Remote Source Document Verification- Frequently Asked Questions

Remote Source Document Verification Platforms (Functionalities, Features & Support)

What are the available options to sites for Remote Source Document Verification (rSDV)?

1. *Veeva SiteVault Platform*- This will be handled directly by sites, through a free subscription from Veeva Systems. This option may require a signed agreement between the site and Veeva Systems, Inc.
2. *Site Controlled SharePoint or Cloud-Based Portal-* Site may already have an existing platform which allows for sharing of participant source documents, that could be extended to allow monitor's access for a specific protocol and limited time.
3. *Direct Access to Sites' Electronic Medical Record (EMR) system*- Site provides monitor(s) direct access to their EMR for a specific protocol and limited time.
4. *Medidata Rave Imaging Solutions*- This will be an additional module to the existing Medidata Rave EDC system that's currently being used by sites to complete eCRFs. As such, it will be provided to sites through the Data Management Centers (DMCs). This option does not require a separate agreement by the sites.

For options 2 and 3- Sites need to work through their internal procedures to secure the necessary institution approval and signed agreements to provide access to the monitors. These options must be 21CFR Part 11 and HIPAA compliant as applicable.

Can Veeva SiteVault and Medidata Imaging be used for managing Regulatory Documents?

Yes, regulatory documents can be uploaded by the site for remote review by the site monitor. This reduces the extra burden of uploading the same documents multiple times for different studies, as some documents such as CVs, licenses, and HSP/GCP training documentation only need to be uploaded once and are referenced across multiple studies.

Do the systems provide long-term storage of electronic documents in the cloud (no need to keep paper)?

This depends on the selected option:

Veeva SiteVault - Once certified copies of source documents and other essential documents are uploaded into the cloud storage system; they are controlled and accessible to sites as needed for up to 25 years.

Medidata Rave Imaging Solutions - Certified copies of source documents and other essential documents are uploaded into the cloud storage system hosted by the DMCs and are accessible to the sites for the duration of the agreement between the DMCs and Medidata.

The FDA issued guidance document entitled "FDA Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency", provides the following guidance*: "Regarding retention of copies of source documents used for remote review, it would not be necessary to retain the certified copies of source documents used for remote review, provided the clinical investigator retains the original source documents according to FDA regulations for the retention of records"*.

For options 2 (Electronic Medical Record (EMR) System) and 3 (Site Controlled SharePoint or Cloud-Based Portal), it is expected that sites would have in place policies and procedures for complying with regulatory records retention requirements.

Do sites manage the monitor's access to the selected rSDV system?

With the various options proposed, sites can control the monitor's access to specific protocols and specific participant information except if they are using Medidata Rave Imaging Solutions where access is managed by the DMCs.

What assistance does DAIDS provide to sites with setting up rSDV systems?

Sites should work with their DAIDS POs to address questions that may arise during implementation of rSDV platforms. Questions regarding Medidata RAVE Imaging Solutions should be directed to the applicable DMC for assistance. Questions for Veeva Site Vault can be directed to: sites.comms@veeva.com

Our site has a HIPAA compliant Box and Office SharePoint, and our DocuSign is Part 11 compliant. Can we use the two systems together and use the DocuSign for things that require e-signature, or do we need to have the same system that meets both requirements?

21 CFR Part 11 applies to both records and signatures. While DocuSign which you intend to use for electronic signatures is Part 11 compliant, Box and Office SharePoint should also be Part 11 compliant.

Uploading source documents will be time-intensive and would require better equipment to scan more pages. Do either of the rSDV options upload faster than Box?

This depends on whether the site plans to upload redacted or unredacted source documents. For redacted source documents, Medidata Rave Imaging Solution has a web-based redaction tool, which would make the uploading process less burdensome. However, for unredacted source documents, it is uncertain if there is any difference between these options since they all utilize a cloud-based storage system. The upload time may depend more on the type and size of documents, scanner specifications and internet speed, rather than the selected rSDV option.

Can you clarify why the file sharing system must be 21CFR Part 11 compliant, especially if it is HIPAA compliant and already being used within the institution?

In addition to HIPAA requirements, compliance with 21CFR Part 11 comes into play since this file sharing system is not only being used for clinical care but also for clinical trials and the data is intended for submission to the FDA.

Our source documents are paper-based, and we would be scanning our paper source documents into the SharePoint system. Any revisions to source documents would occur on the original paper source document, not on or through the scanned version on the SharePoint system. Could you provide a rationale for the CRF 21 Part 11 compliance requirement for paper source documents?

Even though the electronic signatures requirement aspect of Part 11 does not apply, scanning paper source into SharePoint is akin to conversion to electronic format. Part 11 applies to "Records that are required to be maintained under predicate rules, that are maintained in electronic format in addition to

paper format, and that are relied on to perform regulated activities". We are utilizing the electronic format in place of the paper format for monitoring, so the SharePoint system still needs to comply with the areas of Part 11 that pertain to electronic records.

Are cloud-based SharePoint platforms 21 CFR Part 11 compliant?

SharePoint is available in different forms and can be configured to be Part 11 compliant. The site should have system configuration and validation documentation, as well as applicable SOPs on file to show that their SharePoint satisfies the requirement of Part 11.

Where can we obtain additional information regarding Veeva SiteVault other than the description in the memo?

Sites can sign up at sites.veeva.com and questions can be directed to: sites.comms@veeva.com. Online resources are available at: https://www.veeva.com/products/sitevault/. In addition, sites can contact Bree Burks at Veeva systems for any additional information that is needed for IRB/EC submission or implementation of Veeva SiteVault. Her email is: bree.burks@veeva.com. The site should inform her that they are part of the National Institute of Allergy and Infectious Diseases (NIAID), Division of AIDS (DAIDS) network.

Does DAIDS have a contract with Veeva Vault?

DAIDS does not have a contract with Veeva Systems. The Veeva Site Vault platform is presented to sites as an option to facilitate rSDV. Should this option be selected, the signed agreement is between your site/institution and Veeva Systems, Inc.

What are the next steps for sites that selected Medidata Rave Imaging Solutions?

As of June 24, 2021, the following 12 studies have been added to MDR Imaging**: HPTN 083, HPTN 084, IMPAACT 2019, IMPAACT 2017, IMPAACT 2014, IMPAACT 2010, IMPAACT 2032, P1093, A5360, A5379, A5300B, and A5359**. DAIDS continues to work with both DMCs to extend the Imaging Solutions platform for most ongoing/active studies.

The DMCs will continue to send out notification memos as additional studies are configured in MDR Imaging. Please note that access to Rave EDC will be blocked until completion of the required 10-minute eLearning "Medidata Remote Source Review: Site Users Training". For additional information, please reference the FAQs in the DMCs memos and your site can also contact the Medidata support center at support@intelemage.com or 877-464-7473 or 513-996-6113.

Implementation of Remote Source Document Verification (rSDV)

What is the target timeline for starting rSDV?

In the DAIDS memo dated January 21, 2021, rSDV monitoring visits were expanded to all DAIDS sponsored protocols at sites with a secured rSDV platform and all required approvals.

Remote monitoring, system upgrades and trainings on any changes to the rSDV system requires that data personnel have adequate internet access. Are there alternatives in the scenario where a country shuts down internet infrastructure for an extended period?

We recognize that some countries face challenges with internet connectivity, and this directly impacts their ability to conduct remote monitoring visits, in addition to other clinical activities. We encourage sites to engage their POs and PPD monitors to determine ideal timeframes for remote monitoring visits and timelines for implementation of the rSDV platform. If on-site monitoring visits are feasible in your site location and there are no travel restrictions in place, this can be an alternative to remote monitoring.

When CRAs come for on-site monitoring, do they still need to go back to all files monitored remotely to verify what is in the EDC?

No. Study data that have been verified through rSDV, will not require re-verification during an on-site visit. Source data verification will only be applicable to data points that were not verified during the remote monitoring visit.

Are the POs expected to approve the access method for rSDV?

No, the POs do not need to 'approve' the site's choice for rSDV platform. The site can choose any of the platforms that were outlined in the rSDV memo (dated 28Jul2020 or 13Jan2021), or any other secured platform.

During a remote monitoring visit, the CRAs did not review participants' clarifying notes documented on the site progress notes, and only relied on what was entered in EDC. How could the CRA have reviewed the complete participants' information?

The CRA may not have reviewed the complete participant files supporting the data in the database if the visit type was a remote monitoring review. However, for rSDV all source documents need to be uploaded into the secured platform for verification by the site monitor.

Is remote monitoring mandatory? Can sites have the choice to select which option they prefer for a visit?

Remote monitoring is not mandatory. If your institution allows for on-site monitoring this should be communicated to your PPD monitor in planning your next monitoring visit. As the COVID-19 pandemic continues to disrupt travel, kindly note that while your institution may allow for on-site monitoring there may still be local and/or national travel restrictions limiting travel of monitors to your site. As these disruptions remain fluid, DAIDS prefers that you select a rSDV option for your site to maintain continuity in monitoring.

How will on-site monitoring and remote monitoring work together?

On-site monitoring visits will continue to be conducted where institutional, local, and national regulations allow. Remote monitoring visits will take place when these regulations are restrictive to an on-site visit, to maintain continuity in study monitoring. If your site has fully implemented an approved rSDV option, your PPD monitor will conduct rSDV during the remote monitoring visit as they would if they were on-site.

Can sites use other secured rSDV platforms for protocols that are available in Medidata Rave Imaging system?

Yes, sites can use any of the systems that were outlined in the DAIDS rSDV memo dated July 23, 2020, for all active studies regardless of their availability in Medidata Imaging. At this time not all studies have been configured in the Medidata Imaging Solutions available through the DMCs (FSTRF and SCHARP).

Can sites use more than one option to provide access for remote source document verification?

Yes, it is acceptable for sites to use any number of options to provide source documents for remote verification. Some sites may provide direct monitor's access to their EMR and also upload other source documents through Veeva SiteVault or Medidata Rave Imaging, provided all appropriate agreements and approvals are in place. We recommend that sites planning to use Medidata Rave Imaging for rSDV to consider more than one option, due to the phased approach in the configuration of studies in Medidata Rave Imaging by the DMCs.

Source Documents Upload Challenges and Redactions

Capacity issues at sites to upload source documents.

We realize that it will be an extra burden on the site's limited resources to upload study documents. Recognizing this, our monitoring strategy is to focus rSDV on studies in the order of their estimated database freeze/lock (DBL) dates with emphasis on studies with DBL dates within 12 months, so as to limit the number of studies that will be monitored during each remote monitoring visit. In addition, all PIDs will be announced on the Work Order to allow ample time for your site to upload the requested source documents. PPD monitors will work collaboratively with your site on the number of PIDs' source documents that need to be uploaded and ensure that visits are scheduled at convenient dates when feasible. It is anticipated that the workload will normalize once the backlog of source documents for enrolled participants has been completed, and source document upload for rSDV is incorporated into the site's clinical research operations routine practices. We encourage you to communicate with your PO if your site continues to experience challenges with uploading source documents.

Should sites redact source documents?

Both Medidata Rave Imaging and Veeva SiteVault options allow for redacted and unredacted source documents to be uploaded into the cloud storage system. This decision should be made by each site based on their institutional guidelines regarding privacy and confidentiality. In addition, each site should consider the extra resources that may be required to redact the documents. Even though one of the options, Medidata Rave Imaging Solution has a web-based redaction tool, it may be more suited for electronic documents as opposed to scanned documents. An uploaded document must retain all of its original attributes to be considered a certified copy. For redacted source documents, it should be clearly noted that they are certified copies of the original, redacted for Personally Identifiable Information (PII) /Protected Health Information (PHI). Our recommendation is that the sites do not redact the source documents since the upload is to a secure platform. However, your institutional policies, National/Country regulations and IRB/EC will determine the final decision.

What type of information should be uploaded to these platforms? Does NIH require upload of the clinical records or laboratory reports? Will these copies be de-identified?

All source documents (medical history, visit notes, diagnostics, lab tests, etc.) which the monitors need to ensure participant safety and verify data accuracy should be uploaded into the selected platform. In addition, pharmacy documents may need to be uploaded as applicable. PPD monitors will specify 100% of PIDs to be reviewed during the remote monitoring visit on the Work Order. They may OR may not be redacted depending on the Institutional policies regarding upload of documents containing PII/PHI. For redacted source documents, it should be clearly noted that they are certified copies of the original and redacted for PII/PHI. Sites are expected to upload complete documents for specific participants noted on the Work Order (WO).

Since the proposed rSDV systems are 21 CFR Part 11 compliant, is it necessary to redact the source first? Or is this an IRB/EC decision?

Even though the proposed systems are 21 CFR Part 11 compliant, the decision on whether to redact should be determined by the IRB/EC and or based on institutional requirements.

FDA and other regulatory agencies conducting inspections have requested that documents be redacted for protected health information (PHI) prior to being uploaded into a secured platform.

For regulatory inspections, sites must follow each regulatory agency's requirements for upload of documents for inspection.

Scanning and uploading documentation is time-intensive and sites lack sufficient staffing to manage these processes. Sites will likely need to request more funding support for data personnel and clinical staff to manage the document upload process.

Due to the continued travel and other restrictions associated with the pandemic, the option for rSDV is needed to supplement on-site visits. The monitors will work collaboratively with the sites on how best to lessen the strain of rSDV on their operations and processes. We encourage you to inquire about availability of any additional funding to support this activity from your PO.

National/Country and IRB/EC Approvals and Documentation

Would sites need IRB/EC approvals to implement these rSDV options?

IRB/EC approval is required as DAIDS' protocols and other relevant study documents language specifies that monitoring is performed via on-site visits. In addition, sites also need to comply with their institutional guidelines regarding confidentiality and privacy. It is possible that some sites have issued a new guideline or amended existing ones to include rSDV. In such instances a copy of this guideline along with the DAIDS memo (dated 28Jul2020 or 13Jan2021) on rSDV can be filed in the Regulatory Binder as documentation on why IRB/EC approval was not sought. Also, site SOPs may need to be amended to include the process of rSDV.

Is Country/National approval required to conduct rSDV?

This varies by country; while the US/FDA does not require approval to be sought, other countries, i.e. most African and Latin American countries, do require National Regulatory Agency review and approval prior to the implementation of rSDV. Each site should contact their Country/National agency to obtain relevant information on rSDV approval as applicable.

Do you require IRB/EC approval for the specific rSDV platform?

No, not for the specific platform. However, DAIDS requires IRB/EC approval to conduct rSDV using any secured platform that is HIPAA and Part 11 compliant. Also, it is suggested that sites seek a general IRB/EC approval that applies to all active studies instead of individual protocols. Some sites submitted the DAIDS memo (dated 28Jul2020 or 13Jan2021) regarding use of rSDV for all ongoing protocols to their IRB/EC for approval.

Some IRB/ECs are requesting that remote monitoring with the selected rSDV platform be included into the individual protocol consents. This poses a significant workload to revise each consent for each protocol.

Sites must follow their institutional requirements for rSDV. DAIDS recognizes the challenges and burden in IRB/EC submissions for rSDV acknowledgment and/or approval. For studies under the purview of a single IRB (sIRB), the networks will make the submission to the sIRB on behalf of the participating US sites. In addition, remote monitoring language will be incorporated by DAIDS into any protocol undergoing amendment to ease the IRB/EC submission requirement for rSDV.

Would all options require IRB/EC approval including Medidata Rave Imaging Solution if a site already uses this system for several studies?

Yes, the expectation is for the site to obtain IRB/EC approval for the use of Imaging Solutions for rSDV as well. However, if this is currently being used at the site for other studies, IRB/EC approval may already be in place.

Should sites wait until the signed agreement is in place for Medidata Rave Imaging to submit to the IRB/EC or go ahead with IRB/EC submission before that is ready?

The Medidata Rave Imaging will be an additional module to the existing Medidata Rave EDC system that's currently being used by sites to complete eCRFs. As such, it will be provided to sites through the DMCs. It does not require a separate agreement by the sites, so they can proceed with IRB/EC submission.

Typically, IRBs/ECs do not review/approve specifics about study monitors and/or how they access study records. What exactly are DAIDS's expectations about what constitutes "IRB/EC approval"?

Yes, we agree that the IRB/EC does not typically review/approve how monitors and sponsor representatives will have access to study records, modality of access or the study monitoring plan as a "stand alone " document, however if the IRB/EC approved protocol specified on-site monitoring visits for source data verification, then IRB/EC review and approval is required for remote source data verification.

If sites have used the language below in the privacy section of their site-specific ICFs, is there anything else that DAIDS would like IRBs/ECs to review/approve?

Site staff will have access to your study records. Your records may also be reviewed by groups who watch over this study to see that we are protecting your rights, keeping you safe, and following the study plan. These groups include:

- The US National Institutes of Health and its study monitors,

Yes, IRB/EC review and approval of the protocol is still required if on-site visits were specified as the modality of study monitoring. We recognize that the normal practice is that ICFs will state monitors and sponsor representatives will have access to study records and the modality of access is usually not included. If the ICF does not provide specifics about the process of source data review, then no changes are needed, and IRB/EC review is not required.

Some sites provided institutional rSDV guidelines in lieu of IRB/EC approval. Is this adequate documentation to conduct rSDV?

Sites should follow institutional requirements regarding submission/informing their IRB/EC of rSDV. IRB/ECs may formally approve or just acknowledge receipt of the submission. For institutions with a new or revised guideline to address rSDV that do not require researchers to obtain IRB/EC approval to transition from on site to rSDV, the site should file the applicable DAIDS memo(s) along with the institutional guidelines in the regulatory files as documentation for not seeking IRB/EC approval.

Due to the small number of documents requested for review during the next monitoring visit, the site and the monitor decided to use ZOOM for the visit to conduct rSDV. Does the site need IRB/EC approval for this as well?

Yes. For rSDV to be conducted, IRB/EC approval needs to be in place.

Our site does not have IRB/EC approval for use of the system yet, but PPD has requested participant files be sent for review. Is there an alternative system that sites have used to share participant files with PPD monitors?

Prior to the implementation of rSDV, PPD monitors were sometimes requesting various documents to be emailed for remote monitoring review, but this would only be documents with no PII/PHI. The IRB/EC approval requirement is to conduct rSDV and not necessarily for the use of a specific platform. If there is no IRB/EC approval, the monitor may have to conduct the remote visit without completing any SDV.

Is it considered adequate documentation if a site provided an e-mail communication from the IRB/EC Coordinator stating that the IRB/EC approves of using Microsoft Teams as a SharePoint site for rSDV?

IRB/EC approval documentation may vary from site to site, depending on IRB/EC guidelines, Institutional policies/procedures, Regulatory requirements, etc. The e-mail approval documentation from the IRB office will suffice. A copy of this e-mail should be filed along with DAIDS rSDV memos in the Regulatory binder as documentation of IRB/EC approval.

When the sites send POs their rSDV system selection, will it suffice for them to say that their IRB is aware / approved of the system chosen, or do they need to send more formal IRB/EC documentation?

Yes, a form of written documentation of IRB acknowledgement or approval of rSDV is required and should be filed in the Regulatory binder.