SPAULDING CLINICAL
First in Phase I

The Paperless Site: How to Overcome eSource Obstacles for Faster Database Close and Final Results

Cassandra Erato, CEO, Spaulding Clinical

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TAKING YOU TO THE NEXT MILESTONE BY DELIVERING QUALITY DATA, FAST.

INTRODUCTION

Regulatory agencies and industry groups have long promoted the use of electronic source data, or eSource, to streamline data collection for clinical trials. Despite recognized benefits such as higher data accuracy, real-time access, and greater overall efficiency, Phase I CROs have not embraced the technology as readily as one would expect in their Phase I units.

Instead, many Phase I units continue to collect ECGs, vital signs, and other data on paper. Manual data entry leads to more time spent on data cleaning and clinical monitoring, as well as higher risk of error. Considering most (91%) clinical trial sponsors use electronic data capture (EDC) according to a Veeva Systems report,[1] why not embrace digital?

Technical limitations, data security concerns, lack of resources, and simple resistance due to lack of familiarity have all kept Phase I CROs from embracing electronic solutions for source data. As clinical trials become more digital, organizations that overcome their eSource limitations will gain a competitive advantage.

Researchers gather data from more sources than ever before: electronic health records (EHR), wearables and apps, non-case report forms (non-CRFs), and direct data capture (DDC), to name a few. Efficient, paperless data collection is crucial to maintaining quality and compliance throughout all phases of clinical trials. In Phase I, eSource — a solution that leads to faster database close and faster final results — can positively influence a sponsor's entire program.

WHAT IS ESOURCE?

The term eSource simply refers to electronic source data or data captured electronically. This source data fills predefined fields in an EDC system, also known as an electronic case report form (eCRF).

Nonprofit TransCelerate BioPharma categorizes eSource into four categories:[2]

- EHR data
- Devices and mobile apps, including data from wearables, sensors, and apps, including electronic clinical outcome assessments (eCOA)
- Non-case report forms, which include data from internal sponsor sources (e.g., specialty lab results) or external vendors (e.g., lab results, diagnostic imaging, ECG results) not entered into an eCRF
- Direct data capture (DDC), which is clinical data directly entered by site staff into a mobile app or EDC system

THE MANY BENEFITS OF ESOURCE

In its 2013 eSource guidance document, the FDA promotes eSource as a way to further streamline and modernize clinical trials. Because of the following benefits, interest in eSource continues to grow.

Faster database close. A database build at the beginning of a trial can take months. By partnering with a Phase I CRO with eSource expertise, you can cut that process down to weeks.

Reduced data entry time. Data fields populate automatically using eSource — no pen required. A 2016 eSource study found the method reduced overall data capture time by 37% compared to traditional methods.[3] Staff can devote the time saved to higher-value tasks.

Shorter timelines. Faster database build, combined with dramatically reduced data entry, leads to shorter overall timelines.

Improved data quality. That same eSource study found eSource reduced transcription error frequency — 9% with manual entry — to zero. Reduced data entry errors lower the time required for source data verification.

eSource vs EDC: What's the Difference?

eSource is the source data. In Phase I trials, data are recorded when the patient is in the room (e.g., taking someone's pulse or getting a blood pressure reading). EDC is the capture of this source data. Sponsors and CROs use EDC systems to aggregate and analyze source data. Sponsors interested in eSource can eliminate the need for an EDC and receive study reports directly from the eSource system.

Risk mitigation. Because data is transparent and uploaded immediately, the project team can spot data anomalies earlier and address them before the audit stage. eSource also complements risk-based monitoring, an approach promoted by the FDA.

Ease of use. eSource modernizes and streamlines data collection, monitoring, and reporting. CRAs and data monitors appreciate when these processes go more smoothly.

Streamlined audits. Auditors have quick access to documents, data, audit trails, and other necessary information.

Real-time sharing of data. An instant view allows for a more efficient analysis by investigators, site staff, and sponsors.

Analytics capabilities. eSource consolidates data across a variety of systems, allowing project teams to track values, analyze trends, and flag points of concern.

CLEAR THE HURDLES TO ESOURCE ADOPTION

Not many Phase I sites use eSource, and not all sites that use eSource use it correctly. Some sites record data on paper and transfer it into their EDC. Others use eSource to collect some data, but not all. A select few use eSource exclusively. Admittedly, eSource comes with a steep learning curve. Templates don't look or work the same and real-time EDC doesn't "feel" the same as paper-based data collection.

A Phase I site experienced in eSource has likely faced these and other barriers and developed processes to overcome them. However, sponsors and Phase I CROs alike have common concerns around eSource. Here, we take a look at a few of those in depth.

Data Integration

A Phase I study may collect ECG/EEG values, lab results, vital signs, and other types of data during the trial period. Integration issues occur when values don't match up with the CRF. Software updates may also throw off integration and reporting.

eSource-optimized EDC platforms allow integration with vital signs monitoring equipment. The eSource Implementation Consortium is working to accelerate software applications that integrate EHR, EDC, and clinical data management systems (CDMS).

Paper-based methods create integration issues of their own. Imagine a physician deciding to review ECG results at home. The physician emails results back to his assistant, but the assistant applies the results to a different study. Or even worse, the email gets intercepted and other parties have access to protected health information (PHI).

These sorts of problems can be easily eliminated with eSource. Physicians and sponsors have real-time access to data, which allows them to spot and address anomalies instantly. Further, studies can save three to four weeks by eliminating time spent validating the paper source against eSource.

Integration also allows for efficient single ascending dose (SAD) reporting. When a SAD study has an ECG analysis component, typically sponsors have to wait three to four weeks before analysis can start. When that data is integrated via eSource, sites can send it for analysis immediately.

For studies that rely on regular lab results, the site can implement checks to flag high and low values. They can also instantly view trends and results over time. You can't see trends with each data point on a different piece of paper.

Data Security

Sponsors and Phase I sites have understandable concerns around privacy and security of PHI. FDA guidance says sponsors should include information about security measures taken when using "computerized systems in the protocol or data management plan."[3]

Security is paramount whether using paper or digital formats. When using eSource, be sure to implement additional controls, such as password protections, data encryption, and specific procedures that specify roles and access privileges.

Sites also need to make sure their EDC vendors maintain HIPAA and GDPR compliance.

Regulatory Concerns

eSource raises FDA 21 CFR Part 11 and EMA concerns. Some sponsors and CROs resist eSource due to risk of audit and additional documentation required from the FDA and/or EMA. Others may fear rejection of their new drug application (NDA) if they use paperless data collection.

The FDA has become more familiar with, and accepts, eSource. Auditors do, however, want full access to every part of the source data to the extent that it could recreate the trial from that data. To provide the data the FDA requires, sponsors and sites need easy access to archival data. Pulling data from disparate, disorganized systems, or from deep storage, won't allow sponsors to access what they need quickly enough to ensure the audit goes smoothly.

21 CFR Part 11 applies to electronic signatures. The electronic signatures provided by investigators after reviewing the eCRF must be voided when data is changed on a signed record. The meaning of the signature must be documented, and signers must use two-factor authentication when signing in.

When implementing eSource, Phase I sites must establish access points to restrict access to certain data. To accommodate the FDA's robust data requirements, be sure your Phase I vendor establishes an archiving process that keeps archived data readily available.

Ask your Phase I vendor if it has the appropriate systems in place to meet FDA requirements. These sites will need to change their auditing process to be prepared for deep dives. It may take several tries to get the process down; sites that do have systems in place can expect a more streamlined experience when responding to FDA inquiries.

Lack of Standard Process

TransCelerate envisions a future for eSource that includes Clinical Data Interchange Standards Consortium (CDISC) and Health Level Seven International (HL7) standards.[4] These standards would allow for direct, secure exchange of data across organizations. It would also allow for easy integration of EHRs and EDCs, improving efficiency for clinical trials overall.

Standards are emerging; however, sponsors and sites don't currently have a uniform eSource data collection process to follow. Without them, transitioning from paper to eSource presents process challenges. Where's the playbook for eSource data collection?

In the absence of a published uniform standard, sites can establish and document a specific data collection process and keep it consistent for every trial. Trial and error will help you refine that process to make it as efficient as possible. *Rule Number One: Phase I sites should not let their monitors revert back to paper.*

Data Transfer to Sponsors

Once a site captures all its Phase I study data, it may have to transfer that data to the sponsor's EDC. Using paper-based methods, staff have to manually enter that data — a time-consuming, error-prone process. What if this transfer could happen automatically?

With eSource, it can.

CROs and/or sites can use an EDC optimized for eSource or an API to integrate the eSource system and the EDC. The time spent on this IT issue will save sponsors thousands in labor costs and accelerate their timelines by weeks.

Internal eSource Challenges

Stakeholder resistance prevents many Phase I CROs and sites from adopting eSource. Internal challenges include:

- **Fear of change.** Sponsors, CROs, and sites all have established processes in place. Letting go of old ways to adopt modern technology intimidates many individuals.

  Clinical trials have largely adopted eCOA, EDC, wearables, and mobile devices. eSource is the next best step in the digital transformation of clinical trials, but it requires change management.

  Be sure your Phase I provider develops a detailed eSource migration plan. Communicate the financial value to leadership. Inquire whether your Phase I provider has the IT resources to manage a smooth implementation process.

- **Perceived lack of resources.** While moving to eSource does require technology and staff training, over time, sites will require fewer resources.

  Sponsors should seek out Phase I CROs that are either experienced in eSource or that have made eSource fluency a priority. It takes time for a study team to become familiar with the system and its processes.

  Take Note: It can take up to two years for a CRO to become fluent in eSource.

- **Don't see the benefit.** How much money does a Phase I study save when it gains two to three months? Sponsors can save anywhere from six to 12 weeks when they partner with an experienced Phase I CRO.

CONCLUSION

As clinical trials continue their move to digital, eSource is the logical next step in designing efficient, cost-effective clinical trials. Moving away from outdated paper-based processes improves data accuracy and can shorten timelines, which dramatically improves quality.

Biopharmaceutical sponsors outsourcing Phase I studies to CROs should look for an EDC platform optimized for eSource. In addition, they should partner with eSource-fluent Phase I CROs that have developed established policies and processes around using the technology to its fullest. The efficiency gains and improvements in audit readiness are more than worth the discomfort of change.

References

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Founded in 2007, Spaulding Clinical is a full-service, state-of-the-art paperless Phase I clinical pharmacology unit. Our facility, originally a hospital, features fully integrated bedside electronic data capture and sets the standard for patient care. We specialize in IND-enabling clinical pharmacology studies, cardiovascular safety, and clinical proof of concept. We provide expertise on study design, offering in-house medical writing, clinical data management, biostatistics, project management, clinical laboratory, and PK/PD analysis. For high-quality data to inform your decisions, Think Spaulding First. To learn more, visit **spauldingclinical.com.**

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