CRIO™

Case Study

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The High Cost of Hesitation: Breaking Free from Process Paralysis in Clinical Trials

OVERVIEW

This case study examines a leading pharmaceutical company's implementation of CRIO's eSource solution to modernize data collection. The collaboration aims to address process paralysis while maintaining quality standards. Expected improvements include standardized data collection, increased CRA productivity, and substantial cost savings through enhanced remote monitoring. The eSource solution is designed to provide real-time data validation and streamline processes, with projected results including significant improvements in data quality and reduced query volume. This implementation approach represents a step towards digital site focused transformation in clinical research, potentially contributing to industry-wide improvements in trial methodologies and accelerating drug development timelines. This case study is complemented by early indicators from a similar, more advanced trial, providing additional insights into the potential impact of eSource implementation on study start-up metrics and overall trial efficiency.

I. Breaking the Status Quo

Clinical research stands at a crossroads. For decades, the industry has been caught in a paradox: the processes that have successfully brought life-changing medications to millions are now holding it back. Large pharmaceutical companies, having refined their methods over 20-30 years, find themselves trapped in a state of process paralysis.

This paralysis isn't born of failure, but of success. However, in an era of rapid technological advancement, even proven methods can become obstacles to progress.

One of the world's leading pharmaceutical companies recognized this dilemma. Despite its impressive track record, this industry leader saw that its clinical trial processes were not optimized for the digital age.

In a strategic decision, the company partnered with CRIO, a pioneer in clinical research technology. CRIO's eSource platform, utilized by over 2,000 sites across their study portfolios, offers a unique site-centric approach to clinical trial management. CRIO's dedication to enhancing efficiency aligned with the company's desire to improve processes without compromising quality.

Breaking the Status Quo (cont.)

This case study explores how CRIO's eSource solution was implemented across multiple study sites, introducing new efficiencies in clinical trial management. Specific examples of how eSource addresses common challenges are examined, including:

1. Leveraging CRIO's eSource capabilities to standardize data collection, reducing protocol deviations and improving endpoint data accuracy.
2. Increasing CRA productivity by combining SDR and SDV, allowing for more efficient monitoring and fewer on-site visits.
3. Achieving cost savings through remote monitoring, increasing remote IMVs from 20% to 70%, reducing monitoring costs and travel expenses.

By combining the Pharmaceutical Company's industry knowledge with CRIO's innovative approach, this collaboration created a model that respects established practices while utilizing modern technology. The following sections will detail the benefits and improvements achieved, providing insights into how eSource can transform clinical trial operations and deliver cost savings.

To further illustrate the potential impact of eSource implementation, this case study also references early indicators from a similar, more advanced Phase III trial. While these comparative metrics are not direct results of the primary case study, they offer valuable insights into the potential outcomes of eSource adoption, particularly in the critical study start-up phase.

II. CRIO eSource: A Site-Centric Approach

CRIO is a pioneer in eSource technology for clinical research. Founded by clinical research site experts, CRIO has developed a comprehensive platform that addresses the complexities of the clinical trial process, focusing on optimizing site-level operations.

CRIO's distinction in the clinical research technology landscape comes from its understanding of site workflows. This expertise is based on CRIO's established presence, with over 2,000 sites using CRIO as their comprehensive workflow tool across their entire study portfolios. The platform manages various aspects of site operations, including regulatory documentation, patient databases, electronic informed consent, visit scheduling, and reporting.

CRIO eSource: A Site-Centric Approach (cont.)

CRIO's eSource capabilities benefit all sites, whether long-term clients or single-study users. Features include intuitive interfaces aligning with familiar source documents, built-in edit checks and form logic, real-time data capture, automated calculations, and customizable templates.

For sponsors, CRIO's site-centric design offers improvements in study efficiency and data quality. This alignment facilitates adoption and efficiency, regardless of whether all sites use CRIO as their primary workflow tool.

CRIO's focus on site usability addresses site needs while providing advantages for sponsors. The site-centric approach contributes to user adoption, data quality, and faster data entry, leading to more efficient trials. While replacing traditional paper source documents, CRIO maintains the sites' role as data originators and custodians, while providing sponsors with timely data and enhanced monitoring capabilities.

In the clinical research technology landscape, CRIO offers sponsors a site-centric system that can facilitate site adoption, improve data quality, and enhance efficiencies in monitoring, data management, and overall study conduct.

CRIO's position as both a site management tool and a sponsor-oriented eSource solution creates mutual benefits, potentially leading to faster study start-up and more cost-effective clinical trials.

III. Standardizing Data Collection and Improving Endpoint Accuracy

In clinical trials, the protocol is the foundation. Sponsors meticulously craft these documents, detailing every aspect of the study to ensure scientific validity and patient safety. However, a gap often exists between this carefully articulated plan and its execution across multiple research sites.

Traditionally, each site creates its own paper source worksheets based on the protocol. This leads to inconsistencies in data collection methods from site to site. When patients arrive for visits, staff record information on these varied paper forms. Later, usually one to two weeks after the visit, they transfer only the endpoint data values into an Electronic Data Capture (EDC) system. This marks the first standardized data collection point in the legacy process and the first time sponsors or CROs can access the information.

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Standardizing Data Collection and Improving Endpoint Accuracy (cont.)

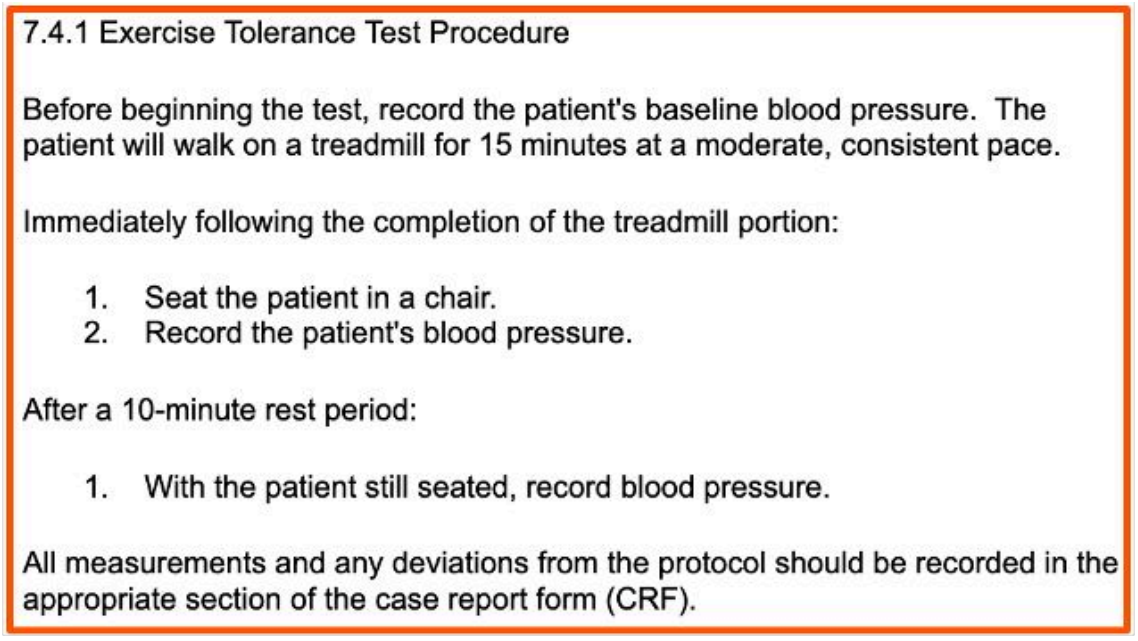
This approach presents several challenges, including inconsistent source documentation, lack of real-time error checking, and delayed data visibility. Paper records require physical storage and on-site review by monitors. Additionally, coordinators risk confusing requirements across multiple trials. A significant concern is the potential for backdating, particularly with Principal Investigator (PI) signatures. In busy clinical research sites, PIs may fall behind on reviews and sign-offs, potentially backdating documents days or weeks later. Paper systems lack robust audit trails, creating a blind spot in data quality assurance that could impact study validity and regulatory compliance.

Beyond Trust: Verifiable Protocol Adherence with eSource

To illustrate the benefits of eSource in ensuring protocol adherence, let's consider a common scenario in clinical trials: measuring vital signs before and after a treadmill test.

Protocol Requirements:

In a paper-based system, there's no real-time method to verify if the coordinator followed these steps precisely. The eCRF might simply ask for the pre- and post-treadmill vital readings, leaving room for potential protocol deviations.



7.4.1 Exercise Tolerance Test Procedure

Before beginning the test, record the patient's baseline blood pressure. The patient will walk on a treadmill for 15 minutes at a moderate, consistent pace.

Immediately following the completion of the treadmill portion:

1. Seat the patient in a chair.
2. Record the patient's blood pressure.

After a 10-minute rest period:

1. With the patient still seated, record blood pressure.

All measurements and any deviations from the protocol should be recorded in the appropriate section of the case report form (CRF).

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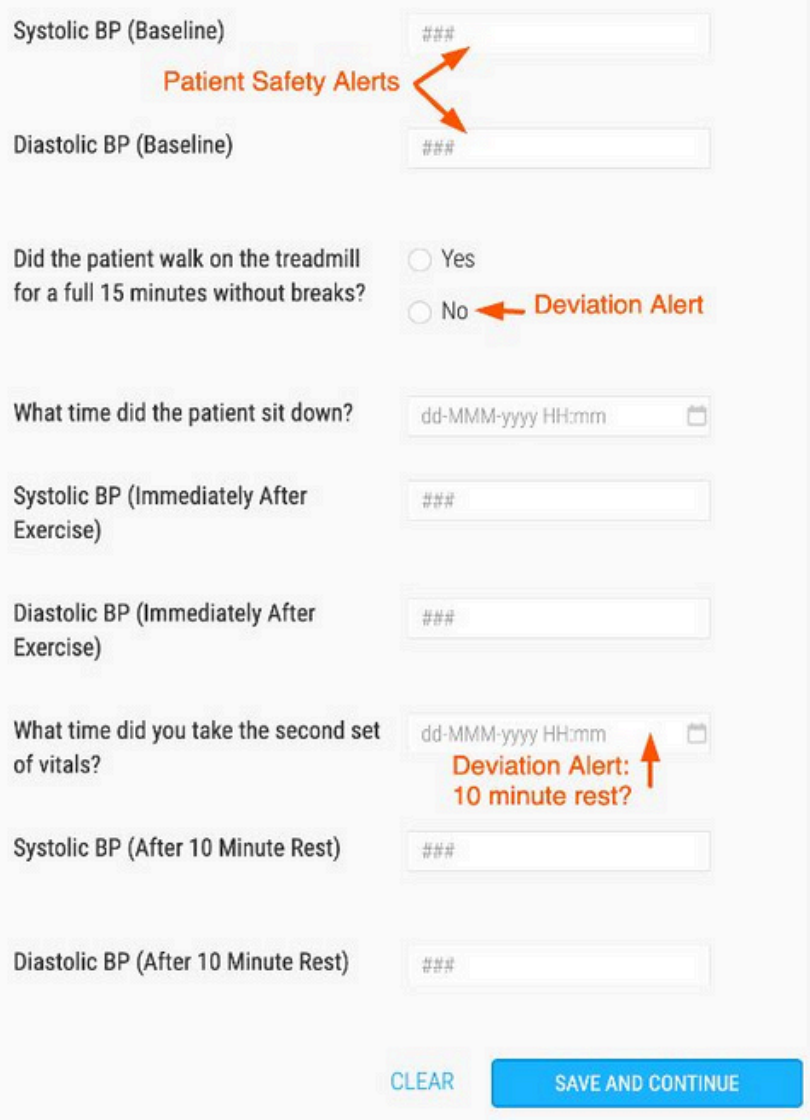
Beyond Trust: Verifiable Protocol Adherence with eSource (cont.)

CRIO's eSource solution addresses this by incorporating protocol requirements directly into the data collection process. By structuring the source data collection in this manner, CRIO's eSource solution provides several advantages:

1. **Real-time Protocol Enforcement:** The system guides the coordinator through the correct procedure, reducing the likelihood of protocol deviations.
2. **Immediate Data Validation:** Alerts for out-of-range values or incorrect patient positioning allow for real-time correction or explanation.
3. **Precise Timing Documentation:** By capturing exact times, the system ensures and documents the required rest period between measurements.
4. **Standardization Across Sites:** All sites, regardless of their familiarity with CRIO, follow the same structured data collection process, ensuring consistency across the study.
5. **Audit Trail:** Each step is time stamped and recorded, providing a clear audit trail for monitors and auditors.



This approach not only improves data quality but also provides sponsors with greater confidence in protocol adherence. It transforms the data collection process from one of hope ("You hope they followed the protocol") to one of certainty, backed by structured, time-stamped evidence.

Beyond Trust: Verifiable Protocol Adherence with eSource (cont.)

CRIO's eSource solution addresses these issues by integrating endpoint fields and supporting documentation into a single, standardized electronic form. Developed collaboratively between the sponsor/CRO and CRIO's study design team, this tool maintains consistency across the study while accommodating site-specific needs. Core questions can be locked while allowing sites to add custom fields, ensuring standardization where crucial.

The system provides real-time edit checks, flagging potential safety concerns and preventing protocol deviations. Automated calculations and skip logic further enhance data accuracy and efficiency. A robust audit trail captures exact times of data entry and PI sign-offs, eliminating undetected backdating and providing a clear, verifiable record for sponsors and regulators.

IV. From Partial to Full Integration: A Progressive Approach to Remote Monitoring

In traditional clinical trials, the monitoring process is often fragmented and inefficient. Clinical Research Associates (CRAs) typically perform separate Source Data Review (SDR) and Source Data Verification (SDV) tasks, requiring on-site visits with extensive travel. CRAs often lack access to critical data for weeks or months, delaying issue identification and potential protocol deviations.

CRIO's eSource solution addresses these inefficiencies by enabling a combined SDR and SDV process. There are two variations of the CRIO Model:

CRIO eSource with Sponsor's EDC: Sites collect data in CRIO's eSource system but transcribe it into the sponsor's EDC. This approach:

- Enables remote monitoring, reducing travel costs and time.
- Streamlines the SDV process through side-by-side screen comparisons or creative reporting solutions.
- Improves data quality at the point of entry, with 40% higher quality data at visit time.

Direct Data Capture with eSource: This model represents the full potential of the CRIO system:

- Significantly reduces SDV needs, though some verification is still required for third-party data.
- Provides instant access to cleaner, more sortable data for CRAs.
- Increases CRA productivity by eliminating most transcription verification.

From Partial to Full Integration: A Progressive Approach to Remote Monitoring (cont.)

The CRIO Model drives substantial efficiency gains and cost savings by enabling remote monitoring and streamlining SDR and SDV processes. This allows CRAs to focus more on critical tasks ensuring data quality and patient safety.

Overall, this strategy allows for immediate efficiency gains while paving the way for future improvements, demonstrating a commitment to relieving site burden and improving trial efficiency.

By leveraging CRIO's eSource solution, sponsors can increase CRA productivity, reduce costs, and improve study quality and efficiency. This approach represents a fundamental shift in clinical trial monitoring, aligning with the industry's move towards streamlined, technology-driven processes.

V. Achieving Substantial Cost Savings

The implementation of CRIO's eSource solution offers significant potential for cost savings across multiple aspects of clinical trial operations. By leveraging technology to streamline processes and improve efficiency, sponsors can realize substantial financial benefits while enhancing overall study quality.

One of the most immediate and tangible areas of savings comes from reduced monitoring costs. By enabling remote monitoring capabilities, the CRIO Model can increase the percentage of remote Interim Monitoring Visits (IMVs) from approximately 20% to 70%. This shift decreases travel expenses by up to 60-65% and boosts CRA productivity. With the ability to remotely review more Case Report Forms (CRFs) per day, monitoring efficiency can potentially double, leading to an overall reduction in site monitoring costs of about 30-35%.

Improved data quality and data management contribute significantly to cost savings. The real-time edit checks and automated calculations in CRIO's eSource reduce protocol deviations and data entry errors, resulting in up to 40% higher quality data at visit completion. This improvement, coupled with streamlined Source Data Verification (SDV) and Review (SDR) processes, can decrease query volume by as much as 80%, cutting data management costs by up to 80%.

The streamlined data collection and processing eliminates duplicate data entry, accelerating study timelines. Some sponsors have reported reducing time to database lock by several weeks. Administrative burdens are also substantially reduced, with savings of up to 50% on study setup and support costs.

Achieving Substantial Cost Savings (cont.)

A significant, though less quantifiable, area of cost savings comes from mitigating the risk of costly study delays. Real-time data access and faster issue resolution help keep studies on track, crucial given that delays in bringing a drug to market can cost pharmaceutical companies millions of dollars per day in lost revenue.

The CRIO Model also helps reduce regulatory and compliance risks, potentially saving sponsors from costly remediation efforts or regulatory penalties. Finally, optimized resource allocation allows for more efficient use of CRA time and better staff distribution across multiple studies, leading to significant savings in personnel costs and improved trial management efficiency.

While exact savings percentages can vary by trial, the comprehensive nature of these cost reductions demonstrates the substantial financial benefits of adopting CRIO's eSource solution. As more sponsors implement this technology, we expect to see even more precise quantification of these savings across various types of clinical trials.

VI. Comparative Insights: Early Indicators from a Similar Trial

While our primary case study is still in progress, valuable insights can be gleaned from early indicators observed in a similar, more advanced Phase III trial. This comparative data, while not direct results of our main study, provides a compelling preview of the potential impact of CRIO's eSource solution, particularly in the critical study start-up phase.

The comparative trial, also utilizing CRIO's eSource platform, involved 140 research sites across Australia, Canada, and the United States. The sites were divided into two groups: 56 sites using CRIO's eSource platform (Group A) and 84 sites not using CRIO (Group B). Key early indicators from this trial include:

1. Time to First Patient Screened:
    a. CRIO users: 81 days
    b. Non-CRIO users: 112 days
    c. Improvement: 31 days faster (27.7% reduction)
2. Time to First Patient Enrolled:
    a. CRIO users: 123 days
    b. Non-CRIO users: 167 days
    c. Improvement: 44 days faster (26.3% reduction)
3. Site Activation Rate:
    a. CRIO users: 87.5% (49 out of 56 sites screened patients)
    b. Non-CRIO users: 75% (63 out of 84 sites screened patients)
    c. Improvement: 12.5% higher activation rate

Comparative Insights: Early Indicators from a Similar Trial (cont.)

These early indicators align with the projected benefits of CRIO's eSource solution discussed in our main case study:

- Faster study initiation: The significant reduction in time to first patient screened and enrolled suggests that CRIO sites can begin generating valuable data more quickly.
- Improved site engagement: The higher site activation rate among CRIO users indicates better site readiness and engagement, crucial for study success.
- Potential for accelerated timelines: These early gains in study start-up phases hint at the possibility of earlier study completion and faster time to database lock.

While these results are from a different trial, they provide a tangible illustration of the potential impact of eSource implementation. As our primary case study progresses, we anticipate observing similar efficiency gains, which are expected to translate into the broader benefits seen in previous CRIO implementations, including improved data quality, reduced query volumes, and overall cost savings.

VII. The Future of Clinical Trials: Lessons from eSource Implementation

The adoption of CRIO's eSource solution by this leading pharmaceutical company marks a significant shift in clinical research methodology. While this implementation is ongoing, the case study, complemented by early indicators from a similar, more advanced trial, demonstrates how CRIO's platform addresses key challenges in clinical trials:

- Standardization of data collection reduces protocol deviations and improves endpoint data accuracy.
- Combined SDR and SDV processes increase CRA productivity and facilitate remote monitoring.
- Cost savings are realized across multiple areas, from reduced travel expenses to decreased data management costs.

While this implementation is ongoing, projected benefits based on other CRIO case studies (available at www.clinicalresearch.io) consistently show:

- 30-35% reduction in site monitoring costs
- Up to 80% decrease in query volume
- 40% improvement in data quality at visit completion
- Accelerated study timelines, saving weeks in time to database lock

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The Future of Clinical Trials: Lessons from eSource Implementation (cont.)

The early indicators from the comparative trial are particularly encouraging, showing significant improvements in study start-up metrics. CRIO eSource users demonstrated faster times to first patient screened (31 days faster) and enrolled (44 days faster), as well as a higher site activation rate (87.5% vs 75% for non-CRIO, paper sites). While these results are from a different study, they align with the projected benefits of our main case study and suggest the potential for accelerated overall study timelines and improved site performance throughout the trial.

The company's approach demonstrates a commitment to continuous improvement and site-centric solutions. The success of these projects underscores the value of prioritizing site-centric solutions to improve overall trial efficiency, even when not all sites use CRIO as their primary workflow tool.

Early indicators align with proven results from other CRIO implementations. As more companies adopt eSource solutions that prioritize site operations, we anticipate continued transformation in clinical research methodologies, leading to more efficient, accurate, and cost-effective trials.

Embracing such innovation is essential for the future of clinical research. The combination of our ongoing case study and the comparative data from a similar trial provides a compelling argument for the adoption of solutions like CRIO's eSource. By implementing these technologies, the industry can drive meaningful improvements in efficiency, data quality, and patient care, ultimately accelerating the delivery of life-saving treatments. As more data becomes available from our primary case study, we expect to see further validation of these early indicators, reinforcing the transformative potential of eSource in clinical trials.