WHITE PAPER

Top Five Reasons You Need IRT Expertise (Not Just Software)

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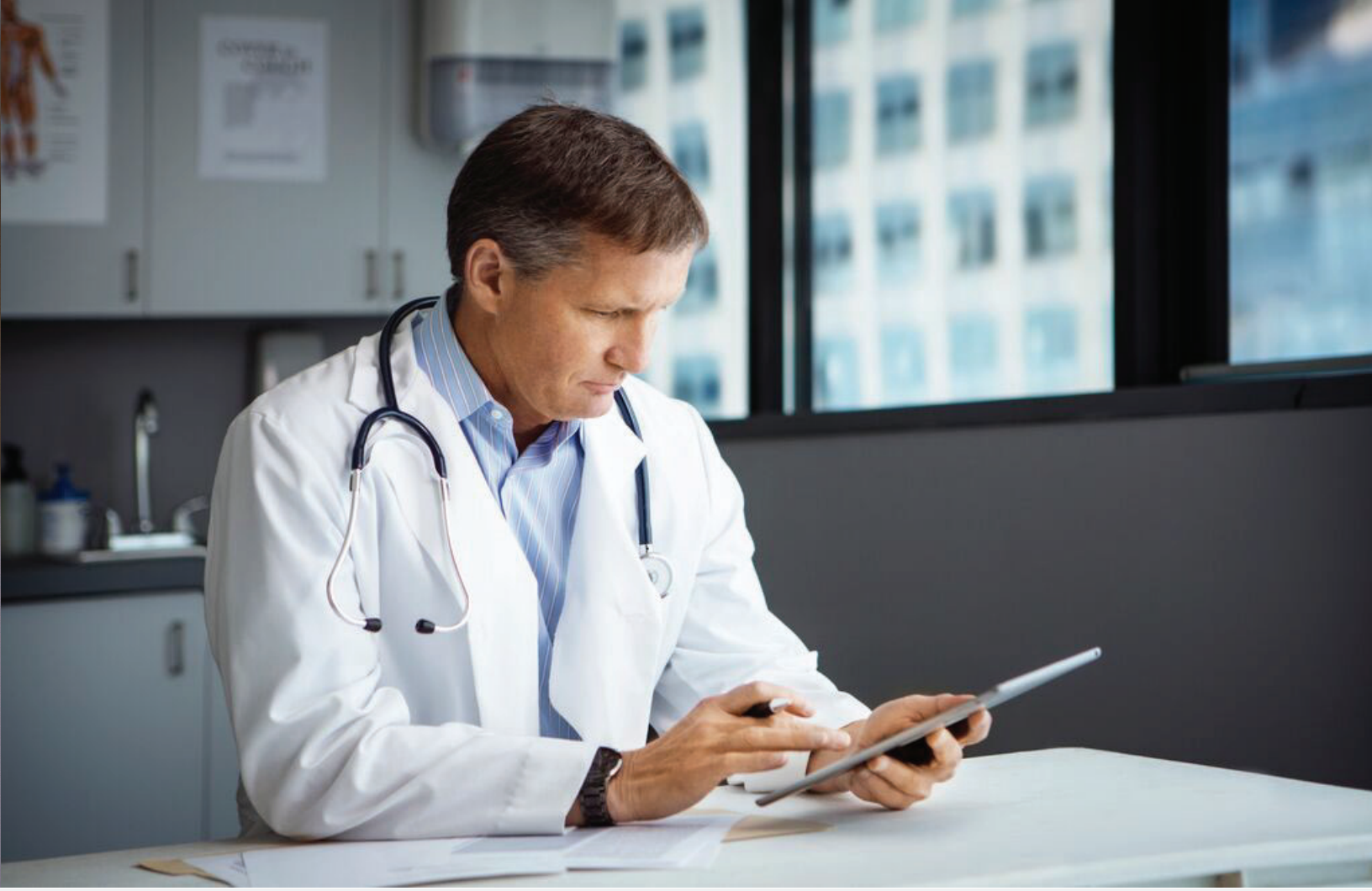

Top Five Reasons You Need IRT Expertise (Not Just Software)

Today most Interactive Response Technology (IRT) vendors have developed modern, configurable systems and much has been written about Agile development and delivery methodology as well as faster builds that improve system quality, reduce risk and simplify validation requirements. These system developments over the past several years have certainly brought many benefits to Randomization and Trial Supply Management (RTSM) delivered on IRT. Interestingly, though, while some eClinical technologies, such as Electronic Data Capture (EDC), are readily brought in house by biopharma companies and Contract Research Organizations (CROs), IRT is rarely "tech transferred" by comparison. Instead pharma companies generally seek IRT vendor relationships to ensure high quality builds that meet their needs and avoid the potential pitfalls associated with RTSM.

The speed and agility benefits being realized by configurable systems can be likened to creating a faster car with better handling. Yet even the best high-performance car needs a skilled driver–a driver who can navigate effectively, anticipate and avoid risky situations and at the same time, make sure that all passengers are comfortable throughout the ride. Likewise, even with an effective, modern platform, tapping into the experience of an IRT specialist is essential to get the best performance out of the system.

While there are many areas where an IRT specialist can add great value to a study, this paper will focus only on the top reasons to seek such expertise. The factors selected are based on interviews with experts with years of experience and "rescue studies" performed in the past several years to save clinical trials that were heading for failure.

While timelines have been greatly compressed in recent years, pharma companies who engage with their IRT vendors earlier in the study process reap much greater benefits.

Reason #1: More Effective Planning

This first reason to consult expert advice for RTSM may also seem like the most obvious, yet it is not at all uncommon for sponsors to delay in choosing an IRT vendor. As a result, time to fully plan the study, supply chain strategy, effective integrations, essential customizations and other vital factors is often rushed. At times, it is simply too late to make changes that a specialist may suggest.

While timelines for the actual study specification, build and delivery have been greatly compressed in recent years, pharma companies who engage with their IRT vendors earlier in the study process reap much greater benefits in terms of optimal configuration, planning efficient packaging and pack types, establishing specific study and supply chain health monitoring plans and so on. These factors go a long way in establishing efficiency, enhancing analytics, such as those used for risk-based monitoring, and in controlling costs associated with wasted supplies.

There are several areas where early planning with an expert team can help, including complex trials involving titrations, adaptive designs, open label studies or maintaining balance across a large number of stratification factors. For example, in open label studies, investigators often feel they can bypass the IRT when dispensing drug to their patients since they know what each patient should receive. However, this causes problems downstream in controlling inventory, logging drug accountability and managing expiry dates. So what are the factors that will motivate investigators and staff to use the IRT? How can a sponsor ensure that they do not bypass the system? Experienced vendors have a number of tools and methods that reduce these risks and enhance study design and quality. Because they've surely seen these and similar challenges in the past, they can readily point out and plan for the potential issues well before go-live.

Reason #2: Setting Up and Maintaining Optimal Supply Chain Performance

A faulty clinical supply chain is perhaps the most common pitfall in IRT setup and maintenance. This is because each trial has its own unique requirements and there are many factors to consider during setup. The main goals of an effective supply strategy are ensuring that every patient gets their medication on time while minimizing any

waste due to over-supplying depots and sites. These two goals are obviously at odds with each other and require balancing a number of factors. Some of the key considerations include the countries, regions, depots and sites that will be used, the regulatory requirements for shipping drug to each of these regions, minimizing shipping costs, planning the volume and frequency of shipments to avoid stock-outs at depots and sites, the medication pack types being used, frequency of patient visits, varying patient recruitment patterns and managing expiry dates just to name a few. (See Cenduit Trial Supply Management white paper for more details.)

IRT specialists have a great deal of experience in balancing all of these factors to ensure that every patient gets the right drug at every dosing visit, while simultaneously making sure that the number of costly shipments is minimized. Managing all of these factors is not simply a matter of plugging in a few parameters in a "set-it-and-forget-it" manner. It requires ongoing vigilance, the ability to anticipate and foresee potential risks and when necessary, taking appropriate actions to keep the supply chain on track.

Another issue that affects the supply chain is accurately forecasting drug requirements. Many biopharma companies use forecasting methods or systems that are detached from the actual IRT system to estimate the amount of drug required to run a study. This means that the baseline forecast is often out of sync with the IRT algorithms for identifying the need to ship more drug to a depot or site, how much drug will be sent with each shipment, whether any pack type (e.g. other drug type, such as comparator or placebo) should be sent and so on. Then as the study progresses, the additional forecasts may become further detached from the actual supply chain if the real-world information from the IRT system is not regularly fed into the predictive models. (See Cenduit Forecasting white paper for more details.)

Once again, IRT subject matter experts (SMEs) can provide the insights and advice necessary, not only for baseline forecasting, but also for ongoing modeling of the supply chain using real-world data directly from the system.

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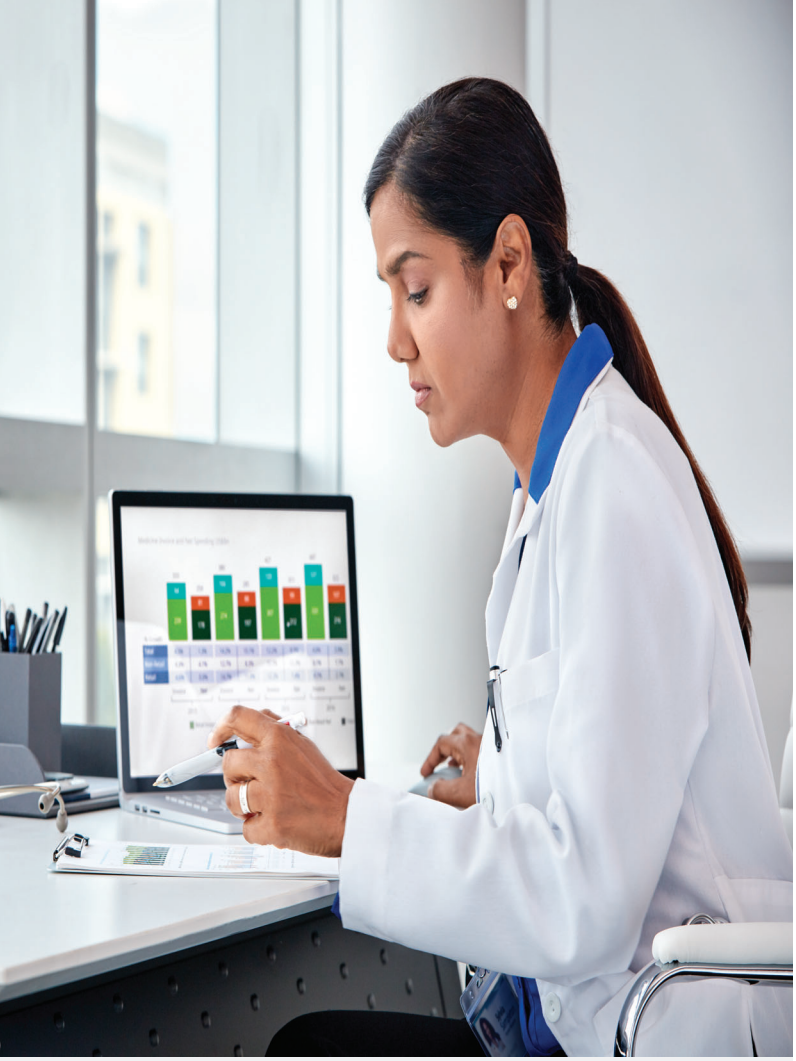
Further, vendors who are deeply integrated with international supply companies that specialize in global logistics can provide sound advice on setting up and optimizing your supply chain. They can also offer effective forecasting solutions and advice on using these to ensure success.

Reason #3: Overall Study Health

Many systems offer reports and dashboards that report on study health factors such as recruitment, enrollment, compliance, drug supplies and more. Further, many vendors talk about tools for "data-driven decision-making" or "predictive analytics." However, while these systems are helpful in identifying potential issues, they rarely give users advice on how to mitigate risks or solve problems that may be arising. There is still a great need for an expert to perform additional analysis and review of the data to make recommendations and to take action.

Consider an example.

The project team may have set up a practical randomization



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plan that, in theory, would lead to a balanced number of patients in each of several strata, such as gender, age and smoking status. This balance may be desired at the overall study level and also by country or region. Yet, in the real world, the random nature of recruitment and enrollment often leads to unexpected consequences, which can affect study balance. If no specialist is checking the study for indicators of balance on a regular basis, this could lead to disaster. Imbalance at the end of the study could undermine the intended statistical analysis plan and as a result, the entire study. Having a reliable team of experts who can identify such risks and then take action is critical. (See Cenduit Randomization white paper for more details.)

Randomization balance is just one study health item that must be monitored and maintained. As noted above, dashboards and reports may track a host of other trends and data patterns, any of which may warn of risks. Going back to the issues with the supply chain, suppose a dashboard indicates that a problem is likely if current trends continue. What action should be taken? Should additional drug be manufactured and sent? Should recruitment be capped for some regions? Can the drug be relabeled? An IRT specialist deals with these challenges regularly and can draw on experience from hundreds of previous studies to take proactive measures and mitigate any risks.

Reason #4: Avoiding Unintentional Unblinding Issues

The risk of unblinding or partially unblinding clinical trial participants or stakeholders should never be underestimated. And since the IRT system typically contains a great deal of information about the study medications and the blind, the RTSM data must be carefully protected. Additionally, the study setup should not lead to any partial unblinding, meaning that a study participant can discern which patients are on the same drug. IRT vendors have Standard Operating Procedures (SOPs) governing their systems, handling of potentially unblinding information, data transfers and reporting, setup of users who may or may not view unblinded data and so on. They also have experienced, well-trained personnel who make sure that all data-handling procedures are properly followed to protect the study blind.

This is especially important when performing data transfers or generating study correspondence to the sponsor or a site.

Partial unblinding can occur when the study is poorly configured, such as when the randomization list is linked directly to pack numbering or when reports are sorted on data linked to the study blind. These and similar situations allow site personnel to determine which groups of patients are on the same study medication. A previous paper covered these risks and several scenarios that could lead to partial unblinding. The scenarios described are drawn from actual studies that some sponsors have set up before consulting SMEs and illustrate the need for domain expertise. (See Cenduit Unintentional Unblinding white paper for more details.)

Reason #5: Intelligent Integration with other eClinical systems

In addition to rapid setup and configurable systems, many vendors also offer Cloud-based integration platforms that have greatly accelerated and simplified data exchanges between systems. Even so, experience with "rescue studies" has demonstrated that integration is not just a plug-and-play task; rather, it requires proper setup in several areas. For example, as mentioned in the section above on unblinding, rules for data sharing must be carefully implemented. Also, role-based user security is essential to make certain that no unbinding data is shared inappropriately. This is just one vital consideration.

Additionally, each clinical trial has important nuances and specific needs that can require a measure of customization. Take as an example a migraine study where patients were required to have a minimum severity score during the run-in period to qualify for randomization. Patients used an electronic Patient-Reported Outcome (ePRO) device to score their headache symptoms on a daily basis and in turn, the data were shared with the IRT database so that the severity score could be calculated in real time. If the patient reached the minimal severity score, the IRT would then allow the site staff to randomize the subject; otherwise, the system would prevent the randomization.

IRT specialists can also make recommendations for deeper, enterprise level integrations with a variety of systems to more effectively manage the supply chain and data flow.

This type of integration has been set up by experienced IRT professionals for many trials.

IRT specialists can also make recommendations for deeper, enterprise level integrations with a variety of systems including your internal Clinical Trial Management System (CTMS), Drug Supply Management System (DSMS) and modules of your Enterprise Resource Planning (ERP) software to more effectively manage the supply chain and data flow. Such deep integrations enhance efficiency by eliminating redundant data entry, sharing information across systems in real time and avoiding transcription errors.

Conclusion

Modern technology has brought many benefits to RTSM delivered on configurable IRT platforms, including faster timelines and simplified validation. Returning to the analogy of a high-performance car, it is critical to have the right "driver" to navigate effectively and to skillfully negotiate risky situations. It is also vital to have an experienced "pit crew" to maintain your investment and make sure it continues to function optimally and at the highest levels to lead you to success and ultimately, to victory. As discussed in this paper, such an experienced IRT team can ensure many benefits, including:

- A truly optimized supply chain that ensures every patient gets the right medication at every visit without creating overage that leads to expensive wastes.
- Avoiding risks such as unintentional unblinding.
- Maintaining overall study health for critical factors such as treatment balance.
- Establishing more efficient and intelligent integrations.
- Effective planning that results in getting the most out of your IRT configuration.

Who's driving your IRT?

About the author

Kevin Landells, M.D. Vice President, Business Head Cenduit IRT, IQVIA

Kevin has over 24+ years of experience in the IRT/ RTSM industry, having worked across many technical and project management leadership roles. Experienced with developing and leading global teams delivering managed services spanning Operations, Project Management, Client Partnerships and Business Transformation. Kevin is passionate about improving healthcare and utilizing technology that makes a real difference to patients' lives.

Kevin holds a Bachelors' Degree in Computer Science from Hertfordshire University in the UK.

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