KNOWLEDGE SHARING SERIES

User Acceptance Testing and RTSM System Validation

Demonstrating Joint Responsibility (Vendor and Sponsor) for Ensuring RTSM Validation in a Highly-Regulated Environment

Bringing crucial medicines to those who need them, faster.

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About 4G Clinical

4G Clinical is driven by a single purpose: bring crucial medicines to those who need them, faster. 4G Clinical believes that the way to accelerate clinical research is by disrupting the way trials are executed. That's why we have revolutionized RTSM (randomization and trial supply management) and supply forecasting capabilities and services from the ground up.

4G Clinical is committed to helping sponsors and CROs follow the science, wherever it may lead, as quickly and as safely as we can. While we will not discover the next novel compound in the lab, we are doing our part by leveraging our extensive experience and technological innovations to bring speed and agility to clinical trials.

"We reduce the time it takes to commercialize vital medications by delivering validated, easily extendable RTSM capabilities to Pharma and CROs faster than anyone in the world."

About 4G's RTSM

4G's RTSM platform, Prancer RTSM®, utilizes natural language processing alongside integrated clinical supplies forecasting and management functionality to slash development timelines, increase operational efficiencies and offer exceptional quality.

"Our 100% configurable and agile RTSM is built for the clinical trials of today and tomorrow."

Purpose

When implementing a randomization and trial supply management (RTSM) system for a clinical trial, there is a shared responsibility between the RTSM vendor and sponsor organizations to ensure the system performs as intended according to predefined requirements. The vendor is responsible for ensuring the system is properly validated to perform to requirements prior to the client accepting the system for use. According to guidance documents, regulations and industry best practices, the sponsor is responsible for supplier oversight, validation of the system in their environment (i.e. fitness for use) and to plan for risk and mitigation. This whitepaper outlines a proposed strategy for sponsors to follow that demonstrates joint responsibility for ensuring overall RTSM validation, without duplicating the efforts already taken by their vendor and ensuring proper oversight by the sponsor company.

History of RTSM Systems Validation

The pharmaceutical industry is heavily regulated and generally risk-averse. Twenty years ago, auditors manually sifted through binders of SOPs, test cases and training summaries. Ten years ago, computer systems validation came into play. Auditors had to shift their focus to technology auditing, which changed the quality process. In this new wave of agile development, the quality process for cloud technology needs to undergo a fundamental shift a second time. Quality systems and auditors will have different requirements.

In such a conservative industry, the concept of storing data in the "cloud" can be met with uncertainty even though it is due to an evolution in technology. The "cloud" is simply a large data center. Just like any data center, there are servers, machines, and people that service those systems. The cloud also enables the flexibility to determine where in the world the data is stored (which is important in many EU countries) as well as ensures fool-proof disaster recovery and in the end, provides full traceability and much more robust security and expandability.

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Overview of Guidance Documents and Regulations

GAMP® 5 A Risk Based Approach to Compliant GxP Computerized Systems

According to ISPE, **GAMP® 5** "provides pragmatic and practical industry guidance to achieve compliant computer systems fit for intended us in an efficient and effective manner." In section 7, **GAMP® 5** outlines the requirements of software vendors. It is the responsibility of the sponsor organization to ensure the vendor complies with such requirements either through an audit, questionnaire, working meeting, etc., to ensure proper oversight.

21 CRF Part 11

21 CFR Part 11 outlines the FDA's current thinking regarding the scope and application of part 11 of Title 21 of the Code of Federal Regulations as it relates to electronic records and electronic signatures. Within the regulations, it is stated that sponsors must use validated systems, such as RTSM. Computer systems validation includes systems acceptance as a key step but does not dictate the scope of user acceptance testing.

ICH E6 Rev2

E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1). The GCP section of ICH E6 Rev2 includes updates that require a risk-based approach as well as a focus on ensuring systems are validated. Sponsors should work with their RTSM vendors to ensure the appropriate processes are in place. It is strongly recommended to complete a thorough qualification and ongoing oversight of that vendor. This is not limited to the initial qualification of the vendor from an audit perspective, but also includes ongoing management of the experience, operational issues, etc., to oversee the complete quality picture.

The RTSM Validation Process: Vendor Responsibilities

The vendor is responsible for ensuring the system is properly validated to perform to requirements, specifically study specifications laid out in the protocol. The vendor's process should include validation of the product functionality and the study configuration, and must be outlined in their quality system procedures.

Validation of a 100% Configurable, Fully Cloud-Based RTSM

The core RTSM product itself is validated with each product release, in compliance with 21 CFR Part 11 and GAMP 5. Validation at the core product level ensures that all features and requirements of the product are functioning according to detailed acceptance criteria outlined for each requirement. Traceability between requirements and test cases and results ensures that all requirements are addressed and verified. For validation of a study, the vendor verifies the study configuration matches the requirements captured in the study specification.

The study validation process begins with a validation plan that highlights areas of risk that should be tested. These include any feature that could impact patient safety (e.g. randomization, dispensing) or data integrity (e.g. maintaining the blind) even though these features are also fully validated in the product validation. These areas are important enough to merit a second layer of validation.

In addition, the RTSM vendor verifies the configuration of the study as part of the overall validation. Each study has a different visit schedule and patient flow, so these are always tested. Additionally, individual features that may be used for the study, such as temperature excursion monitoring or cohort management, are also verified. The study validation covers the entire workflow of the study, to ensure that each user role's experience matches what has been defined in the specification.

Lastly, the vendor is responsible for including additional testing for any feature that is new to the product. These features are heavily tested during product validation, but as they haven't been used in the 'real world' before, they merit a second check. The RTSM vendor writes test scripts to verify all the areas outlined in the study validation plan, performs the testing, and records the results in a validation report.

The RTSM Validation Process: Sponsor Responsibilities

According to the regulations, the sponsor does not need to repeat the validation performed by the RTSM vendor. It is the sponsor's responsibility to provide oversight and ensure acceptance of the system in a fitness for use scenario in their environment.

Since a fully cloud-based RTSM is hosted by the vendor, the system is already in the environment in which the sponsor will use it. In this case, the sponsor must then identify all risk areas and demonstrate confirmation that RTSM features are functioning properly when configured with their roles and study data. This process is typically done in a user acceptance testing (UAT) environment which is provided by the vendor.

The sponsor then needs to accept the system for use, by signing off that the system works as intended, that it is fit-for-use-purpose. Unlike the vendor responsibilities which are very clear, the sponsor is only required to demonstrate adequate oversight and ensure that they have sufficiently verified high risk areas to provide themselves a level of comfort that the system is indeed functioning as expected.

"UAT is meant to be acceptance of a system as fit for use, not as a requirement for sponsors to completely revalidate the system."

Regulations and guidance documents touch on validation, but do not prescribe a process or detailed requirements for validation or UAT. For example, in the TMF Reference model, UAT documentation/ system acceptance is listed as a requirement. There is no mention of what is included/necessary for this documentation. However, based on current regulations, UAT is meant to be acceptance of a system as fit for use, not as a requirement for sponsors to completely revalidate the system.

Recommended Practice

At the barest minimum, the sponsor could ask their RTSM vendor to give demos of high-risk functionality to confirm that it functions as intended. While this would meet the regulatory requirements, it is easier to confirm software functionality by doing rather than watching. It is highly recommended that sponsors log in and use the system to explore the functionality.

At the other extreme, the sponsor could repeat the RTSM vendor study validation process and write/ execute test scripts for every requirement of the system. This is not recommended as best practice, however, this practice is not uncommon due to the risk-averse nature of the pharmaceutical industry.

Decision Criteria for Using Test Scripts

Test scripts very clearly track the progression from requirements to results, confirming that each requirement has been tested. Because they are static, they require a very specific test environment with a precise data setup. If the step in a test script says to add a patient, if the site hasn't been opened the step will fail and the script will fail. For that reason, using test scripts in the first round of testing will test data setup and the scripts themselves.

Considerations when deciding to use test scripts:

- Writing scripts and verifying that they work takes a great deal of effort. If the up-front work isn't done to dry-run the test environment and the scripts, the testers will likely be frustrated by issues that are due to the script and not to the RTSM software.
- If the up-front work is done to dry-run the test environment and the scripts, the testers are only repeating what has already been proven to work.
- Test scripts, by definition, follow a pre-determined path for the user, which does not simulate real user experiences where people often follow hunches rather than user manuals.

Test Scenarios – An Alternative to Test Scripts

As an alternative to test scripts, the sponsor can identify high-risk areas that should be tested, much like the vendor validation plan, and use these to define scenarios to be tested. The RTSM specification should be used as a guide to identify the features included in the system.

For example, the scenarios can mimic general study workflow:

WORKFLOW CATEGORIES	POTENTIAL TEST CASE SCENARIOS
Study Startup	Add lots, release, and approve for use in countries Add sites and users Ship to sites
Site Inventory Management	Receive Shipments Perform temperature excursions Mark inventory as lost or damaged
Patient Flow	Screen a patient Randomize a patient

Once the scenarios have been defined, the sponsor assigns different users to perform each of the scenarios. The RTSM vendor should provide user manuals and training on how each feature functions. Some scenarios can be performed in parallel and some must be performed in sequence, but by the end of the testing each of the scenarios has been performed.

The sponsor should keep a record of who performed each scenario. The RTSM vendor should be present during the testing to capture any results that do not meet the expectations defined in the RTSM specification.

Advantages of Scenario Testing

When using scenarios, the sponsor gives comprehensive instructions on **what** to test, but gives more freedom around **how** to test.

- It is much less effort to define scenarios than to write scripts.
- Scenarios more accurately represents the end user experience, where people will click on just about anything and do things in unusual ways.

The sponsor, if asked by an auditor, can share the list of scenarios that were tested, the people who performed the testing, and the results. This will confirm that all high-risk areas were tested, and that the sponsor has provided adequate oversight to confirm that the software is functioning as expected.

User Acceptance Testing (UAT) Best Practices

Preparation for UAT is far more labor-intensive when using test scripts, but even when using scenarios the process should begin with planning. Just as the RTSM vendor does in preparation for study validation, the sponsor must ensure that the scenarios to be tested address the high-risk areas. The goal is for the testing to be targeted so the sponsor spends time on the areas most likely to produce errors.

It is crucial to have key roles represented in the planning process to ensure that all perspectives are heard. An RTSM subject matter expert or dedicated RTSM group will have the experience to know what areas to address, but members of study teams may not participate in RTSM development more than once a year. In this case, the sponsor should ensure that the testing plan receives input from Clinical Supply, Clinical Operations, Biostatistics, and usually Data Management.

Since UAT requires that the testers can perform the tasks outlined in the scenarios, the RTSM vendor should get the sponsor comfortable in the system before beginning the official testing. It is highly recommended that the sponsor spend time with the system, either directly or through demos, throughout the design process. This resolves two common roadblocks during UAT:

1) **Testers are not trained in the system**
   To overcome this, allocate enough time before UAT to make sure the testers know how to log-in and perform the tasks needed to complete the scenarios. An intuitive RTSM streamlines this process.

2) **Design changes cause issues in UAT**
   Very, very frequently the issues that arise during UAT are design changes – a question on a screen that isn't clear, a report that should really have a few more columns. These 'issues' have nothing to do with functioning according to the specifications, they are new ideas. Generally, these are good ideas, because the sponsor is seeing the system from the point of view of the site, or experiencing how the resupply functions when lots of patients are added. The sponsor should encourage their RTSM vendor to share the system BEFORE getting in a room to perform UAT. There should be no surprises at UAT.

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Conclusion

RTSM systems validation is a critical process. It is important to familiarize yourself with the regulations and requirements as well as understand the responsibilities of the sponsor to ensure proper oversight as well as what should be expected of the RTSM vendor. It is recommended that UAT is used to check high-risk areas and not as a process to find quality errors in software. Remember, it is the vendor's responsibility to ensure the system is properly validated to perform to requirements per the protocol.

About the Authors

Kathleen Greenough, Director of Client Solutions at 4G Clinical, has 16 years of experience in life sciences spanning Clinical Operations, Finance, and IT. Her wide range of solutions implementation expertise includes RTSM, CTMS, trial costing tools, OLAP financial suites and patient enrollment planning. Kathleen has also spent many years as a Clinical Financial Planner and Analyst at a major biotech in Cambridge, MA, gaining a broad and deep understanding of the challenges inherent in Clinical Development. Specializing in software adoption and a frequent speaker at industry conferences, Kathleen is most in her element when working within a user community to facilitate solutions that are insightful and truly helpful.

Laura Araujo, Vice President of Quality at 4G Clinical, has over 30 years of experience in Quality Assurance and Technology, holding various positions in Software Development, Quality Assurance, Software Auditing, and Technology Management. She has had positions in, or related to, the pharmaceutical industry for 25 years. Prior to joining 4G Clinical, for 10 years, Ms. Araujo was the President and owner of Ojuara, LLC, an independent consulting firm servicing the health care and pharmaceutical industries, as well as, technology development companies.

Download our White Paper: RTSM Best Practices

Still have questions? Contact us today to start a conversation.

Bringing crucial medicines to those who need them, *faster*.

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