



Reader ROI

- Process optimization is essential to reducing costs and time.
- Opportunities exist to reduce source data verification.
- Many companies are reducing the workload for site monitors by lowering the amount of source data verification.
- Efficient site monitors can build strong relationships with clinical investigator sites.

Process Optimization: Reduced Source Data Verification

In today's environment, the typical pharmaceutical company faces multiple challenges in order to stay competitive. Shrinking product pipelines, increased generic competition, and ongoing regulatory compliance efforts all impact company operations. Within this landscape, companies are seeking to analyze process optimization opportunities to lower their development costs and timelines. Process analysis initiatives can lead to streamlined processes, reduced duplication of efforts, and greater use of technology. Among the latest processes being examined is the reduction in the rate of source data verification (SDV).

Source data verification

Every clinical study requires the capture of subject information. The sponsor provides the paper case report form (CRF), or electronic CRF (eCRF), and may provide the source documents that accompany many electronic data capture (EDC) studies. Any information that is captured on a paper CRF or electronic CRF (eCRF) is verified against the source documents during a site-monitoring visit. Every subject visit is captured and transcribed, resulting in thousands of pages of information. Often source document verification (SDV) is done at the rate of 100 percent of the documentation for 100 percent of the subjects (or patients) in the study. In some instances, it can take a full day or more to complete SDV on a single patient's data. Companies that have minimized their risk of data errors through efficiencies gained from other process optimization initiatives are now refocusing site monitoring efforts on other, more productive and value-added activities such as developing and maintaining good relationships with clinical investigator sites.

EDC: not the end of SDV

The promise of cleaner, faster data with EDC has been realized. However, what is not widely discussed is the creation of source documents that accompany the eCRF to the site. These are hard copy documents created by sponsors and supplied to the sites to provide a uniform source document that closely matches the eCRF. This enables the investigator, study coordinator, or study nurse to complete a form when evaluating a subject during a visit and easily transcribe the information into the EDC system later.

Not all sponsors or EDC systems require paper source documents. Typically, offline EDC systems allow the computer accessing the eCRF page to be portable and taken into the examination or patient's room. When this is the case, the eCRF can fill the need of the source document.

Regulatory information regarding SDV

While regulatory bodies require that SDV be performed, there is no specification regarding the amount of data required.

The level of SDV is decided by each sponsor based upon the level of risk to the accuracy of the data they can manage without impacting safety and timelines, as well as what downstream risk mitigation processes are in place.

Company-specific requirements

Some companies have specific standard operating procedures (SOPs), working guidelines, or practices that detail SDV requirements. If these documents are ambiguous, SDV requirements may be detailed in the site monitoring plans for each specific trial. In many companies, SDV templates may be used, as those writing the site monitoring plan may not understand the level of effort required or may not need to differentiate among sites.

To avoid compliance issues, it is important to understand where and in what detail SDV requirements are specified before undertaking an SDV reduction project. This is true whether the project is undertaken as a pilot or as a time- and cost-saving strategy.

Determining the data correction rate

Many of the current EDC systems have the functionality to track SDV; when data is changed, it typically includes the reason for change (e.g., transcription error). Using information on data corrections captured by the company's EDC or clinical data management system (CDMS), it is possible to determine

the current (pre-reduced SDV) rate of SDV correction. Using the CDMS, the sponsor can identify fields or CRF modules that have a high rate of SDV correction. This may show where additional site training or a redesign of the CRF or source documents may be needed. It will also focus on where continued high rates of SDV should be applied. When fields or CRF modules that have lower SDV correction rates are identified, the sponsor can reduce the level of SDV performed without incurring an increased risk of errors. This can be applied to current or future programs, maximizing the reduced SDV benefit.

It is important to note that safety and efficacy must not be negatively impacted by SDV reduction.

SDV around the industry

Information gathered through industry relationships and experience is presented below as an example of SDV algorithms and methodologies used by many of the top pharmaceutical companies. The below bulleted items are not all-inclusive, but provide an overview of some industry standards to consider when determining whether to reduce the SDV for a trial.

- 100 percent SDV of all subjects' screening, randomization, and first on-drug visit

Other variations of this include:

- 100 percent of first two subjects screening, randomization, and first two on-drug visits.
- 100 percent of all subjects' inclusion/exclusion criteria
- 100 percent of all consent forms
- 100 percent SDV of 100 percent of the documents for the first one to five subjects' entire study participation

After selection of the first one to five subjects for 100 percent SDV, further SDV is done at 100 percent for 20 percent of the subjects (selected randomly by monitor or through technical solution).

- 100 percent SDV for 20 percent of the subjects (selected randomly by monitor or through technical solution)
- X percent of 100 percent of subjects (X is determined by the clinical team.)
- 100 percent of all consent forms, SAE and AEs, and con-med pages (This was consistent through all companies that had reduced SDV initiatives.)

In addition to the above, there are cases in which the clinical trial team has established SDV rates and specific data points that must be validated throughout the study. In addition, phase I and II trials consistently required 100 percent SDV for all subjects.

Further considerations

When undertaking a reduced SDV initiative, thought must be given to technology enablers such as the CDMS, EDC, AE/SAE reporting, and statistical sampling. Determining how these tools can be leveraged in order to provide the monitor with random sampling, notification of upcoming SDV intensive visits, or easy review of the necessary documents will increase the compliance and efficiency with which a reduced SDV initiative is accomplished. In addition, personnel at the clinical sites must be appropriately trained so that they understand their responsibility for the accuracy of the source data.

Continuing optimization

Reducing SDV can provide benefits when accomplished within the context of a process improvement initiative or as one part of an all-encompassing clinical process excellence initiative. While it has proven to be a time- and cost-saving benefit, it is important to utilize the time saved to further improve downstream processes or to provide additional benefits to the clinical process through other value-added activities.



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