

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

R validation Hub 2018

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

- 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(.))
```

package	version	license	export_help	has_vignettes	has_bug_reports_url	bugs_status	has_news
riskmetric	0.1.0.9001	NA	1	0	1	0.5667	0
utils	3.6.2	NA	0.996	1	0	0	0
ggplot2	3.2.1	NA	1	1	1	0.6333	1
Hmisc	4.3.1	NA	1	0	0	0	0
survminer	0.4.6	NA	1	1	1	0.2333	1
coxrobust	1.0	0	0	0	0	0	0

Risk Assessment App

The screenshot displays the Risk Assessment App interface, divided into two main sections: PACKAGE CONTROL PANEL and MAINTENANCE METRICS.

PACKAGE CONTROL PANEL:

- SELECT PACKAGE:** dplyr
- SELECT VERSION:** 1.0.7
- STATUS:** UNDER REVIEW
- RISK:** 0.14
- SELECT OVERALL RISK:** A slider ranging from Low to High, currently positioned at Low.
- SUBMIT DECISION:** A red button.
- WRITE OVERALL COMMENT:** A text input field.

MAINTENANCE METRICS:

- VIGNETTES:** 9 (Number of vignettes)
- NEWS CURRENT:** Yes (NEWS contains current version)
- SOURCE CONTROL:** [https://github.com/tidyverse/...](https://github.com/tidyverse/) (Package source control url)
- MAINTAINER:** Hadley Wickham <hadley@rstudio.com> (Package maintainers)
- REPORT BUGS:** [https://github.com/tidyverse/...](https://github.com/tidyverse/) (Public url to report bugs)
- DOCUMENTATION:** 99.7% (% of documented objects)
- NEWS FILE:** 1 (Number of NEWS files)
- WEBSITE:** [https://dplyr.tidyverse.org...](https://dplyr.tidyverse.org/) (Package public website)
- BUGS CLOSURE RATE:** 50% (% of the last 30 bugs closed)

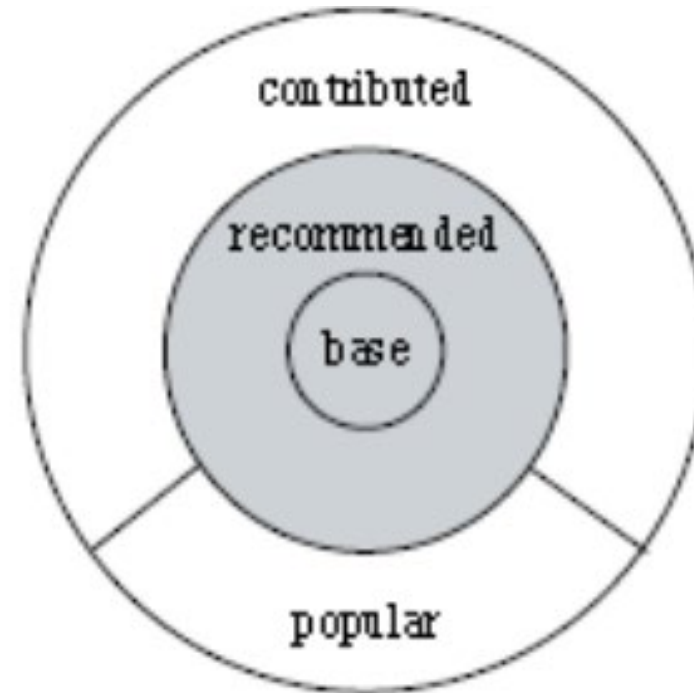
Partner Initiatives

- 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



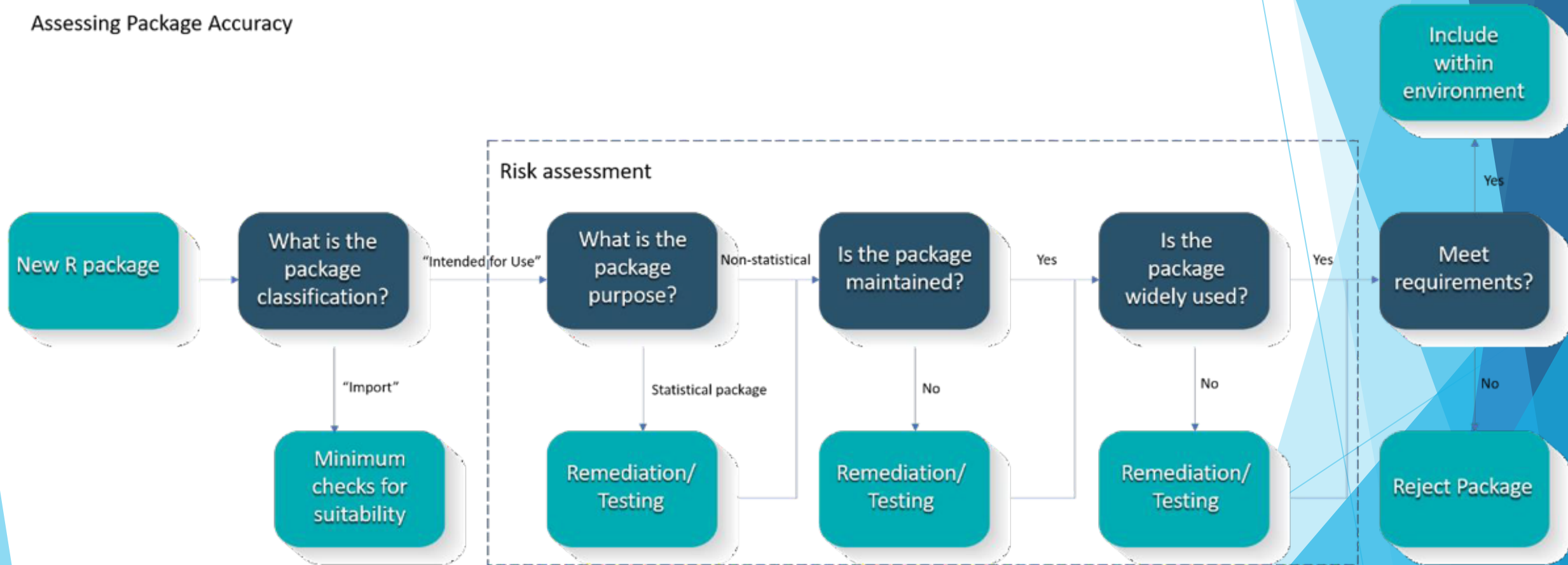
White Paper

- 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



White Paper

Assessing Package Accuracy



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.

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.

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.

Case Studies: Common Challenges

- R package assessment is a resource-intensive 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

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]