

R Adoption Series

# Review Experience with R based Submissions

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# Disclaimer

This presentation reflects the views of the author and should not be construed to represent FDA's views or policies.

# Outline

1. What is Important to FDA?
2. R based Submission
3. Findings / Issues
4. Recommendations

# What is Important to FDA? (In R based Submissions)

# Conformance



# Reproducibility



# Traceability



## Conformance

Follow FDA application submission guidance and meet requirements

- Study Data Technical Conformance Guide – Technical Specifications Documents
- CDISC
- Electronic Common Technical Document format (eCTD)
- Etc.

## Reproducibility

Obtain consistent results using the same data

## Traceability

Enable the understanding of the data's lineage and/or the relationship between an element and its predecessor(s)

# R based Submissions

# R Submission Working Group Pilot Project

## Pilot 1

(completed)

- To test an R-language based submission package can meet the needs and expectations of the FDA

## Pilot 2

(completed)

- To test a Shiny application created with the R-language can be bundled into a submission package and transferred to FDA

## Pilot 3

(Reviewing)

- To re-test the pilot 1 with ADaM datasets generated using R



# Application Review

## Clinical Trial Submission

- There have been a few SAS and R hybrid submissions.
- There have been some challenges in replicating the sponsor's computational environment.

# Findings / Issues

# R versions / R packages

- Different versions of R may not perform as desired.
- Switching between R versions in RStudio can be problematic.
- ‘renv’ package can create reproducible environments and manage package dependencies; however, it might not be ideal.

# Different Environments

- Different operating systems (Linux vs. Windows)
  - Different operating system may cause some differences.
  - In the Pilot review, some file names and file paths had to be changed.
- Warning messages may appear differently.
- In the 'renv' set up, the reviewer may need to select different options to proceed.

# Flexibility

- R offers greater flexibility.
  - Multiple ways to calculate values
  - Diverse packages
  - Different default settings for functions and representing missing data
- Shiny app's interactive features could be inappropriately used to enable p-hacking and for cherry picking.

# Recommendations

# For Future R based Submission,

- Let FDA know at the design stage.
- Use CRAN or a curated repository for sourcing packages.
- Use standard packages and minimize dependency on sponsor developed packages.
- Provide thorough documentation and detailed comments.

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