11 Hidden Features of electronic Trial Master Files (eTMFs) to Optimize the Value of Your eTMF

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eTMFs are rapidly replacing paper trial master files in CROs, Pharmas, Biotechs, and the Device industry. An industry coalition, the TMF Reference Model (TMF RM), meeting under the auspices of the Drug Information Association (DIA), has been instrumental in developing a reference model to standardize TMF document collection and management (1).

Quinn and Ross reported on a TMF RM survey collected in Spring 2012 reported that 48% of Clinical Operations responders were using an electronic TMF. By 2015, the number had inceased to nearly 70%(2). In 2012 47% of the respondents reported an eTMF eases the burden of internal and regulatory audits and inspections and by 2015 remote TMF access for auditors and inspectors was expected to double within the next two years to 65%.

Having an eTMF for Sponsors, and Vendors and an associated electronic Investigator Site File (eISF) for sites is the most efficient and cost effective approach. The electronic document management systems hold all the documents supporting the conduct of the trial, not just the essential regulatory documents.

The 11 hidden features of eTMFs and associated eISFs are as follows:

1. Robust Access Control

   Everyone associated with conducting the trial should have access to the eTMF and know how to perform actions related to their documents and functions.

   Sites should have an eISF available. Sites need to access and control the documents within their eISF. Even if sites request a separate paper version, SOPs can be developed defining the electronic version and the official Site TMF.

   When using an eISF, there is no need to send regulatory binders, do onsite checks of site regulatory binders during site visits, or make copies to reconcile documents in the Sponsor's TMF.

   When the eTMF holds Vendor files, all documents supporting the management of the trial (e.g., Monitoring plans, EDC specifications and approval, system validations, lab transmittals, validation, and approval) are in one place and available for review and access from anywhere at any time.

2. Unlimited Roles

   When systems are designed to enable unlimited roles to fit user's needs, Sponsors and CROs achieve maximum benefit.

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Roles should determine which documents a user can see and what actions are authorized on that document (e.g., upload, read, electronically sign). This enables many users to work within the system and only access the documents related to their study function.

Roles should also include an association by study and by site. This enables the system to be used for multiple studies. Users can be associated with different sites and have different roles. Access to certain folders holder Personal Health Information can be limited to site users, monitors, and auditors.

3. Customizable archiving

   Proper archiving of documents for clinical trials ensures the documents supporting proper Good Clinical Practice (GCP) conduct and oversight are available at any time.

   With a robust eTMF, many of the documents stored in the TMF are used for study conduct but are not essential documents needed for an audit. It is essential to have a system that enables you to determine which documents will be archived for which user.

   A robust eTMF enables remote review of informed consents and other patient source documents after they have been converted to certified electronic copies. The informed consents should not be included in the Sponsor archive (unless Personal Health Information has been redacted), but are a key component of the Site archive.

4. Missing Essential Documents Report

   Knowing which documents are required within the TMF and site's eISF is one of the biggest challenges to TMF management. While locating the documents expected at the start of the study is simple, finding new required documents based on the changes that occur during trial conduct presents a challenge if there is not a systematic way to capture what new documents are required based on changes in the study.

   Creating a dynamic report that adds new essential documents based on actions within a trial saves time, cost, and ensures a more complete TMF for both the sites and the Sponsor. It is also a powerful compliance tool to alleviate errors that may occur when there is staff turnover.

5. Electronic Notifications

   Electronic Notifications save time and enhance cross-functional communications. When you use a common eTMF across different functional teams, electronic notifications assure each team member can take action quickly.

   For instance, if all documents are stored in the eTMF to enable approval to ship the Investigational Product (IP), the team member responsible for approval can be notified electronically when all the documents are available

in the eTMF. This eliminates the time needed to collate a separate email with all the documents required to approve IP shipment.

Investigators are notified if there is a new IND Safety Report, eliminating the need for a separate overnight mailing and all documentation remains in the same system.

Coordinators can be notified if a document needs to be changed or if a document is going to expire.

6. Electronic signatures

   Electronic signatures can significantly enhance the value of an eTMF system. Electronic signatures linked to a document having full audit trail and customizable language associated with the electronic signature eliminates the need for wet signature documents. This saves significant time and cost and assures all documents remain together.

   Electronic signatures should be available to multiple roles based on the specific document (e.g., Principal investigator, Study Coordinator certifying electronic Source). When many users can sign different documents within the eTMF, it can be used for multiple tasks such as certifying electronic source or signing contracts or 1572's.

7. Managing Communications

   Collating and searching email, electronic, and paper communications associated with a trial is a complex and costly component of the eTMF. When selecting a system, it is critical to determine specifically how you will manage this component of the eTMF and eISF.

8. Robust, Flexible Reporting and Search Capabilities

   You cannot underestimate the value of reporting and search capabilities in an eTMF or eISF. You need the capability to search documents that are going to expire, documents of a certain type, documents from a specific site, or documents that have been uploaded within a timeframe. eTMF/eISF utility strongly correlates with its reporting and search capability.

9. Account Management

   Account management is a critical hidden feature. It that has a huge effect on effectively and efficiently using the eTMF.

   For example, does the system enable the validation of each role at the time the system is set up? If so, adding a new user to a role is extremely fast and efficient. This approach also eliminates errors, since the role goes through a full validation process during the User Acceptance.

   Additionally, can users be easily added to a new study? How can the training documents from one study be transferred to another study, saving the user from undergoing a second round of training?

The eTMF account management should identify the investigational products (IP) each site user is studying. This is extremely valuable when IND Safety Reports or Periodic Safety Update Reports are posted in the eTMF.

10. Metadata

    Metadata are the associated data linked to the document in the eTMF. It includes the date and time the document was uploaded, the person who uploaded the document, and the status of the document. Additional metadata helpful to the CRO or Sponsor include data on the Trial number, Investigational Product, Phase, Indication, Country, and Site number (for site specific documents).

11. TMF Processes

    The largest cost and time savings are achieved by carefully evaluating the process for collecting, reviewing, and managing the TMF.

    For instance, instead of having documents collected by monitors during a site visit, the process can be streamlined to have a team member collect the documents proactively, directly from the site, independent of the site visit. With this approach, monitors have more time to conduct training, have meetings with the Investigator, and trial documents are kept up to date throughout the trial.

As you define your requirements for a single study or a system to support an entire organization, evaluate the hidden features and your processes to get the most value for your clinical research dollar.

References:

1. Drug Information Association Special Interest Area Community for Trial Master Files. Version 1.2 released December 2011. http://www.diahome.org/en/homepage/EDM+Corner.htm
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