



October 2020

Attendees

Andy Nicholls
Paulo Bargo
Michael Carniello
Eli Miller
Joseph Rickert
Juliane Manitz
Lin Taft
Mark Padgham (ROpenSci)
Mark Penniston
Mike Stackhouse
Satish Murthy
Sean Lopp
Nash Delcamp
Reinhold Koch
Lyn Taylor
Søren Klim
Matthias Trampisch
Yilong Zhang.

Agenda

- R/Pharma Conference summary
- Updates from streams
 - Website
 - Riskmetric
 - R Consortium
- Discussion on stats methods catalogue (Mike Stackhouse)
- App to interaction with riskmetric

R/Pharma Conference

- R Validation Hub materials:
 - Workshop: <https://pharmar.github.io/rpharma2020/>
 - Presentation: https://pharmar.github.io/rpharma2020_pres/
- Other notable mentions of validation
 - Douglas Robinson, Novartis - Validation vs qualification
 - Ellis Hughes, Fred Hutch - Validating internal packages
 - Adrian Olszewski, 2KMM - Numerical validation
 - Paul Schuette, FDA - Looking forward to the first submission in R!
 - Others?

All very relevant at the conference and mostly in line with our thinking. Adrian's talk was focused more on a comparison of R to SAS in a validation R, however that's not our intention since there may not be one method better than the other. We plan to avoid "validation" or "identical replication" but instead detail why they are different.

Michael Carniello described plans to do a late phase submission/re-analysis submission fully in R. FDA requested all R packages, versions, and SAS transport files to be able to replicate the analysis that was done but so far going OK.

Reinhold provided the FDA guide on creating transport files using R or python:
<https://www.fda.gov/media/132457/download>

Website

- Recent updates
 - Minor facelift
 - R/Pharma presentations
 - Regulations page
 - Mailing list
- Coming soon...
 - ROpenSci blog post

Blog post will come out from ROpenSci – by Mark Padgham, which demonstrates automatic testing, where they put riskmetric through testing and demonstrate how automatic testing is being developed.

riskmetric

- Recent progress
 - [GitHub project](#)
- Future plans

Yilong provided a riskmetric update. The plan is to launch the 1st version of riskmetric to CRAN by end of this year.

We want to make it easier to update app when riskmetric has new metrics added to it. So we are ensuring the app is modular. App was demonstrated at the R/Pharma conference. Updates to the app are being made to make it more robust. Yilong asked to be able to run the outputs in batch and be able to get the metrics out into a report. Individual package report on the output objective.

R Consortium

- Initiation of R Consortium RTRS (Tables) Working Group
 - rconsortium-wg-rtrs@lists.r-consortium.org
- Pharma Hierarchy

This group are looking at creating a set of TLFs created in R, which meets 21CFRpart11 standards so could form part of submissions. Joe Rickert and Michel Cain (Yale) started RTRS (R tables for regulatory submissions) working group. One meeting to date bringing together companies to work together on common goal. Will be looking at gt (which can now create PDF and RTF), gtsummary type packages for creation of tables and bring people together to drive forward progress in this area. Next meeting is November 5th. If you want to attend please email Joseph.rickert@rstudio.com

Testing

- Strong desire for shared test framework
- Brief white paper to cover:
 - Appropriate response to risk
 - Testing for statistical functions
 - A requirements-based test framework

Keaven & Andy working on white paper on this area. Used the R/pharma conference to get feedback and that can form framework for the paper. You can streamline production using markdown. Will be creating test framework which allows people to submit tests to it. Volunteers wanted!

Discussion

Stats Catalogue

- Attempting to compare R with SAS will yield differences:
 - Rounding
 - MMRM
 - Hazard ratios
- Our interest is in demonstrating statistical correctness of R, not comparing to SAS
- A catalogue of methods and implementation in R might prove a useful reference guide
 - Risk assessment
 - Regulatory discussions
- Examples could be used as qualification test cases

The objective is not to compare R to SAS to get the same answer, but to have documentation that describes why the difference exist and identifies reasons.

Mike Stackhouse described the Phuse proposal shown below. It would be great for any interested R Validation Hub members join the Phuse proposal to help so that we don't duplicate work, but work together to focus the effort and drive towards a single aim. So Phuse led, but would be great to work together. Could advertise on pharmaR website that this work is going ahead and volunteers required: <https://www.pharmar.org/>. If you are interested please contact Mike.Stackhouse@atorusresearch.com

Phuse Proposal

Clinical Statistical Reporting in a Multilingual World

- Provide a framework for assessing the fundamental differences for a particular statistical analysis across languages
 - Identifying common statistical analyses performed during submissions
 - Providing necessary documentation to produce equivalence
 - Evaluating and documenting differences
 - Provision of sample code
 - Promoting sound statistical reasoning

- Timelines

Recruit team members	Oct 2020
Initial collated (extensible) list of common statistical analyses across the industry	Dec 2020
GitHub Repository documenting identified differences between statistical analysis implementations (based on R and SAS use cases as a starting point)	March 2021
Expand repository to provide comparable syntax across languages (based on R and SAS use cases as a starting point)	June 2021
Expand GitHub repository to incorporate Python and/or Julia	Sep 2021
White Paper providing framework for addressing language discrepancies in statistical analysis implementations, including specific use cases as examples	Dec 2021

Volunteers needed for phuse project, the App and the testing. The risk assessment project is relatively well supporting for now, but any interest in joining the other groups please get in touch.

Risk Assessment App

Marly discussed Risk Assessment app. It's having it's bug fixes now, but what is the path for the next steps for the application? What would be wanted next? How will the app be used?

Andy (GSK) plans the following however, others to please feedback their needs/likes/dislikes/future preferences to Marly.

- 1) Visualize results from riskmetrics (graphs) and extension to work with new metrics when available in riskmetrics
- 2) Generate report in rtf, docx - including the addition of overall comments which are not autogenerated and more subjective.
- 3) Sign-off of the reports would likely be done in a different system.

Mark Padgham – ROpenSci – will have a bot trigger assessment of packages, and it will deliver a report from riskmetrics, but the bot will provide a GitHub entry for the report. See the following for more information: <https://github.com/openjournals/buffy>

We may see that if you are not a programmer developer, you may prefer to use the App, but if you are a developer then you may more often use what Mark is describing.

R Validation Hub mailing list.

Invites for this meeting went out through the mailing list. Please ensure others are registered at that mailing list so that they get the invites to the meeting. We did see a drop off when we moved to this method, so if you know people who were a member, please remind them to re-register with the [mailing list](#).