix is to document the traceability of key output 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 legacy analysis and ADaM data, and explains how ADaM represents the equivalent data.

Conversion Data Flow

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

Rationale:

(Text here)

Converted Data Summary

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.

Outstanding Issues

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