21st Century Trials Demand 21st Century Technology

Contributed by

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The pharmaceutical industry can pride itself on its use of state-of-the art technology in drug discovery using such advances as robotics, molecular modeling, and powerful computational software. Oddly, though, the industry has been slow to take advantage of technology to support clinical operations. Consequently, clinical trial systems are notoriously inefficient as they depend on many siloed databases and manual, error-prone processes that extend development timelines and inflate costs.

Given the increasing demands on the development function, sponsor companies and their contract research organizations (CROs) can ill afford to operate this way. In the past five years, the industry has seen a 58% increase in the number of sites per trial and a doubling of the median number of countries per trial.[2] And, the average number of endpoints collected increased 71% between 2002 and 2012. All this means more data, more data sources, and more systems in an environment where budgets and people are ever more strained. Against this backdrop, performance metrics are underwhelming. Less than 10% of trials end on time and nearly half of all sites under-enroll study volunteers.

So, the question is: Why are so many industry leaders still willing to collect, aggregate, manipulate, and report clinical trial data manually when automated solutions are available and are proven to streamline operations and yield better results while reducing trial costs and timelines?

Automated Data Capture

For the past 20 years, sponsors and CROs have collected patient data from investigational sites electronically via electronic data capture (EDC) systems. Unfortunately, sites are not the only source of trial participants' clinical data. Data are now routinely collected directly from patients or their caregivers, as well as from external sources such as labs and imaging centers. In many cases, these data sources are still paper-based.

According to a survey by Industry Standard Research (ISR), "nearly half of all studies that collect patient outcome data do so using primarily paper solutions."[3] Many sponsors have clung to the use of paper-based patient diaries to collect patient-reported outcomes (PRO) and clinical outcome assessments (COA) based on an outdated notion that it is less expensive than electronic methods (ePRO/eCOA). Today that is simply not the case. The cost of poor quality data gleaned from paper collection and transposition — bundled with the cost of not knowing study results until well after study close — far outweighs the cost of electronic data collection from patients, clinicians and caregivers. Paper data collection involves heavy back-end costs, as responses must be manually checked and entered into a database. Plus, data quality suffers from a combination of waning patient compliance and data-entry errors. There's also patient preference to consider. A recent ISR survey found that more than half (55%) of respondents strongly prefer electronic PRO systems over paper diaries and that 86% "somewhat prefer" them.

Objective data can also be integrated with electronic PRO/COA data, however few sponsors elect these efficiencies. Medical device data — such as spirometry tests, electrocardiograms, and medical imaging — are often interpreted at sites and then entered manually into EDCs, a process that can introduce inconsistencies in interpretation and transcription errors, which jeopardize data integrity, clinical outcomes, and patient safety. Instead, with the availability of today's digital, centralized solutions, machine output from these tests can be uploaded automatically to centralized facilities where software can evaluate the results with subsequent validation by medical professionals as appropriate. The result is quantitative, reproducible, and objective data — obtained with less manual intervention in less time, and with lower costs.

Data Integration and Clinical Trial Management

Clinical Trial Management Systems (CTMS) do not live up to their name. Rather than providing a centralized resource for all trial-related activities, analysis, and oversight, they merely support some of the trial's administrative functions such as site feasibility, on site monitoring, and study documents and serve as yet another disconnected information silo. Teams must rely on a number of other systems — an average of seven to 10 per trial — to manage trials in their entirety. In addition to the CTMS, these systems commonly include EDC to collect clinical data, Interactive Response Technology (IRT) to manage patient randomization and dosing, and

Proven Benefits of ePRO/eCOA

ePRO/eCOA systems provide tremendous resource savings for sponsors in that incoming data are eSource data — they do not have to be manually checked and entered into a database. This frees trial staff to focus on more strategic or value-added work. In addition, ePRO/eCOA provides:

- **Better clinical care/communication between provider and patient:** When patients report their symptoms electronically, they go on to discuss their symptoms and health-related quality of life (HRQoL) issues with their physicians more often than when they use paper diaries.[1]
- **Improved data quality:** Specified parameters prevent the entry of outlying data.
- **Stronger patient compliance:** Advances in smartphone and other portable technologies are providing ever-better digital patient engagement and data capture. It's easy for patients to complete questionnaires and diaries on mobile devices in a way that integrates into their everyday lives and improves participation and adherence.
- **Unlimited participation:** ePRO/eCOA technology can be extended to large, heterogeneous populations across different diseases and conditions. The technology enables translation and localization to each patient.
- **Flexibility.** It's easy to reflect the seemingly inevitable mid-study design or protocol changes within ePRO/eCOA systems.

ePortals that capture data from patients such as core, central, and specialty laboratories.

Because these various systems are not designed to "talk" to one another, the information that trial managers need is locked in silos and maintained in an assortment of spreadsheets, emails, and various extracts. This lack of integration burdens study teams with manual data aggregation and compilation that is time-intensive and prone to human error.

The ISR survey mentioned above found that "better integration of the data between EDC software and other systems" was the solution that most respondents thought would "have the biggest impact on reducing the time needed to conduct a trial." Fortunately, there are now data-agnostic solutions that can amalgamate all of the necessary data into one repository. These new cloud-based solutions can integrate data from any number of key eClinical systems, with access controlled by role-based permissions.

Sponsors that have invested in these solutions prevent the risk of human error in their data management processes, improve operations and dramatically reduce trial times and costs. One CRO found that by integrating data from five different data capture systems into a single trial oversight solution it saved approximately 200 operational hours per month across the 10 studies being managed.

Centralized Trial Oversight

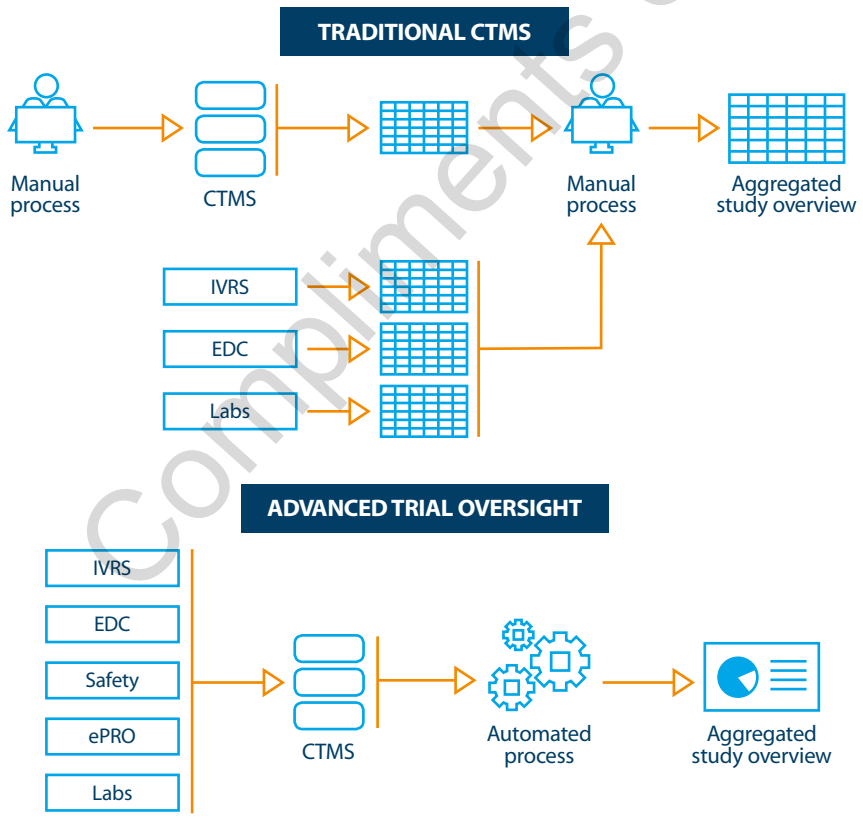
When incoming data remain in silos, trial staff tasked with managing a trial's performance must cobble together data from various systems and spreadsheets, reconcile it, manipulate it, run it through the proper quality controls, then turn it into something actionable. One CRO complained that staff members were spending "80% of their time entering and tracking data, building reports, and checking data accuracy."

This lack of integration poses a huge oversight problem for sponsors and CROs. Without a clear view of performance and risk indicators, they're hamstrung when it comes to making decisions. The solution is to aggregate all incoming data into a centralized oversight solution (as mentioned above) overlaid with trial management workflows and data analytics that help make sense of incoming data, presenting it in pre-configured reports and dashboards (See Fig.1.) These can be used to:

- Leverage historical data to develop baseline assumptions
- Rapidly identify study-level patterns and proactively address potential problems
- Manage and mitigate risk across the trial life. This includes the ability to perform risk-based monitoring of site performance, patient safety, compliance, and outcomes data.
- Support mid-study decisions to improve study performance
- Identify emerging trends at the study, site, and country level

When all stakeholders — study teams within the sponsor and vendors — share a single, secure interface that they can access 24/7, they can work seamlessly together to manage operations.

Figure 1: How CTMS Must Evolve To Provide a Complete Picture of All Trial Data



Conclusion

Although too many sponsors and CROs are still relying on paper data collection and management approaches and are struggling with multiple, siloed databases, the pressure to improve trial efficiency will bring about change. It is forecasted that ePRO/eCOA will become the norm, superseding paper diaries and questionnaires. And, technologies for capturing and interpreting other clinical data electronically will also quickly replace less efficient, error-prone methods. As the amount of data generated in trials grows exponentially, neither sponsors nor their CRO partners will be able to continue coping with data sources that are not integrated and that do not provide a central platform for shared work, progress monitoring, risk-assessment, and reporting. Only electronic technologies can manage these issues.

With the myriad of technology advances that are now available and proven to overcome the challenges of paper-based approaches, the methods used to conduct and support clinical trials can be as cutting edge as the industry's research capabilities and therapeutic innovations. Sponsors and CROs that are slow to adopt integrated software and automated tools in their clinical operations will risk falling behind their more progressive and efficient peers. PV

Notes:

[1] Tufts Center for the Study of Drug Development, Phase II and III Enrollment Performance on a Multi-Center Study;

[2] "EDC and eCOA/ePRO Market Dynamics and Service Provider Performance," ISR, 2015;

[3] Taenzer, et al., 2000, Psychooncology, 9:20