A Topic Brief Series on eSource

Society for Clinical Data Management (SCDM)

eSource Implementation Consortium

Playbook 1: Practical advice for vendors and CROs

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Authors

- Linda S. King, SCDM, Astellas
- Jonathan Andrus, SCDM, CRIO
- Alex Crawford, ICON
- Kristen Harnack, Castor

Reviewer

- Patrick Nadolny, SCDM, Sanofi

Author notes:

SCDM eSource Implementation Consortium, Linda S. King, SCDM Facilitator

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Correspondence relating to this article: Linda S. King
(linda.king@astellas.com)

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Abstract

Clinical research is in the midst of a digital transformation, with the emergence of eSource data promising to accelerate drug development timelines, enhance patient centricity, and unlock previously unseen insights. While much has been written on the rationale for eSource approaches, practical advice on their implementation has been less widely available. As the world's leading advocate for the discipline of clinical data management, the Society for Clinical Data Management (SCDM) is in a unique position to fill this knowledge gap. To achieve this aim, the group has produced a series of podcasts in which leading experts from across the clinical research ecosystem share their case studies and practical advice on moving eSource from theory into practice. We then distilled their learnings into four playbooks, each from the standpoint of one of the main stakeholder groups: CROs and vendors, pharma, regulators, and academia/sites. This paper focuses on the technology vendor and CRO perspective.

Methodology

The eSource Implementation Consortium is publishing an eSource topic briefs series intended to serve as orientation guides on eSource, which are contributing directly or indirectly to the evolution of Clinical Data Management (CDM) into Clinical Data Science (CDS). Due to the absence of a comprehensive and authoritative literature base regarding the wide implementation of eSource within the Drug Development industry, this content was gathered from industry leaders through an opinion-based methodology. As eSource implementation matures and technology evolves, the Consortium anticipates that literature on this topic will blossom.

Podcast interviewees were selected for their eSource expertise according to SCDM Board recommendations and/or were members of the SCDM eSource Implementation Consortium. Efforts to reduce bias included using a standard set of questions, based on input from the SCDM eSource Implementation Consortium, and conducting interviews with 17 contributors from four different perspectives. Contributors were asked to share their thoughts on barriers to eSource adoption and implementation from their personal experiences of the approach, and to provide case studies.

Post-podcast recording, the recordings were grouped into four perspectives: CROs and vendors, pharma, regulators, and academia/sites. The transcripts were reviewed to identify key themes, which were then summarized to form a narrative, playbook-style report. Podcast contributors were asked to review the drafted content to ensure their viewpoints had been represented faithfully.

Interviewees: *

Name	Job title / Organization	Sector
Jonathan Andrus	President and COO at CRIO, and SCDM Treasurer	Vendor/CRO
Alex Crawford	Director of Decentralized Clinical Trial Products, DCT Operations, ICON	Vendor/ CRO
Kristen Harnack	Director of Solutions Consulting, Castor	Vendor/CRO
MD Naqib Alam Ansari	Senior Manager, Clinical Data Strategy and Operations, AbbVie R&D	Pharma
Magda Jaskowska, PhD	Global Director/Leader Oncology, Data Strategy and Management, GSK	Pharma

Lauren McCabe	Associate Director, Clinical Data Sciences, Pfizer	Pharma
Muzafar Mirza	Senior Group Lead, Clinical Data Sciences, Pfizer	Pharma
Joseph Angiolelli	Director, Information Management/Clinical Trial Solutions, Pfizer	Pharma
Peter Casteleyn	Director, Data Collection Solutions-EHR, Janssen R&D	Pharma
Rakesh Maniar	Executive Director and Head of eClinical Technologies, Global Clinical Trials Operations– Global Data Management and Standards, Merck & Co., Inc.	Pharma
Nadir Ammour, DDS	Global Lead for external engagement, Transformation & Performance Office, Clinical Science & Operations/Development, Sanofi R&D	Pharma
Mitra Rocca	Senior Medical Informatician, FDA	Regulatory
Jeff Stein	President of Stamford Therapeutics Consortium	Sites/academia
Michael Buckley	Associate Director of Product Management, Clinical Research Informatics and Technology, Memorial Sloan Kettering Cancer Center	Sites/academia
Elena Christofides, MD	Owner, Endocrinology Research Associates	Sites/academia
Cory Ennis	Director of Information Technology- Engagement and Assistant Dean for Research Systems, Duke University School of Medicine's Office of Academic Solutions and Information Systems	Sites/academia
Denise Snyder	Associate Dean for Clinical Research, Duke University School of Medicine Office of Clinical Research	Sites/academia

* All interviewees consented to use of their quotes. All information included in this report has been reproduced with the permission of the interviewees and the SCDM.

Introduction

Clinical research is in the midst of a digital transformation, with the emergence of eSource data promising to accelerate drug development timelines, enhance patient centricity, enhance sponsor and site efficiencies, and unlock previously unseen insights. eSource refers to the direct collection (entry or acquisition) of clinical data into an eSource system from site staff, clinical trial participants, or care givers. It can include direct from device, such as wearables or sensors, direct from clinical trial participants or clinician/site staff, such as eCOA, or direct from an electronic health record (EHR).[1] The approach reduces the need for source data verification (SDV), minimizing the need for transcription and providing real-time guidance on illogical or inconsistent data at the point of collection. If implemented correctly and in compliance with ICH-GCP, it can reduce site burden, boost patient centricity, and improve data quality.[2]

As the industry moves from the "why" to the "how" of eSource, however, it is clear that adoption can sometimes present just as many challenges as it does opportunities. The new paradigm often requires the integration of disparate data sets, using multiple technologies, and redesigning

existing work and data flows, for example. While much has been written on the rationale for eSource approaches, practical advice on their implementation has been less widely available.[3] As the world's leading advocate for the discipline of clinical data management, the Society for Clinical Data Management (SCDM) is in a unique position to fill this knowledge gap.

SCDM eSource Implementation Consortium

SCDM is one of several industry bodies backing the use of eSource, which offers a wide range of benefits. The consensus is that it can "improve protocol design and clinical trial participant recruitment, modernize and streamline data collection, monitoring and reporting"[2], thereby improving healthcare and outcomes. It can enhance "site and participant experience, reduce data entry errors, minimize the 'burden of source data verification', and 'facilitate' the use of 'risk-based monitoring (RBM)', as well as enable real-time data review and generate the outcomes-based evidence sponsors need to demonstrate the value of their products"[2].

Despite the well-documented advantages and wide availability of eSource tools, challenges around implementation mean adoption has been slow. SCDM eSource Implementation Consortium, which includes representatives of leading biopharmaceutical companies, academic medical centers, regulatory bodies, and healthcare technology providers, was established in 2017 to further the adoption of eSource approaches.[4] As part of that work, the group has produced a series of podcasts in which leading experts from across the clinical research ecosystem share their practical advice on moving eSource from theory into practice. We have also distilled their learnings into an eSource Topic Brief series of four playbooks, each from the standpoint of one of the main stakeholder groups: CROs and vendors, pharma, regulators, and academia/sites.

Playbook 1: Practical advice for vendors and CROs

As part of the Playbook project, three representatives from clinical trial technology companies and CROs shared their experiences:

- Jonathan Andrus, President, and COO at CRIO, and SCDM Treasurer, has more than 20 years of experience in the direct data capture space.
- Alex Crawford is the Director of Decentralized Clinical Trial products in ICON's DCT operations group. He has been working with clinical technology for 15 years, and eCOA for over five.
- Kristen Harnack, Director of Solutions Consulting at Castor, where she advises customers on using electronic health records (EHR) in clinical trials. She has been working with EHR for the last decade.

Typical challenges to adoption

eSource adoption can present vendors and CROs with a range of challenges. There can be, for example, a certain level of sponsor and site reluctance to apply these new processes as they are not always germane to legacy data collection and management practices. This roadblock has been compounded by the recent rapid roll-out of decentralized clinical trials (DCTs), accelerated by the COVID-19 pandemic, which has left many sites drowning in technology. In addition, those responsible for compliance within CRO and sponsor organizations can often misunderstand how regulations pertain to eSource data. Regulators tend to be open to looking at new, more effective, and more efficient ways of collecting data, yet this is not always widely understood. Ultimately, this means that vendors need to understand – and be ready to demonstrate – how their technologies fit into existing workflows and regulatory frameworks.

"A site might work with six sponsors or CROs, and each might ask them to use a different technology to collect data. None of these will necessarily be optimized to how a site operates," Andrus.

Case study: eCOA and Complex cognitive assessments

The proposition: Increasing inclusivity and cohort diversity in an Alzheimer's study by deploying remote monitoring, via an eCOA system.

The challenges:

- Enabling the effective, consistent, and compliant conduct of complex cognitive assessments in a completely remote environment
- Ensuring system ease of use for participants as well as caregivers of all ages

The solution:

- Vendor developed a thorough understanding of the assessment, data sources, and possible "in-visit" scenarios
- A robust telehealth technology, with built in 24/7 help desk for all parties, was deployed

Direct from patients

Collecting source data directly from participants can pose challenges. These include ensuring the patient engagement needed for continued use, which makes easy to use, easy to understand interfaces essential. It is worth noting that asking participants to interact with multiple solutions, such as separate eDiary and pedometer apps, for example, can make protocol adherence more burdensome, so integrated solutions are always the best option.

"Device data is shifting from being a secondary to a primary endpoint. It really needs to work seamlessly for the patient." Crawford.

Direct from EHR

Data access rights are another important consideration. Retrieving information from an EHR, for instance, will need agreement from the patient to obtain their health/medical records, and a legal agreement with the specific hospital or a third-party provider before the software build can take place. If technology vendors start work without these contracts, the negotiation process, which can take several months, must be accounted for in project timelines.

There also can sometimes be a knowledge gap on the part of sponsors around the nuances of EHR data. Vendors will often need to work closely with their clients in order to ensure the needs of the specified use case and advise accordingly.

Considerations include:

- Optimizing the solution to the project timeline: for a three-month trial, for example, the most appropriate integration solution is likely to be a straightforward CSV export, rather than a direct EHR integration
- Optimizing integration path to the required information: not all data will be accessible from patient portals, for example

Data integration

The most appropriate integration method will usually depend on the use case. For short, simple projects, a CSV export is often the easiest, most practical and cost-effective approach. For

deep integrations, such as those needed to connect multiple studies over a long period of time for example, an API is the best ideal solution. APIs can be used to integrate eSource with EDC either unidirectionally, meaning from eCOA or ePRO to EDC, or bidirectionally, which would allow queries and other data to be sent back the other way. While the latter can be challenging to implement, it is often preferable to prevent additional site burden associated with manual data transcription. As direct from patient eSource can generate huge volumes of data from disparate sources, simple integrations are often the most effective here.

> *"With something like a continuous monitoring device, you're looking at more data than you really know what to do with. Ideally, you need to parse out the data you need, and bring it into whatever application the site is using, along with anything like the eCOA data. The industry is finding clever ways of doing this: reducing applications on patients' phones and cloud-to-cloud integrations, for example. But we're also getting more and more data, so it's very important to keep that in mind as you design your studies."* Crawford.

Regardless of data integration methods, vendors need to consider how data points from different sources will map to each other. This is particularly true in EHR eSource, where disparities in coding and, more importantly, in the use and purpose for collecting, for example billing versus for pure research protocol compliance, are common.

Case study: Managing multiple device data sources across a large trial

The proposition: To reduce site and participant burden and increase and enable the real-time review of primary and secondary endpoint data in a large global COVID vaccine trial.

The challenges:

- the volume and geographical spread of participants: 42,000 people across 12 countries on three continents
- multiple direct from device elements, including eDiary, COVID surveillance log, and multiple memory aid questionnaires
- 30% bring your own device (BYOD) – 70% of participants were provided with a device
- urgent need for rapid enrolment

The solution: The Interactive Response Technology (IRT) was integrated with an eCOA platform that brought patient identification and medication management information into a single system. An API between this system and EDC fed into the CRFs. Each system extracted into a third-party reporting tool via a simple CSV.

All queries were raised in the EDC and sent to both data management and the clinical teams, who discussed them at daily scrum meetings. Issues were logged, investigated, and, if necessary, corrected contemporaneously.

Data cleaning

Trials are seeing huge amounts of data coming from multiple sources, making efficient data cleaning essential. Tools with built in data discrepancy identification or data discrepancy management are available. Front-end logic can interrogate data, based on protocol requirements, as the clinician enters it. Many eCOA platforms, however, do not currently have query functionality, meaning queries are raised in the EDC. Fortunately, powerful reporting tools that can bring all the data from disparate sources together are emerging. By providing a base for all the data, such tools can facilitate data management access, query resolution, data cleaning, and reporting.

Centralized monitoring approaches can add another layer of assurance. Such approaches analyze datasets at the full clinical trial level and can flag outliers that could signify discrepancies.

Real-world data

At the EHR level, it is important to consider what the data is needed for and how it will be used. While coding around fields like vital signs and medications is quite standardized, clinician notes and nurse assessments will be more challenging to analyze and map.

Clinical terminologists can help vendors to understand the nuances of real-world data points, but they are in short supply. The next best option is ensuring the clinical and technical teams work together on forming the data maps.

Duplicate records are common in EHR data but identifying them can be complex. The medical records number may not always be accurate, and using demographic information can threaten anonymization. One solution is tokenization, in which a sensitive identifier is issued with a non-sensitive equivalent, or token, with no exploitable meaning or value.

> *"Mapping of EHR data is not always simple. Local hospital workflows can change where and how information is documented and, if you're not accounting for those nuances, then you could be missing data as it's imported in the EDC."* Harnack.

Case study: Identifying cohorts from Real World Data (RWD)

The proposition: Use EHR data to identify people who would be eligible for a clinical trial in diabetes

The challenge: Aggregate EHR data will provide an inaccurate selection population if searching on a single data point such as diagnosis alone. Recorded diagnoses may be inaccurate or irrelevant.

The solution: Algorithms that search by diagnosis and supportive material, such as a relevant medication prescription or recorded HbA1c results, were developed. Upon deployment, this solution returned a much better-defined population of eligible participants than would have been possible by searching for diagnosis alone.

Standardization and terminology

With an ever-widening volume of data being generated and collected, the challenge is to develop ways to work with and organize that information. What's more, the rise of decentralized clinical trials has made the evolution to clinical data science more crucial than ever. Standard naming conventions, such as CDASH and SDTM, can be applied to front-end eSource data capture tools to enable the export of downstream submission data.

> *"There needs to be collaboration and harmonization on how we are transferring that data as well as an agreement on standards and terminology, so that data is moving back and forth in an efficient manner,"* Crawford.

While there are levels of standardization within the separate silos of healthcare and clinical research, currently the two do not always cross over. However, much work is going into the Fast Healthcare Interoperability Resources (FHIR) standard as a set of rules and specifications for exchanging electronic health care data that could fill this gap.

Data flow

Data flow approaches tend to depend on the desired export requirements. When sponsor requirements are for data to flow from eCOA or ePRO to a downstream warehouse in near real time,

the CDISC ODM model is useful. If the data is not needed in real time, it can be exported using an extraction, transformation, and loading (ETL) tool and posted to a secure file transfer protocol (sFTP) site. The sponsor would then use a routine command to pull the data into their data warehouse.

A good way to understand the data flow is to map the pathway from the point of view of the patient. This might include site and/or remote appointments, which data capture systems they will use and when, and the visit windows. Next, vendors can do the same from the site point of view, looking at which systems they would be logging into at which points, whether eCOA data is being delivered to the EDC or a third-party reporting tool, and the parameters of data cleaning and study data lock.

From a technical standpoint, API integrations are key for real-time touch points. Examples might mean moving information provided in clinic from an IRT to an EDC to enable randomization and material release.

The future of eSource

When our three experts shared their views on the future of eSource, there was one common theme: The approach was here to stay. At SCDM, there is an important focus on the evolution from data management to clinical data science, and how to best utilize all available sources for protocol analysis and submission purposes.

> *"In the future, I would like to see eSource treated as a true source, just as ECG or lab data are sources. I hope we can use eSource tools and technologies to pull these data into data marts and data warehouses. This aggregation of data will allow data management professionals to elevate their role, from a data science perspective, and look at things more analytically, from a trends and outliers standpoint."* Andrus.

All in all, the future of eSource is "very exciting", said Harnack. "There's an opportunity to make the process more streamlined for clinicians on the front end. The dream state is a single experience for the end users where APIs create a truly seamless experience in which everything can be done in one tool, then parsed out to all the different stakeholders on the back end," she explained.

Crawford pointed to the opportunities to, and benefits of, leveraging eSource to make research more patient centric. "I think we are going to see very user-friendly front-end interfaces for the powerful reporting tools that collect and clean data, bringing things like query functionality to the forefront and enabling queries to be addresses in systems other than the source system."

Crawford further states, "By utilizing the capabilities of eSource, the industry will be able to reach more participants, driving up inclusivity and build more diversity into trial cohorts."

References

1. U.S. Department of Health and Human Services Food and Drug Administration, Electronic Source Data in Clinical Investigations: Guidance for Industry. September 2013. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/electronic-source-data-clinical-investigations. Accessed July 17, 2023.
2. Parab AA, Mehta P, Vattikola A, et al. Accelerating the adoption of eSource in clinical research: a TransCelerate point of view. *Ther Innov Regul Sci.* 2020;54(5):1141-1151. DOI: 10.1007/s43441-020-00138-y.
3. Jennings DG, Nordo A, Vattikola A, Kjaer J. Technology considerations for enabling eSource in clinical research: industry perspective. *Ther Innov Regul Sci*. 2020;54(5):1166–1174. DOI: 10.1007/s43441-020-00132-4.
4. eSource Implementation Consortium. Society of Clinical Data Management. Date unknown. Available at: https://scdm.org/esource-implementation-consortium/ . Accessed July 17, 2023.