

Let's get to the Source and Streamline it to the End

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ABSTRACT

Esource is simply the use of the original source data as collected, without requiring transcription. Using source data provides many advantages, but also challenges. I will review successful implementations, challenges, TransCelerate, SCDM and CDISC activities and best practices.

INTRODUCTION

We all agree that esource is a great idea with strong benefits, however adoption has been very slow and painful. In my work with the CDISC eSource Stakeholders group, the Trancelerate eSource project, and our customers, I have witness the struggle firsthand.

WHAT IS THE SOURCE?

Clinical Data can come from many different places. The final submission data is a compilation of data from many sources including:

- Patient Health/Medical Records
- Patient assessments and physical exams
- Patient interviews
- Laboratory Data
- EKG Data
- MRI's or other Imaging modalities
- Patient Diary
- Wearables, Sensors and Devices

REGULATORY CONSIDERATIONS

The FDA has made it clear that they encourage and support the use of eSource as seen in the following statement:

"In an effort to streamline and modernize clinical investigations this guidance promotes capturing source data in electronic form, and it is intended to assist in ensuring the reliability, quality, integrity, and traceability of data from electronic source to electronic regulatory submission. " (Guidance for Industry: Electronic Source Data in Clinical Investigations)

Section 6.10 of ICH E6⁹ Good Clinical practice states that *"The sponsor should ensure that it is specified in the protocol or other written agreement that the investigator(s)/institution(s) will permit trial-related monitoring, audits, IRB/IEC review, and regulatory inspection(s) by providing direct access to source data/documents."* There are no statements that paper records must be kept, just that there needs to be direct access to source data/documents.

Sponsors have indicated several other concerns:

- Data privacy,
- Data providence
- Data security

BENEFITS OF ESOURCE

There are many benefits of collecting data from the source:

- Eliminate Data Entry, reducing transcription errors
- Eliminate the need to 'source verify' all data fields
- Closer to 'real-time' data access

DATA COLLECTION CHALLENGES

Today we collect clinical research source data in a variety of ways based on the type of data being collected. Some data collection such as the collection of centralized laboratory data are straightforward and done in a uniform way for all trials. Clinical trials are run in a variety of settings, and the data collection tends to be related to the process these unique settings have used historically to collect data. The most typical settings are listed below with their typical data collection methodology and suggestions for collecting this data electronically.

HOSPITALS:

- Patient data is stored in the Hospital Electronic Health/Medical Record (EHR/EMR). Any additional data required for the clinical trial is typically collected on paper, but could be collected directly in the Electronic Data Capture (EDC) system.

SOLUTION: The struggle with collecting data from EHR systems is not necessarily a technical one, the technology exists and has been demonstrated at industry events such as the CDISC Intrachange and PhUSE Connectathon events. The challenge is mostly one of obtaining permissions to access the healthcare data from the healthcare provider. An additional challenge is that each site may use a different EHR provider, so the sponsor would need to obtain a methodology and technology solution to collect data from multiple facilities using multiple EHRs. This solution is the most challenging and requires up-front planning, testing and validation for each site being used in the clinical trial. The challenges in this solution typically are not able to be overcome for a single study.

MULTIPLE RESEARCH CLINICS:

- Some research sites collect all patient data on paper source. As an example, a site may have ten patients involved in several different trials and need to collect data for all ten quickly. It makes sense to have the same collection mechanism for all ten, even though they are in different trials. For all ten patients, they will collect vital signs the same way, on the same form. This allows them to minimize the time the patient is required to be in the clinic. This is a 'patient centric' approach. Having to login to a different EDC for each patient and navigate to different screens in each to enter vital signs would significantly slow down the process.

SOLUTION: There are eSource software solutions that the site can deploy that duplicate this paper binder process. The data collected in this type of eSource software can be integrated into various EDC systems. This requires a mapping exercise for each EDC vendor, then a specific mapping and QC for each study. This mapping is typically done once per eSource/EDC vendor, then adapted for each unique study if needed.

SINGLE RESEARCH CLINIC OR ACADEMIA:

- A single clinic or an academic site is ideal for direct esource data collection. Some sponsors have dedicated clinics that run research studies on their products. This is ideal because it allows the sponsor to provide the method of collecting source to the research clinic. In fact, this data can be 100% in the EDC system. Examples of real-life implementations have shown this solution to be successful. This direct entry process works best when reusing standard forms to collect all data. This method allows the site to be comfortable with the collection forms, since they are standard

and re-used. This method also allows for a very fast study build time in the EDC system, since there is so much re-use.

SOLUTION: The challenge in this solution is to work with the sponsor and site to adapt the site processes to make entering data directly into the EDC as efficient as entering into their paper source. This requires training and dedication by the site. Sites may need to revise and update their SOPs to include this direct entry practice.

ESOURCE DATA COLLECTION IMPLEMENTATION EXAMPLES

Today we collect this source data in a variety of ways. Below is a figure showing the typical type of data collection where the site is entering data directly into an EDC system and acquiring data from an EHR:

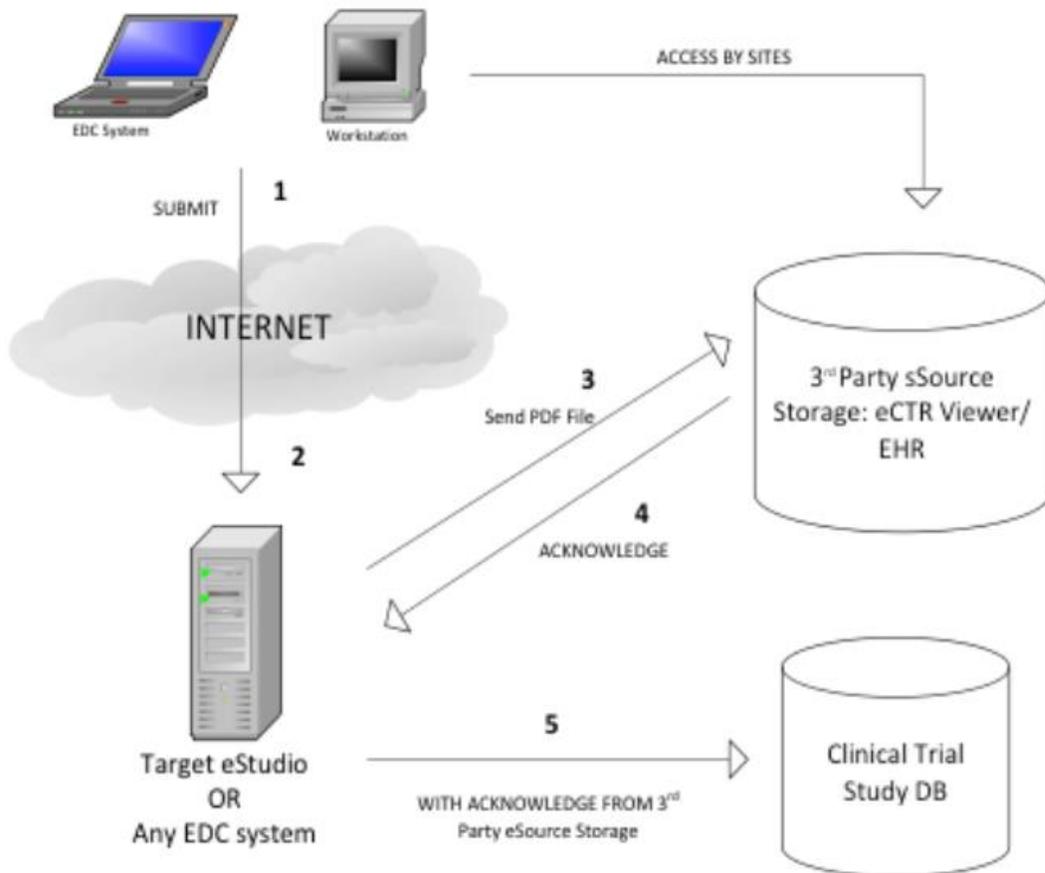


Figure 1 (Jules T. Mitchel, 2015) eSource Data Flow

The successful use of 100% eSource collection requires up-front planning before the first patient is screened. Ideally, this would happen when sites are being selected. Some of the methods require training of the sites and providing electronic data transfer practices. In some cases, simple re-training and help with SOP creation can provide the advantages of using an eSource methodology, and in some cases, the technology solutions required may not be feasible due to refusal of cooperation or access by a site IT infrastructure.

Below is a list of different data types showing how this source data may be collected electronically:

Domain/Datapoint/Field	Collection Method	Electronic Source
LB Laboratory Panel	Blood is collected from the patient and sent to a central laboratory for analysis.	Central lab data vendor
DM Demography Data MH Medical History Data SU Substance Use IE Inclusion / Exclusion Criteria	This data may be collected as a patient is screened or may already exist in the site electronic record.	EDC, eSource app or EHR
FINDINGS Patient Reported Outcome (PRO) or Diary Data	In many studies, safety and efficacy data is collected directly from the patient by using questionnaires or scales. This patient diary can be provided in many forms such as paper, a device provided by the sponsor or an app. This data can also be entered using a website.	PRO vendor
AE Adverse Events CM Concomitant Medications	The data collected for adverse events and concomitant medications is typically obtained verbally from the patient. This data can be collected over a length of time.	EDC, eSource app or EHR
CO Comments	The collection of comments in the CRF is discouraged. Any relevant clinical data that may be contained in a comment should be provided in the domain for which it is intended. The collection of comments on CRF pages originated with the paper based collection process and is not considered best practice today.	NA
DS Disposition DA Drug Accountability	The dispensation and accountability of study drug is typically collected in an Randomization and Trial Supply Tracking system (RTSM) if such a system is used for Randomization and dispensation. If an RTSM system is not used, this data can be entered directly into the EDC system using specially designed collection pages.	EDC, eSource app or RTSM
EG ECG Test Results	The collection of ECG/EKG data is typically done electronically by the collection device.	ECG vendor
EX Exposure	The collection of exposure data typically depends on the type of clinical product. Some products are dispensed and consumed by the patient directly at the study site and is therefore documented directly in the EDC system. If the clinical product is provided to the patient to be used outside the study site, the site typically provides a method to collect the date/time and any other relevant information required as proof of exposure.	EDC, eSource app or PRO
PE Physical Examination	The collection of physical exam data typically isn't required in a clinical study. Any findings from this	NA

Domain/Datapoint/Field	Collection Method	Electronic Source
	type of data are provided in other domains such as medical history or adverse events.	
PV Protocol Deviations	The collection of protocol deviations are typically collected by clinical research associates and documented electronically in a system (Clinical Trial Management System (CTMS)) provided by the sponsor. Some protocol deviations can be derived from the clinical data. Examples are visits occurring outside the study window or medications taken before the allowable period as defined by the protocol.	NA
SC Subject Characteristics	Subject Characteristics can be entered directly into the EDC system. Some Subject Characteristics may be found in the EHR data and mapped.	EDC, eSource app or EHR
VS Vital Signs	Vital sign data is obtained by the site and can be entered directly into the system provided. This is typically a eSource or EDC system, but can also be from a collection device.	EDC, eSource app or EHR

IMPLEMENTATION

The implementation steps below require an overall implementation plan for each site, and a supplemental plan for each study being deployed. The idea is that most of the data collected and transferred to the EDC system can be identified, mapped and tested initially. Each study would require identifying any unique data types within the study. If anything may be reused, it should be amended to the overall implementation plan. Prior to every new study, all data being transferred should be identified and a study plan should point to the documentation that shows how this data mapping is documented and tested.

1. For each site, determine the process that the site currently uses for collecting patient data. This should be documented in an overall implementation plan.
2. Determine if each site is willing to implement an eSource methodology. Outline and document the steps that may be needed for each site since they may be unique. Keep in mind that this process may involve utilization and coordination of resources from their IT department.
3. Assure that key variables such as site ID, subject ID, visit identifiers are present and consistent within all systems used. This may require a work instruction identifying a consistent structure for all key variables.
4. Put a plan in place with the site to map the data to the EDC system. This may involve coordinating multiple vendors and may incur initial costs. There should be a reusable work instruction identifying all steps required for the mapping process.
5. Test the solution by entering several test subjects with various information. This should involve a formal test plan and findings.
6. Once successful, determine a plan that determines the unique characteristics of each study, identifying the different data types and referring back to the eSource implementation plan and adding a plan for any data that may be unique to the given study.

CONCLUSION

Collecting data electronically undeniably provides the most streamlined data collection approach. The benefits of eliminating transcription from paper are widely acknowledged. The challenge with collecting data electronically lies within the processes used by the sponsor, sites and vendors and requires all the parties to commit to a data collection plan that incorporates these eSource best practices.

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