Learnings and Reflection from RvalHub Case Studies

Juliane Manitz, Doug Kelkhoff, Andy Nicholls, Lyn Taylor, Joseph Rickert, Paulo Bargo, Keaven Anderson, Eric Milliman, Aaron Clark and Preetham Palukuru

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

R Validation Hub

Outline

1. Recap
2. White Paper
3. Case Studies
4. Breakout Rooms

R validation Hub 2018

R Validation Hub

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.

R Validation Hub

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

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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

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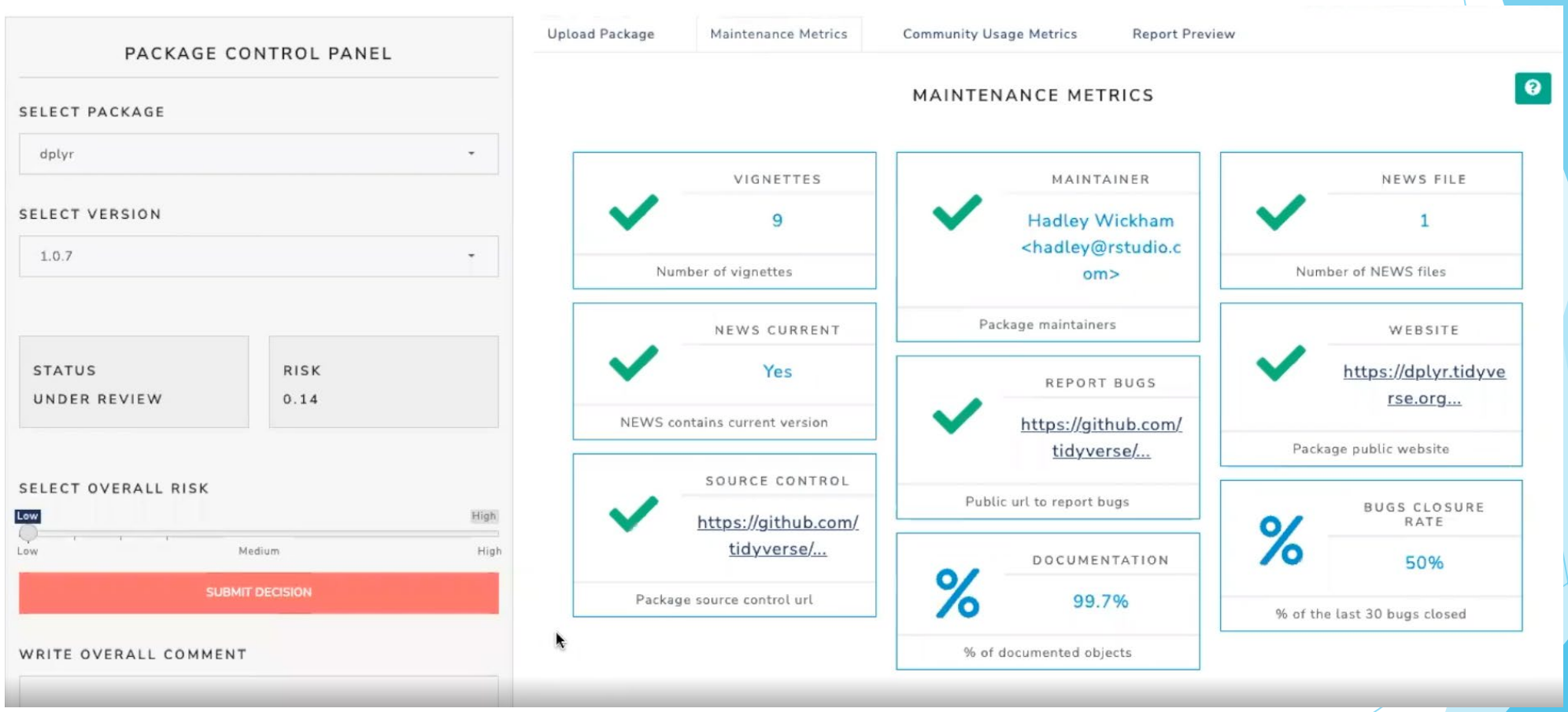
https://cran.r-project.org/web/packages/riskmetric

Risk Assessment App



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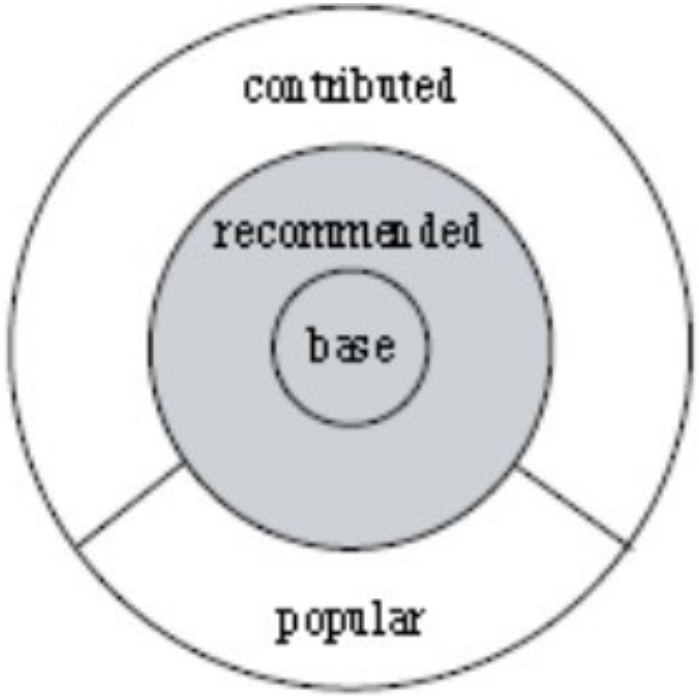
https://github.com/pharmaR/riskassessment

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
- Comparing Analysis Method Implementations in Software (CAMIS)
  - Seeks to provide a framework and repository 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



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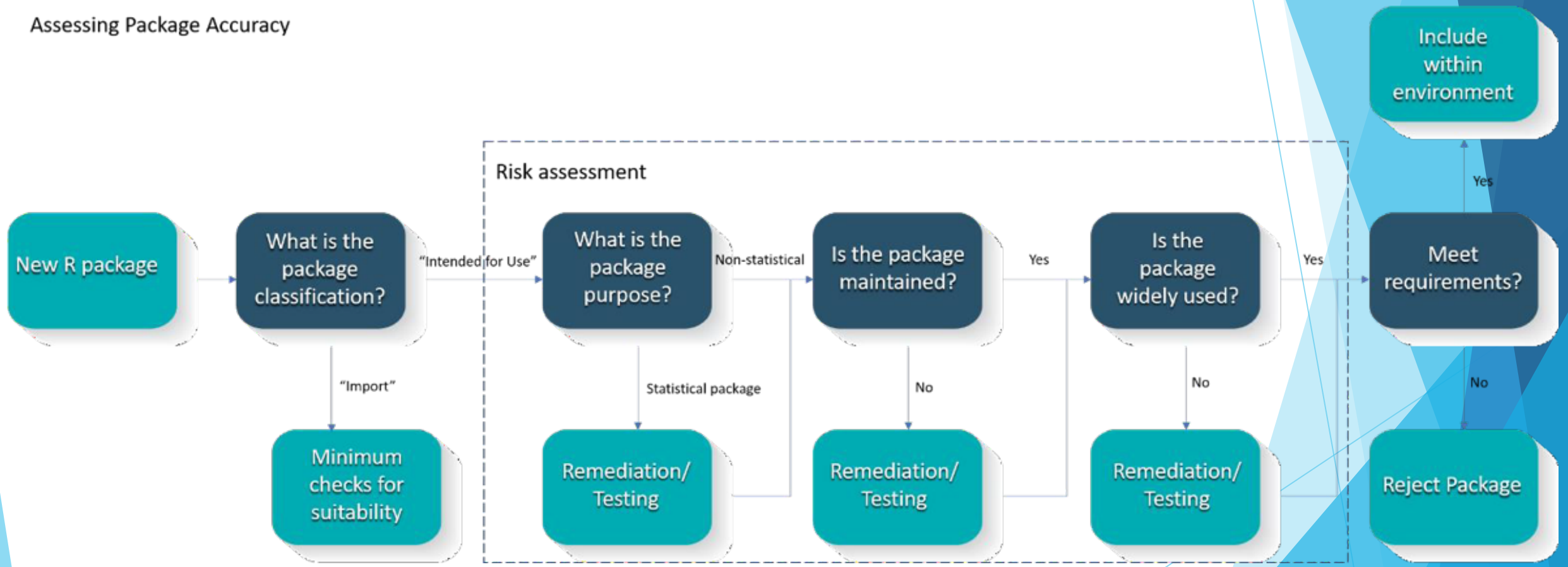
https://www.pharmar.org/white-paper/

White Paper



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.

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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.

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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.

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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

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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]

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