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OPINION PAPER

Real-Time Perspectives on the Transition to eSource: SCDM Best Practice Consensus Recommendations for Implementation and Scalability

Linda S. King*, Michael Buckley†, Amy Cramer‡, Muzafar Mirza§, Cory Ennis‖, Lauren McCabe¶, Cal Collins** and Aruna Vattikola††

The transition from traditional to modern data collection, in the form of eSource, has spawned an entire new ecosystem of approaches and vendors. This has created a complex web of considerations that leave many clinical research stakeholders unsure of where to start.

A study from the Society of Clinical Data Management (SCDM) eSource Implementation Consortium, published in Contemporary Clinical Trials Communications in December 2024, found there were 36 steps research sites needed to traverse before they could even get started with eSource – all of which were associated with their own challenges.[1]

Scalable implementation relies on the clinical research ecosystem, in collaboration with regulators, coming together to overcome these barriers. To this end, SCDM hosted a series of workshops and meetings in 2024, that brought leading subject matter experts from across the clinical research ecosystem together to share their knowledge, insights, and case studies. The initiative included three working groups, which focused on site readiness, contract readiness, and technological readiness. They were followed by a roundtable discussion, which reviewed and discussed the working groups' findings, the challenges and, crucially, the potential solutions of eSource implementation.

This document summarizes those talks and sets out a range of best practices, all aimed at building a consensus that can act as a foundation for the wide-scale adoption of eSource clinical trial data collection and transfer across the industry.

Keywords: Manage Clinical Research Data; Collect data; Record Data; eSource; Electronic Health Record

What is eSource and why does it matter?

The US Food and Drug Administration (FDA) defines eSource, or electronic source data, as data that are initially recorded in electronic format. It can refer to "information in original records and certified copies of original records of clinical findings, observations, or other activities captured prior to or during a clinical investigation used for reconstructing and evaluating the investigation".[2] eSource dataflow is the electronic transfer of data after it is initially entered at a single point of entry into an electronic health record (EHR) or similar source system. There is no subsequent manual data entry involved post-original eSource entry.

Examples include direct from device data capture, such as via wearables or sensors; direct from patient or clinician, such as an electronic clinical outcome assessment (eCOA); or direct from an EHR or electronic data capture (EDC) system used as an eSource system.[3] It reduces the need for source data verification (SDV), minimizing the need for transcription, and provides real-time guidance on illogical or inconsistent data. It can reduce the volume of automated and manual queries, which has the potential to decrease the workload of data review and circular back and forth reconciliation activities with sites. If implemented correctly, it can reduce the burden on sites and sponsors, boost patient centricity, and improve data quality.[4]

With new International Council for Harmonisation (ICH) Good Clinical Practice (GCP) guidelines recommending that researchers avoid unnecessary transcription of data, the drive to eSource is accelerating.[5]

* Astellas Pharma, US
† Memorial Sloan Kettering Cancer Center, US
‡ Johnson & Johnson Innovative Medicine, US
§ Pfizer, US
‖ Duke Medicine, US
¶ Everest Clinical Research, US
** OpenClinica, US
†† Merck & Co., Inc., Rahway, NJ, US
Corresponding author: Linda S. King (lindasking40@gmail.com)

eSource Implementation Consortium

eSource is an evolving space. While the FDA has published a general framework for its use, highlighting its benefits and the body's commitment to Health Level-7 (HL7®) Fast Healthcare Interoperability Resources (FHIR®) standards,[6] there are currently no standard guidelines regarding implementation.

The 2024 SCDM working group meetings and roundtable aimed to accelerate the adoption and scaling of eSource clinical trial data collection and transfer by building the foundations of a consensus for implementation. The program of work tasked key stakeholders from across the research ecosystem—including biopharmaceutical firms, sites, and technology vendors—with sharing their knowledge and best practice examples, in a bid to provide best practices for the implementation and operation of HL7® FHIR® data transfer. *See Author Contributions section for participants.*

This report summarizes those discussions and best practices in three key areas:

- The feasibility of existing and theoretical eSource approaches
- Contracting considerations by eSource approach
- Technological readiness

eSource approaches

Site readiness is a challenge, in no small part, because eSource is not a single pathway. Over the last five to ten years, there has been an influx of solutions, vendors, technologies, and methods all aimed at reducing or eliminating dual data entry between site EHR and sponsor/clinical research organization (CROs) EDC systems. With such a wide range of different approaches, navigating this new, complex landscape is difficult.

The eSource Implementation Consortium identified seven different eSource approaches, or scenarios, currently being used in industry:

- Site identifies preferred EHR-to-EDC technology
- Sponsor identifies preferred EHR-to-EDC technology
- Clinical research-focused eSource application
- Sponsor and site each use their own technology
- Direct data capture (DDC)
- EHR research module
- Mixed use of technology within same study

Of the seven identified approaches, two will be described in detail with case studies. These were site-provided and sponsor-provided preferred EHR-to-EDC technology, using a mutually agreed upon, system-agnostic technology vendor, and with HL7® FHIR® as the data exchange standard.

Currently, the Consortium are aligned that these two are the most widely used approaches for eSource dataflow using EHR systems meaning they have the richest base of use case examples, and for eSource EHR dataflow approaches are the least challenging to implement. As such, the eSource Implementation Consortium believe they have the greatest potential for scalability.

> *Demonstrating the value of eSource data collection could help to aid scalability by generating excitement. Early adopters, for example, can share examples that encapsulate the benefits, such as greater consistency and efficiency, to highlight the potential gains in productivity and data quality.*

Approach 1: Site identifies the preferred technology

When sites establish technical connections with the EHR-to-EDC technology of their choice, the sponsor's EDC system receives data from multiple site technology systems (see **Figure 1**).

For sites, it means all security and privacy documentation and approvals, system/vendor qualifications, contracts (e.g., site-vendor agreements, Clinical Trial Agreements), and other agreements are done upfront, before study set-up, and assigned study staff are already trained on the system. As the technology vendor already has experience of the site's EHR set-up, there can be some reuse of mapping across sponsors and/or studies. In addition, the

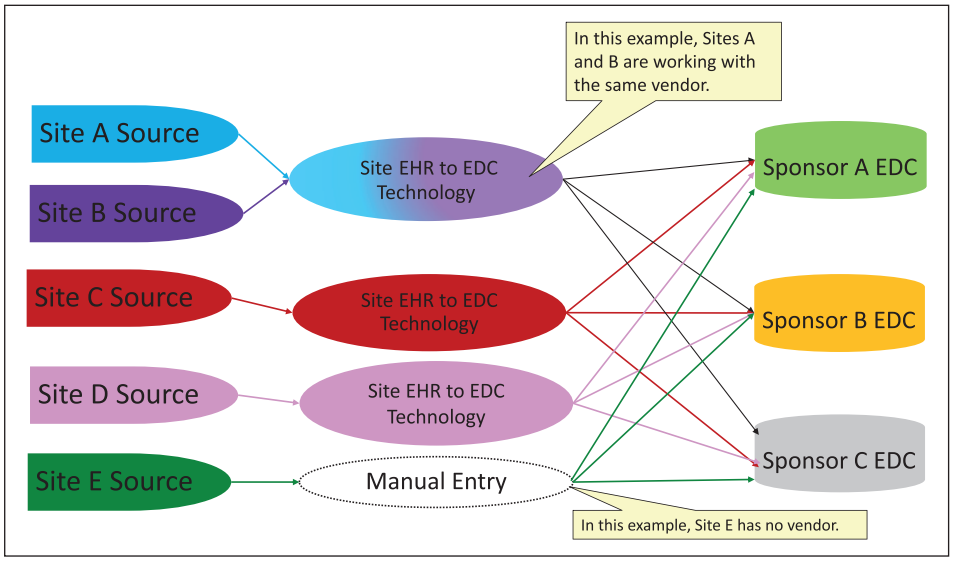

Figure 1: Sites identify their preferred technology eSource approach.

single set-up can enhance efficiency by minimizing the need for on-site IT (Information Technology) expertise and infrastructure. Technology vendors should share appropriate validation reports as required by sponsor and regulators.

Furthermore, once the solution has been established, the site can then expand its use to any or all of its pharma-sponsored studies, as applicable.

Sponsors tend to work with hundreds of sites, and this model means they will need to have relationships and mappings with many vendors. However, not all technologies will integrate well or seamlessly with the sponsor's EDC system, and some sites may not have the resources necessary to maintain their own technology solution.

One proven option is that sponsors look to work with vendors that have relationships with high-volume preferred study sites. The large number of studies, patients and data elements available for exchange at such sites can contribute to economies of scale, thereby accelerating adoption. In addition, it does not put pressure on sites to implement a vendor they may only use once.

Case study: Site-identified technology in action

The Memorial Sloan Kettering (MSK) Cancer Center, USA, has made scaling eSource EHR-to-EDC a top priority. It has been working with a system-agnostic technology vendor to deploy a cloud-based virtual research assistant that provides interoperability between EHR and key research systems, such as EDC. It provides seamless, secure transfer of high volumes of structured clinical trial data. The two started working together in May 2023, with implementation taking place in September 2023, and the first studies going live two months later, in November 2023. As of January 2025, MSK is using this technology with four sponsors and 15 protocols and continues to scale.

MSK analysis of the first five live studies in the fourth quarter of 2023 found the system reduced the time and effort of data entry, based on data point per second, by 49% in commercially sponsored studies, and 68% in investigator-initiated trials. A validation study found the platform increased data entry throughout by 55%, from 10 data points/min with manual entry to 15 data points/min with the vendor technology platform and reduced data entry error by 99%.

The team also carried out a user satisfaction survey. They found all users preferred using the platform over manual data entry. It was easy to learn, easy to use, and resulted in fewer queries from sponsor/site monitors.

Case Study: Site-identified technology in action

Johnson & Johnson Innovative Medicine (J&J) conducted a comprehensive global analysis to identify site preferences for eSource vendors. As part of our commitment to enhancing clinical trial efficiency, J&J undertook an extensive evaluation of eSource solutions focusing on those typically favored by our site partners. Through this exercise and aligning with our internal business requirements, we ensured that the selected vendors met the diverse needs of multiple sites. The initiative included a request for proposals and subsequent pilot programs with several vendors preferred by our site partners. Importantly, our vendor selection criteria include the ability to be agnostic to both Electronic Health Record (EHR) and Electronic Data Capture (EDC) systems, which is vital for operational flexibility and integration. Our requirements were based on The European Institute for Innovation through Health Data (i-HD) vendor selection criteria.[7]

Following the alignment process, J&J decided to proceed with a vendor that garnered preference from multiple sites and was committed to partnering with us to meet our business requirements. In 2023, we initiated our first live study at one site and in 2024 we successfully scaled operations to six sites in two countries—specifically the United States and the United Kingdom. Looking forward, rollover work from 2024 provides a solid foundation to scale operations to an additional 14 sites, bringing the total to 20 sites with 56 integrations across countries in North America, the European Union, and Asia Pacific, as well as the United Kingdom. We plan to continue to pragmatically scale up in line with the maturity of the solution in this still emerging space with a goal that all studies that are using sites that are eSource enabled will source data using this solution.

The strategic expansion of eSource integration at J&J represents our dedication to innovation in clinical trials and our commitment to our critical site partners to reduce the burden of data collection. By leveraging site preferences and fostering a collaborative environment with our sites and vendors, we aim to enhance the quality and efficiency of our research initiatives globally advocating for greater data interoperability to benefit clinical research.

Approach 2: Sponsor identifies preferred technology

In this scenario, sites establish technical connections to each sponsor's preferred technologies via middleware (see **Figure 2**). If a site is working with more than one sponsor, which is often the case, they will have to make multiple connections. Sponsors or their contracted vendors work with sites to establish mappings between site EHR data outputs and the sponsor's standard or study-specific case report forms (CRFs) entered into their EDC system.

All EHR data coming into a sponsor's EDC system will be via a single vendor. This provides simplified, more consistent data flow management—for example, for snapshots or locks—than when working with each site's individual vendor. It also means the sponsor can be confident that the technology will work with their chosen EDC solution. Once the connection has been established with a site, the sponsor can then extend the solution to be used on any or all studies being conducted at that site.

However, this can lead to a longer start-up time for the first study. Each vendor will need to be assessed by the site's security, privacy, and compliance processes before the program can be initiated. In addition, the sponsors technology vendors may not have experience with each site's EHR set-up and security/privacy expectations and protocols.

It can also place additional burden on sites as it requires staff and resources to work with each sponsor and vendor. Site users also need to learn, adopt, and use multiple systems.

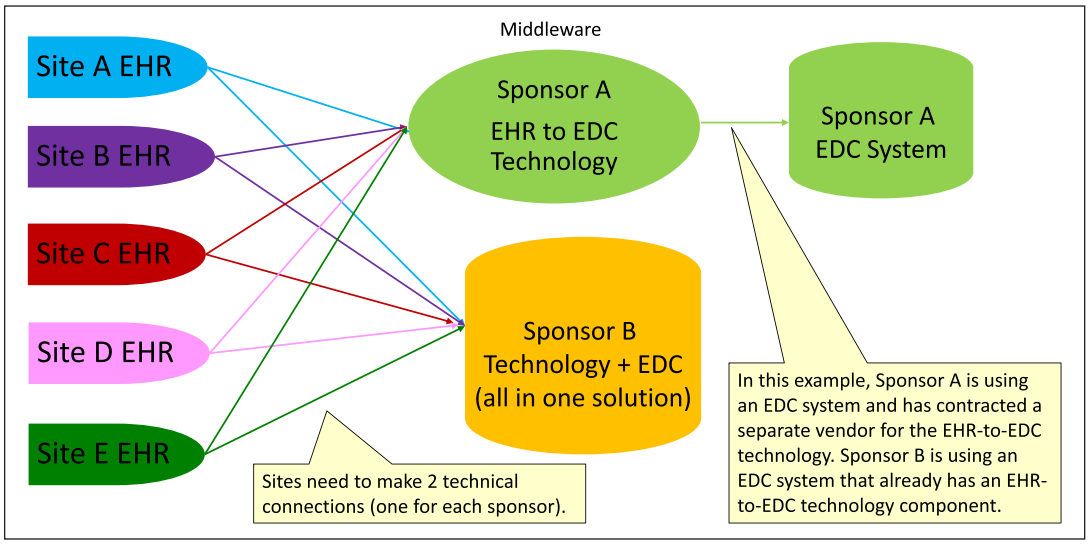

Figure 2: Sponsor identifies preferred technology eSource approach.

Case study: Sponsor-identified technology in action

Since 2018, **Pfizer** has been working with a technology vendor to develop middleware to enable EHR to EDC data transfers.[8] The approach has proven successful from a data flow perspective.

The team started small, first focusing on demographic and vitals data with a small number of sites before moving on to include laboratory data to enable developing the technology solution further.

When scaling up the number of sites, there were several considerations. Firstly, not all sites across a large study were open to electronic data transfer and sites had variations in EHR structures. This led to scalability challenges with initial set-ups on a site-by-site basis taking a significant amount of time. Once a site was configured, however, the data transfer was successful with production data transfers enabled using this solution.

Case study: Sponsor-identified technology in action

Quantum Leap Healthcare used a hybrid model when implementing a vendor technology solution of an EHR-EDC integration framework. Sixteen of 35 sites working on a Phase II platform trial adopted the system, which allows patient health record data to flow directly from site EHR systems into electronic case report forms (eCRFs), while those without integration readiness continued to enter data manually.

After eight of 16 site deployments were activated, the team studied the impacts of EHR to EDC integration and recorded:

- A 16-minute per form saving for elapsed data entry time on the primary daily eCRF – a 61% reduction compared to manual entry;
- For just 52 patients studied at one site with a 15-day treatment course, 208 hours of clinical research coordinator time was saved;
- The elimination of data errors by the automated, validated EHR-loaded data and the downstream costs associated with cleaning and SDV;
- Low implementation costs
- Reusability across sites

Quantum Leap Healthcare has since deployed the integration to three trials, across 24 sites, and continues to scale.

Alternative eSource approaches

The eSource Implementation Consortium outlines the use cases and implementation challenges of the remaining five eSource approaches below.

Clinical research-focused eSource application

This scenario is an option for research-dedicated or non-traditional research sites, such as for-profit multi-site networks, pharmacies, meta sites, and mobile research nursing organizations, that use their own eSource system rather than an EHR system. It utilizes an application specifically designed for capturing source data in clinical trials, which is typically paired with the clinical trials management system (CTMS). Additionally, sponsors may establish this model of eSource as a central eSource system for all of their sites to use (i.e., similarly to how sponsors may provide site payment tools through a third party). All the same considerations, challenges, regulations and requirements for an EHR apply to this approach.

Sponsor and site both use their own preferred technology

In this scenario, sites and sponsors continue to use their own EHR-to-EDC solutions, requiring the technologies to exchange data via two sets of middleware. While this may streamline data upload and retrieval from site EHR systems, the technologies may not be designed to easily communicate with one another unless mitigations, such as FHIR-based application programming interfaces (APIs)/exchanges, are identified. The multiple translation of data between systems introduces opportunities for errors and decreased data quality, while the complexity of multiple system integration places additional burdens on audit trails. In addition, coordinating and overseeing the two vendors may require increased site and sponsor resources.

Direct data capture (DDC)

Direct data capture (DDC) is defined as sites directly entering data into the sponsor's EDC system. DDC can work well where the site does not have an EHR system. No technical connection is needed to facilitate this approach; however, data is not entered into the patient medical record and can have potential patient safety risks. In the evolution of site maturity for eSource, some sites do not capture data electronically and utilize paper, and this method, although not recommended, can be utilized.

If the site has an EHR system, this data may need to be appended or transcribed. This poses data structure challenges as data may not be in machine readable or shareable formats (for example, as PDFs). In addition, transcription is not likely to be in real time. It is vital that sites with EHR systems keep eSource DDC data as PDF copies in patient charts, or upload eSource DDC data, whether as PDFs or via APIs. The EMA's Qualification Opinion highlights this necessity, stating that sites must have contemporaneous access to eSource DDC data.[9]

EHR research module

Here, the EHR vendor creates study-specific modules, such as CRFs, within their platform, and no EDC system is used. It is rarely utilized for a number of reasons. It can be costly to implement in terms of set-up, testing and training, and can blur the line between clinical and research activities, with complexities around aspects such as blinding. The site will need to create study-specific data collection tools that require additional coordination and input from the sponsor, and the approach runs the risk of not collecting all data points necessary for study analysis. In addition, the data will still need to be mapped and transferred to the sponsor's data warehouse.

Mixed use of technology within same study

In this scenario, sites and sponsors will use the technologies they deem to be applicable to the situation. Sponsors allow a limited number of technologies that are validated for integrating with their EDC systems, and sites allow a limited number of technologies that are accepted for integrating with their source system. While this is included as a possible eSource approach, it is not one that is being used in practice.

Strategy-first

The eSource Implementation Consortium agreed that eSource dataflow approaches one (site identities preferred technology) and two (sponsor identifies preferred technology) are the most commonly used and hold the most potential for scalability. All other approaches are based on non-EHR solutions or on combinations of technologies within a study that may make it difficult to scale beyond the single study, and one (the mixed use of technology within same study method) is largely theoretical.

Overall, teams should select technologies and approaches based on the site and sponsor needs, and on clinical protocol design.

The continuation of cross-sector work in this area is vital as we move forward. Leveraging the eSource Implementation Consortium can connect sites and sponsors, enabling them to learn from each other in real time. Furthermore, the SCDM's collaboration with HL7®'s Vulcan, a global community of more than 45 patient, sponsor, site, and technology organizations within the clinical research space, facilitates the sharing of standards and best practice for data transfer. Consortium members, including MSKCC, Duke Office of Clinical Research, IgniteData, OpenClinica, and J&J, for example, are actively participating in the Vulcan Interoperability Bridge Project to facilitate the more efficient exchange of data. This multi-stakeholder approach can help to aid site readiness and facilitate eSource adoption.

Contract readiness

Contracting was identified as a challenge to EHR-to-EDC transfer adoption and scalability, representing a significant bottleneck in moving eSource from theory into practice.

The eSource Implementation Consortium recommend understanding an organization's contracting requirements at the outset. This can ease the journey and shorten the time to study set-up.

Overall:

- most contract groups will need to confirm that all security/compliance requirements have been met;
- most contract groups will require confirmation that the technology needed to support the validated software can be provided, both from a functionality and a resource perspective, and the validation documentation should be available for audit/inspection;
- each contracts office will have boilerplate language related to data, security, privacy and Intellectual Property that the vendor will need to agree to, as well as standard implementation, change management/amendment policies;
- contracts cannot be executed if the required functionality is not present; and
- every implementation of eSource has a cost, and contracts cannot be executed until budget feasibility has been confirmed.

It is also worth noting that navigating regional variations in regulations can take time. While this part of the process does not tend to impact contracts with sites, it does require different procedures and, potentially, different language within vendor contracts.

As execution of the contract is dependent on all the listed components, the timeline is largely driven by their complexity and achievability.

Contract readiness considerations

It is also worth noting that the contracting process will differ according to the selected eSource approach. Each will have its own advantages and disadvantages, for sites and sponsors, and these will need to be factored into the contracting process.

Approach 1: Site identifies preferred EHR to EDC technology.

	Security/Compliance	Technology	Contracting	Functionality	Costs	Timelines
Advantages	· Site can choose a vendor that meets institutional requirements. · Site can carry out comprehensive review for general use. · Site has control over all aspects of the system and vendor in compliance with the ICH GCP.	· Solution should meet all site compliance and security and privacy requirements. · Site can leverage work to implement solutions for multiple studies.	· Site can include contract language amenable to all stakeholders. · Site can leverage existing Clinical Trial Agreement with sponsor ensuring appropriate article in place allowing sponsor to contract with site preferred vendor.	· Sponsors can draw from site experiences with EHR data transfers. · Solution can be selected based on site needs.	· Economies of scale and growing familiarity should lower costs over time. · Opportunity to charge sponsor for study-specific eSource costs.	· Once the solution has been implemented for a sponsor, study set-up timeline should be short.
Disadvantages	· System may not be chosen centrally, and there may be insufficient vetting, requiring rework.	· Vendor may be purchased or go out of business. · Solution may not work with all sponsor EDC systems. · Site/vendor is responsible for maintenance and support.	· Site must negotiate Master Service Agreement contract with vendor. · Sponsor must also negotiate a study-specific contract with the vendor.	· Solution may not meet current or future sponsor needs. · EHRs may not have an e-signature functionality and corresponding audit trail. · It may be harder and costly to change solutions when a need for new functionality arises. · Solution may not work for all studies.	· Sites are responsible for ongoing support and maintenance costs. · Vendor may raise costs during the lifetime of a trial. · Studies may not have the budget to cover the costs of the technology. · An institution may not want to fund all costs.	· With the site and sponsor responsible for contracting considerations, time to implementation can be extended.

Approach 2: Sponsor identifies preferred vendor for the EHR to EDC technology.

	Security/Compliance	Technology	Contracting	Functionality	Costs	Timelines
Advantages	· Sponsor will cover the cost of review and accept liability for data security. · Low liability for site reduces complexity for review. · Sponsor contracts are generally standardized and do not require addition of terms. · Payments to vendors can be streamlined, reducing burden on sites.	· Sponsor-provided technology should have clear requirements. · Licensing or other usage fees will be handled by the sponsor, as applicable. · Low number of EHR variations means a high likelihood of a working solution.	· Sponsor contracts tend to be standardized	· Sponsor should be able to choose a solution that works with site EHRs and delivers the needed data. · Use at multiple sites should ensure good results and deeper knowledge of the system.	· Sponsor covers the cost of software and implementation work.	· When sponsor is responsible for vendor technology it shortens the time needed for sponsor reviews. · No need for a request for proposal. · Once installed, the solution could be leveraged quickly for future studies with the same sponsor.
Disadvantages	· Review/approval is typically for single study use. · Resources for testing and implementation may not be available at site. · If installation of application is needed, site may require penetration test or other artifacts.	· Mappings may not support data needed at every site. · Site may not have the technical knowledge or staff to implement the solution. · Solution may not be supported by site tech stacks.	· Confusion around vendor's relationship to parties, and which parties need agreements with each other.	· System may not provide the functionality the site needs. · Site staff may not be able to effectively utilize the system, which will increase learning time as each sponsor solution could be different. · Implementation may not be able to be leveraged for any other studies due to licensing.	· Investment in a system that may only be used once.	· Agreements between site and vendor may still be required to cover privacy and security aspects, adding to the timeline. · Sponsors may not consider the additional IT, security, and compliance aspects of contracting for eSource, and assume timelines would be similar to traditional approaches.

Technological readiness

The numerous considerations when approaching technological readiness can be grouped into the following categories:

- **Implementation:** Includes installation, testing, validation, performance and re-verification triggers
- **Protocol:** Includes evaluation/feasibility; schedule of activities; change management/amendments
- **Data standards and mapping:** Includes transfer specifications
- **Data cleaning:** Data integrity checks, data reconciliation with different sources, or data consistency within a source. Includes SDV, source data review (SDR), data changes, queries, audit trail review, investigator sign off
- **Compliance and provenance:** Includes ensuring data origin/authenticity

The eSource Implementation Consortium recommends that these categories be considered as early as possible in your planning.

Technological readiness: Best practice recommendations

The eSource Implementation Consortium made a number of technological best practice recommendations, matched to each eSource approach.

> *In 2020, the final rule entitled "21st Century Cures Act: Interoperability, Information Blocking, and the ONC Health IT Certification Program" (85 FR 25642; May 1, 2020) was published by ASTP/ONC, establishing the HL7 FHIR standard as a nationwide standard for access, exchange, and use of data for healthcare delivery organizations.*[10,11]

Approach 1: Site identifies the preferred technology

Technological readiness advantages:

- Sponsor does not require in-house eSource/FHIR® expertise
- Provides scalability to all sites the vendor has connections with
- Faster access to clean data due to decreased monitoring burden and queries
- Increases data transparency by minimizing user intervention

Best practice recommendations:

- Implementation:
  - Site/vendor has standard implementation scripts/procedures that are re-usable for each study, though some parts may need to be customized to the sponsor, study, or EDC system.
  - The EHR-to-EDC vendor and EDC vendor may or may not be the same.
- Protocol:
  - Mapping of EHR data to clinical research domains should be conducted, and study-specific needs identified, prior to engaging sponsors/studies.
- Standards:
  - Where the EHR is not compatible with FHIR®, data transport should be via CDISC ODM-XML. Flat file is also a possibility.
- Data cleaning:
  - Review/cleaning should be conducted in the sponsor system, whether that is EDC or integrated eSource/EDC.
  - Any updates to data based on cleaning, queries, or review should be made in source system and the data re-sync'ed.
- Compliance and provenance:
  - The site should instate a vendor qualification Standard Operating Procedure (SOP).
  - When vendor qualification SOP is in place, the site can rely the on vendor's GCP software validation procedures, testing, and documentation.
  - The site should consider using eClinical Forum eSource Readiness Assessment Tool (eSRA) regulatory criteria.[12]
  - Site-to-data broker sharing of phase I/II data should already be covered by data confidentiality and data use agreements.

Approach 2: Sponsor identifies the preferred technology

Technological readiness advantages:

- Site does not require in-house eSource/FHIR® expertise
- Provides scalability to all sites the vendor has connections with
- Faster access to clean data due to decreased monitoring burden and queries
- Increases data transparency by minimizing user intervention

Best practice recommendations:

- Implementation:
  - Sponsor/vendor has standard implementation scripts/procedures that are re-usable for each site, though some parts may need to be customized to the site or EHR.
  - The EHR-to-EDC vendor and EDC vendor may or may not be the same.
  - Sponsor should consider the site's regulatory readiness for eSource implementation using their EHR systems. The eClinical Forum eSRA criteria can be helpful.[12]
- Protocol:
  - Evaluation of data elements versus likely EHR data should be conducted globally, prior to engaging sites, and then customized on a site-by-site basis. Sponsors should seek to provide as much "off-the-shelf" mapping as possible.
- Standards:
  - HL7® FHIR® standard use is recommended and supported by the FDA.[6]
  - Coded data, such as RxNorm meds or LOINC labs, could be translated into structures aligned to study CRFs.

- Data cleaning:
  - Review/cleaning should be conducted in the sponsor system, whether that is EDC or an integrated eSource/EDC data warehouse.
  - Any updates to data based on cleaning, queries, or review should be made in source system and the data re-sync'ed.
- Compliance and provenance:
  - Implementing the FDA eSource and EHR data guidance enables EHR data to be considered a certified copy of source.
  - The sponsor should validate any transformation that occurs after site sign off.

Sponsors should reassess the EHR system's fitness-for-purpose if software updates are made to it or to the EDC system during the conduct of the trial, to ensure they do not affect the integrity and security of transmitted data.

Sponsor review of the data broker system documentation may be acceptable to confirm data integrity, provided it is sufficiently comprehensive to identify any risks to the data, conduct appropriate risk assessments, and integrate/implement effective risk mitigation strategies.

Conclusions and next steps

Overall, the working groups concluded that approaches one (site identifies the preferred technology) and two (sponsor identifies the preferred technology) are currently operationalized and are the most scalable eSource EHR dataflows. Approach one is the most commonly used of the two. These two approaches are widely used, meaning they have the richest base of use case examples, and, importantly, are the most feasible for implementation. While DDC into EDC is arguably the least challenging to adopt from a technological perspective, the approach although manageable adds complexity elsewhere, particularly around the potential threat to contemporaneous updates to EHR data as applicable.

When the sponsor or site identifies the preferred technology, they do so in partnership with a vendor. These vendors have extensive experience and expertise in areas such as data standards, mapping, and transfer processes—experience and expertise that sites or sponsors may not necessarily have in-house. They will also have access to a wide range of use case examples to help guide best practice implementation. While there is still a question regarding which of the two is preferable, these options, which narrow down the wide range of potential starting points, are an important step in the direction of scalability.

There is also now a consensus, built on the FDA's support, surrounding the use of HL7® FHIR®, and its use as standard for US trials is incontrovertible. However, there are still issues to be fleshed out, particularity in the context of global trials. There is a need for clear regulatory guidelines that consider privacy and security laws across countries. Currently, such documents tend to be FDA-generated and US focused, but trials are often multinational. A global Office of the National Coordinator for Health Information Technology (ONC) Certification could help teams to roll out eSource more widely.

One large area of discussion was a lack of standardized mapping, leading to repeated work and wasted time and effort at every study set up. There are often, for example, hundreds of LOINC codes for glucose measurements, and understanding which should be used for each trial can be time consuming and resource draining. Creating a library of common mappings, with collaboration between sites, vendors, standards organizations and sponsors, could help to overcome this barrier, but regulatory guidance is required. Adverse event domains need particular attention, as definitions, workflows, and data requirements vary across patient monitoring, clinical intervention, FDA safety reporting requirements, and clinical trials monitoring use cases. Fortunately, work is ongoing on this area. The United States Core Data for Interoperability (USCDI+) project, for example, has seen the ASTP/ONC, National Cancer Institute (NCI), and FDA working with EHR vendors to identify a minimum dataset and deploy the HL7® Vulcan Adverse Events (AE) Implementation Guide. Moving forward, a project to acquire more information on AEs, and how sites and EHRs are capturing them, would be useful. The SCDM will continue to support work to improve domain mapping availability.

In addition, the metrics required to measure success are still under discussion, though the roundtable did reveal a general trend toward focusing on site satisfaction.

Teams need to be aware of the complexity of moving unstructured EHR data to EDC systems. There may be a role for innovative solutions, such large language model (LLM) AI technology to extract data from unstructured clinical notes. It is up to the sponsor to decide which technology to use, but to move this approach on, sponsors could conduct pilots and share the learnings with the FDA.

Developing a standard process for archiving EHR data, which is needed to ensure inspection readiness, is the last piece of the puzzle. Organizations cannot, after all, use clinical research data for its intended purpose if they are unable to demonstrate its provenance. Such a process could be based on the historical transition from paper to EDC, which led to eCRF, eCOA, and other third-party data being returned to site in archive packages, and sites being required to keep a certified copy of any eSource data as a document noted in the sponsor Data Management Plan (DMP). The FDA's EHR eSource guidance (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-electronic-health-record-data-clinical-investigations-guidance-industry) includes principles for tracking data originators and data element identifiers in the audit trail to demonstrate data provenance and chain of custody. To build recommendations in this area, the community needs to work with regulatory agencies to understand how they access submitted EHR data.

In conclusion, there are ongoing projects and initiatives aimed at improving data standards and interoperability, and new technologies and approaches to enhance data integration and improve efficiency in clinical research. There is still much work to be done as a hybrid world of traditional data collection and modern eSource dataflows compete today, but the SCDM hopes the best practice recommendations set out in this paper will help the sector to continue to move toward wide-scale eSource adoption.

Competing Interests

Linda S. King – employee of Sponsor company, Astellas Pharma
Michael Buckley – none
Amy Cramer – employee of Sponsor company, J&J Innovative Medicine
Muzafar Mirza – employee of Sponsor company, Pfizer
Cory Ennis- none
Lauren McCabe – previous employee of Sponsor company, Pfizer, current employee of CRO, Everest
Cal Collins – employee and shareholder of OpenClinica LLC
Aruna Vattikola – employee of Sponsor company, Merck &; Co., Inc.

Author Contributions

Working Group Leads: Lauren McCabe, Muzafar Mirza, Cory Ennis, Cal Collins, and Michael Buckley; **Roundtable Leads:** Aruna Vattikola and Michael Buckley.

Working Groups and Roundtable Participants: Ben Baumann, OpenClinica; Amy Cramer, Johnson & Johnson Innovative Medicine; Christopher Dunn, Pfizer; Linda S. King, Astellas Pharma; Joseph Lengfellner, Memorial Sloan Kettering Cancer Center; Dalia Mack, Duke Medicine; Rakesh Maniar, PKR Health and Life Sciences LLC; Catee Mullen, Duke Medicine; Dhwani Patel, Bristol Myers Squibb; Anna Patruno, Memorial Sloan Kettering Cancer Center; Denise Snyder, Duke Office of Clinical Research; Zach Taft, IgniteData; Ira Togo, Duke Medicine; Thanh Tran, Astellas Pharma; Barry Treichel, Advarra; Chris Weiss, OpenClinica; Veronique Wilson, Premier Research.

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