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RTSM and EDC: The Unified Experience

Integrating and streamlining complex processes to better clinical trials

The familiar methodological framework that supports the planning, conduct and evaluation of clinical trials is changing—again. Just as manual methods for randomization, data collection, product dispensing and other core elements were replaced by electronic applications, those best-in-breed products designed to perform a single function are being replaced by integrated product suites that are up and running 24 hours a day, seven days a week, with intuitive, easy-to-follow instructions for investigators, site monitors, and users. These solutions aim to provide unified solutions with a single user interface, automatic data interchange, more reliable, robust security measures and other features that improve efficiency and quality at a lower overall cost.

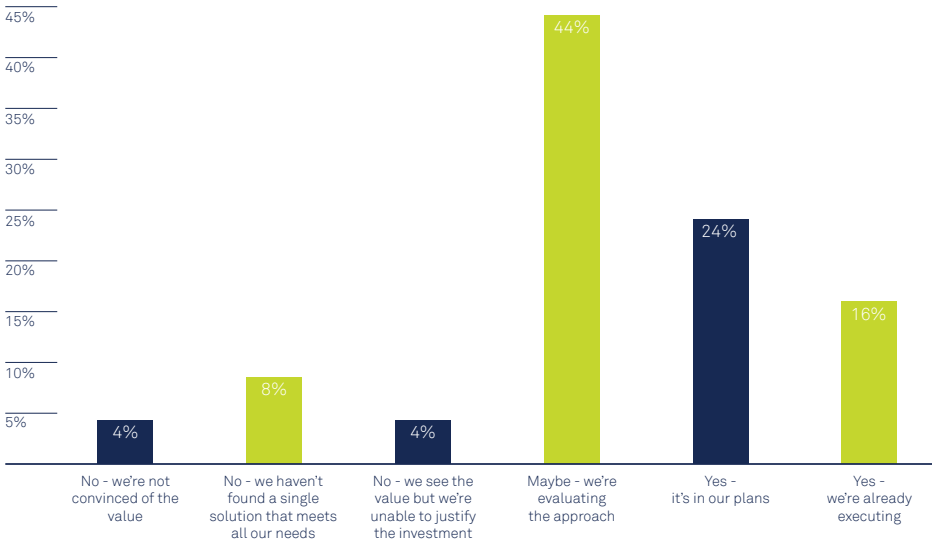
The new generation systems that integrate traditional randomization and supply management (RTSM) and electronic data capture (EDC) have not yet developed a common name or description. Some observers describe a unified experience, others as part of the clinical cloud or as part of a clinical trial suite. And yet there are some that still rely in data imports/exports and batch uploads to collect data in one place. Whatever the name, integrating and streamlining the complex processes that make up a clinical trial is a win for sponsors, technology providers, contract research organizations (CROs), investigators, regulators and, in the end, patients.

Sponsors/CROs still rely on heavy data import/ export agreements to manage data uploads from data collected in various disparate data systems.

Under the Gun

Trial sponsors have a simple mandate. They want studies to be completed on time, within budget and with the highest quality. One of the most direct and cost effective methods to meet all three goals is to integrate traditional Randomization and Trial Supply Management (RTSM) requirements and EDC.

FIGURE 1: Is your organization adopting a unified solution for RTSM & EDC?



But integration is a task easier to describe than to accomplish. To even be able to talk about standardization is a major improvement especially considering that not so long ago, the industry still relied on traditional call and web services to randomize subjects and dispense treatment. Manual entry resulted in erroneous data and reconciliation remained a costly and time consuming task with the same data captured in disparate systems.

Trust But Verify

Clinical trial sponsors and investigators were among the earliest adopters of electronic versions of traditional RTSM solutions and EDC. Both entered the industry as stand-alone systems. And while there is some degree of integration, those various RTSM solutions and EDC remain separate universes in too many clinical trial programs. Some data can be pushed from some RTSM systems into some EDC systems, some data back from EDC to RTSM. And reconciliation remains a problem despite robust testing during the development phase.

The industry needs ease and flexibility conducting clinical trials. Randomization and trial supply management needs to be flexible to accommodate protocol changes that come with adaptive trial design and increasing design complexity.

Even more important than easy configuration and flexibility is a good experience for end users—the investigators, monitors and staffers who must use the system successfully in order to complete a trial. The user interface has to be easy to use and intuitive across multiple cultures and levels of experience. Any training that is needed must be just as easy and just as fast. And the entire system must be available any time, anywhere, for any authorized user.

CROs, like drug sponsors, are focused on managing the time, cost and quality of clinical trials while working to get drugs into and through Phase III and approved more quickly.

Making Do

That kind of seamless integration is a tall order. While not impossible, it is difficult, time consuming and resource intensive.

CROs, like drug sponsors, are focused on managing the time, cost and quality of clinical trials while working to get drugs into and through Phase III and approved more quickly. They relied heavily on manual labor to import and export data, countless hours spent reconciling data between one source and another. Additionally, they provided extensive programming support to meet regulatory demands.

The Vision

Is the traditional way of integrating data from one disparate source to another reaching this goal? Are there ways that we can move away from data import agreements and specifying variables to match between one system and another for the purpose of including data in final datasets. Will there be a time that we can completely eliminate reconciliation of RTSM data and EDC data? Are there better ways by which RTSM data can be collected and ***automatically*** integrated with EDC?

Cloud-based RTSM arrived around 2010, leveraging the concept of Software as a Service (SaaS) to produce pre-validated capabilities that let sponsors and CROs prototype and build systems as needed, no programming required. That was when interactive links between traditional RTSM systems and EDC moved from dream to possibility.

Sponsors are expecting an increasing degree of interconnection across what were once separate domains within the clinical trial world.

Integrating RTSM and EDC is just the beginning for cloud-based services. Sponsors are expecting an ***increasing degree of interconnection*** across what were once separate domains within the clinical trial world. Users now expect systems that share design elements across different sites and functions as well as data. They expect clinical data to be pulled from services such as electronic patient-reported outcomes (ePRO) or electronic medical records.

"The time is actually here when conducting clinical studies in disparate technological silos over different clinical applications with a type of one-off integration will cease to be the best option," Lebowitsch said. "These one-off integrations are better than no integration at all, but they still leave a lot of room for improvement."

The real question is whether it is better to integrate multiple systems or to create a single, unified system.

The Comparison

Integration of multiple systems from multiple vendors is not an impossibility. Nischal described an inVentiv integration of three different systems for a straightforward double-blind Phase III study with two treatment arms and no international study sites or other complications.

The company used eCRF from Medidata, a clinical trial management system (CTMS) database from a second vendor and RTSM services from a third vendor. Site information in the CTMS database needed to be shared with the RTSM database, while randomization and drug information needed to be shared with the eCRF. All three systems had to work seamlessly and provide a single log-on so trial users did not have to maintain IDs and log-ons for three distinct systems.

The solution was to gather project managers from the data management team and the RTSM team to figure out which data points would be moved from which system(s) to which system(s). Next came development and testing teams looking at the different database designs in the three systems, mapping fields and tables, and looking at details such as the frequency of data transfers, how to handle updates and inserts, and how to create a single user interface that included the appropriate functions from all three programs.

"They came up with a very detailed but very lengthy requirement document that was taken by our development team, coded, and then the validation team would test the entire transfer," Nischal explained. "We had to get our IT team involved because we had to set up secure FTP sites where different teams and different systems teams could pull data in a secure manner. The clinical lead was sitting on top of everything, managing and coordinating the process."

Nischal reported that the integration worked. But was the result worth the effort?

"The process was extremely resource heavy," Nischal said. "We had many people working across many different organizational groups talking to each other, figuring out how to code these transfers. We had developers and we had validators. We had IT involved and we had QA sitting on top of the entire process. We addressed some of the challenges of data integrity by making these systems talk to each other so we are not collecting duplicate data or reconciling duplicate data. We did overcome the challenge, but the question is at what cost?"

At what cost is it best to continue integrating data from disparate systems?

The Unified Challenge

The real question is whether it is better to integrate multiple systems or to create a single, unified system. While there are arguments both ways, practicality says to go with a unified system. Look no further than the evolution of desktop applications.

In the 1980s, the buzzword was "best-in-breed." Get the best application for document creation and editing, the best spreadsheet, the best database, the best presentation program. It was awkward; one couldn't easily drop a presentation graphic from Harvard Graphics' ProPresentations into a WordPerfect document, nor did Lotus 1.2.3 play well with Ashton-Tate's dBase III.
"At the time, it was the right choice to make," Lebowitsch said. "You had to choose the best-of-breed. The market was still evolving, there were big differences between various applications in the space. You had to have the best separate applications for each task."

Microsoft Office changed the dynamic. Instead of figuring out how to integrate different applications, a single suite did it all with a common look and feel. It didn't matter that WordPerfect was a better writing tool than Word, or that Lotus Notes was better than Excel.

"The value of the unified solution was so much higher than the marginal advantages these best-of-breed applications had," Lebowitsch explained. "Microsoft delivered the unified Office Suite that made it easy to move content from one app to another app. You could copy and paste, you could embed graphs in presentations and tables in documents. The whole was easier to use than the parts because they all had a unified user interface."

There have been similar evolutions in other market segments. Enterprise resource planning started with a host of competing products that eventually coalesced into unified product suites. The clinical trials market is now mature enough to support, even demand, that same level of unification in the basic applications that power the industry.

"We have all been seeing signs of this happening for some time," Lebowitsch said. "Based on standards and open application programming interfaces (APIs), there have been numerous data integrations between EDC and RTSM systems (or IRT systems). There is a lot of integration between CTMS, lab systems and exports to SaaS. Many times the integrations have been cross-vendor and I don't think this is going away. It is very important that we as vendors remain committed to open standards and open APIs."

The clinical trials market is now mature enough to support, even demand, a level of unification in the basic applications that power the industry.

But those one-time, cross-vendor integrations are just the beginning. Some Medidata customers have managed to centralize some functions to provide a single user sign-on across multiple applications.

"The boundaries between some of these applications are becoming blurred," Lebowitsch continued. "But this is still not what we mean by a unified application or a unified solution. A unified solution eliminates all the artificial boundaries across apps."

The Unified Future

The ultimate clinical trials suite has yet to appear. What is clear is that a successful suite needs multiple elements. Sponsors and CROs are looking for:

- Unified and uniform user and site management
- Unification of core study design elements
- Unified data model
- Common terminology
- A unified user interface that promotes the appropriate user flow and movement
- The ability to maintain the relevant context (i.e., the study, the site and the subject, as the user moves from the EDC to the RTSM system and back again)
- Standardization across studies
- Better reporting and overall visibility
- Increased site compliance and satisfaction
- Reduced total cost of ownership
- Reduced operational risk
- Increased study agility
- Better internal resource utilization

"That's not to say there shouldn't be boundaries at all," Lebowitsch added. "There should certainly be access boundaries in a clinical system. There should be modularity. Not everyone should be able to see or do everything. You need modularity to help break the problem o taking a study live into pieces that can be managed separately—a problem has to be managed in its parts. But whatever the boundaries are, they should be based on business reasons, not on technological limitations."

It may seem obvious that the value of a unified suite is greater than the sum of the value of its individual parts. But clinical trials are based on evidence, not seemingly obvious conclusions. Medidata tested the hypothesis that using a single system or EDC and RTSM solution can reduce the time to form completion, the time between a visit and the submission of the completed visit form and data capture. The study used Medidata's own RTSM, based on Medidata Rave EDC.

"The result," Lebowitsch said, "was a dramatic drop from a median of 14 days between visit and form completion to just nine days," a 35 percent reduction.

Reduced data collection time is just the beginning. *Because the unified system uses a single data model, there is no data integration or reconciliation. There are none of the risks associated with custom coding because there is no custom coding. The entire system and each of its elements have already been validated. Reconciliation goes away! Timelines are reduced and data quality improves.*

The unified system is more agile than a customized integration. Changing the study design and adding an arm, or example, can be done on the fly. Amendments are a feature in the system via Edit Live Design functionality, not a custom change that requires special coding and verification.

Resource utilization is also changed. A unified system is easier to set up and implement, which suggests being able to do the same amount of work with less staff time.

The move to a fully unified, end-to-end platform is a journey that, for some, will begin with a unified EDC and RTSM solution. Once this initial step is achieved, the value of a comprehensive clinical cloud platform—inclusive of unified design tools, CTMS, ePRO, monitoring tools and reporting tools—will be self-evident. It will transform clinical trials.

Trials using Medidata's unified RTSM/Rave solution can experience a reduction in form completion time of 35 percent.

The Challenge of Implementation

But simply having a unified approach does not mean organizations will adopt it. Moving from best-in-breed solutions to a unified solution means changing long-standing habits and practices. That kind of change requires strong internal leadership.

"You must have a very senior-level advocate within your company to drive this," Leonatti said. "We had a very high-level advocate from the top saying we are going to be a company that uses EDC. The same thing has to happen to get a single unified solution between EDC and IRT."

Making the change may take senior-level support, but good ideas don't always start at the top. Change begins when someone in the organization recognizes an opportunity and promotes the advantages of doing things differently.

"Be the change you want to see in your organization," Nischal said. "Lack of executive direction is usually because they are locked into the existing system. Push the vision with your own management and show them the dollar value of a unified system. Even though you are getting the efficiency of time and cost savings, you're not compromising on the quality of your trial product. Push this vision within your teams, discuss it at every opportunity within your organization. Show them the process savings, show them that your data is more secure within one system, that you are reducing or completely mitigating any kind of data integrity issues. They will listen."

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