Learnings and Reflection from RvalHub Case Studies

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on behalf of the R Validation Hub, an R Consortium-funded ISC Working Group
Outline

1. Recap
2. White Paper
3. Case Studies
4. Breakout Rooms
It’s time to integrate PhaRma?
What is the R validation Hub?

- started by the PSI AIMS Special Interest Group
- R Consortium Working Group
- approx. 100 members; > 50 organizations

**Mission:** R Validation Hub is a cross-industry initiative whose mission is to enable the use of R by the Bio-Pharmaceutical Industry in a regulatory setting, where the output may be used in submissions to regulatory agencies.
Resources / Achievements

Website [www.pharmaR.org](http://www.pharmaR.org)
- White paper
- Blog posts
- Presentations at several conferences
- Case Studies
- ASA BIOP report publication

**Tools** available on GitHub / CRAN
- R Package **riskmetric**: provides a number of metrics to help quantify R package quality; led by Eric Milliman
- **riskassessment App**: Shiny Application for riskmetric package; led by Aaron Clark
R package riskmetric

library(riskmetric)
pkg_tbl <- pkg_ref(c("riskmetric", "utils", "ggplot2", "Hmisc", "survminer", "coxrobust"))

res <- pkg_tbl %>%
  pkg_assess() %>%
  pkg_score() %>%
  mutate(risk = summarize_scores(.))

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<tr>
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<th>version</th>
<th>license</th>
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https://cran.r-project.org/web/packages/riskmetric
Risk Assessment App

https://github.com/pharmaR/riskassessment
Partner Initiatives

• R Tables for Regulatory Submissions Working Group
  • Create tables that meet the requirements of FDA submission document standards

• R Submission Pilot WG
  • Focus on IT and platform challenges to make “all R” regulatory submissions

• Clinical Statistical Reporting in a Multilingual World
  • Seeks to provide a framework for assessing the fundamental differences for a particular statistical analysis across languages

• R/Pharma
  • Annual conference focus on the use of R in clinical drug development
White Paper

• Provides arguments that there is **minimal risk in using Core R** for regulatory analysis and reporting

• Suggests a pipeline for risk-based assessment of contributed R packages based on
  • Intended use
  • Type of implemented method
  • Maintenance quality
  • Community usage
  • Remediation and testing

https://www.pharmar.org/white-paper/
Assessing Package Accuracy

1. New R package
2. What is the package classification?
   - "Intended for Use"?
     - Yes: Continue
     - No: Reject Package
3. What is the package purpose?
   - Statistical package
     - Yes: Remediation/Testing
     - No: Import
4. Is the package maintained?
   - Yes: Remediation/Testing
   - No: Remediation/Testing
5. Is the package widely used?
   - Yes: Include within environment
   - No: Reject Package

https://www.pharmar.org/white-paper/
Case Studies

• R validation hub initiated a three-part presentation series on “case studies”
• Eight pharma companies participated a case series sharing different experiences on building a GxP framework with R
• Highlight aspects that were easy to implement which those which were more challenging.
• Recordings of these sessions are available on the R Validation minutes page.
• Discussion and exchange to be continued on GitHub, where you are welcome to contribute and learn from others.

https://github.com/pharmaR/case_studies
Case Studies: Common Themes

- All implementations follow the risk validation process for R packages as outlined in the white paper.
- Classification of package quality into high/medium/low or a binary high/low categorization, however the approach to the assessments themselves varies.
- High importance of test coverage as assessment metric.
- Trusted resources: R Foundation, thus core R (base and recommended packages) are treated as a collective of “low risk” packages; some organizations also trust Rstudio developments, i.e. tidyverse, etc.
- The majority focused risk assessments only on “Intended-for-Use” packages but several also ran metrics on the Imports.

https://github.com/pharmaR/case_studies
Case Studies: Differences in Approach

- Varied degrees of automation in risk classification and qualification i.e. either complete automation or no automation
- Different weights were assigned to the testing coverage and various suggested metadata metrics: acceptable threshold for test coverage ranges between 50-80% for low-risk packages
- Different risk remediation strategies have been applied:
  - some organizations will immediately introduce their own unit tests,
  - others restrict package use to only the tested subset of package functionality.

https://github.com/pharmaR/case_studies
Case Studies: Common Challenges

- R package assessment is a resource-intense activity
  - Time has proven to be a considerable challenge.
  - Ensuring R package reviewers have the right technical expertise
  - Alignment of different contributors across the organization: IT, Quality Assurance and with their own Statistics, Data Science, or Programming lines.
- Finding appropriate test datasets, test cases and expected model output
- Long-term management and maintenance as well as oversight of the risk-based package assessment process

https://github.com/pharmaR/case_studies
Breakout rooms (15mins)

Please select one of the following breakout rooms:

1) Package score thresholds (low, medium, or high vs accepted/rejected) and metric weights [Eric]
2) Repository for common packages and their metrics [Doug]
3) Sharing test data and test cases [Juliane]
4) Ensuring and documenting R package reviewers have the right technical expertise [Preetham]