



R Validated Environment

A Platform for and Analysis of Clinical Studies

PHUSE EU Connect 2021



CONTACT INFORMATION

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Agenda

Microsoft's Contributions

R default package source: „Comprehensive R Archive Network“ (CRAN)

Microsoft contributions to the community:

1. Daily CRAN snapshots: „Microsoft R Application Network“ (MRAN)^[1]
2. R Distribution „Microsoft R Open“ (MRO)
 - Enhanced performance by multi-threaded math libraries (optional)
 - Additional bundled non-CRAN packages
3. R packages: **checkpoint**^[2] and **miniCRAN**^[3]



^[1] <https://mran.microsoft.com/>

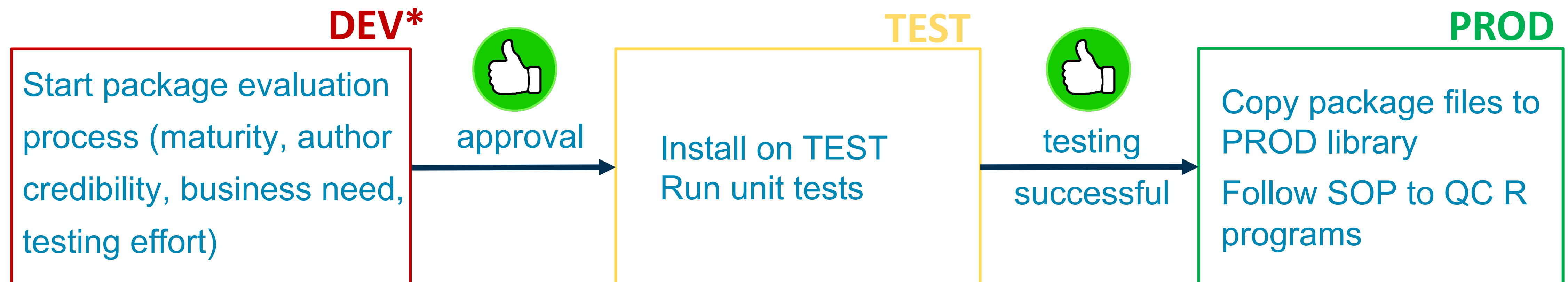
^[2] <https://cran.r-project.org/web/packages/checkpoint/index.html>,

^[3] <https://cran.r-project.org/web/packages/miniCRAN/index.html>

Maintaining the Validated State of R Environment

“Any changes to a validated computerized system, including configuration changes, should only be made in a controlled manner in accordance with a defined procedure.” – EU Annex 11

- Cannot download and install new packages in PROD freely by users
- Cannot update the version of a package in PROD freely by users
- System controls should be implemented besides SOPs



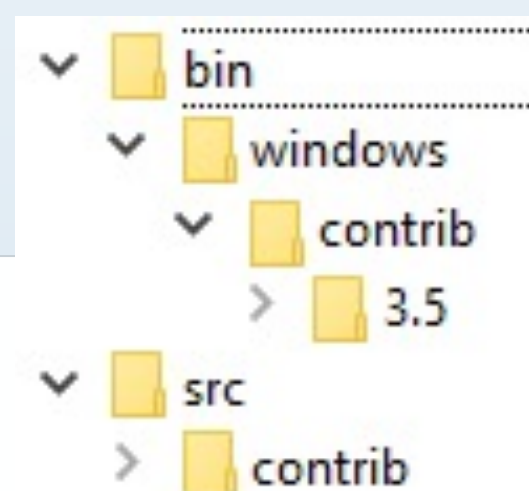
Solutions for reproducible package management

How R handles packages:



miniCRAN :

- creates **local repository** for package source or binary files
- downloads package files from public mirror of choice (CRAN or MRAN-snapshot)
- preserves folder structure expected by R for package installation



checkpoint :

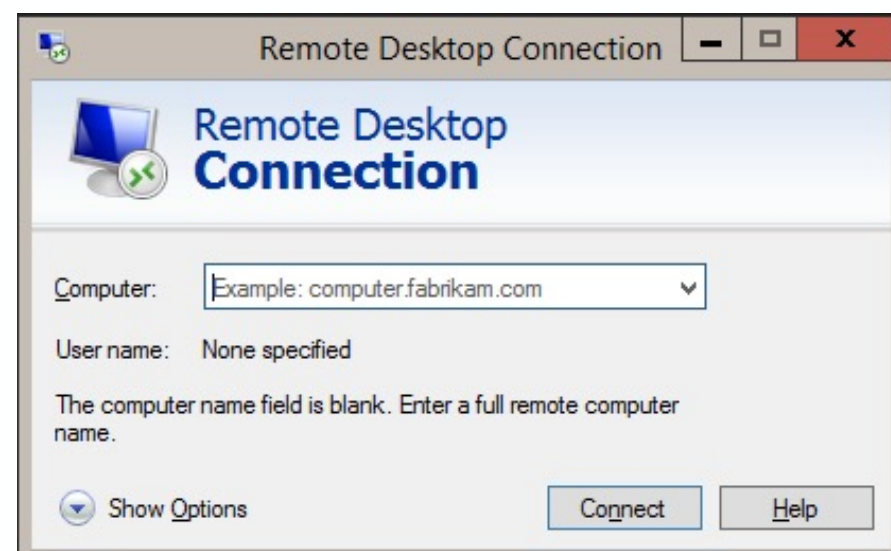
- creates a **local library** of installed packages
- local library: all packages versioned at same date
- repository used: MRAN or local miniCRAN (reflecting a date snapshot)
- scenario: you receive a script and want to reproduce results. `checkpoint()` function installs same package versions as on original date. Does not overwrite your default libraries.

RStudio

- Integrated Development Environment (IDE) for R
- Open source and commercial editions
- Base R Installation necessary

RStudio Desktop

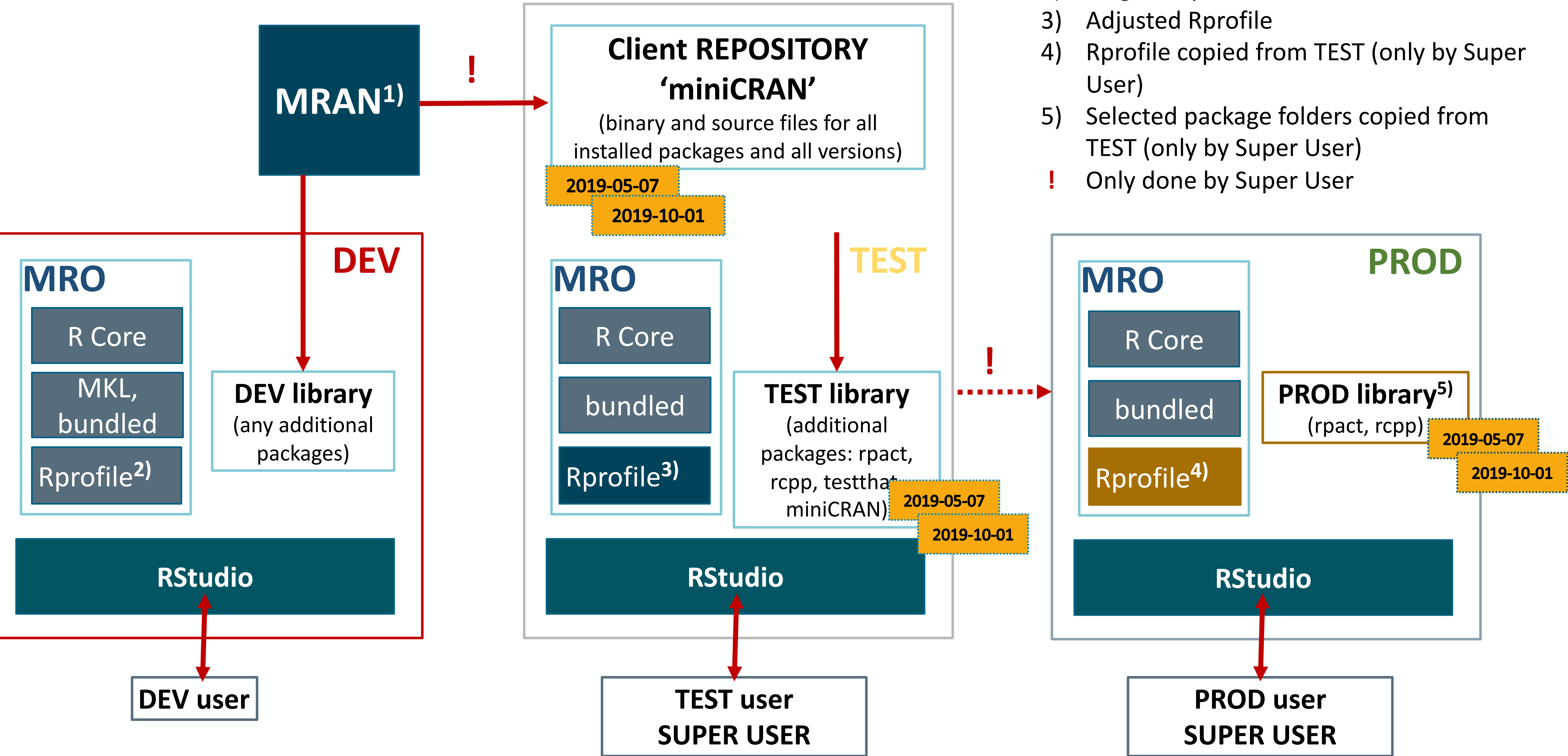
- Available for Windows, Mac, Linux
- Free under Affero General Public License (AGPL)
- Installed
 - locally on PC, Notebook ...
 - on a server accesible via Remote Desktop (RDP) or Secure Shell (SSH)



RStudio Server (Workbench)

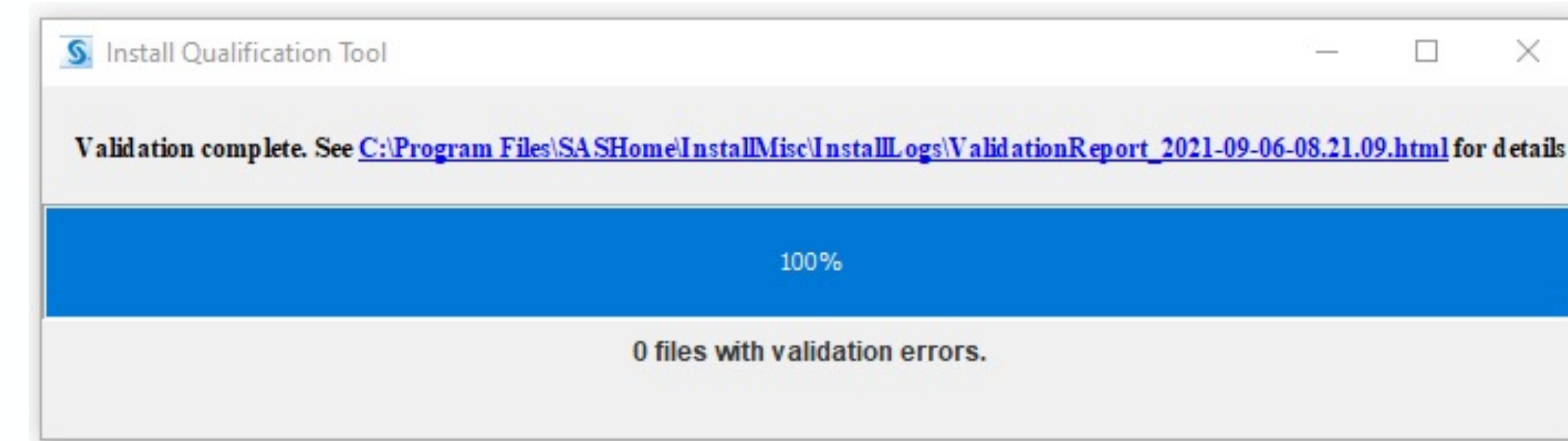
- Installed on Linux Server
- Access via a web browser
- Business Context: License Fees, but enhanced features:
 - Administrative Tools, Metrics and Monitoring
 - RStudio as Frontend
 - Native SSO support
 - Jupyter Notebooks & Python connectors

R environment



Unit Tests

- Not as comfortable as SAS IQ/OQ Tools
- Many Warnings concerning:
 - non English OS – lacking internationalization
 - Concerning timestamps



Regular Reviews & Upholding a Validated State

Periodic review of validated systems is mandatory

- “Systems and processes should be periodically evaluated to verify that they are still operating in a valid manner” [1]
- GAMP 5: “Periodic reviews are used throughout the operational life of systems to verify that they remain compliant with regulatory requirements, fit for intended use, and meet company policies and procedures” [2]

Review Release Notes of all installed package:

- New available features
- Found and fixed bugs: concerning security, in statistical packages ...
- Breaking changes and deprecation warnings

Assess impact: Reason to update?

[1] ICH Harmonised Tripartite Guideline, Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, ICH Q7 (2000)

[2] GAMP5, A Risk-Based Approach to Compliant GxP Computerized Systems, Section 4.3.5, ISPE (2008)

