

eSource Arising: Clinical Data Automation Possibilities Beyond Data Capture

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ABSTRACT

When implementing the 1st generation of eSource system at SGS, the focus was on facilitating data capture and converting clinical data directly to a Study Data Tabulation Model (SDTM), making eCRF redundant. After getting familiar with eSource, we are now ready to use our knowledge and expertise and take eSource clinical automation to the next level with the 2nd generation of eSource system.

This paper will highlight our acquired insights and the challenges faced from both systems, resulting in improved efficiencies. The focus on standardized data and the use of code lists to convert easily to SDTM are key for efficiencies. With a proper test environment set up in the 2nd eSource system, it is now possible for data management to enter dummy data, making it easier to set up SDTM conversion. Data visualization and accessibility have improved significantly, and the new query management seems to allow for shorter data cleaning-timelines.

In order to keep improving, we are already thinking of other functionalities that could be explored in the 2nd eSource system. Future plans such as coding and handling of blinded data are being considered.

INTRODUCTION

In 2012, the SGS Clinical Pharmacology Unit (CPU) specialized in Phase I trials started using an automated software system to capture source data electronically, allowing for easy access to clinical real-time data as one of the main advantages.

When implementing the 1st generation of the eSource system at SGS, the focus was mainly on facilitating data capture and converting clinical data directly to the SDTM making eCRF redundant. Over the years, the 1st eSource system of our CPU in Antwerp has proven highly efficient for several user groups. However, as clinical trials are getting more complex and require the handling of more data, we are now ready to take eSource clinical automation to the next level.

Our experience and knowledge gained with the 1st eSource system helped us with the design of the new eSource user requirements and challenged us to further enhance its capabilities and functionalities.



ESOURCE IN CLINICAL TRIALS AND THE ADVANTAGE OF A GOOD COLLABORATION BETWEEN THE SITE AND DATA MANAGEMENT

An eSource system is far more than a digital replacement for paper sources. With an appropriate eSource solution in place, electronically captured data can be shared in real-time from the capture device to the eSource database, and transferred subsequently into the clinical SDTM database, dissolving the boundary between source and CRF. However, eSource systems must be seen as part of a larger entity that integrates data capture, site automation, sample management, data flow facilitation, data visualization and data management.

SGS’ cross functional teams designed the new user requirements of the 2nd eSource system starting from the familiar functionalities of the 1st eSource system. In Figure 1, an overview of the benefits of the 1st generation of eSource system are listed. One of the first and best known benefits for the site when working with data management (DM), was the possibility to eliminate the (e)CRF and diminish manual data entry. Error rates were highly reduced due to the integration of devices, as data entry errors were avoided at source-level. By using a setup library, forms could be created and made reusable for other trials making it easier to set up a trial. Lab data were directly uploaded from the local lab in the eSource and did not have to be entered manually. The interface with the ECG and vital signs devices allowed data to be uploaded immediately and even the evaluation and assessment of test results could be performed within the system.

An important feature of using an eSource system at the site is the barcode driven sample management which reduces data capture errors. In eSource barcodes are used to scan subjects, sampling tubes, assessments and administration drugs. It is not possible to save data when the barcode of the sample or drug does not match with the subject and/or action to be performed. Even more beneficial for the barcode driven sample management in particular, is that it allows for a sample tracking and visualization of the sample path that would not be available without eSource.

It was not just the site that benefitted from the 1st generation of eSource; remote data monitoring of real-time data and copying of existing annotations and mappings of the SDTM conversion over trials also facilitated the work of (medical) monitors and data management.

BENEFITS 1ST GENERATION ESOURCE SYSTEM
Eliminates data entry in (e)CRF
Easy access to real-time data
Setup library: forms can be re-used
Reduces error rate
Reduces missing fields
Automated (barcode driven) sample management
Data from devices are captured immediately
Lab data are uploaded into eSource
Remote date monitoring
Re-use of SDTM annotations and data conversions

Figure 1 - Benefits 1st generation eSource system

With all these advantages already in place, one might wonder what made SGS investigate the use of another eSource system. The main reason was because our first eSource system was reaching end-of-support.

As all site personnel, monitors and data managers were already familiar with eSource, the challenge was no longer to get everyone on board, but to encourage them to think of how eSource could be improved to match the growing complexity of trials; how eSource could facilitate the workflow even more and how data entry errors could be reduced even further. The defined limitations and difficulties encountered when working with the 1st eSource system, motivated the search for a system that could provide solutions for these difficulties. As different groups relied on the eSource system for a variety of tasks, all user requirements needed to be considered (Figure 2).

SITE	DATA MANAGEMENT	CRAs	MEDICAL MONITOR (DRUG SAFETY PHYSICIANS)	CLIENT
Subject recruitment	View real-time data	View real-time data	View real-time data	View real-time data
Trial setup	Data cleaning: querying capabilities	Source verification	Medical monitoring	View real-time data
Data collection	Converting data to SDTM	Querying capabilities	Querying capabilities	Data accessibility by dashboards
Sample management	Possibility to create dummy data to set up conversion	Site management		
Data assessment				

Figure 2 – A general overview of the use of eSource by different groups

TRIAL SET-UP

The study specific setup of the eSource is carried out by dedicated CPU staff. During the setup of a trial, the set-up CRF (sCRF) is extracted from the eSource system and reflects the available forms and time and event schedule of the study containing all data that should be captured in the SDTM database. Several reviews are held to have the sCRF reviewed by DM, the client and other possible user groups until no further updates are needed and the setup can be finalized together with the sCRF.

For the 1st eSource system, SGS decided to use an external software solution program to create the sCRF. Separate templates were needed to generate the blank sCRF used for SDTM annotations and the completed subject CRF containing subject data. This implied that should updates to the eSource database be needed, the entire process to generate the blank sCRF and the subject CRF would need to be performed twice and outside the eSource system. This is no longer the case with the 2nd generation of eSource system. Both the sCRF and completed subject CRF can easily be extracted directly from the system itself. When the setup of a trial is updated, both sCRF and subject CRF will automatically reflect the same updates.

From DM perspective, reviewing the sCRF has become easier with the 2nd eSource system because the available information from the setup is now printed on the sCRF. This means reviewers have a better understanding of the setup of the study eSource database, which results in more constructive feedback. Errors or inefficiencies are now detected and adjusted during the setup phase, resulting in fewer problems during the trial when it is difficult to update the setup of the eSource study database.

The increased design possibilities from the new eSource system allowed the site to reevaluate all the assessment forms and how they should, or could, be completed. Coding lists were added to simplify and standardize the completion of the events, resulting in fewer data entry errors. The coding lists from the 2nd eSource system allow for the forms to be completed in the local language while being captured in English at the same time. The forms created for data collection by the investigators have been made more user-friendly in order to save time and to allow investigators to focus more on subject safety rather than data collection.

CONVERSION TO SDTM WITH THE NEW ESOURCE SYSTEM

As efficient as it is for the site to extract the sCRF directly from the 2nd eSource system, more advantages are seen by DM who use XPT-files exported from the eSource system for conversion to SDTM datasets (see Figure 3 for the full eSource dataflow). Extra information on the setup of the eSource printed on the set-up CRF allows DM to give comments on e.g. the field data types (text field, numeric field, ...), the name of the variables, the domain to which the variables are exported in the XPT-files, the specified ranges, the variables that will be printed on the set-up CRF (and included in the SDTM datasets). By enabling DM to check this information at such an early stage, future queries may be avoided at this point.

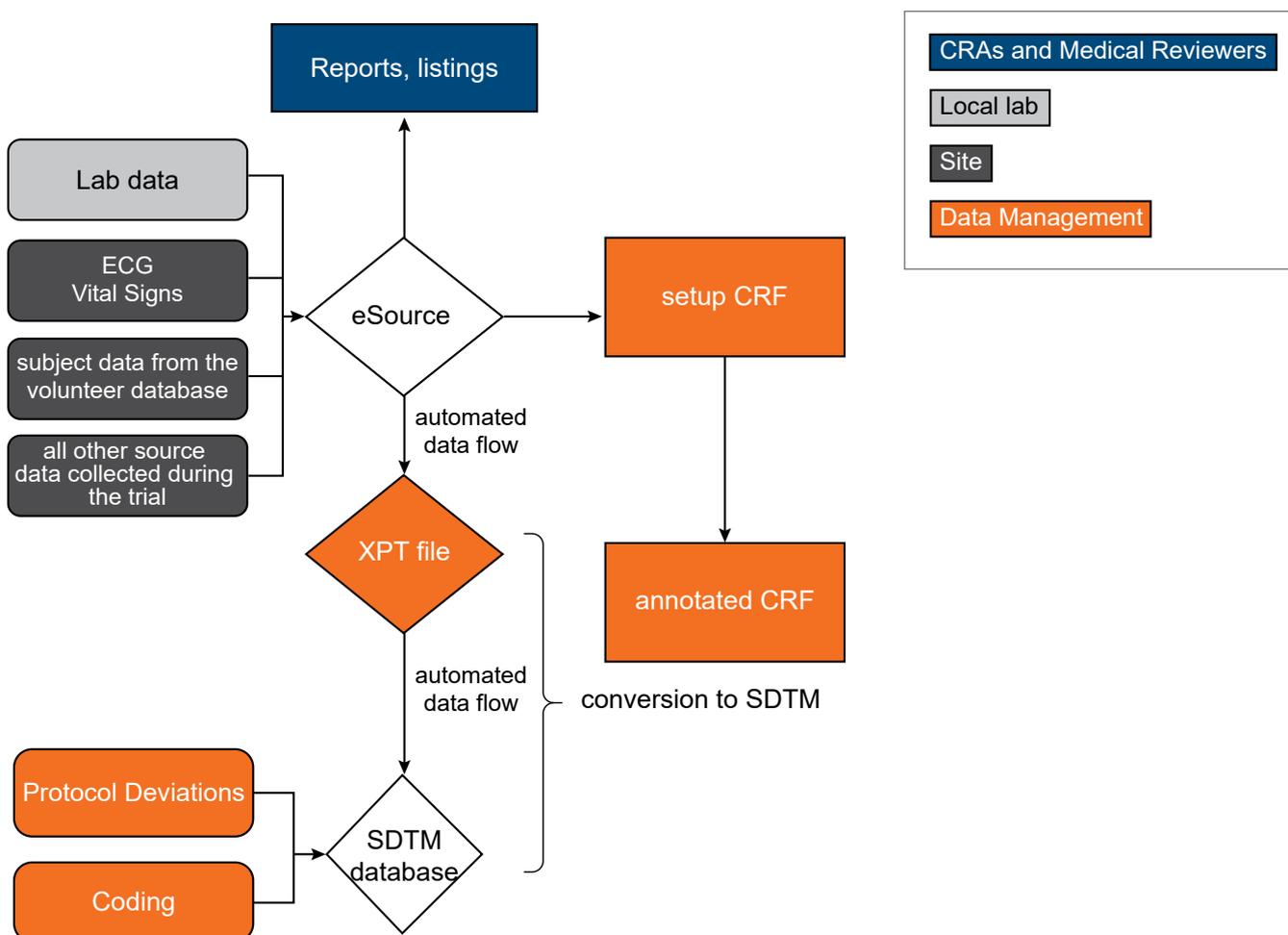


Figure 3 - eSource dataflow diagram

In the new eSource system, two environments are used: the test and the main environment. The trial is created in the main environment. After finalization of the sCRF and the set-up, it is pushed to the test environment. The main environment will be used to collect the actual live data. Within the test environment, it is possible for DM to enter their own dummy data, contributing to the setup of the SDTM conversion and making it easier to add additional dummy data when protocol amendments require updates in the SDTM conversion. From the moment the setup and corresponding sCRF are finalized, DM can start entering the dummy data while simultaneously CPU can enter data to test the trial specific eSource system requirements. This saves time at both ends and reduces the dependency on one another.

BLOOD FOR LAB SAFETY (screening) Origin: CRF

LB_STATUS Origin: CRF; Repeating: No; Domain: LB

LB_STATUS	<input type="radio"/> NOT DONE <input type="radio"/> COMPLETED	LBSTAT Format: S Data Type: string Origin: CRF
LB_REASON NOT DONE	[_____]	LBREASNO Format: \$200 Data Type: text Origin: CRF Conditionally Visible

LB_BLOOD FOR LAB SAFETY (screening) Origin: CRF; Repeating: No; Conditionally Visible; Domain: LB

LB_FASTING	<input type="radio"/> Y <input type="radio"/> N	LBFAST Format: S Data Type: string Origin: CRF
LB_SAFETY BLOOD SAMPLE DATE/TIME (screening)	[][][][] - [][] - [][][][] : [][] : [][] yyyy-MM-dd HH:mm:ss	LBDTG Format: yyyy-MM-ddTHH:mm:ss Data Type: datetime Origin: CRF Lab Panel: Blood (screening) Requires Barcode Verification

Figure 4 - Form Blood for lab safety (screening) from the sample CRF extracted from the eSource system

As Figure 4 illustrates, the variables to which the values will be exported in XPT are named closely to SDTM-terminology, which facilitates the mapping of the variables to SDTM. The variables are named by SGS, by the eSource study designers at CPU who work closely with DM to get the naming as much aligned to SDTM-terminology as possible.

Reports
Results

Clinical Data

Generate reports encapsulating clinical data. If no fields are chosen, all will be included.

Subject(s)	<input type="text" value="x 1001 / L001 / S001"/>
Study Event(s)	<input type="text" value="x AE/CM"/>
Form(s)	<input type="text"/>
Data Status	<input style="border: 1px solid #ccc;" type="text" value="All"/>
	narrow to item groups with status:
Show Item Name?	<input style="border: 1px solid #ccc;" type="text" value="Name"/>
	Display item name or item prompt.
Output Type	<input style="border: 1px solid #ccc;" type="text" value="Excel"/>

Generate ↕

Figure 5 – Example to run a report on all available data in the 2nd eSource system

ACCESS TO REAL-TIME DATA

Where data were extracted from the first eSource system by using an external software solution, the new eSource system provides the opportunity to extract reports directly from the system. Not only set-up CRFs and completed subject CRFs as mentioned above can be exported separately, but also lab reports, query reports and reports from all different executed events. This can be useful for DM, (medical) monitors, the investigator and the client. Since (medical) monitors can extract these reports themselves, they will always have all real-time data present in the reports up to the moment the reports are created (Figure 5). The study data are now more accessible and easier to consult.



Figure 6 - The dashboard of the 2nd eSource system

The dashboard, the eSource homepage for each trial, visualizes all relevant study information on one screen (Figure 6). Furthermore, the dashboard and the ability to run ad hoc customized reports (Figure 7) gives other user groups such as medical monitors and clients a clear indication on the progress of the trial at any given time.

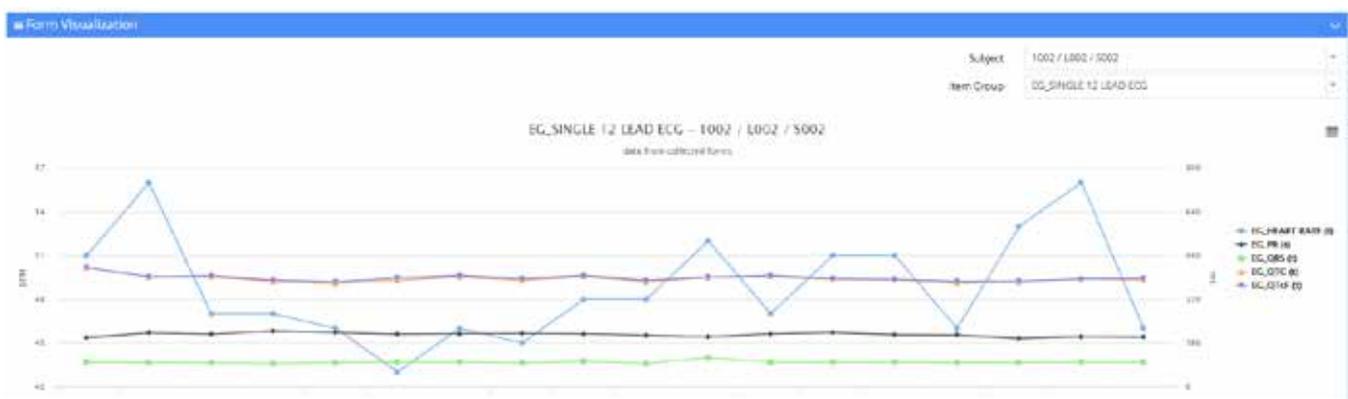


Figure 7 – Example of a dashboard for trends visualization in the 2nd eSource system

QUERY MANAGEMENT

In the 1st eSource system, performance was slow and query management was not user-friendly because of the different views for query creators (data managers, monitors) and query resolvers (site). A form’s data fields could not be left blank – a comment was required, and no conditional form or field completion was foreseen. In the 2nd eSource system, the option to conditionally complete forms or fields implies that only certain fields will be visible and will only need to be completed depending on the outcome of a previous field. For example, when the question ‘Is the adverse event serious?’ is answered ‘Yes’, all the questions related to a serious adverse event will appear. If the question was answered ‘No’, then the questions will not pop up, they will not have to be completed and it will not seem as if there are ‘empty’ fields in the eSource transfer. For the 1st eSource system these ‘empty’ fields led to a high number of queries and reissues for both site and DM.

The development of a Global Rulings Document (GRD) was required at the start of the DM activities and described all evident corrections and global rules that were applied to the clinical database. The GRD, which allowed DM to make the necessary structural updates to the clinical database of the trial without issuing queries, was a very elaborate document with many system specific properties and characteristics that needed to be translated to the SDTM structure. For the 2nd eSource system, the GRD still exists, but it has been reduced.

Compared to the 1st eSource system, all users are now able to see queries using the same view. With the previous eSource system, a separate module was used to create queries, making it very difficult for data managers and site users to track and understand the precise issue the query was referring to. This hurdle is no longer the case in the 2nd eSource system; a question-mark icon now illustrates the fields that require attention. By using a filter, users can select only the relevant queries that still need to be addressed. Using the same views has certainly improved query resolution timelines.

Since the 2nd eSource system has become more user friendly, the medical monitor may be more eager to request access to the eSource system. The drug safety physician can perform a medical review by viewing real-time data in the eSource system and by extracting the desired data via listings from the system, without the interference from DM. Therefore, medical monitoring can be performed simultaneously with the DM cleaning and CRA monitoring. This workflow offers the possibility that study data may be cleaned in a shorter timeframe.

THE IMPORTANCE OF ROLES, RIGHTS AND RESTRICTIONS

Performing clinical trials in an era when the General Data Protection Regulation (GDPR) determines how personal data may be collected and processed, requires a thorough and well considered management of roles to access, complete and consult eSource database. The system contains action roles. With these action roles a role is build. A role is assigned to each staff member. CPU maintains a document with the role actions assigned to a role. These role actions can differ in the test and main environments. This ensures that data managers can complete dummy data in the test environment, without there being any risk for personal subject data to be exposed; these data are only present in the main environment. Collection role restrictions can be assigned at form and even field-level.

SUGGESTIONS FOR FUTURE IMPROVEMENTS

At DM, after the successful completion of the first trial using the 2nd eSource system, we can already see some improvements compared to the 1st eSource system, as listed in figure 8.

The first trial was a good opportunity to get familiar with the 2nd eSource system, but also a starting point to question what other possibilities the system may hold.

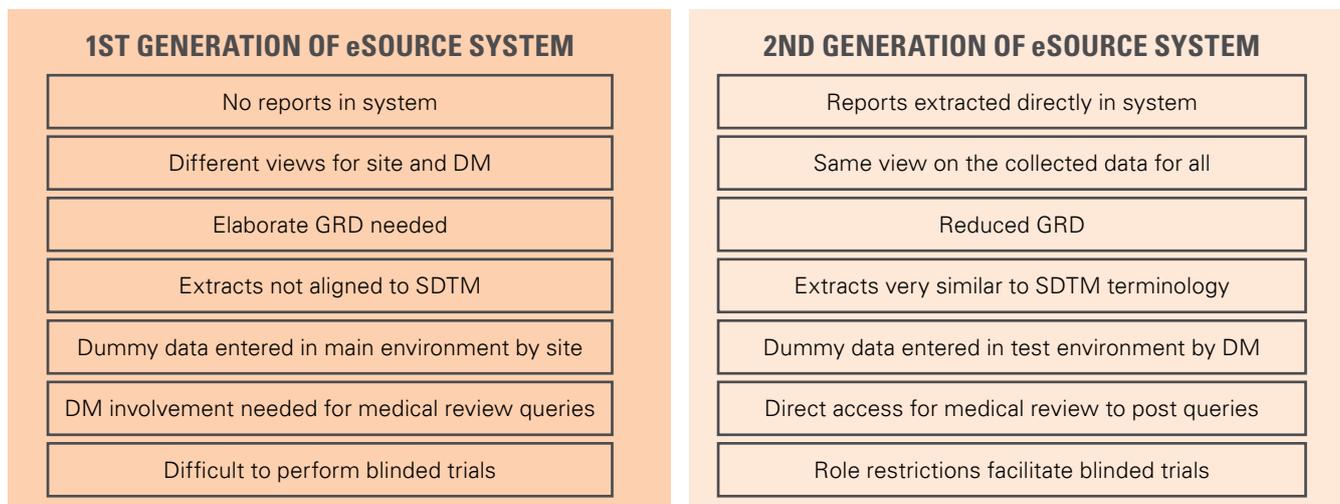


Figure 8 - Improvements compared to the 1st eSource system

In the meantime, the site has explored the recruiting options in the 2nd eSource system and is using the feature to batch SMS and e-mail directly from within the system to reach large groups of people.

Although the 2nd eSource system has already made the GRD less elaborate, it has still not become redundant. The global rulings that are still in place are mostly limited to one domain: lab data. Since these data are provided by a local lab which works independently of SGS, it will be a challenge to completely disengage from the GRD.

By defining and using the right action roles, clients should be able to get access to blinded trials. The blinded data from the drug exposure-form could be blinded for all user roles except for the unblinded staff who will collect the data, but this feature must be tested upfront.

A coding module is present in the new eSource system, but it is not yet being used by SGS. In time, when the new eSource system is completely up and running, it may be interesting to focus on using this coding module. If coding could already be performed at source level, then both review and correction can be performed prior to converting the data to the SDTM database.

Another interesting feature to explore is capturing subject data such as questionnaires and diaries electronically. Currently, this patient data is captured on paper and entered manually into the eSource system. Perhaps the integration of an electronic patient reporting outcome (ePRO) system with the eSource system is feasible, or a questionnaire module in the eSource system that is accessible for subjects to complete their data directly in this module?

CONCLUSION

The efficiencies implemented in the 2nd eSource system have shown benefits for all eSource users. The first case study with the new generation of eSource system started in September 2019 and had the eSource and SDTM database locked at the beginning of February 2020. SGS will continue to explore and test the boundaries of the 2nd generation of eSource system, while finetuning it for upcoming trials.

As more trials are set up in this new eSource system, there will be more reusable forms ensuring more standard data. With all improvements already in place, we are confident that this 2nd eSource system will allow us to save time in the setup of the trial, the conversion to SDTM and during data cleaning. Still we see some challenges ahead if we want to keep growing our efficiencies; such as making the GRD completely redundant, exploring the option to perform coding in eSource by developing the coding module and thinking of paper-free data collection by subjects.

CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the author at:



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