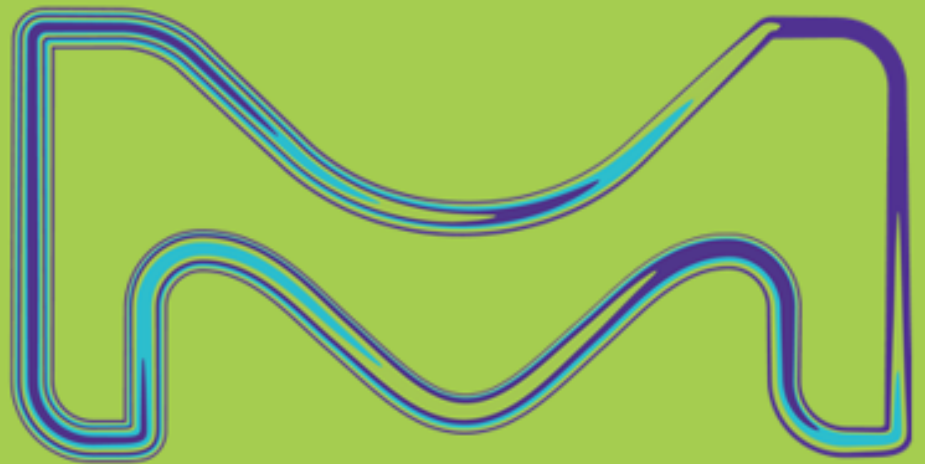


# RISK-BASED ASSESSMENT OF R PACKAGES

AT MERCK KGAA/ EMD SERONO

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R/Pharma  
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# Abstract

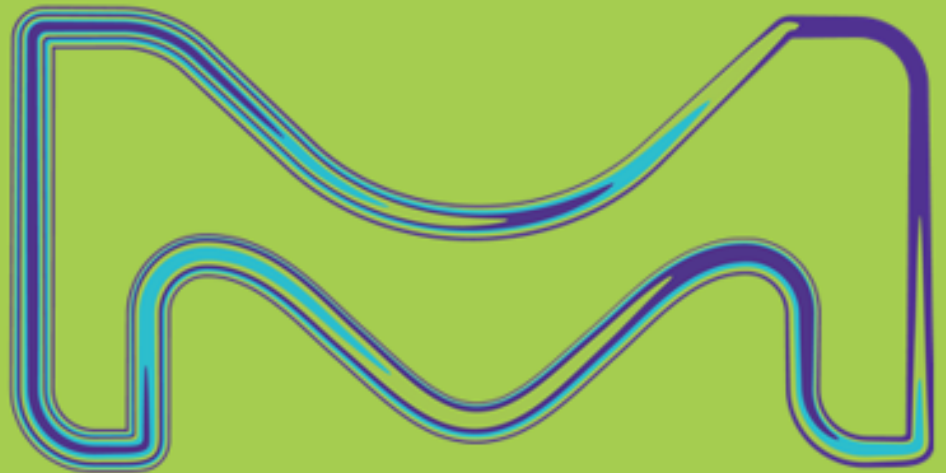
Like many other companies, **Merck KGaA/EMD Serono** has embarked on their journey to enable the use R for regulatory submissions. Following the framework introduced by the R validation hub (Nicholls et al., 2020), we started to develop an algorithm to qualify a CRAN package as a Merck standard package in our GxP environment.

**In a nutshell:** If an R package passes the installation qualification and successfully executes available tests, the package will be made available to the user. Then, an **automated risk assessment of R packages** is performed based on the test coverage score (more is better) and the riskmetric score generated from the meta-information (smaller is better). If **pre-defined thresholds** are fulfilled, the package is qualified as Merck standard package, otherwise an explicit (manual) risk assessment is needed.

In this presentation, we introduce our pathway to a risk-based assessment of R packages at Merck. We provide relevant details on the **statistical analysis** which led to the definition of thresholds supporting a robust classification of CRAN packages as Merck standard packages. **We want to inspire other companies and seek feedback from the community.**

# Outline

1. R Package Validation
2. Merck Validation Framework
3. Algorithm for Assessment
4. Definition of Riskmetric Score
5. Derivation of Classification Threshold
6. Summary & Next Steps





# R Package Validation

## Validation

[...] establishing documented evidence which provides a high degree of **assurance** [accuracy] that a specific process **consistently** [reproducibility] produces a product meeting its **predetermined specifications** [traceability] and quality attributes

FDA's Glossary of Computer System Software Development Terminology

## This presentation

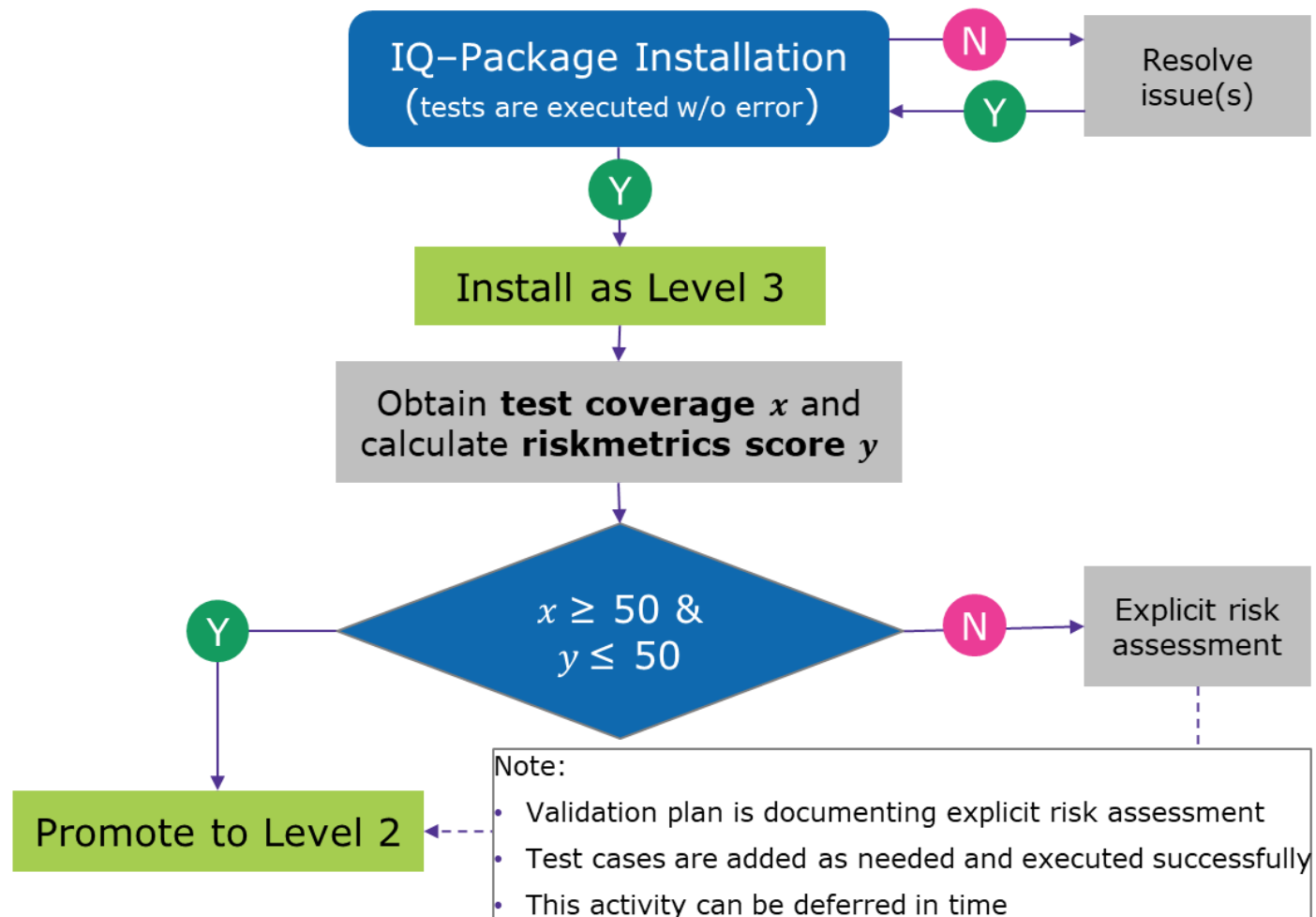
- Outlines the development of a Merck framework for the assessment of the accuracy of R packages
- While focused here on R, the proposed framework can be generalized to other programming languages (e.g. Python, SAS, ...).

# Merck Validation Framework



- Process of validation to ensure quality output of statistical analyses.
- Classification of external CRAN packages into three levels of confidence in the accuracy, reliability, and trustworthiness of their functionalities:
  1. **Core CRAN Packages** which are generally accepted to be accurate based on published documentation by the R Foundation
  2. **Merck add-on standard packages** which have sufficient documented evidence establishing trustworthiness.
  3. **Other R packages** for which the user is expected to ensure proper quality control and respective documentation that the specific package functionality results in the accurate outcome.

# Algorithm for Assessment





# Riskmetric Score

The riskmetric score has the following components and weights:

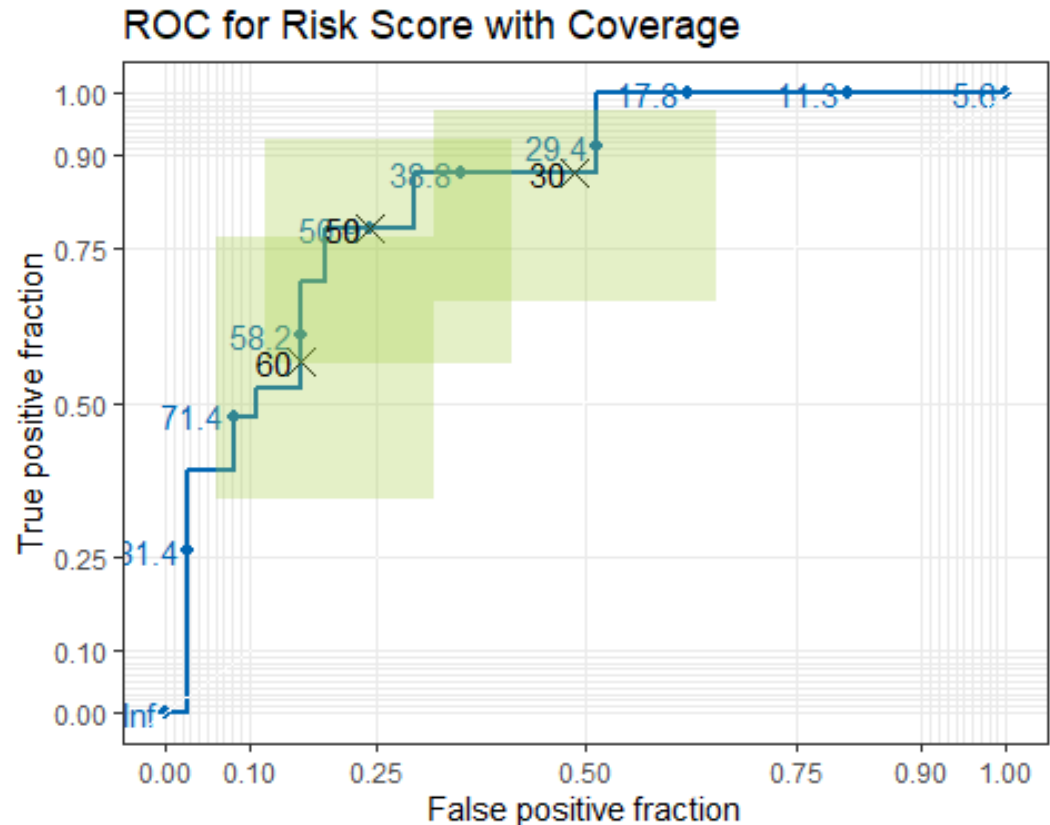
- 50% **code coverage**: unit testing, examples, vignette
- 15% **good software development practices**: maintainer, public code base, news file
- 15% **bug resolution**: url, status
- 10% **community usage**: downloads
- 10% **usability metrics**: documentation, help, vignette

Note that the riskmetric components are not independent, but the overall score has been found to be robust.



# Classification Threshold

- ROC analysis derives an optimal threshold for package classification given continuous riskmetric score at  $y = 50$
- Training data of 61 manually evaluated CRAN packages
- Empirical accuracy: 77% [64; 87]





# Stay-Home Message

## Summary

- Automated risk assessment of CRAN packages
- Derivation of an optimal two-dimensional risk score
  - test coverage  $x = 50$
  - riskmetrics score  $y = 50$
- Classification specificity of 88.5%

## Next Steps

- Empirical evaluation of threshold using a test set of packages
- Seek feedback from the community - *Please let us know what you think!*

