eBOOK

How to Select the Most Effective RTSM Technology for Early Phase Studies

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In the wake of pandemic-related lockdowns, healthcare cost inflation, supply chain issues, and the state of the economy at large, clinical trials are rapidly changing. The right technology can help you manage and reduce volatility.

With 42 percent [1] of sites logging into more than 6 platforms for an average study, evaluating additional solutions to add to your eClinical technology stack can feel daunting. Anticipation of near-term implementation strain may make it hard to envision the long-term payoff of introducing and training diverse staff roles on yet another technology; however, selecting and implementing the right randomization and trial supply management (RTSM) solution is more critical than ever to study success.

Sponsors who don't implement RTSM risk:

- Selection bias impacting randomization
- Potential unblinding incidents
- Regulatory non-compliance
- Lack of visibility into drug accountability
- Waste and overages driving budget inefficiencies

In this eBook, we will explore RTSM in detail and look at how to determine when to use RTSM, considerations when evaluating RTSM vendors, and best practices when implementing a new randomization and trial supply management solution.

Changes in the Clinical Trial Industry are Putting Studies at Risk

Developing a new medicine, therapeutic, diagnostic, or device is a high-stakes endeavor. Organizations face tremendous financial and operational risk balanced against the high reward of helping to improve the health and quality of life of vulnerable populations. The race to not only develop and prove the safety and efficacy of these new compounds, components, and treatments but also to bring the innovations to market as quickly as possible is hyper-competitive. Inefficiencies or delays in product development and testing in the early phases can mean delaying a key go-to-market window, missing customer commitments, or even putting the company's solvency and reputation at risk.

With evolving study designs, the COVID-19 pandemic, scientific advancements, and ongoing global supply chain and economic issues, clinical trials are growing even more complex:

- Employee churn: Sites face a 30 percent turnover rate for clinical research associates (CRAs) (~10 percent higher than the US average)[2]
- Supply chain issues: Around 87 percent of life sciences companies still faced pandemic-related supply chain issues as of late 2021[3]
- Increased amendments: The average number of amendments per protocol rose by 33 percent in Phase I and 23 percent in Phase II from 2018-2020[4]

These issues may seem relatively benign, but if left unchecked, they put your clinical trials at risk – or at least over timelines or budgets. Employee churn produces a lack of consistency in trial operations and may cause delays or errors related to learning curves. Supply chain issues risk whether you receive your investigational product in time or whether it is even usable (e.g., temperature control issues). Protocol amendments necessitate changes to systems that were designed to meet a certain study design, and require quick, thorough responses from vendor teams.

Leveraging technologies traditionally used in later-phase trials provides a way to overcome these issues and fuel successes in early-phase studies, which is crucial in a competitive market.

The Role of Clinical Trial Technology in Enabling Early Phase Trial Success

Technology has long underpinned clinical trial operations, particularly in the areas of data capture and study management. Yet research teams often still rely on manual methods of randomization and trial supply management for early phase studies. Their perception is that the investment in technology solutions makes sense only in studies with large numbers of sites, sizable patient pools, and broader global reach.

Today, organizations running studies of all phases and sizes are looking to integrate RTSM solutions into their technology stacks to remove risks associated with manual, error-prone processes for randomization and supply management and gain greater real-time transparency to supply status. They are finding that RTSM is just as valuable for early phase trials as it is for Phase III and beyond.

In a dynamic and complex trial environment, having the right RTSM tools in place helps ensure supply chain issues are managed before they become problems – no matter what the study phase.

The Drug Supply Evolution: IxRS to RTSM

Technologies to streamline randomizations or manage trial supply have been in existence in some form or another since the 1990s, but they have gone under a variety of names including:

- IRT - Interactive Response System
- IWR(S) - Interactive Web Response (System)
- IVR(S) - Interactive Voice Response (System)
- IXR(S) - Any of the above

Today's RTSM is unique compared to its early technological predecessors because it recognizes the importance of not just randomization, but also supply management, and getting the investigational product (IP) on shelves when and where it's needed. Combining these two functions together elevates overall study management and bridges organizational silos. Whatever name it goes by, RTSM is a powerful tool that can improve efficiencies, regulatory compliance, data visibility, sustainability, patient safety, and more.

According to a McKinsey[5] report, elevating clinical supply strategy to include RTSM solutions has the potential to:

- Provide better investigator and patient experiences
- Reduce drug launch timelines by one to two years
- Deliver 15 to 20 percent cost savings in clinical drug supply

What Is RTSM, Precisely?

Randomization and trial supply management can encompass several basic functions, some of which can theoretically be done manually. However, the automation of these activities by an electronic solution has the potential to improve the efficiency of a clinical trial.

- Participant management: RTSM can support study teams as they manage the participant journey from the eligibility decision through the enrollment process. The technology delivers participant-specific dosing schedules and instructions for reporting adverse events.
- Randomization: RTSM guarantees that selection bias is removed from your study data while automating the process of maintaining balanced cohorts, even if participants drop out.
- Supply chain management: RTSM tracks inventory from initial receipt through eventual return and destruction.

The Right Time for RTSM

As with any technology, there is always a question of when is the right time to adopt it. In early phase studies, manual methods of randomization and supply management based on paper or in spreadsheets have been the status quo, and change can be challenging to navigate. However, clinical trials increasingly require eClinical technologies that can help study teams manage the complexities of early-stage clinical research. In fact, in some therapeutic areas, like oncology, early-phase studies are actually more complex.

Organizations have learned that by relying on manual processes, they're exposing themselves to unnecessary risks. The smaller size of early phase studies means there's less room for missteps; automation can provide relief by removing human error. Dose-finding studies and studies with adaptive designs, both common in Phase II, are also highly complicated, and study teams can benefit from the support of technologies that ensure they're managing dosing and allocation correctly.

You may have maintained the status quo thus far, but if you are experiencing any of the following red flags, it may be time to bring RTSM upstream into your early phase studies:

You're Relying on Manual Randomization Methods

How do you randomize your study participants? Some biotech, biopharma, and device research companies are still relying on manual randomization methods, especially in smaller, early-phase studies. Then, they keep track of this information in spreadsheets.

Any manual method introduces the risk of human error as well as selection bias in the randomization process, meaning your sample will not be fully representative of the efficacy of the drug across the wider population. This jeopardizes potential regulatory approval.

You're Struggling with Lagging Site Inventory

Scheduling participant site visits and not being able to complete their treatment due to a supply management issue is one surefire way to cause both patients and sites to disengage from a study, risking compliance and retention rates. RTSM can help manage site inventory and ensure you get your investigational products in time so you don't miss participant visits due to not having the right inventory on hand, and reduce overcorrections in ordering excess inventory that leads to waste and cost overages.

You're Concerned About IP Transportation

Without a randomization and trial supply management tool in place, you lack visibility into IP transportation, and ensuring IP safety and quality becomes a highly manual process. An RTSM solution, however, may automatically flag a shipment in the case of a temperature excursion, and send a notification to the appropriate role, eliminating the need for site staff to spend valuable time combing through a temperature log. It can also facilitate easier replacement or disposal of a product if it becomes unusable for any reason.

You're Dealing with Excessive Product Waste

Last-minute shipments or maintaining large volumes of drug supply can drive up study costs. According to McKinsey[5], as of November 2021, the median waste level for investigational medicinal product (IMP) kits was 50 percent. The primary cause associated with this value was poor planning. Without forecasting and algorithms, it's nearly impossible to maintain leaner trial supply management.

You're Not Confident in Your Drug Accountability Best Practices

Drug accountability starts with dispensing IP to study participants and comprises how much they take, what they are taking, and what they return. The process ends with unused IP being destroyed. RTSM provides drug accountability oversight from start to finish, which can become critical, especially when working with controlled substances, such as opiates. The precision offered by RTSM is also important in establishing pharmacokinetics (PK) or pharmacodynamics (PD) as well as meeting regulatory requirements. For instance, FDA 21 CFR Part 312[6] requires studies to maintain drug disposition records. Is your study able to reconcile the amount of IP given vs. the IP taken for every patient? If not, an RTSM can help.

Critical Features to Look for When Selecting an RTSM

There's feature parity throughout the RTSM market. Most, if not all, RTSM solutions are going to provide the basic functionality your clinical trials need.

These baseline capabilities include:

- Randomization
- Single or double blinding
- Shipment tracking
- Inventory management

This parity can make choosing a vendor difficult. How do you compare apples to apples? What matters most is that you secure the features and system flexibility that are most important based on your study design.

While the list of functions offered by many RTSM vendors on the market can be quite long, and every protocol is unique, Medrio recommends ensuring your chosen RTSM solution delivers the following key features:

Integration

When you're done using the RTSM in a particular study, that data needs to be exported relatively quickly as the trial moves towards database lock. When this process is done manually, site users need to transcribe the RTSM's data, introducing delays and the potential for human error.

Choosing a modern RTSM solution that is integrated directly with an EDC will ensure that the data flow is seamless and automatic, eliminating need for complex and time consuming integrations between different vendors.

Flexibility

Before you settle on an RTSM vendor, make sure that the solution can deliver the flexibility needed to best serve your studies. For example, early-phase data on dosing may require the elimination of a treatment arm. A flexible solution, backed by an expert team, can easily plan for and accommodate this change. Out-of-the-box solutions may come with functionality limitations; an RTSM optimized for your study will allow you to make the most of the technology.

Dose Escalation Management

Dose escalation schedules can be calculated manually but doing so increases the risk of introducing human error. By making dose escalation management part of an automated system, you get the right dosage simply by entering the relevant patient data. This is especially crucial in Phase I studies, which are focused on finding the correct PK, PD, and dosing range of an IP.

Automated Notifications

Any robust RTSM solution will include an automated notification feature. This capability can break down the organizational informational silo, pulling information out of email or messaging channels and highlighting critical data in real-time.

The ideal system should automatically let people know when a participant is randomized, when shipments are needed, and so on. For instance, the clinical operations director should be notified when a participant is unblinded, and the supply manager should receive an alert when they need to review a shipment.

Ability to Build a Partnership and Provide Guidance

This is particularly important if you are running an early phase study or using RTSM for the first time. Ensure that your solution provider has experience guiding organizations with a similiar size or study design to yours to learn how to bring your master protocol master protocol to life within their RTSM solution. Ensure that your partner is prepared to educate and guide your team on best practices based on their experience.

THE REGULATORY RISKS OF MANUAL RANDOMIZATION

When you've completed your study and are ready to submit the data to the regulatory body for review, it can feel like a celebratory milestone. However, your manual randomization methodology can quickly become a roadblock.

According to experts, the more manual processes for data collection and randomization that are used in your study, the more likely you are to get flagged for follow-up by regulatory agencies. This can slow down approvals and jeopardize your ability to get to market quickly.

Key Questions to Ask Before Selecting an RTSM Vendor

Once you've defined your purchasing criteria and have put out RFIs to RTSM vendors, the selection process begins. As you start having conversations with your shortlist of potential vendors and watching demos of their solutions, remain focused on your requirements and imperatives. It is critical to use each conversation to ensure the vendor is prepared to support your unique organization and meet the specific needs of your study protocol.

By asking potential vendors the right questions, you can find a partner to help you elevate your randomization and supply management strategy without introducing additional complexities. As a guide to get started, here are a few foundational questions we recommend asking based on our own experiences with customers running studies of all sizes and phases.

How Will You Support My Study Design?

This is a basic question, but it is also the most essential. Protocol design drives the complexity of the RTSM build. We've already established that protocols are becoming increasingly complicated, a trend that shows no sign of slowing down any time soon. It's vital that your vendor will take the time to understand your protocol and its unique nuances. Without that understanding, they shouldn't be prepared to guarantee that they can deliver the solution you need.

How Do You Prepare to Handle Protocol Amendments?

Understanding that both the frequency and quantity of protocol amendments are increasing, it's fair to say that no protocol is ever truly final. Change is nearly inevitable in today's clinical trials, especially in the early phases when data is continuously being reviewed.

Many times, IP is packaged and at a warehouse awaiting shipment before an RTSM vendor is engaged, but that is short-sighted. Bringing your chosen vendor in as early as 6 months or more in advance of the first-patient-in (FPI) milestone can deliver a plethora of benefits.

Involving an experienced RTSM vendor in the early planning stages allows experts to identify and plan for potential risks, provide recommendations on packaging and labeling, and ensure alignment between your protocol and RTSM strategy.

That's why it's critical to engage a vendor who has the experience to think proactively and identify potential areas of change, even when there's no reference to them in the protocol. This allows the vendor to introduce capabilities up front that can help you avoid cost- and time-intensive changes later on in your study. Of course, planning for change isn't always possible. In those cases, the vendor must have a flexible process for responding quickly, and with agility, when change arises.

What's the Background of the Vendor Team Supporting the RTSM?

Unlike other elements of a clinical trial, drug supply information isn't frequently documented in the study protocol and occasionally is not formally documented anywhere at all. As a result, sponsors may find themselves relying on the expertise of a vendor to know what questions should be asked and what information is required to build a robust supply management strategy. Pressure test the industry experience and tenure of the RTSM team that your organization would work with.

How Does Your RTSM Support Our Decision-Making Process?

Even small studies can generate a lot of data in RTSM. It is vital to consider how you can take that data and make it actionable to save time, reduce costs, eliminate waste, and improve site efficiencies. Make sure that the RTSM platform you choose has configurable reporting capabilities to help you access the data you need and turn it into something impactful that informs future supply management decisions. Verify the level and types of reports that are included and what requires extra customization and additional fees.

How Well Can Your RTSM Integrate with Other Technologies?

To operate most efficiently at the site level, it's critical that your RTSM solution plays well with other eClinical technologies, including eConsent, eCOA, EDC, CTMS, and RBQM.

Be aware that many integrated solutions only push through data updates once every 24 hours, or sometimes even less frequently.

This can leave you in the dark for hours or even days when it comes to your data – blinding you to compliance trends and data quality or participant safety issues. A seamlessly integrated solution should be able to reflect data updates immediately or within minutes so you can maintain control over your study.

Do You Consider Yourself a Vendor or a Partner?

Take the time to discuss whether an RTSM supplier will be a vendor or if they can offer the guidance of a partner. Vendors provide software. When you need help, you may talk to an IT expert who can diagnose issues in the technology but won't be able to provide any other insights. RTSM partners are completely different. While you still run your trial autonomously, their product, project, and subject matter experts provide collaborative support and guidance on best practices so that your studies move faster and with fewer obstacles to navigate.

WHY SHOULD YOU CHOOSE AN INTEGRATED RTSM?

Patient Safety

The combination of ePRO, EDC, and RTSM allows study teams to respond quickly to adverse events (AEs) in the early phases of a trial; all the information they need is up-to-date and accessible. RTSM enables emergency unblinding for the affected participant while preserving the blind for the rest of the study. It also prevents a participant from being randomized incorrectly or receiving the wrong treatment, which can potentially lead to AEs.

Operational Visibility

Using manual or otherwise non-integrated systems can lead to informational blind spots, miscommunications between teams, and uninformed decision-making. This shortcoming can lead to mismanagement of inventory or even accidental unblinding, which can jeopardize study success.

Regulatory Submissions

Filing a regulatory submission or submitting an audit trail can be much more arduous and error-prone when data is collected and collated manually. Integrated solutions that feature automatically generated audit trails and easy data export can simplify this critical, time-sensitive process.

Data Quality and Visibility

Integrated platforms reduce the need for data transcription and validation by automating data sharing between solutions, preventing timeline delays, and reducing costs. Real-time visibility into data also allows study teams to spot trends sooner and intervene as needed. For example, if participant visits logged in RTSM show up in EDC in real-time, and a participant doesn't complete a visit as required, study teams can take action to ensure compliance.

Prepare for a Successful Implementation

Once you've selected your vendor of choice, there are two simple, strategic pillars to ensure a smooth and successful implementation.

Assemble a Project Team

Start by bringing the right people to the table to support the implementation effort. Assigning critical roles will help ensure accountability. The exact combination of roles involved may vary by organization, but should involve stakeholders who oversee:

- IP packaging and labeling
- Participant randomization and the subject journey
- Drug shipments
- Data and any eClinical or EDC integration

This group should work collaboratively to define the following in advance of meeting with your RTSM vendor:

- Key roles, responsibilities, and contact information for the study team
- Kit and subject randomization list needs
- Study drug dispensation rules
- Finalized contracts with sites and depots

If any data transfers are required, your vendor team will need to gather details including the type of transfer, frequency, how the data will be delivered, and all required data parameters.

While some of these elements may not be a direct part of the RTSM solution, they can have an impact on your vendor's ability to deliver a finished product on time.

Develop a Communication Plan

The benefit of communication isn't limited to your internal team. Work with your vendor to approve a detailed project plan, outline deliverables, and share study-specific information based on the latest protocol. If you can create and agree to detailed specifications for the RTSM build as a team, you'll improve your odds of success.

You also should encourage open communication between your team and the vendor. Meeting regularly to monitor project progress and stay aligned is ideal. This allows you to set proper expectations on both sides around responsiveness and avoid unexpected delays that can impact study timelines.

UNNECESSARY COMPLEXITY IS A BIG RISK TO IMPLEMENTATION SUCCESS

Robust RTSM solutions are capable of handling massive amounts of data - but that doesn't mean that they should. Collecting extraneous data increases the complexity of your RTSM system unnecessarily, potentially reducing platform speed and making it more difficult to find the information you need.

The Bottom Line

Today's RTSM systems have matured from IRT services into randomization and trial supply management solutions that make clinical trials safer and faster. However, not all RTSM products have evolved equally.

In the current clinical trial landscape, mid-study protocol amendments are standard and IP supply chains require unprecedented flexibility. Even aside from the question of whether the RTSM integrates into your eClinical suite, each randomization and trial supply management solution is a little different. You need to carefully consider whether a particular RTSM can keep up with your therapeutic, diagnostic, device, or drug development protocols.

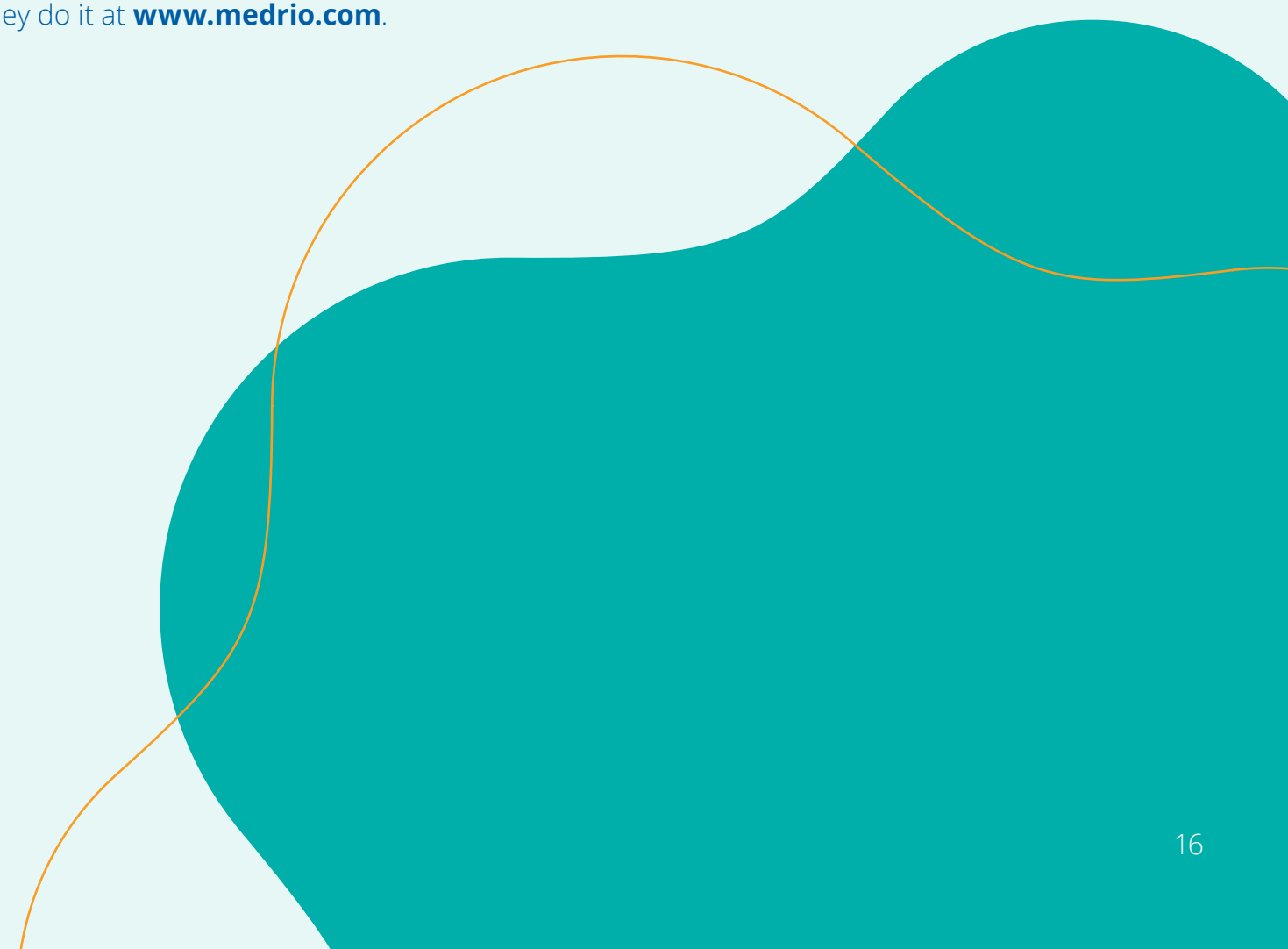
Medrio RTSM's modern and intuitive user interface brings randomization and trial supply management technology into the 2020s. A simple experience for the user means less stress for site staff, and reduces the potential impact of employee turnover at sites on trial operations.

Behind the interface lies a powerful platform intentionally built to remove unnecessary complexity from your study data. In combination with insights from our team of experts, you can effectively manage the randomization or supply chain challenges you may face in running your trial, whether they're big or small.

ABOUT MEDRIO

Medrio is on a mission to ease complexity in today's hybrid, decentralized, and site-based clinical trials by delivering a flexible suite of eClinical technologies and services, including EDC, eCOA, ePRO, eConsent, Direct Data Capture, and Randomization and Trial Supply Management (RTSM).

Trusted by contract research organizations (CROs), sponsors, and sites across all therapeutic areas and trial phases from study startup and feasibility to post-market approval since 2005, Medrio is industry-recognized for delivering eClinical software with intuitive interfaces and time-saving "drag and drop" configurations as well as high-touch customer engagement, onboarding, and support services. Learn how they do it at **www.medrio.com**.



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