**Validation & Test Plan for R**

**Document Properties**

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# Introduction

The purpose of this document is to describe the activities and deliverables required to validate R base installation version *insert software version number* *for which this plan is applied first* and higher based on *insert references to local computerised system validation policies and SOPs, if applicable* as well as SCTO R Validation Policy and associated SOPs. The deliverables/activities described in this plan will provide the documented evidence that R base installation performs per its intended use and has been thoroughly tested on a risk-based approach.

# System Description

R is a ‘language and environment for statistical computing and graphics’. It is an official part of the Free Software Foundation’s GNU project and is released under the Free Software Foundation’s GNU Public License. CTUs use R primarily, but not exclusively, in the preparation and analysis of data from supported studies. Internal use for other reporting, visualisation and business management might also take place, according to individual CTU needs, but is not the focus of this policy.

## System components / Architecture

Several components are installed on a standard R-user workstation:

1. The **operating system** (infrastructure software)
2. The R base installation, which includes the R base and recommended packages (as defined in “A Guidance Document for the Use of R in Regulated Clinical Trial Environments”, 2021) and is available via the Central R Archive Network (CRAN)
	1. Contributed **R add-on packages**, provided by the R community and available via CRAN or other sources (e.g., Bioconductor, Github, and various websites)
	2. Additionally, R packages may be developed in-house (for internal use only and not distributed via any of the channels mentioned above)

If R add-on packages or some of their functions are used in the GxP context (e.g., clinical trials), they must also be validated (see Scope below).

R base installation requires validation as per the outcome of the High-level Risk Assessment. All R add-on packages or functions within that packages used with GxP data have to be validated as well to ensure the “R system” as a whole is validated when used in the GxP context.

# Scope

## In Scope

In scope of this Validation & Test Plan are

* the validation of new major versions of **R base installation (official distribution),** including:
	+ R programming language
	+ R base packages
	+ R recommended packages
* R base system-specific process deliverables (SOPs)

For each major release distributed, the following minimum steps and rules apply for selecting and using a new R base installation version in the GxP context:

* The System Owner decides that a newly distributed version shall be used at the CTU
* The Validation Responsible or IT change responsible creates a change plan to document the required activities (see chapter Validation Strategy)
* Once all validation activities are completed, the Validation Responsible creates a Validation & Test Report
* All major versions accepted for productive use in the GxP context are documented in a repository accessible to all R users (e.g., on SharePoint) - details have to be defined in respective SOPs.
* Minor releases and bug fix & technical improvement releases of R base installation distributed may be accepted and used without separate validation.

## Out of Scope

Out of scope of this Validation & Test Plan are:

* **R-add on package validation**
	+ covered by SCTO R Validation Policy and associated SOPs
	+ *Note:* The process for validating R add-on packages as outlined in the SCTO Validation Policy and associated SOPs should be used whenever feasible before using an R package in the GxP context, even if the R package is not shared with the SCTO community.
* **R add-on package management** to ensure traceability and reproducibility on R product/ outcome level
	+ covered by Statistical Analysis SOPs
* **R Products and data analysis processes** related to that products
	+ covered by Statistical Analysis SOPs
* **Hardware and infrastructure** related qualification activities
	+ The infrastructure software and hardware used is provided *by the D&ICT department of the University Hospital Basel. A SLA with the D&ICT department ensures that the infrastructure used by DKF Operations is sufficiently controlled in order to host GxP relevant systems.*
* User training and business processes for external users
* Validation of any interfaced applications, for example
	+ Version control software or system (e.g., subversion repository, git etc.)
	+ User interface software (e.g., R-Studio IDE)

# Roles and Responsibilities

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| --- | --- |
| **Validation Responsible** |  |
| **System Owner** |  |
| **Technical Lead** |  |
| **IQ Tester** | *Members of the Data Analysis/ Statistics team* |
| **PQ Tester** | *Members of the Data Analysis/ Statistics team* |

# System Classification

## High Level Risk Assessment

The outcome of the High-level Risk Assessment indicates that the system is:

* GxP relevant

Further risk assessments are performed according to *local SOPs, if applicable and the SCTO R Validation Policy.*

## GAMP category

R base installation is categorised in the High-level Risk Assessment according to GAMP5 as:

* Category 1: Infrastructure software – established or commercially available layered software.

# Validation Strategy

The validation strategy folllows the *local SOPs, if applicable and the SCTO R Validation Policy.*

The following table describes the activities and documentation required for the validation of R base installation Active:

| **Activity/ Document** | **Location** |
| --- | --- |
| **High-Level Risk Assessment (HLRA)*** Reviewed and updated at least:
	+ With new R base installation releases introducing new system functionality impacting HLRA aspects **or**
	+ periodically (every 3 years).
 | *<reference/ link to High-level Risk Assessment document>* |
| **Vendor Assessment Statement** | *<reference/ link to Vendor Assessment Statement document>* |
| **Validation & Test Plan (this document)*** Reviewed and updated at least:
	+ if the validation strategy changes **or**
	+ periodically (every 3 years).
 | *<reference location, where documentation is stored>* |
| **User Requirements Specification*** Reviewed and updated at least:
	+ if new user requirements are implemented or existing requirements require updating with a release **or**
	+ periodically (every 3 years).
 | *<reference location, where documentation is stored>* |
| **Functional Risk Assessment*** Reviewed and updated at least:
	+ if new user requirements or new application areas are implemented or existing requirements require updating with a release **or**
	+ periodically (every 3 years).
 | *<reference location, where documentation is stored>* |
| **Software Installation Instructions*** **No** R base installation Active **specific software installation instruction document is created**
* R is installed according to R Foundation installation guidelines using only R official distribution from CRAN.
 | Not applicable |
| **Test Protocols (User Acceptance Test)*** Reviewed and updated at least:
	+ if new user requirements are implemented or existing requirements require updating with a release **or**
* periodically (every 3 years).
 | R (Script) |
| **Execute & document Software Installation o**n **TEST*** New R base installation versions are installed on a dedicated TEST environment (server location) or a local machine used for testing purposes before releasing the new version for productive use.
* Documentation of installation should contain (at least):
	+ Location where the new version was installed (for testing)
	+ Version installed.
	+ Date and time of installation.
	+ Who performed the installation
 | *<reference location, where documentation is stored/ required information is documented>* |
| **Execute Test Protocols (User Acceptance Test)*** At least with every major release.
 | R (Report) |
| **Traceability Matrix*** Reviewed and updated at least:
	+ if new user requirements are implemented or existing requirements require updating with a release **or**
	+ **if new test protocols are created/ existing protocols are significantly updated or**
	+ periodically (every 3 years).
 | *<reference location, where documentation is stored/ required information is documented>* |
| **Validation & Test Report*** This document summarizes all validation and testing activities, any open action items (incl. an impact assessment and plan for completion) as well as any open defects and their impact on productive use.
* With the approval of this report the system is accepted for productive use (with or without restrictions).
* **The approval of this report is the prerequisite for the productive use (creation of R products with GxP relevance) of a new R base installation version.**
 | *<reference location, where documentation is stored>* |
| **Execute & document Software Installation o**n **P**ROD* New R base installation versions are installed/ selected for use on productive machines.
* Documentation of installation should contain (at least):
	+ Location where the new version was installed (for testing)
	+ Version installed.
	+ Date and time of installation.
	+ Who performed the installation
* **If the new version is installed on a central server and only selected by users, the documentation of the version selected may be covered by the metadata recorded with each analysis.**
 | *<reference location, where documentation is stored/ required information is documented>* |

# Testing strategy

The testing strategy folllows the *local SOPs, if applicable and the SCTO R Validation Policy* and the relevant tests are described in the table above.

## Test and Test Defect Management

For User Acceptance Testing, a script is prepared in R that covers the user requirements. The result of that script (and verification of the requirement to be able to export data) is an R report. This report is added to the Validation & Test Report as PDF.

In case of errors/ defects, the error message in R has to be documented in a screenshot and the screenshot added to the Validation & Test Report.

Each defect needs to be assessed to work out the root of the problem and the impact of the issue. The classification of the defect will determine if re-testing is possible with the current R base installation version and which steps need to be taken. Configuration and script errors may be resolved, and the resolution (changes to the configuration/ script) has to be documented in a format that can later be added to the Validation & Test Report (e.g. before and after screenshots), before executing a re-test.

# Traceability

Traceability between requirements and tests is maintained in R and visible in the report created.

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# Acceptance Criteria

The fulfillment of the following acceptance criteria will constitute an acceptable execution of this plan:

* The system hardware and software (infrastructure & application) have been installed and documented, according to specifications.
* The system has been shown to meet its intended use (i.e., tests are completed and accepted).
* Procedures are current and adequately describe how the computerised system will be operated.
* Training materials (as applicable) are available and training has been completed and documented before system access is granted to end users. Trainings may still be ongoing at the time of Go Live as long as it can be assured that only trained users have access to the productive system.
* Documents are reviewed and approved according to local document management and approval processes.
* Any exceptions/ deviations from this plan are justified, and any open issues are documented and assessed.

# Maintaining the validated state

## Operational procedures

Following the conclusion of the validation activities and issuing of the validation & report, operational SOPs and procedures must be in place to maintain the validated state of the system.

The following operational documents / procedures are needed:

* User management and training procedures R base installation:
	+ Tutorials and SOPs
* Change management procedure
* Tools / processes for managing issues and problems:
* Business continuity / disaster recovery:
* Backup and restore procedures

## Periodic review

See *local SOPs, if applicable OR SCTO R Validation Policy*

# References

|  |  |
| --- | --- |
| **Reference Title** | **Description** |
| R: A Guidance Document for the Use of R in Regulated Clinical Trial Environments | R: Regulatory Compliance and Validation Issues - A Guidance Document for the Use of R in Regulated Clinical Trial Environments (2021): R Foundation for Statistical Computing guidance document for the validation of R for the use in regulated environments. |
| SCTO R Validation Policy and associated SOPs | A framework provided by the SCTO (Swiss Clinical Trial Organization) to validate R and its add-on packages.Associated to the policy are SOPs to guide through the process of add-on package validation. The SCTO also provides a repository for all network members to share validation documentation for add-on packages validated based on the policy and processes set forth by the SCTO. |
| *SOPs of the Data Analysis team* | *References to applicable local SOPs* |