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Remote Source Document Verification (rSDV)

A Sponsor Perspective and Results of Implementation

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There is a critical need to make the entire process of source data verification (SDV) more efficient and cost effective while assuring that study data are accurate. Technology is now available that enables the efficient SDV of most clinical trial data remotely. Efficient remote SDV (rSDV) is done through scanning of source documents into a central repository, where they become viewable to an inhouse rSDV specialist. The rSDV process saves significant cost in monitoring visits and associated travel, and also makes monitoring visits less disruptive and more valuable to the site and the sponsor.

This paper presents one sponsor's implementation and evaluation of a pilot study concerning rSDV, as well as the results of a survey of site acceptance. The results showed shorter and less frequent monitoring visits and extremely high site satisfaction. The sponsor and 92% of sites said they would do another study with rSDV.

Implementation of the Case Study

Our company had the unique opportunity to run two pivotal, U.S.-based Phase III studies over three years, with the first utilizing traditional SDV methods in a paper data collection environment. The second used a combination of rSDV and onsite monitoring with electronic data capture (EDC). This arrangement provided an optimal environment to assess the impact the rSDV function had on trial conduct, and also became the basis for evaluating the initiative.

The key difference between the two trials is the first study's use of paper case report forms (CRFs) and no technological product to enable any data to be source verified without a monitor being physically at the site. The second trial ran with an EDC system in place that had an electronic trial master file (eTMF) component tied to the EDC system, which served as the central repository and work area for the rSDV specialist. The system automatically created a subject file in the eTMF, which was then used as a container to capture necessary documents (source data) for each subject in order to perform the tasks related to rSDV.

The sites scanned the source documents into the subject's file using scanners provided by the sponsor. All source documents were study-specific standardized worksheets. Any requested alterations to a standard worksheet were permitted, but required review and approval by the sponsor to ensure that no inappropriate subject identifiers were added. Any known documents with subject identifiers were first electronically deiden-

tified by the system before being visible to any viewers of the eTMF, in accordance with the requirements of the Health Insurance Portability and Accountability Act (HIPAA)—that is, protected information was deleted from the electronically scanned source.

We conceptualized the rSDV role to function as a point-to-point data verification role, comparing an entry on the electronic CRF (eCRF) to the source worksheet.

To be prepared for the tasks involved in rSDV, an initial assessment was required to determine what portion of the data could be verified via rSDV. We conceptualized the rSDV role to function as a point-to-point data verification role, comparing an entry on the electronic CRF (eCRF) to the source worksheet. To assure data quality, we used this point-to-point comparison of data for items that were not of a critical nature to the study's primary or secondary endpoints. Data that were more clinical in nature (i.e., adverse events) were left in the hands of the experienced clinical monitors that visited the sites.

For randomized subjects, 85% of the data could be monitored remotely. Specific categories not appropriate for the rSDV process were inclusion/exclusion criteria, adverse events, concomitant medications, and medical history. If any data point lacked clarity (such as having an extraneous comment on the source, or a checkmark placed in the middle of two questionnaire responses instead of a clear choice being selected), it would not be remotely verified, and would instead be flagged (within the system) for the clinical monitor to address. Examples of data points checked through rSDV included date of

birth, race, gender, vital signs, questionnaire responses, diary responses, study visit dates, etc.

Once we established this information, we assigned personnel to fill the rSDV role. A strategic determination allowed only one person the role of rSDV, which would make it easier to identify areas for improvement and to test the true capacity of such a role. The one rSDV specialist supported 10 clinical research monitors across 120 sites in the U.S. The rSDV specialist tracked upcoming monitoring visits and performed all rSDV for a research site two to three weeks prior to the onsite visit. In addition, the rSDV specialist reviewed the eTMF for any missing or out-of-date essential documents (*curricula vitae*, 1572s, financial disclosures, etc.).

Upon completion of an rSDV site review, the site-assigned clinical monitor and the project leader, via e-mail, would be supplied with a listing of what was verified, what issues were observed, and also what data points could not be done via rSDV due to lack of source information or lack of clarity in the source.

The Benefits

Numerous efficiencies were targeted to be realized by using rSDV. Several expected, as well as some unexpected, benefits were identified throughout the course of the study. Some of the more significant items were:

- **rSDV summaries provided faster awareness of issues needing investigation at the site prior to the site visit.** If an issue was still outstanding once the monitor was on a site visit, this was typically indicative of a larger problem. With the traditional monitoring process, it took two onsite visits (up to four months) to establish this pattern; with rSDV, the pattern was established in two to three weeks.
- **rSDV activities are helpful in identifying potential problem sites.** If the rSDV specialist

encounters an excessive proportion of unverifiable data points while performing remote monitoring activities, this flags the project lead and clinical monitor to collaborate more closely. Site issues can be assessed and a course of action can be established prior to the scheduled onsite visit.

- **Improvement of quality of monitoring activities and decrease in onsite rework.** The rSDV role created a checks and balances system, because there was a dual responsibility for each site, which increased accountability. Additionally, a process was in place for necessary follow-up activities to be performed remotely, which saved time and money.
- **Significant improvement in the utilization of the clinical research monitor's experience.** Because the clinical monitor was not tied down verifying nonclinical data points, he or she had more time available to be a valuable resource for the site. Overall reports from our field monitors conveyed more time available for such activities as offering suggestions to assist with enrollment and providing protocol training.

The one rSDV specialist supported 10 clinical research monitors across 120 sites in the U.S.

Cost Savings

Because this was a pilot study with rSDV, we had a general goal of cost savings, but were not certain what a reasonable target would be for true cost savings. Through various assumptions, we established that in a "perfect world" scenario, rSDV could have saved us nearly a million dollars in our large Phase III trial (8% of the total

study budget, including costs associated with investigator payments, data management, monitoring, statistics, advertising, etc.).

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Although we did not realize that level of cost savings on this first attempt, the cost savings achieved were substantial. Specific areas and amounts for cost savings included:

- **Wage savings per rSDV "visit conducted" of $725.** We conservatively estimate the rSDV rate to be four times faster than onsite source document verification because (a) all documents were on one uniform system and ready to review and (b) the remote monitor had no onsite distractions. This factor was combined with a lower hourly rate for the rSDV specialist. We then multiplied the wage savings times the number of rSDV visits throughout the course of the study.
- **Savings on trip expenses.** We estimate that we were able to save a minimum of 120 (one per site) study visit per-day expenses by having rSDV in place. The remote activities eliminated the need for many multiday trips to sites. Additionally, activities performed by clinical monitors remotely, such as eTMF review and some source document review follow-up work, eliminated, we estimate, at least 35 onsite visits.

- **Overall estimated savings due to rSDV in the pilot study = $375,000 (3% of total study budget).** This amount, while considerable, could have been much higher had we been able to roll out rSDV when the study first kicked off five months earlier. We also learned valuable process improvements and best practices from the pilot study regarding what does and does not work in rSDV. We could make refinements to the process in the future that would significantly increase our cost savings.

HIPAA Considerations and Concerns

As stated previously, we created standard source worksheets for our site to use for collection of study visit information. Personal information for the subjects was not included on the source documentation, and the sites were instructed not to alter the worksheets to include such items. Many sites are bound by internal standard operating procedures to use standard worksheets that include private patient information. The system allowed deidentifi-cation of such worksheets prior to uploading into the eTMF for rSDV.
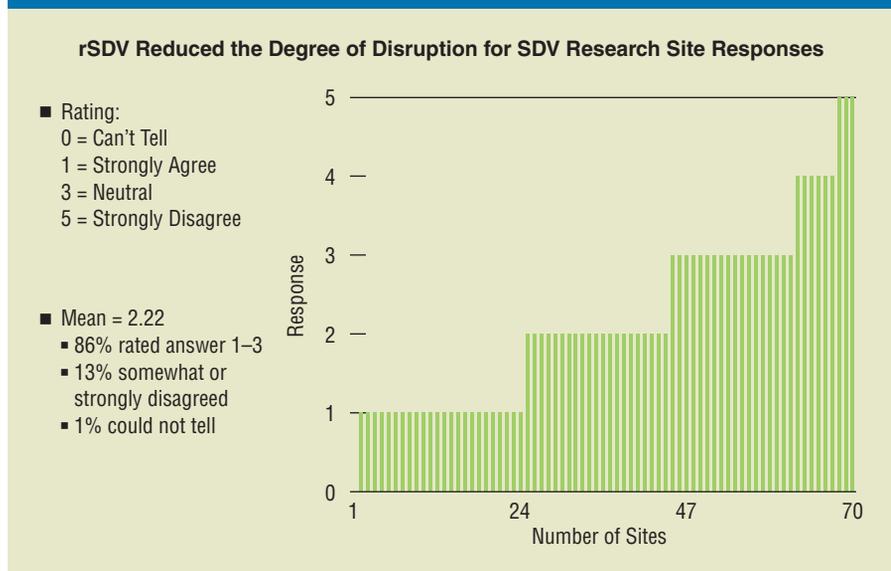
Differences in Query Rates

Several questions arose concerning how to determine the differences in query rates between the pilot study and the original paper study. However, we could not attribute the differences in query rates noticed in the study using rSDV solely to this initiative. We believe factors that contributed to the decline in the number of queries were related to paper vs. EDC, the reuse of some sites, and their familiarity with the compound and the study, as well as to the rSDV process.

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Some of the automatic checks launched in the EDC system could be easily resolved by the rSDV specialist. For example, when an edit for a seemingly erroneous date was launched in the system, the rSDV specialist was easily able to confirm that the date was accurate based on the source doc-

Figure 1 Site Survey Responses to Whether rSDV Reduced the Degree of Monitor Visit Disruption

rSDV Reduced the Degree of Disruption for SDV Research Site Responses

- Rating:
  0 = Can't Tell
  1 = Strongly Agree
  3 = Neutral
  5 = Strongly Disagree

- Mean = 2.22
  - 86% rated answer 1–3
  - 13% somewhat or strongly disagreed
  - 1% could not tell

uments and the protocol deviations that were uploaded into the eTMF. Obvious transcription errors that launched queries were still expected to be resolved and corrected by the sites, especially when changing data was involved.

The Site Perspective

The rSDV process was created primarily to benefit the sponsor and the monitor in terms of efficiencies and cost savings. In order to fully evaluate the success of rSDV, we recognized the need to survey site personnel to obtain their opinion of their experience with the initiative. Results were received from 64% of the 120 sites. Of those, 78% noted that scanning documents was easy or that they were neutral to scanning. Other findings determined that rSDV offers benefits to the site, including decreases in the frequency and length of monitoring visits and more personal attention from the onsite monitor to focus on items important to the site. Specific responses to a portion of the questions are detailed in Figures 1, 2, and 3.

Lessons Learned

In reflecting on our pilot study with rSDV, we observed many critical items important for the use of rSDV in future trials, which we can categorize as follows:

Clinical Monitoring

The traditional clinical monitor may not be the ideal fit for a trial using rSDV. If the clinical monitor holds to the concept that he or she alone should verify everything onsite, rSDV can shift from being a cost saver to being an added expense.

The clinical monitors' attitudes toward rSDV have direct impacts on the sites' attitudes. Although our monitoring team fully embraced the rSDV concept at initiation, the ups and downs in enthusiasm for the process as we ironed out the details did have some effect on our sites.

A thorough assessment of attitudes about rSDV, as well as any clear expectations being set for clinical monitors to eliminate role ambiguity, should effectively eliminate the issues we experienced in our pilot study. For sites, this means a detailed introduction to the process during the site assessment phase, prior to final site selection.

Study Sites

We anticipated that there would be initial resistance to scanning documents. In an effort not to overwhelm sites with scanning activities, we opted to scan documents related only to those subjects who were actually randomized into the study. However, most sites needed little training with scanning devices. Thus, including screen-fail subjects for rSDV in future trials might not overwhelm the sites as much as originally thought, which

Figure 2 Site Survey Responses to Whether They Would do Another Study Using rSDV
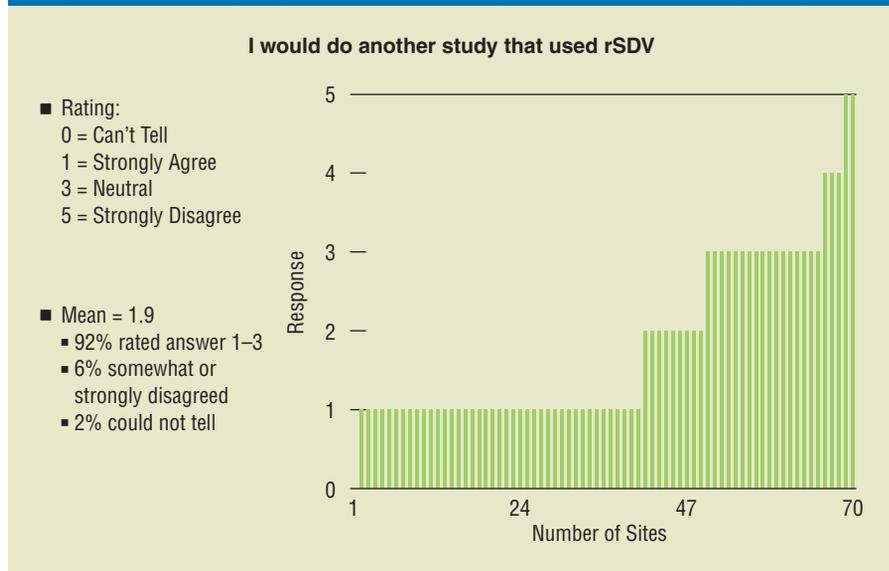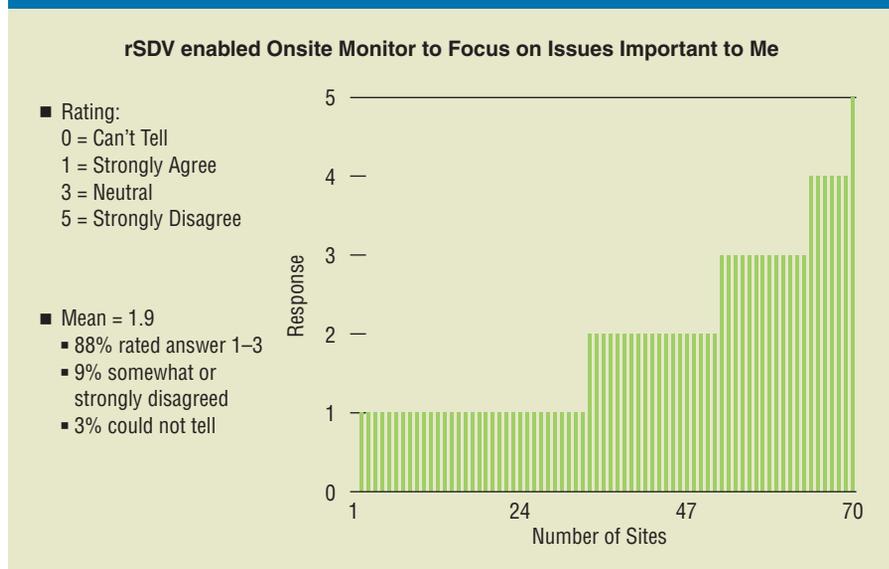

I would do another study that used rSDV

- Rating:
  0 = Can't Tell
  1 = Strongly Agree
  3 = Neutral
  5 = Strongly Disagree

- Mean = 1.9
  - 92% rated answer 1–3
  - 6% somewhat or strongly disagreed
  - 2% could not tell

Figure 3 Site Survey Responses to Whether rSDV Enabled the Onsite Monitor to Focus on Issues Important to the Site

rSDV enabled Onsite Monitor to Focus on Issues Important to Me

- Rating:
  0 = Can't Tell
  1 = Strongly Agree
  3 = Neutral
  5 = Strongly Disagree

- Mean = 1.9
  - 88% rated answer 1–3
  - 9% somewhat or strongly disagreed
  - 3% could not tell

then could have increased the total savings of the pilot study by an additional 2–3% of the overall study budget.

The plan for implementation in future trials with rSDV would include scanner training sessions as part of the site initiation visit. We would also have detailed descriptions of the scanning process in the pretrial site assessment.

Special Consideration

As is the case with EDC, sites are now being asked to provide more service to sponsors. One key to successful rSDV is obviously the site or sponsor managing to upload study source documents into the eTMF. Many sites may ask for a budget increase in order to account for time to scan. Thus, the sponsor should consider if it wants to have a technology vendor scan all documents into the eTMF, to provide its own centralized scanning resource to sites unable or unwilling to scan on

location, or to provide increased budget costs for sites to scan independently. Although it was considered a site task for the pilot study, we, as the sponsor, provided resources as needed if the site became overwhelmed or fell behind in scanning. This was especially important during the end stages for data lock.

The traditional clinical monitor may not be the ideal fit for a trial using rSDV.

Ultimately, the pilot study was an encouraging beginning to what we expect will be a significant history of the effective use of the rSDV model. We have not yet used the full potential of the process, but look forward to refinements and progressions that will make the rSDV process

even more time- and cost-effective in future trials.

Acknowledgements

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