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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 SDTM, making eCRF redundant. After getting familiar with eSource, we are now ready to use our gained 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 challenges faced from both systems resulting in improved efficiencies. 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, handling of blinded data and subject recruitment form within the eSource system 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 eSource system at SGS, the focus was mainly on facilitating data capture and converting clinical data directly to SDTM making eCRF redundant. Over the years, the 1st eSource system of our CPU in Antwerp has been 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 the 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 enhance the eSource capabilities and functionalities even more.

ESOURCE IN CLINICAL TRIALS

An eSource system is far more than a digital replacement for paper source. 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.

The 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 main known benefits for the site was the possibility to eliminate the (e)CRF and diminish manual data entry. The error rate was highly reduced due to the integration with devices, as

data entry errors were avoided already at source-level. By using a setup library, forms could be created and made reusable for other trials making it easier to set up the 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 to reduce the data capturing errors. Barcodes are used to scan subjects, sampling tubes 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. Not only the site was benefiting 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.

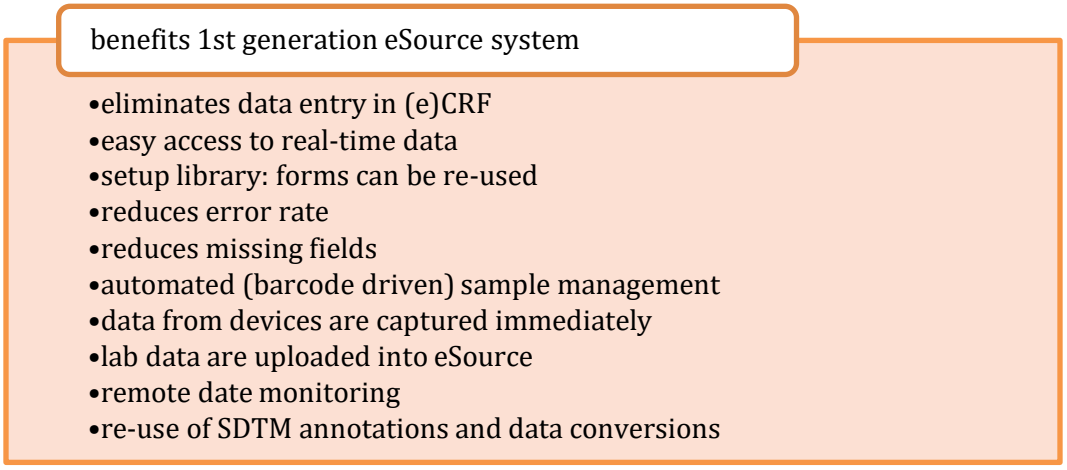

Figure 1 - benefits 1st generation eSource system

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.

Given the fact that all site personnel, monitors and data managers were already familiar with eSource, the challenge was no longer to get everyone on board, but to make them think of how eSource could be improved to meet up with the growing complexity of trials. Defining the limitations and difficulties encountered when working with the 1st eSource system resulted in discovering new possibilities. As different groups were depending on the eSource system for various tasks, all user requirements had to be considered (Figure 2).

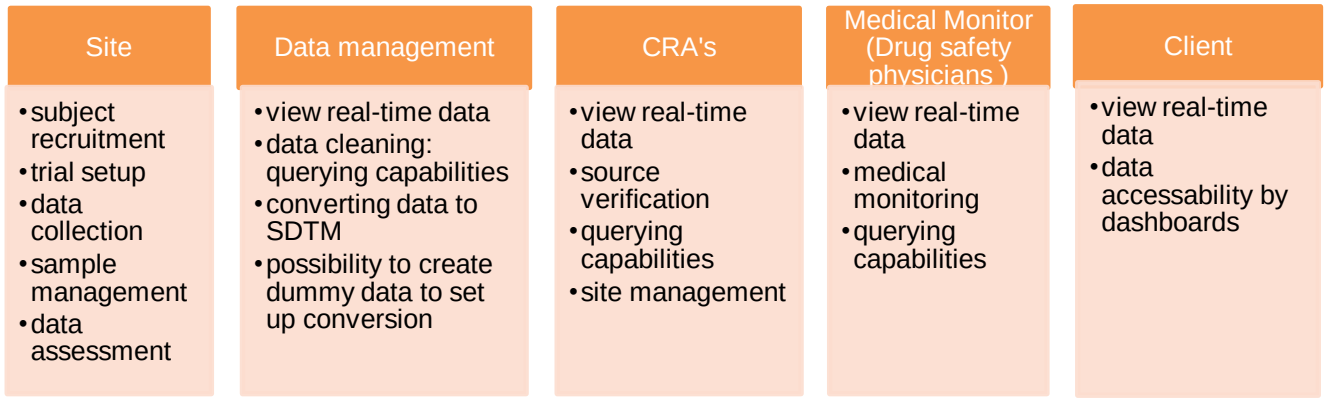

Figure 2 - Use of eSource by different groups

TRIAL SET-UP

The setup of an eSource study database is done 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 review rounds are held to have the sCRF reviewed by data management (DM), the client and other possible user groups.

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 in case updates to the eSource database were needed, the entire process to generate the blank sCRF and the subject CRF had to be performed twice and outside the eSource system. This is no longer the case with the 2nd generation of eSource system. Both 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 available information from the setup is now printed on the sCRF. The reviewers have a better understanding of the setup of the study eSource database resulting in more constructive feedback. More errors or inefficiencies are now detected and adjusted during the setup phase, causing less problems during the trial when it is difficult to update the setup of the eSource study database.

The need to build forms from scratch for 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 less data entry errors. The forms created for data collection by the investigators have been made more user-friendly in order to save time and allowing the 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, even more advantages are seen by DM who uses XPT-files exported from the eSource system as source 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.

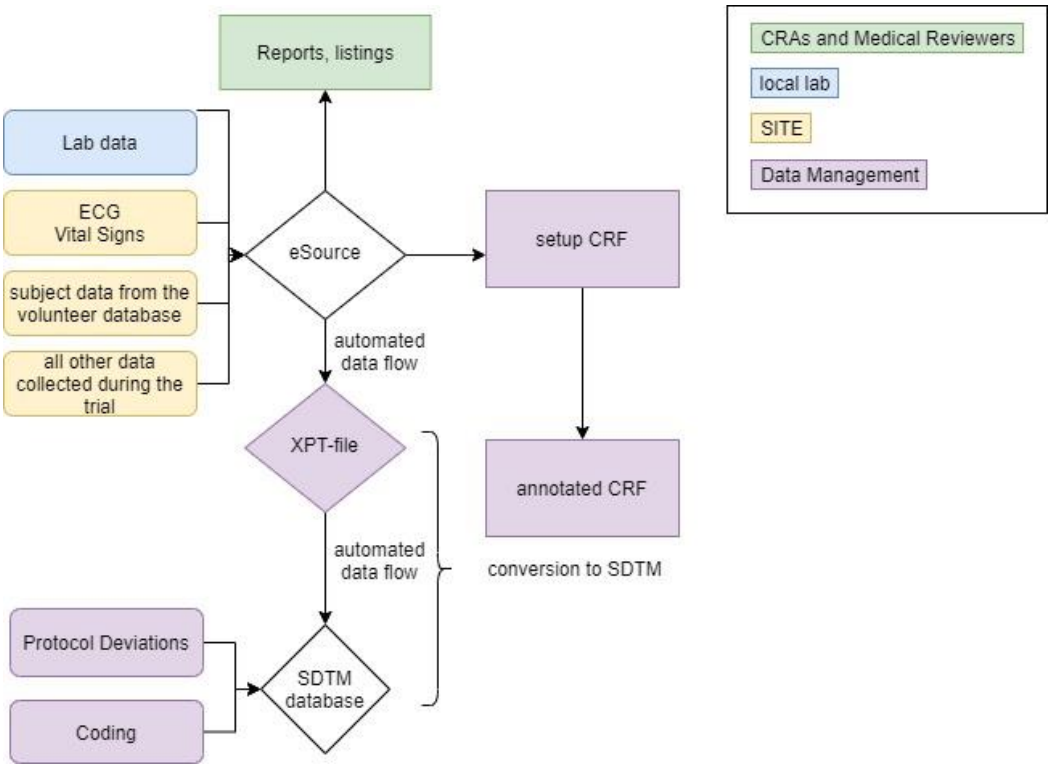

Figure 3 - eSource dataflow diagram

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.

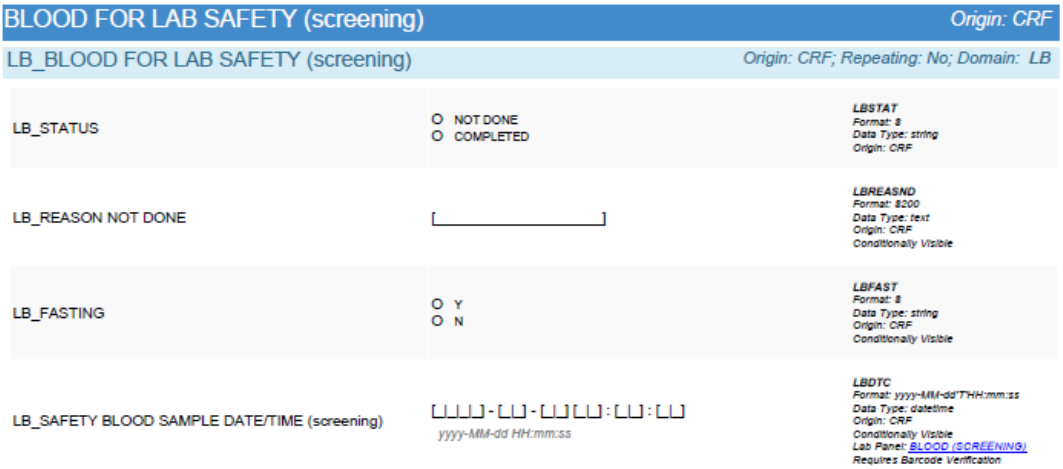

Figure 4 - Form 'Blood for lab safety (screening) from the sample CRF extracted from the eSource system

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.

ACCESS TO REAL-TIME DATA

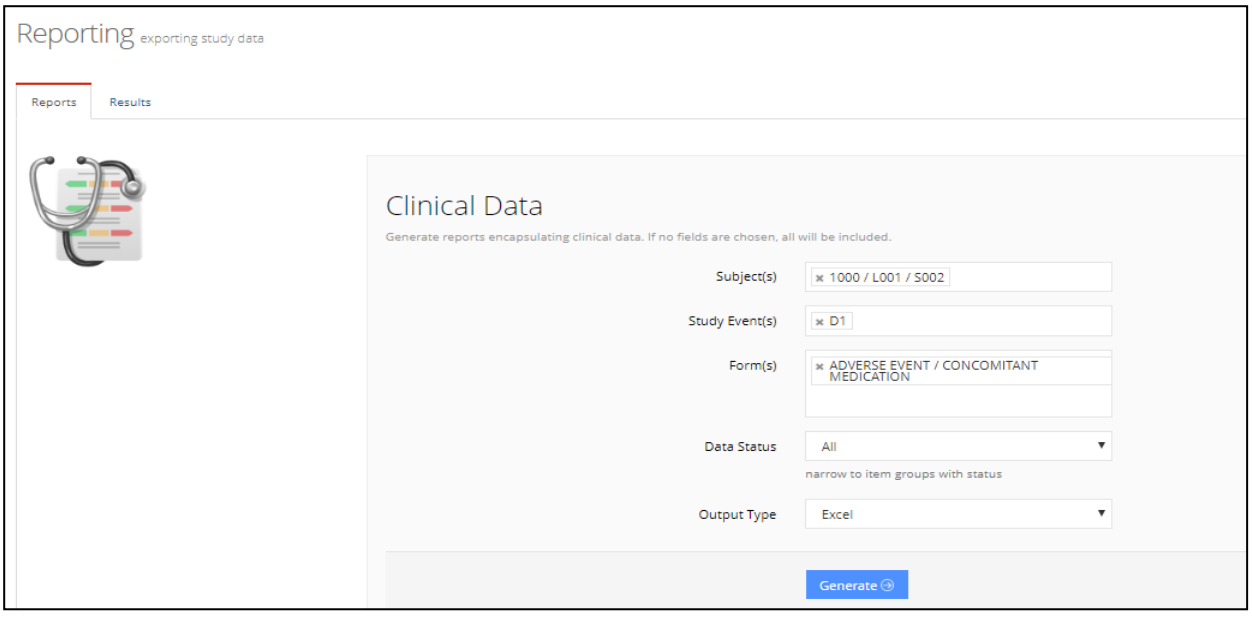

Figure 5 – Example to run a report on all available data in the 2nd eSource system

Where data were extracted from the first eSource system by using an external software solution, our 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, but also lab reports, query reports and reports from all different executed events can be exported separately. 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). This new feature gives data managers an overview of lab data that still needs to be reviewed and assessed for clinical significance which can prevent unnecessary queries. 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.

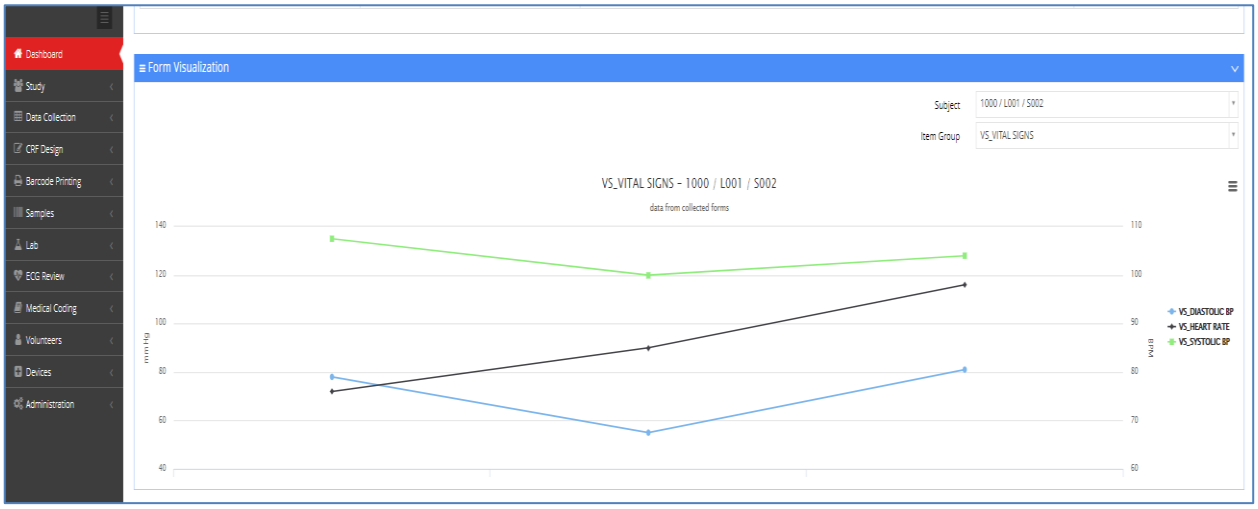

Figure 7 – Example of a dashboard for trends visualization in the 2nd eSource system

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). Data fields of a form could not be left blank without entering a comment and no conditional form or field completion was foreseen. In the 2nd eSource system, the option to conditionally complete forms or fields implies that certain fields will only be visible and will only need to be completed depending on the outcome of a previous field. E.g. 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 and 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 data management.

The development of a Global Rulings Document (GRD) was required at the start of the data management (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 as there were a lot of 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 already been reduced.

Compared to the 1st eSource system, all users are now able to see the 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 speeded up the 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 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. The medical monitoring can therefore be performed simultaneously with the data management 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 where General Data Protection Regulation (GDPR) determines how to collect and process personal data, requires a very thorough and well considered management of roles to access, complete and consult eSource database. SGS CPU created a document listing all roles with their read and write access for all data that can be present in the eSource system. These role definitions allow different access rights to be granted in test and main environment. 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. Role restrictions and permissions can be assigned at trial, 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.

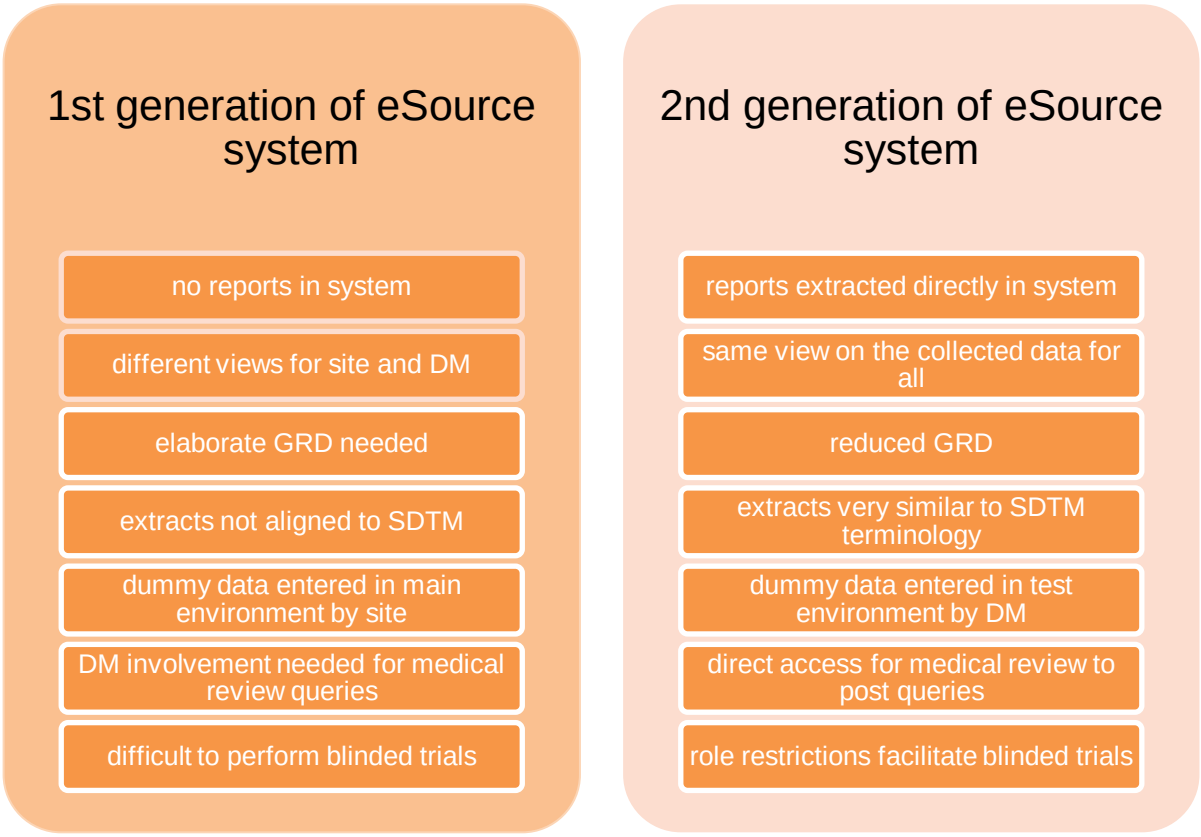

Figure 8 - Improvements compared to the 1st eSource system

Recruiting healthy volunteers and patients with specific eligibility criteria can be challenging and although a subject database is already in place within both eSource systems, there is still room for improvement. The 2nd eSource system allows the recruitment group to batch SMS and e-mail directly from within the system and reach large groups of people. The option is not yet used by SGS but would be interesting to explore further.

Although the 2nd eSource system has already made the GRD less elaborate, it still has not yet become completely 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 independent from SGS, it will be a challenge to completely disengage from the GRD.

By defining and using the right role restrictions, clients should be able to get access to blinded trials when the drug exposure-form is blinded for all users (except for the unblinded staff who will collect the data). This option has not yet been tested by SGS.

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 become 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 an integration of an electronic patient reporting outcome (ePRO) system with the eSource system is feasible or a questionnaire module can be foreseen in the eSource system that is accessible for subjects who can complete their data directly in this module?

CONCLUSION

By customizing the new eSource system for a certain group of users, the efficiencies implemented have shown to facilitate the work for other eSource users as well. The first case study with the new generation of eSource system started in September 2019 and had the eSource and SDTM database locked in the beginning of February 2020. SGS will continue to explore and test the boundaries of the 2nd generation of eSource systems, 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.

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