Zelta

WHITEPAPER

Confidence in clinical trials amid complexity and change

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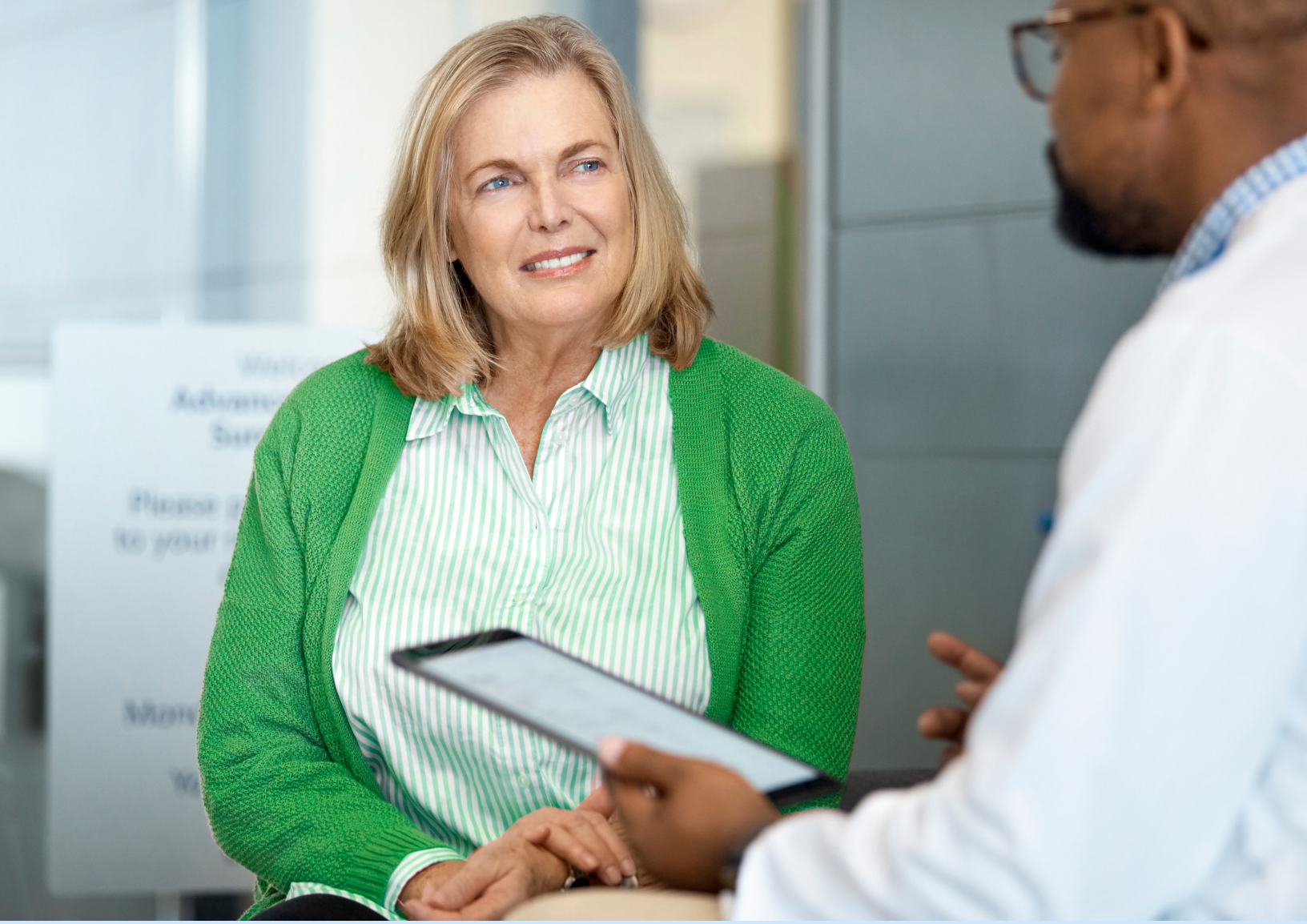
Content



Introduction

The clinical trials industry is navigating a transformative period, driven by dynamic global shifts and evolving regulatory frameworks. Amid these changes, trial sponsors and contract research organizations (CROs) are embracing a more strategic and forward-thinking approach to risk management.

Many sponsors are starting to slow down study starts and defer initiatives that are not considered core to their research portfolio. Instead, they are focused on keeping funding stable and aligning investments with primary business priorities while minimizing financial risk. This has contributed to a slowdown in new trials being launched thus far this year.

These new pressures are compounding challenges from the increased complexity of clinical trials and the associated operational burden. Protocol designs have expanded in the past decade, collecting more data and endpoints than ever before. This has led to costs continuing to rise and mid-study changes such as protocol amendments proving more expensive.

Drawing on insights from Zelta, this whitepaper examines how sponsors and CROs can navigate these industry challenges, and take advantage of a new generation of solutions to help restore stability, boost confidence, and maximize return on investment (ROI) in their clinical research.

Key challenges

Confidence gaps in trial execution

One of the biggest concerns CROs have to address right now is a gap in confidence around clinical trial execution, with sponsors uncertain whether their trials can run successfully on time and on budget.

Consequently, many sponsors have increased the scrutiny of potential CRO partners, moving from a one to three party selection process to sometimes vetting five to six possible CROs to be awarded a trial. When a trial does begin, every operational disruption or sign of underperformance – such as slow enrollment or data issues – can have knock-on effects that increase trial costs. While this increased scrutiny may be in response to proactively getting ahead of these anxious moments during a study, it has the dual effect of reducing willingness to accept recurring or persistent issues.

This has also impacted the willingness to pursue novel research areas. According to recent CRO industry reports, sponsors are increasingly prioritizing lower-risk, high-return studies, with investment in early-phase or exploratory research seeing a measurable decline. When a company does go forward with a trial exploring novel research areas, there is an even further reduced willingness to accept underperformance or timeline delays.

In an environment where every dollar matters more than ever before, and every delay drives up cost and risk, sponsors are being far more selective with their partners. All the more reason why CROs need to be at the top of their game to maintain sponsor partnerships and continue running clinical trials.

Prioritizing site and participant experience

When investigators and coordinators at trial sites become frustrated, overburdened, or disillusioned, they may deprioritize the study or even drop out, and may not support future trials. Likewise, if patients find the trial too onerous, such as too many visits, confusing procedures, or inaccessible eDiaries, they may withdraw consent or become non-compliant, thus rendering their data useless.

Sponsors are understandably anxious about these possibilities, knowing that a trial's timeline and ROI depend on keeping sites and patients happy and engaged.

The key to keeping that anxiety down is retaining high-performing sites for future studies. If execution of a protocol in the real world proves too onerous, that site may choose to not work with that sponsor again. A protocol might look scientifically promising on paper but prove a failure at the site level if it cannot actually be executed in the real world by the site's team. Losing the goodwill of experienced sites is a long-term setback; focusing on site and participant satisfaction must be a key consideration for sponsors.

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Complexity and instability are putting a chill on niche areas of research

Clinical trials have never been simple to build or manage, but over the past decade they have become exponentially more complex. Protocols now often include dozens of endpoints, including elaborate sub-studies, genomic analyses, and digital health data. This rise in complexity has been driven either by a push to address multiple research ideas in a single protocol or because of a highly specific and complex research area. The result is complicated protocols that often attempt to answer multiple questions at once. The volume of data being collected has also grown accordingly, with each additional endpoint and data stream adding burden to the trial's design and execution.

This growing data collection ultimately requires more effort from trial staff and participants. But there are also questions about whether all the additional volumes of data collected are necessary for a trial's outcome.

"More focus is being placed on collecting data that proves the outcomes you are working on," says Mark Laney, senior director of sales engineering and partnerships at Zelta. "If the data is collected and it's not critical, then it's just more work and cost added to the trial with no real benefit."

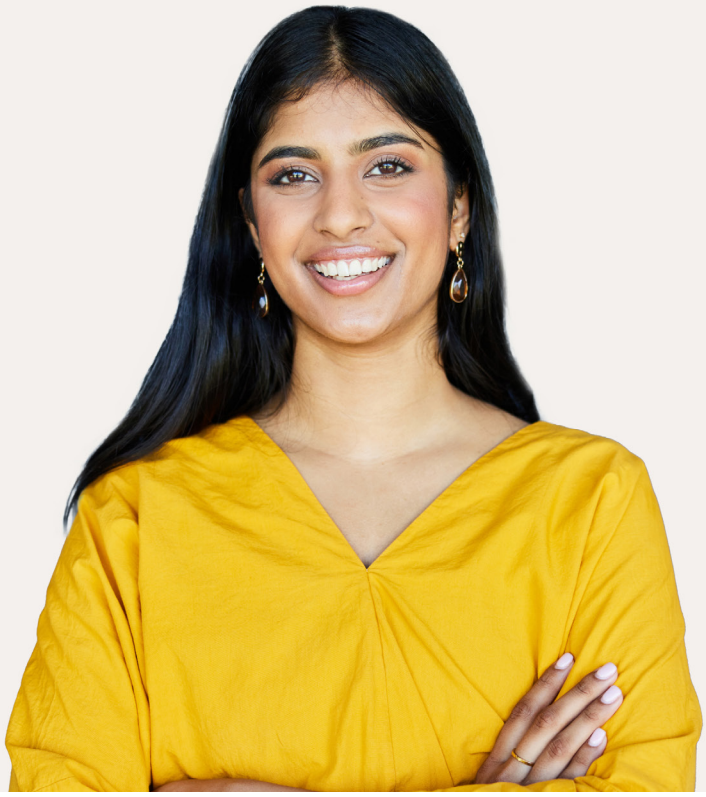
The more complex a trial, the more the potential for aspects of it to go wrong, which directly threatens data integrity and operational efficiency.

Between the pressure to simplify and control costs and timelines, plus the inherent complexity of cutting-edge trials such as adaptive platform trials, many organizations cannot afford to take expensive risks. Thus they are now in a "wait and see" mode about whether they can progress in niche areas such as rare disease or cell and gene therapy trials.

Trial amendments and rising costs

Protocol amendments have become more common, but frequent amendments due to changes in the study design or clinical execution can come at a high cost. Each change can trigger further operational adjustments, from updating electronic data capture (EDC) systems to retraining site staff, notifying ethics committees, and re-consenting participants. One major challenge in recent years is the rising cost, both in time and money, of implementing these changes, especially for complex studies.

If a study is designed in a rigid or overly complex way, an amendment can be difficult to execute, and even if changes are feasible, they often require system downtime that directly impacts trial execution. For example, updating an EDC database for a new protocol version might mean it is offline for a week, during which time sites must either halt data entry or revert to paper to transcribe later. All of this adds to the trial's costs and threatens data quality, and can give the sponsor the impression that the CRO is not delivering well. Many teams will even postpone necessary adjustments, accumulating multiple changes in the process, because they know that their tools for implementing an amendment cleanly will require lengthy downtime. In that calculation, it's better to stockpile the changes and do them all at once instead of taking on recurring downtime. The problem is that this can delay critical updates that are intended to improve trial execution, thus reducing the impact of the intended changes.



Solutions to boost trial confidence and maximize ROI

Providing reassurances of clinical trial success from the start

The more efficient way to bolster confidence in a trial is to set it up for success from day one, including rigorous upfront planning and strategic thinking for how the trial will be executed. Given how costly mid-study course corrections can be, sponsors and CROs should invest time and dedicate expertise to the design and initiation stage. While a degree of disruption is not unusual in a clinical trial, that disruption can be minimized by laying the foundation for a robust trial design that is able to accommodate the real-world needs of sites and participants from the start.

Ensuring a successful start involves a holistic, proactive mindset. Sponsors and CROs need to bring in the right experts from the beginning – not just medical and clinical experts, but those with operational and technical expertise, too. Having experienced operational teams review the protocol early can help identify and mitigate potential pitfalls down the line.

"You have to ask the right questions early on and take feedback on how one might best implement a protocol using the chosen technology, site, and expectations for analysis," says Jennifer Duff, General Manager of Zelta.

For example, if a protocol requires patients to complete a diary within a narrow time window after each dose, the team should discuss whether the sites in question have the tools and capacity to remind patients of this requirement in a timely manner. This includes ePRO apps that send alerts and processes for what to do if a patient misses their window. Pressure-testing this operational plan can also greatly increase the chances of a smoothly run trial with minimal disruption.

Optimized trial design at the foundation

To restore trial confidence, many sponsors are now pursuing simpler, more focused protocol designs that align with key objectives and avoid extraneous complexity by scrutinizing every data point. For example, a quality-of-life questionnaire might be interesting, but if it won't support the trial's primary outcome, it could be left out to streamline the study. This optimization has direct benefits for confidence and ROI, with protocols being easier to execute, faster to enroll, and cheaper to run, as well as reducing the likelihood of amendments and unnecessary change or churn.

Simplicity in execution is not just what you measure, but how you measure it. For each procedure or data point in the protocol, designers should ask how it will be done in practice, and whether it fits into normal clinical workflows or is feasible for a participant to execute. If a protocol requires something unusual or operationally complex, it may undermine its own success.

"If you haven't thought about that human on the other end, it may result in a failure in execution," explains Duff.

"You have to ask the right questions early on and take feedback on how one might best implement a protocol using the chosen technology, site, and expectations for analysis."

Jennifer Duff
General Manager, Zelta

Streamlined startup processes

Even with a robust protocol, a trial can experience pain points if the startup process is slow or disorganized. Study startup covers all activities from final protocol to site initiation, including regulatory approvals, contract negotiations, site training, and system setup.

In recent years, startup times have lengthened as trials become both more complex and spread out around the globe. To maximize ROI, sponsors are seeking to streamline startup so that trials launch faster and more smoothly. An efficient startup not only saves money by cutting idle time, but also boosts confidence by getting the trial on track early.

One key to streamlining this step is to automate and accelerate certain tasks in the trial startup. For example, using integrated EDC platforms can eliminate delays in configuring different systems for the trial. Rather than setting up separate databases for EDC, eCOA, ePRO, et al., an all-in-one platform can be configured once with the protocol and then immediately deployed to sites, reducing the learning curve for those sites.

A well-managed startup process benefits from having a dedicated startup project manager or team that tracks every task and deadline, while checklists and workflow tools help to ensure nothing falls through the cracks. The goal is to eliminate weeks or months of unnecessary delay before the trial begins.

Every week saved in startup is a week earlier that a potential therapy moves toward approval, which likewise significantly increases the ROI for sponsors. At the same time, a smoothly run startup phase builds confidence with sites and internal stakeholders. When sites see a trial that is both organized and responsive during startup, it fosters trust in their sponsor and supports continued engagement for future studies.

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Aligning site selection with key success drivers

Site selection needs to be closely aligned with the trial's success drivers, considering factors such as patient availability, therapeutic area expertise, and prior performance metrics. A common pitfall is choosing sites based solely on the reputation of the clinician or geography, only to find they enroll few patients or struggle operationally. To ensure confidence in trial execution, sponsors must take a more data-driven and strategic approach to site selection.

This data-driven approach can include sponsors and CROs leveraging performance data from past trials to identify sites with a proven track record. These metrics include enrollment rates, data query resolution times, protocol deviation rates, and user feedback scores from previous studies. By analyzing this data, it is possible to shortlist sites that are likely to recruit effectively and follow the protocol diligently, significantly improving the prospects of success.

For example, if a trial needs 100 participants, five high-quality sites enrolling 20 each are far more efficient than 20 mediocre sites enrolling five each. Fewer sites also mean fewer points of contact to manage, which simplifies trial execution. "Data-driven" in this case can also mean leveraging CRO or third-party systems that use real-world data and AI solutions to fine-tune site selection. While these solutions are still in the early stages, they are promising developments to consider for future site searches.

Another success driver to align with site selection is engagement and motivation. A site that believes in the research and has some experience in that area will work harder and likely be more capable of overcoming potential obstacles facing the trial. Part of aligning site selection with success is making sure the trial sites have what they need to succeed, including the right patient population access, adequate infrastructure, and experience with the technologies being used in a given trial. It's counterproductive to select a site that serves the target patient population if the site's staff are uncomfortable with the eClinical platform required for that trial. If a site has no track record of using a proposed system, then that's another potential red flag for risk.

Building in flexibility for operational adjustments

Given that changes during a trial are almost guaranteed, a clinical trial must be built with flexibility in mind. This means having a platform capable of making operational adjustments such as protocol amendments, adding a study arm, or addressing unforeseen issues without derailing the trial's timeline.

To do this, sponsors and CROs should consider adaptive platform trials. They should also consider separating non-critical data collection from critical endpoints – if it becomes too burdensome, it can be dropped via amendment with little impact on the overall trial.

Establishing clear governance for amendments and study changes, including change control boards that evaluate proposed modifications by cost/benefit, can also ensure only necessary changes are implemented. Sometimes, this means batching minor changes together into a single amendment, rather than trickling out multiple amendments.

One of the most crucial enablers of flexibility is a modern eClinical system built to handle changes more efficiently than in the past. Clinical trial platforms such as Zelta have been engineered with agile mid-study updates in mind, including features such as automatic versioning of electronic case report forms so that data already entered remains under the old version and new data goes into the new version without any confusion. This includes features that deliver real-time design feedback to detect and prevent data integrity issues, ensuring a smooth and rapid update through a streamlined publishing interface.

This also helps make training updates more targeted. If a change only affects one procedure, the system might flag that procedure to site users with an in-line note about the change, rather than requiring full retraining. Achieving this level of seamless change has a direct ROI impact because it avoids costly delays and reworking, and helps to maintain the trial's momentum.

Enhancing site and participant experiences

Enhancing the experience for clinical sites and participants is a direct way to improve trial execution and outcomes – and ultimately, confidence in the trial's ROI from the outset. If sites and patients are happier, more motivated, and less burdened, everything from enrollment to data quality improves. Zelta's approach is to design every aspect of trial technology and workflows through this user-centric lens. This prioritizes ease of use, convenience, and support for the personnel who conduct the trial and participants who provide the data.

All too often, technology in clinical trials is chosen for functionality or compliance – with little thought for the actual user experience. Zelta aims to change this. From how a site user logs into the system to how a participant fills out an eConsent form, the focus is on making the user experience intuitive and efficient. This might involve dashboards that display key alerts to a coordinator as soon as they log in, or mobile apps for patients that have clear reminders and progress indicators. The objective is that when a user needs to perform a trial task, the system guides them to do so.

Another aspect of enhancing the user experience is gathering and incorporating user feedback into the trial design. Sponsors are now asking for evidence of site and patient satisfaction with any clinical studies platform they deploy. Net promoter scores (NPS) or user survey results for trial platforms provide a feedback-driven improvement loop. At Zelta, this user feedback has driven numerous refinements to the platform's interface and workflows, all to improve site and participant satisfaction – resulting in an NPS of >95%.

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How Zelta builds confidence in clinical trials

Zelta was purpose-built to enhance the site and patient user experience, seamlessly execute amendments, and instill confidence in trials. Zelta provides the same consistent user experience across complex adaptive mega-trials to straightforward Phase I studies. Teams don't have to switch systems as their trials get more complex; Zelta can be used interchangeably across Phase I to Phase IV trials.

Zelta also emphasizes efficiency and transparency to build up confidence in the build, execution, and ROI of a clinical trial. The all-in-one EDC platform enables teams to accelerate study builds, launch trials faster, and execute with ongoing visibility. Because Zelta consolidates many functions – including electronic data capture, patient engagement, eCOA, ePRO, RTSM, and eConsent – all into one system, sites have total end-to-end visibility into a trial's progress.

At any given point, a sponsor can see real-time enrollment and data status dashboards to assess the success of the study. If results are positive or if any issue is detected, the team knows about it as it happens and can act quickly. Rapid insight enables those go/no-go decisions or protocol optimizations to happen much sooner than in siloed systems.

One of Zelta's strengths is its unifying capability across trial types and phases, which is a benefit for organizations struggling to operate on multiple systems – for example, one EDC for simpler studies, a more robust model for complex trials, and a separate randomization system for adaptive designs. Zelta can be used in place of all of these, with the same platform used for Phase I through Phase IV, for traditional to decentralized trials. This means that sponsors and sites only need to learn one interface, which speeds up new trial startup, eliminates the need for training sites on multiple platforms, and reduces the risk of error.

Zelta is at the forefront of enabling a new era of confident clinical trial execution by simplifying the multiple complexities that affect most studies and streamlining clinical data management. The payoff for sponsors and CROs is that trials on Zelta can start securely, run with fewer disruptions, adapt to mid-study changes with ease, and deliver results that justify the initial investment.

Zelta's mission is to provide sponsors and CROs with a dynamic solution that drives bold research – and with that, the peace of mind that when they launch their study, they have everything they need to be successful, from motivated site staff and engaged participants to a modernized user-centric experience that provides control at every stage of the trial and confidence in its outcomes. By leveraging Zelta, pharma and biotech companies, medical device companies, and CROs starting new clinical studies can regain that confidence, knowing they have the tools and support they need to overcome complexities and deliver on the promise of their clinical trials.

Learn how Zelta can accelerate your clinical trials, providing control at every stage and confidence in the outcome. Contact us to get started.

About Zelta

Zelta by Merative is a clinical trials solution business that includes both a clinical data management and acquisition platform and consulting, enablement, and extension services. Zelta's unified cloud-hosted platform supports all phases and complexities of research, including more than 500 phase III trials.

Learn more at
merative.com/clinical-development

About Merative

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