Analysis Data Reviewer’s Guide

Completion Guidelines

(for Open-source submissions)

These completion guidelines detail the procedure for completing the Analysis Data Reviewer's Guide (ADRG) for an open-source submission package intended for the FDA, specifically focusing on the use of R.

This guideline will focus on Section 7 of the ADRG, as this section addresses technical submission information, including the analysis software utilized, the environment, and the configuration pertinent to the submission.

# Section 7: Submission of Programs

Pertaining to the submission of programs, requires that all programs for analysis datasets and primary and secondary efficacy results be submitted using the specified software and configuration. When submitting using R, or any other open-source solution, please adhere to the following table structure:

For an R submission, the required fields include the programming language (R), the operating system platform (e.g., Windows XX-bit operating system and processor), the software version (e.g., R 4.2.3, 4.x, or future versions such as 5), and the initial date for the software. This initial date represents Time Zero, from which any dates or durations of time calculated using this software are generated. For R, Time Zero is January 1, 1970.

For R submissions, key details include:

|  |  |
| --- | --- |
| **Language** | R |
| **Operating System / Platform** | Windows 10 64-bit OS, x64-based processor |
| **Software** | R version, RStudio version (if used), RTools, WSL, Docker Desktop for Windows |
| **Initial Date (Time = 0) for Software** | January 1, 1970 |
| **R Package Management Tool** | Tool used to manage packages (Posit Package Manager) |

## 7.1 ADaM Programs

Section 7.1 requires a comprehensive listing of all utilized ADaM programs. This listing must include the program name, the resulting ADaM dataset, and, given the use of R, the specific package and functions incorporated within the ADaM programs.

List the program name, the ADaM dataset output, and the R packages and functions used.

|  |  |  |
| --- | --- | --- |
| **Program Name** | **Output** | **Functions** |
| adsl.r | adsl.xpt | {haven} : read\_xpt()  {admiral} : convert\_blanks\_to\_na(),  derive\_vars\_dt(), derive\_vars\_merged(),  derive\_var\_trtdurd()  {dplyr}: arrange(), distinct(), filter(),  mutate(), select(), group\_by(), summarise(),  left\_join(), slice() |

## 7.2 Analysis Output Programs

In Section 7.2, no major changes are required; you should still include the program name, the output number, the title of the output, and the input, which will be the ADAM datasets utilized by the program to generate the output.

List the program Name, Output number, Title, and the Input (ADaM, input files) datasets used.

|  |  |  |  |
| --- | --- | --- | --- |
| Program Name | Output Number | Title | Input |
| tlfdemographic.r | Table 14-2.01 | Summary of Demographic and Baseline Characteristics | ADSL |

## 7.3 Macro/Function Programs

Section 7.3 When submitting programming utilizing open-source languages, presenting a comprehensive list of all functions, including the purpose of each, can result in an excessively lengthy document. As the purpose of functions in open-source programming languages is readily available within the respective package manuals, it is recommended that for an open-source programming language submission, the following information be provided: a list of the packages utilized, their versions, a package description, the primary dependencies, and a classification of whether the package is Proprietary or Open-Source. Identifying the Proprietary versus Open-Source status is essential to inform the Health Authority reviewer that some programs may incorporate sponsor-developed packages, which may necessitate the inclusion of additional validation documentation within the study submission package.

For open-source submissions, list the packages used instead of individual functions and their purposes, as function details are in package manuals.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| R Package | Package Version | Package Description | Dependencies | Proprietary/Open-Source |
| pilot3utils | 0.0.2 | Utilities for the Pilot 3 Submission to the FDA | Imports: dplyr, emmeans, glue, stringr, tibble, tidyr | Proprietary (Identifies sponsor-developed code needing further validation) |
| admiral | 1.4.1 | A toolbox for programming CDISC compliant ADaM datasets in R. | Imports: (admiraldev (≥ 1.4.0), cli (≥ 3.6.2)) | Open-source |