

FDA/Center for Drug Evaluation and Research (CDER)
Central Document Room (CDR)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Re: R Consortium R Submission Pilot 3 (ADaM extension to Pilot 1)

Dear Sir/Madam:

This letter serves as an introduction to the R Consortium R Submission Pilot 3 (an ADaM extension to Pilot 1) focusing on the submission of ADaM data. The objective of this R submission Pilot 3 is to test the concept that an R-language based submission package is aligned with FDA requirements and meets the expectations of the FDA Staff, including assessing code review and analysis reproducibility. All submission materials and communications from this pilot will be shared publicly, with the aim of providing a working example for future R language based FDA submissions. This is an FDA-industry collaboration through the non-profit organization R Consortium.

The R Consortium R Submission Pilot 3 (an ADaM extension to Pilot 1) package follows the eCTD folder structure and contains the following module 1 and module 5 deliverables :

- m1
 - A cover letter
 - The analysis results that were reproduced in Pilot 3 reusing the R code from Pilot 1
- m5
 - SAS transport files (.xpt) of source SDTM from CDISC Pilot 1
 - SAS transport files (.xpt) from R generated ADaM data by R Consortium R Submission Pilot 3
 - R code to generate the 5 ADaM datasets which were used to generate the analysis results from the Pilot 1 R submission
 - R code to reproduce the 4 analysis results generated from the Pilot 1 R submission, which source the ADaMs generated by Pilot 3
 - renv-lock.txt file for Pilot 3 and open source R package installation for analysis reproducibility
 - An Analysis Data Reviewer's Guide (ADRG)

In this pilot, we aimed to provide a working example of R submission in eCTD format to the pharmaceutical industry in compliance with the FDA Electronic Submissions Gateway requirements. Based on the submission package, FDA Staff can review and reproduce submitted R codes. More specifically, we expect the FDA Staff to :

- Receive electronic submission package in eCTD format
- Install and load the proprietary R package (i.e. "pilot3") and open source R packages used in this submission, per instructions in the ADRG
- Reproduce the ADaM datasets and the analysis results
- Share potential improvements to the submission deliverables and processes via written communication

All data, code, material and communications from this pilot will be shared publicly.

Different open-source packages were used when generating each of these ADaM datasets to test wider use case scenarios. Evaluating FDA's acceptance of system/software validation evidence is not in the scope of this pilot.

On behalf of the R Consortium R Submission Working Group, we hope the R Submission Pilot 3 (an ADaM extension to Pilot 1) can establish a working example to guide the industry for future submission using the R language.

Kind regards,
R Consortium R Submission Pilot 3 Team