Getting Started With Remote Trial Management: Webinar Takeaways

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TransPerfect's Trial Interactive and MANA RBM have led the charge for digital and remote trial conduct over a combined 20+ years. MANA RBM CEO, Penny Manasco, M.D. recently contributed to our ongoing webinar series focused on adapting to challenges by enabling remote capabilities.

Below, are some highlights and main takeaways from Penny's responses to learn more about how to get started with remote solutions.

Electronic Investigator Site Files (eISF) & Lessons Learned

Q: Remote monitoring can mean different things to different people. Can you share how you interpret it and what you see as part of that?

A: Remote monitoring is much more than simply performing remote Source Document Verification (SDV). For instance, all of the types of review that traditionally happen on-site must now be performed remotely. Some of the areas that you must consider, based on the "errors that matter (ETM)," include:

- Informed consent review
- Certified copies of source data supporting inclusion/exclusion criteria, safety, and endpoints
- Data and processes for primary endpoint collection
- Investigational product management
- Safety assessments
- Identification of ETM and systematic errors
- GCP and 21 CFR Part 11 compliance

Remote review should identify errors and, more importantly, systematic errors. Systematic errors present a much greater risk to the study and should be identified and corrected as early as possible.

Q: What are the most important aspects of these categories that must be monitored based on risk to the study?

A: The most important areas that affect trial integrity and subject protection are as follows:

- **Human Subject Protection**: Protocol and informed consent approved by the IRB/IEC. The right version, approved by the IRB/EC, is collected before any assessments, and all processes for informed consent administration are followed.
- **Primary Endpoint Collection**—In addition to the data collected, confirmation that the process is followed: the right person performed the assessment, there was training and delegation of authority for the person completing the primary endpoint assessment (if

applicable), and the assessment was done at the right time and using the right processes. If technology is used to collect the endpoint, confirmation that the audit trail reflects the person completing the assessment.
- **Safety Assessment**—Confirmation that all assessments are completed. Safety signals or errors in safety assessments are identified and corrected.
- **Investigational Product Management**—Shipping, receipt, storage, preparation, administration, destruction, and the blinding/unblinding process.
- **Good Clinical Practice and 21 CFR Part 11 Compliance Documentation**—Includes collection and maintaining adequate subject and study records; documentation of selection process for technology systems, specifications, user acceptance testing, and final validation documentation; change management documentation and data transfer specifications.

For each of these areas, it is important to identify and correct systematic errors that occur.

Q: What is the first step you would take to convert a trial from a traditional on-site trial to one that can be performed remotely?

A: I would immediately implement an electronic investigator site file (eISF). As MANA RBM implements this process, we are able to access both regulatory documents as well as certified copies of source documents that were in other systems such as the Electronic Medical Record (EMR). This is helpful because EMRs are not 21 CFR Part 11 compliant and having complete source records in your eISF will help in the event of an inspection.

You can easily set up your eISF to protect PHI using role-based access. The study staff, monitors, and inspectors/auditors can access PHI, as defined in the informed consent, but not other study team members. That way the monitors can do a full review remotely of certified copies.

Generating certified electronic copies requires a specific process as defined in 21 CFR Part 11. It is a powerful tool and allows any document collected on paper or in another system to be certified as the same as a paper document. You can even destroy the paper document after making a certified copy, depending on your SOPs. By using certified copies stored in the eISF, you can more effectively perform remote oversight.

We cleared the process we developed with the FDA office of GCP compliance. It protects personal health information and provides remote access, based on privileges in the ICF, to documents needed for oversight. The critical aspect of using an eISF is that the study site has to have control—meaning they can see all the documents in their eISF, and they can upload and download those files.

Q: Can you use the eISF to do subject ICF review? If so, how?

A:
1. Site uploads the signed consent to the eISF.
2. During upload, document is converted to a certified copy.
3. File ICF in PHI-protected area of the eISF: assuring PHI protection.
4. Complete review of the ICF, raising questions in the document system or EDC.
5. Can be done in near real time with no delay.

Q: How can we have investigational product accountability and do compliance checks in a remote monitoring environment?

A: 1. Identify where all the information is coming from (there can be multiple systems
2. Shipping and receipt
3. Conditions at the site (temp)
4. Preparation including calibration
5. Dosing and compliance
6. Return or destruction

- Blinded or unblinded—different people, different system approach

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Q: What is the impact to sites, and how do we motivate the sites to do this? Are they expecting more money?

A: Sites are NOT the problem. We have had overwhelming endorsement from sites:

- Less space needed
- Access from remote sites
- Less duplication of efforts
- Everything is in one place
- Full records for trial are on a small disk—not in boxes in a warehouse

Q: What are the "gotcha" items that we wouldn't think to ask about?

A: 1. Structure (section 5 of DIA reference model is not enough)
2. Role access and PHI allows for protection of PHI in the eISF
3. Integration between eISF and eTMF
4. Separate archives for site and eTMF (site with PHI, sponsor no PHI)
5. Audit trail may be important; can system be activated for inspections?
6. Reports—not just what you have but what is missing!
7. Certifying documents based on 21 CFR Part 11 requirements
8. Esignature process
9. Defined requirements for system selection

Q: What are the features we should look for in an eTMF/eISF?

A: Some of the features we look for are the system's ability to

- Generate certified copies
- Integrate between eISF and eTMF
- Deliver robust role-based access and PHI protection (granular role-based access)
- Site usability
- Adequate metadata collection to allow powerful reporting
- Electronic signature functionality

Systems can be very basic with more manual processes, or they can be larger, more expensive, and automated, but both types should deliver this functionality. Remember that 21 CFR Part 11 compliance includes both system and process to meet the compliance.

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