



At the Source

Seen by some as the new gold standard for source data generation, eSource is becoming the go-to method for streamlining trials – backed by the FDA and EMA as a modernising force for clinical R&D

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The widespread implementation of eClinical technologies, such as electronic case report forms (eCRFs) and electronic data capture (EDC), has opened new avenues for adopting and integrating many technologies in clinical trials to improve data quality and operational efficiency.

While EDC has become standard practice, with an estimated 88% of Phase 3 clinical trials expected to initiate using this technology (1), it is not without challenges. Volumes of paper still burden clinical trial operations due to continual reliance on 100% source document verification (SDV) and delayed data entry, possibly contributing to questionable data quality. Moreover, uptake of risk-based monitoring (RBM) is advancing at a very fast pace, but many sponsors and study teams have not yet deployed proper eClinical technologies, such as eSource, to generate data in real-time – a key element for effective RBM. In this article, these issues are discussed from the perspective of a sponsor that is a successful early adopter of eSource technology.

eSource Adoption

It has been several years since regulatory agencies in the US and Europe first promoted and encouraged the use of eSource as a replacement for paper source to streamline and modernise clinical trials (2,3). In addition, a July 2015 webinar, sponsored by the FDA, stated that the agency is eager to see industry conducting more eSource trials, first endorsed in its September 2013 industry guidance on the subject (4) (see Box 1 and Box 2 on page 42).

Box 1: eSource Explained

eSource is an emerging cloud-based technology that captures and validates data electronically at the source. This approach eliminates the paper traditionally used to record that first observation, and removes the need to transcribe data into an EDC system – a slow, error-prone and expensive process.

Awareness and adoption of eSource technology are supported by the FDA and EMA. Both regulatory bodies have stated that they actively promote greater use of eSource to improve study conduct. FDA guidance on eSource focuses on its benefits, citing the elimination of unnecessary duplication of data entry, resulting in fewer transcription errors and improving data quality when the patient is still accessible (2). An EMA reflection paper in 2010 identified eSource as pivotal to improving the quality of clinical trial data (3).

Sponsors are beginning to adopt eSource, but the FDA is calling for even greater implementation of the technology. The agency's position was spelled out in a July 2015 webinar on electronic source data capture (4). Dr Ron Fitzmartin, Senior Advisor in the Office of Strategic Programs, commented that in the two years since the release of the FDA eSource guidance, there have been few confirmatory trials conducted. "Hopefully, this is the beginning of the end of paper. We want to see transformational changes, and we are encouraging eSource trials to start as soon as possible," he said.

The webinar also described how eSource can facilitate centralised monitoring, allowing monitors and auditors to view data across the clinical trials continuum, tracking data from a submitted study report to when the data were originally collected at the site. Because eSource makes both the data and the documents in which the data were originally captured visible, fewer visits to the site are needed, providing sponsors with real-time access to critical data.

To elaborate, eSource reflects a reduced need for 100% source data verification, as the emphasis shifts from tedious review of data transcription towards source data review in RBM (8) and a greater focus on study outcomes and relationship-building with investigative sites. Moreover, the technology enables sites to capture data errors through automated triggers on the spot, which can significantly improve data quality, and promotes real-time data entry – a critical factor needed to execute RBM.



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The widespread use of paper-based data collection and sustained regulatory efforts to introduce greater speed and quality into trials has now positioned eSource as the go-to method for streamlining R&D (5), and some sponsors are adopting eSource in their eClinical strategy portfolio to generate breakthrough results.

Although the clinical trials industry has generally exhibited a risk-averse culture towards adopting eClinical technology, Otsuka Pharmaceutical Development & Commercialization was among the first to explore these applications to build study efficiency and improve trial data quality.

As part of a corporate objective to improve the clinical trials process for all stakeholders, Otsuka piloted its first eSource study in 2012. Site staff used tablets to capture patient data directly, instead of using traditional paper source. "The value was that the site added the patient data at the time of the visit – no waiting for sites to complete data entry after the study visit which often falls weeks or even months downstream," says Dr Debbie Profit, Leader of Otsuka Information Technology.

Real-Time Visibility

Profit highlights that some EDC systems are now offering eSource-like functionality, with electronic capture of source data on mobile tablets that can be uploaded to the cloud in real-time. While this feature may be available in some EDC solutions, those systems do not offer real-time electronic access to the patient's chart. "This is a critical feature of true eSource, and truly differentiates this technology from EDC," she explains.

In addition to collecting CRF data via eSource, the technology allows users to record notes, comments and explanations in the patient's chart – information beyond what is required by the protocol, but still needed for the study – and has an electronic audit trail. "With eSource, we have de-identified real-time visibility into notes written by the investigator about the patient, such as the number of times and when a patient regurgitated, and when. With EDC, because the patient charts are still in paper, we have no visibility into that information beyond what appears in the case report form, such as 'patient vomited'. Those patient charts have to be transcribed, which generates lots of queries and extends the process, making it more inefficient," she remarks.

Systems Integration

After conducting a series of eSource studies, Otsuka used the learnings to improve efficiencies and execution of subsequent eSource research. As described by Profit, the company's original vision was to incorporate eSource along with electronic informed consent forms (eICFs) and electronic drug management and accountability technologies. While, in theory, numerous eClinical applications appeared to be a sound strategy, in practice,

Box 2: The Difference Between EDC and eSource

As eSource gains ground, it is sometimes considered a form of EDC, which, in some instances, has evolved into a cloud-based technology that enables direct entry of trial data into the study database. Yet, the two technologies differ significantly.

Most notably, eSource refers to capturing clinical trial data electronically from the outset, as no paper is involved. With this first electronic capture – via desktop, laptop or mobile technology – the data are stored in the cloud and immediately become available to monitors remotely in real-time. In addition, the data can flow into automated reports that the eSource system can generate, allowing stakeholders to evaluate how the trial is progressing, revealing trends in the data and surfacing risks in real-time.

In comparison, EDC has traditionally required data to be captured initially on paper, followed by transcription into the EDC system – typically 2-4 weeks later. Transcription errors are inevitable and the data are not immediately available. This approach causes a delay in detecting issues reflected in the data. It also hinders centralised monitoring efforts as monitors would have to conduct on-site SDV – a task which can take up as much as 75% of the monitoring visit, and has proven to be minimally effective at detecting critical data errors (9).

investigative sites complained they would have to enter the requisite data separately into each of the cloud-based systems, essentially tripling the workload.

Otsuka worked with the three vendors to develop a way of integrating eSource, eICFs and interactive web response systems (IWRS), so the information could flow freely among the solutions. By leveraging eSource as a central hub for administering eICFs and randomising patients, the company realised significant efficiencies in streamlining data and enhancing the quality of clinical trial conduct. "The result has been real-time visibility into study-related information, including trial data – a huge improvement over the way we were conducting trials in that data were typically not available for up to a month or more after initially collected," says Profit. If sponsors are not seeing data in real-time, they are not optimising centralised monitoring and RBM, she adds.

Electronic Informed Consent

Using eSource as the centralised data hub, Otsuka integrated eICFs to replace time-consuming paper-based patient consent forms. Automating patient consent via eICF reduces complexity through features such as video, graphics, pop-up definitions and quizzes. Moreover, eICFs enable sponsors to improve consent through electronic interactions data, such as how much time patients spend with the consent and which sections/terms they find confusing (6).

From a workflow standpoint, when a patient was consented, they were automatically issued a randomisation number via the IWRS, and a subject profile was immediately generated

Box 3: Electronic Drug Supply Chain – In Brief

In comparing two nearly identical Otsuka studies, one used an electronic drug supply chain to manage study supplies, whereas the other used traditional, manual processes. According to the company, the outcome was dramatic:

- The site using an electronic drug supply chain took 4 hours to manage study supplies, compared to 19 hours for the site using manual process
- An electronic drug supply chain helps the study team execute risk mitigation strategies (for example, training) via automatic risk notifications, while reducing queries and data entry time

in eSource. This user-friendly and auditable approach has resulted in improved compliance at the site level – a significant change, since issues related to the informed consent process are among the most frequently cited violations in FDA inspections (7).

Electronic Drug Supply Chain

Integrating eSource with an electronic supply management solution was the final step in Otsuka's eClinical technology suite. Coupling eSource with electronic supply management allowed the study team to manage trial supplies in one system, rather than two. The clinical trial supply chain is long and has many links, each of which involves site, sponsor and/or CRO staff personnel. Trial supplies must be tracked from the distributor to the site, from the site to the patient and, at the end of the trial, from the site back to the distributor. Each link in the chain must be verified by both the site and sponsor/CRO. Traditionally, this entire process is paper-based, expensive and laborious.

The eSource-based process starts with scanning the supply label once it arrives at the site, with information flowing directly into eSource. The scanned data is available remotely to the monitor who manages the distribution of supplies. Once received, the drug label is also scanned when dispensed to the patients, ensuring that the right drug is dispensed to the right patient, and automatically verifying and updating inventory systems. This site-friendly approach eliminates the manual effort exerted by clinical sites and the monitor to manage and verify the supply chain. The supply accountability system moves from paper to eSource, enabling streamlined tracking and remote management (see Box 3).

Paperless Future

From Otsuka's perspective, eSource, eICFs and electronic drug accountability, working together, optimise trial efficiencies by decreasing repetitive data entry and cleaning, improving data quality, supporting RBM, and reducing overall risk to patients. The company, and those following a similar approach, are helping to set a new industry standard by successfully demonstrating that paperless trials offer improvements.

At a time when overhauling study processes for improved efficiency is high on the industry's radar, eSource is becoming key to driving the necessary changes. Indeed, the Society for Clinical Data Management (SCDM), in a June 2014 white paper, stated that eSource is well-justified as the new gold standard for source data generation (5), and its advantages enable sponsors to deliver medical products to patients faster.

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