

Shiny Server Pro: Regulatory Compliance and Validation Issues

A Guidance Document for the Use of Shiny Server Pro in Regulated Clinical Trial Environments

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Purpose and Introduction

The purpose of this document is to demonstrate that the RStudio Shiny Server Pro software, when used in a qualified fashion, can support the appropriate regulatory requirements for validated systems, thus ensuring that resulting electronic records are “trustworthy, reliable and generally equivalent to paper records.”

This document applies to Shiny Server Pro products released in binary executable forms under an RStudio commercial license.

Shiny Server Pro software allows analysts and scientists to share and publish their Shiny applications, authenticate user access, and scale and manage R processes.

For reference, Shiny (<http://shiny.rstudio.com/>) is a web application framework created by RStudio, Inc. and licensed as a free open source R package. Shiny is used to turn analyses created with R into interactive web applications (“Shiny applications”) without requiring web programming skills.

Neither Shiny Server Pro nor Shiny are intended to create, maintain, modify, or delete Part 11 relevant records but to deliver interactive experiences that allow authenticated end users the option of changing input values on a web page and have the results of an R program be written as output values back out to the web page in a reproducible way.

This document is NOT in any fashion, applicable to other R-related software and add-on packages. It is important to note that there is a significant obligation on the part of the end-user's organization to define, create, implement and enforce R installation, validation and utilization related Standard Operating Procedures (SOPs). The details and content of any such SOPs are beyond the scope of this document.

This document is not intended to be prescriptive, does not render a legal opinion and does not confer or impart any binding or other legal obligation. It should be utilized by the reader and his or her organization as one component in the process of making informed decisions as to how best to meet relevant obligations within their own professional working environment.

RStudio, Inc. makes no warranties, expressed or implied, in this document.

Validation of Systems for 21 CFR Part 11 Compliance

Validation is defined by the FDA¹ as: "Establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes."²

It is crucial to note that many validation requirements, as described in the following pages, may be met by the operational characteristics of software systems (i.e. operating systems and database applications) and other technologies or processes outside of Shiny Server Pro, where Shiny Server Pro will be used as a component in an overall data management, analysis and presentation process.

Software Development Life Cycle (SDLC)

Operational Overview

The development, release and maintenance of Shiny Server Pro is a collaborative process.

Most communications among RStudio development team members take place electronically via e-mail and similar means. A non-public e-mail list provides a common forum for discussions along with video conferencing, instant messaging and group chat tools such as Hipchat.

RStudio development team members meet, collectively and/or in smaller groups, with a level of frequency dictated by multiple factors, including regularly scheduled company meetings. These routine communications and meetings ensure that the collaborative efforts are appropriately coordinated and prioritized as ongoing development takes place.

Reasonable software development and testing methodologies are employed in order to maximize the accuracy, reliability and consistency of Shiny Server Pro's performance. While some aspects of development are handled collaboratively, others are handled by members of the team with specific interests and expertise in focused areas.

Importantly, as Shiny Server Pro incorporates RStudio Shiny Server open source components developed by the same team and released under the terms of the Affero General Public License, much of the source code underlying Shiny Server Pro is available for peer review by all members of the R user community. Thus, much of the

¹ General Principles of Software Validation; Final Guidance for Industry and FDA Staff

² Glossary Of Computerized System and Software Development Terminology

functionality embodied within Shiny Server Pro is subject to continuous critique and improvement relative to its accuracy, reliability and consistency.

Additional documentation regarding Shiny Server open source development activities as they pertain to development, goals and related activities, are available here:

<https://github.com/rstudio/shiny-server>

Source Code Management

All of Shiny Server Pro's commercial source code is managed in [git](#), a source code revision control software. The RStudio Shiny Server Pro Repository is access controlled, such that only members of RStudio development team have write access to the source code tree.

Separate source code branches for version control are maintained by RStudio developers. Major features are introduced in distinct branches which can be subjected to thorough Quality Assessment and validation before being merged into the pending Development Version, from which a new Release is made upon further evaluation.

Daily logs of code changes are maintained within the repository and reflect all aspects of code changes.

Changes made between versions of the open-source Shiny Server can be viewed here: <https://github.com/rstudio/shiny-server/blob/master/NEWS>. For each version, we describe the various high-level changes that were made to the software.

Testing and Validation

Within the RStudio development team, guidelines are provided relative to modifications to source code, regression tests, validation tests and similar issues. These guidelines are in place to maximize code quality and to facilitate ongoing code validation during development and during the "run-up" to each version release.

A set of validation tests are maintained and updated to enable the testing of source code against known data and known results. Any errors noted during this testing are resolved prior to release.

A set of tests located in the /test directory of the source code control system validate the code at a component level. Additional tests in other source control repositories validate the end-to-end functionality of Shiny Server Pro.

The Shiny Server Pro product extends the open source Shiny Server product with additional capabilities. Builds of the open source server are tested internally before being released to the

community. Regressions that are not caught in formal validation tests are generally caught within a few days in community testing. Additionally, we evaluate any candidate build on our own hosted Shiny Server Pro services which typically bring to light any additional issues the build may have. Only after both community testing of the the open source foundation and our own use of it as a commercial hosted service do we release Shiny Server Pro builds publicly.

Progressively stronger restrictions are imposed on modifications to the source code during the testing cycles to minimize the risk of unexpected side effects. This provides further opportunities to identify and resolve issues that may have been missed during the development process.

Feedback from the community is facilitated by the use of GitHub issues and support.rstudio.com where users report issues and seek support. This process enables a wider array of code testing and further increases the likelihood of resolving issues prior to the release of a stable version.

Release Cycles

Once the in-development version of Shiny Server Pro has been approved for release by a designated Release Manager, a public announcement is made via the [RStudio blog](#).

Source code archive files for the open source components are made available at <https://github.com/rstudio/shiny-server>

Pre-built executable binary install files for Shiny Server Pro follows on RStudio.com and are made available for common Linux distributions and CPU architectures.

Patch releases are made available when required in order to fix issues discovered in the current release.

Additional instructions regarding the use of Shiny Server Pro, installation requirements and platform and operating system related issues are extensively documented in the Shiny Server Pro Administration Guide, which is available online here <http://rstudio.github.io/shiny-server/latest/>

Availability of Current and Historical Archive Versions

Source code for every open source Shiny Server version we've ever released is available via (note the version number in the URL):

<https://github.com/rstudio/shiny-server/tree/v1.2.0>

Binaries for every version we've ever released are available via (note the version number and build number in the URL). :

https://s3.amazonaws.com/rstudio-shiny-server-pro-build/ubuntu-12.04/x86_64/shiny-server-commercial-1.1.0.379-amd64.deb

Similarly, source and binaries for Shiny Server Pro are maintained for at least three years by version and build numbers in private github repositories accessible only to the RStudio development team.

Maintenance, Support and Retirement

Each Released Version of a Shiny Server Pro is actively supported by RStudio, Inc. with respect to bug reporting, fixes and patches. Binary executable installation files for patched Release Versions are made available at the discretion of RStudio.

As each version of Shiny Server Pro is released, there are a variety of support resources that are made available to end users.

Extensive documentation is provided by RStudio in HTML and PDF formats at <http://rstudio.github.io/shiny-server/latest/> and <https://s3.amazonaws.com/rstudio-shiny-server-pro-build/docs/shiny-server-pro-1.2.0-admin-guide.pdf>

A website devoted to building and deploying Shiny apps with Shiny Server and Shiny Server Pro is available at <http://shiny.rstudio.com>.

A set of published books by members of the RStudio team are available to support the use of R and RStudio products. A periodically updated but partial list of these books is available at <http://www.rstudio.com/resources/training/books/>

Qualified Personnel

All members of RStudio's development team hold qualifying degrees and prior development experience, many with Ph.D. and/or Master's degrees from accredited academic institutions. Many have published in peer reviewed journals. Several have written books on statistical computing technologies and applications. The members of RStudio's development team constitute a widely recognized, international team of experts on statistical computing and software development.

Institutions at which the members of RStudio development team members currently hold appointments or have previously been affiliated include:

University of California - Davis

Harvard University

Iowa State University
Macalester College
Massachusetts Institute of Technology
University of Massachusetts (Amherst)
Northeastern University
Northwestern University
Southern Methodist University
Rice University
Worcester Polytechnic Institute

Physical and Logical Security

RStudio, Inc. maintains its key servers with Amazon. Secure Shell (SSH) private keys protect access in accordance with Amazon's defined security policies.

Amazon requires user names and passwords for all RStudio development team members to gain access to computing systems for RStudio-related activities. User accounts are limited in access based upon standard security policies and functional requirements.

Network access is controlled via the use of typical hardware and software controls, including the use of firewalls, security policies and related mechanisms.

Disaster Recovery

RStudio Shiny Server Pro is installed on customer systems and therefore, subject to customer disaster recovery practices.

For delivery of Shiny Server Pro product purchases and upgrades, we rely on Amazon for availability of our binaries and disaster recovery practices. For development of Shiny Server Pro the RStudio development team relies on Github for the availability of source code and disaster recovery practices. However, because of the distributed nature of our development process and infrastructure, even in the event of a unrecoverable disaster impacting either service, RStudio could continue to make binary products available to customers and source products available to our development team.

21 CFR Part 11 Compliance Functionality

Overview

Within the regulated domain, Shiny Server Pro is intended to be utilized as a component within a larger data management framework, with respect to data acquisition, validation and related source electronic *records* tasks. Shiny Server Pro enables secure, reproducible access via a web browser to reports and interactive data applications created with the R statistical programming environment and specifically the R open source package, Shiny. Shiny Server Pro is focused on securing user access, tuning application performance, and monitoring resource utilization rather than on data management tasks such as transaction/data processing and related functionality.

To that end, the following sections discuss important components of the 21 CFR Part 11 Regulation, provides RStudio's interpretation of each, and discuss how Shiny Server Pro, within an overall data management framework, can meet the guidance interpretations.

Note that sections 11.10(a) and (i), pertaining to system validation and qualified personnel, respectively, have already been covered previously.

In the following sections, the term *record* means an electronic record that is interpreted to fall within the remit of Part 11 as defined in FDA Guidance for Industry Part 11, Electronic Records; Electronic Signatures – Scope and Application (2003).

RStudio Shiny Server Pro is not intended to create, maintain, modify or delete Part 11 relevant *records* but to deliver interactive experiences, typically delivered over the web, that allow the end user to “play” with the data and draw their own conclusions.

11.10(b) The ability to generate accurate and complete copies of records in both human readable and electronic form suitable for inspection, review, and copying

RStudio understands this item to mean that any *records* created or maintained in the system must be accurate and complete. These *records* must be available in both human readable and electronic form.

Shiny Server Pro is not intended to create, maintain, modify or delete Part 11 relevant *records* but to deliver interactive web experiences. It secures user access, tunes application performance, and monitors resource utilization for those interactive web experiences. Because R and the open source R package Shiny provide for the routine

generation of these interactive web outputs as standard features, the output is available in both machine- and human-readable formats (e.g., html) and these *records* are therefore readable independent of the use of R and Shiny Server Pro.

In conjunction with local policies regarding *record* access control, retention and archival, Shiny Server Pro meets the FDA requirements for the inspection, review and copying of *records* as defined above.

11.10(c) Protection of records to enable their accurate and ready retrieval throughout the records retention period

RStudio, Inc. understands this item to mean that all *records* created or maintained in Shiny Server Pro must be stored in a manner that enables accurate and ready retrieval.

Shiny Server Pro is not intended to create, maintain, modify or delete Part 11 relevant *records* but to deliver interactive web experiences.

Therefore, *Records* made available as interactive web experiences by Shiny Server Pro will, therefore, reside within and be managed by a separate host system.

The host system is required to provide for compliance with this part using local policies regarding the retention and archival of such *records* and the mechanisms and access controls in place.

11.10(d) Limiting system access to authorized individuals

RStudio, Inc. understands this item to mean that access to the computer system that creates, maintains or modifies a *record* is limited to only authorized individuals.

The requirement for this section is typically met via system level functionality and is based on user roles, object level security and related security policies.

Shiny Server Pro is not intended to create, maintain, modify or delete Part 11 relevant *records* but to deliver interactive web experiences. However, as a further measure it secures user access to those interactive experiences by enabling or leveraging existing authentication practices, including LDAP, ActiveDirectory, Google Authentication, PAM authentication and sessions, and SSL. Approved users must be supplied unique user account identifiers and passwords.

11.10(e) Use of secure, computer-generated, time-stamped audit trails to independently record the data and time of operator entries and actions that create, modify, or delete electronic records. Record changes shall not obscure previously recorded information. Such

audit trail documentation shall be retained for a period at least as long as that required for the subject electronic records and shall be available for agency review and copying

RStudio, Inc. understands this item to mean that the creation, modification or deletion of *records* must have an associated audit trail describing who, when and why an action was performed. Additionally, any such audit trail will be also considered an electronic *record* within the scope of Part 11.

Shiny Server Pro is not intended to create, maintain, modify or delete Part 11 relevant *records* but to deliver interactive web experiences. No records are created, modified, or deleted by Shiny Server Pro.

Records reside within and are managed by a separate host system. Therefore, any changes to the *record* must have an audit history imposed by the host system. This may be implemented technically via system-level logging as a component of the hosting computer system.

11.10(f) Use of operational system checks to enforce permitted sequencing of steps and events, as appropriate

RStudio, Inc. understands this item to mean that effective user technology, processes, and interfaces must be in place to reduce errors made by an operator to the extent that system errors can be minimized.

Shiny Server Pro is not intended to create, maintain, modify or delete Part 11 relevant *records* but to deliver interactive web experiences which constrain the end user to the input value parameters defined by the R programmer before using Shiny and Shiny Server Pro to deliver their application. The Shiny app enforces with end users whatever permitted sequencing of steps and events the R programmer coded.

Appropriate coding techniques that implement good and defensive programming style are documented and described in many books, including Software for Data Analysis (Chambers)^[2].

11.10(g) Use of authority checks to ensure that only authorized individuals can use the system, electronically sign a record, access the operation or computer system input or output device, alter a record, or perform the operation at hand

RStudio, Inc. understands this item to mean that the system must provide for authority checks to allow users to perform system operations, such as applying electronic signatures, access to input and output devices, the ability to alter a *record* and perform functions.

Shiny Server Pro is not intended to create, maintain, modify or delete Part 11 relevant *records* but to deliver interactive web experiences. Authority checks (such as user name/password controls) which control access to records created, maintained, modified and deleted in another system must be implemented within the host system, as described in section 11.10(d) and can be further enhanced by using features in Shiny Server Pro, which control access to Shiny applications.

11.10(h) Use of device (e.g., terminal) checks to determine, as appropriate, the validity of the source of data input or operational instruction

RStudio, Inc. understands that these checks are warranted where only certain devices have been selected as legitimate sources of data input or commands. The device checks would be used to determine if the data or command source was authorized.

If a Shiny app managed by Shiny Server Pro is coded to be used as a primary-source data entry system, such checks would need to be implemented by the developer of the code and the host environment responsible for the creation, maintenance, modification and deletion of records.

Shiny Server Pro enhances the host environment capabilities as discussed previously, notably in sections 11.10(d), 11.10(f) and 11.10(g).

Shiny Server Pro is not intended to create, maintain, modify or delete Part 11 relevant *records* but to deliver interactive web experiences.

11.10(j) The establishment of, and adherence to, written policies that hold individuals accountable and responsible for actions initiated under their electronic signatures, in order to deter record and signature falsification

RStudio, Inc. understands that individuals must understand their responsibility and accountability when performing actions using their electronic signatures. This must be communicated with documented policies.

Shiny Server Pro is not intended to create, maintain, modify or delete Part 11 relevant *records* but to deliver interactive web experiences. Following from this, they are not intended to allow for signature of *records*.

11.10(k) Use of appropriate controls over systems documentation

21 CFR Part 11.10(k) indicates that these controls must include:

Adequate controls over the distribution of, access to, and use of documentation for system operation and maintenance

Revision and change control procedures to maintain an audit trail that documents time-sequenced development and modification of systems documentation

RStudio, Inc. understands this item to mean that there must be control over who can access and change system documentation and also that there exists revision and change control in place for system documentation.

All releases of Shiny Server Pro include documentation covering installation, administration, programming and related user guides. Documentation is created once per Release Version; thus these documents are uniquely identifiable and associated with a specific release of the software.

This documentation is published and maintained by RStudio as part of the Software Development Life Cycle using the [Git](#) version-control system. This documentation is controlled in the same manner as Shiny Server Pro's source code.

This documentation is provided to Shiny Server Pro users in electronic formats.

The maintenance and distribution of this documentation is the sole responsibility of RStudio, Inc. and is handled in accordance with training and other standard operational procedures.

Section 11.30 Controls for Open Systems - the system shall employ procedures and controls designed to ensure the authenticity, integrity and as appropriate the confidentiality of electronic records from the point of their creation to the point of their receipt. Additional measures such as document encryption and use of appropriate digital signature standards to ensure, as necessary under the circumstances record authenticity, integrity and confidentiality

Shiny Server Pro enhances the host record environment that provides these capabilities (see previous discussion, particularly section 11.10(d)).

It is the sole responsibility of the Shiny Server Pro administrator to ensure that the appropriate safeguards are implemented for a particular Shiny app.

Bibliography

References

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[1]
<https://stat.ethz.ch/mailman/listinfo/r-devel> ⁶
<http://bugs.r-project.org/>

[2] See reference [[Chambers\(2008\)](#)]