A Data Reduction Systems White Paper by James Peters, Director of Professional Services

Implementing an eTMF is not enough. To ensure 24/7 inspection readiness, it must be supported 24/7 by Good Documentation Practices and Risk-Based Monitoring.

February 15, 2018 -- *Migrating essential study documents from a paper-based TMF to an electronic TMF (eTMF) does not automatically relieve sponsor companies from the responsibility of performing certain mandated tasks. Documents, for example, must still be carefully reviewed to make certain they are collected, complete and correct. DRS has seen far too many eTMF transitions go afoul due to sponsors becoming overly dependent on the application and on the submitters' ability to send documents in proper filing condition. Good Document Practices (GDP) requires every document filed in an eTMF to be reviewed for completeness and correctness. The eTMF should (a) produce reports which clearly identify duplicate and/or missing documents and (b) then provide a mitigation process for remediating documents with issues.*

eTMF Background

Prior to 1997, digital media and electronic formats were not acceptable to the FDA. To be compliant, all information stored in Trial Master Files had to be comprised of paper and filed in cabinets. In response to industry requests, the FDA enacted regulation CFR 21 Part 11, which supported the use of electronic records, digital media and digital signatures for use in clinical trials.

Previous Options

As documents began to be collected electronically, they were often stored in tree structures within a shared drive. Occasionally, documents were printed at the conclusion and a paper file was gathered to have a clean file. In those cases, separate spreadsheets were often provided for inventory checks and to assist in searching for missing documents.

Although this showed inventories, it was a manual process for identifying documents collected and then documents missing. The process was often performed at the end of studies and not in an aggressive manner during the conduct of the study.

Additionally, as electronic capture of documents was entered, the following of a naming convention would not be 100% accurate among most document creators and collectors. Closed studies with no or limited partners aside, document collection has demonstrated to not be 100% accurate for defining and differentiating documents.

In the paper world, it was easier to ID individual documents. For example, documents assembled as a packet were stapled, clipped, etc. As they passed through visual inspection, it was quite obvious if they were missing pages, signatures and dates.

Problem Statement

Without GDP, RBM and DRS, an eTMF alone cannot ensure and/or remedy:

- Correctness -- Missing pages, image rotation, pages out of order, poor image quality and missing translations
- Duplicate Identification -- How to ID duplicates with different names
- Submission Difficulty -- Relying on many to submit and file documents following uniform guidelines
- End of Study TMF Cleanup

DRS eTMF was developed with built-in mechanisms to capture and report on poor document submissions and to assist sponsors with vendor reporting. It is a system based on over 30 years' document management expertise particularly in the areas of collection, indexing and the QC of extraordinarily large numbers of documents utilizing Risk-Based Monitoring.

DRS eTMF
TOTAL TRIAL MASTER FILE SOLUTIONS

DRS eTMF Reporting Benefits

- Proactive Risk-Based Monitoring of document inventory
- GAP analysis
- Submission analysis
- Submission timeliness
- Duplicate identification

Mitigation Benefits

- Document Review
- Document issue identification
- Document resolution
- CRO partner training

Inspection Ready Benefits

- Speed of closeout at end of study
- Collection of documents regularly during study conduct
- Documents in good order when audited

Implementation

- DRS eTMF combines the application and services for a great eTMF
- Structure that allows GDP disciplines
- Quality documents
- Tier 3 Certified Data Center to manage the study archive
- Standardized structure incorporating both sponsor and DIA guidelines
- Rapid rollout
- Agile software updates and version releases
- Ability to incorporate Services as required to manage and review TMF
- New tools can be incorporated to manage collection

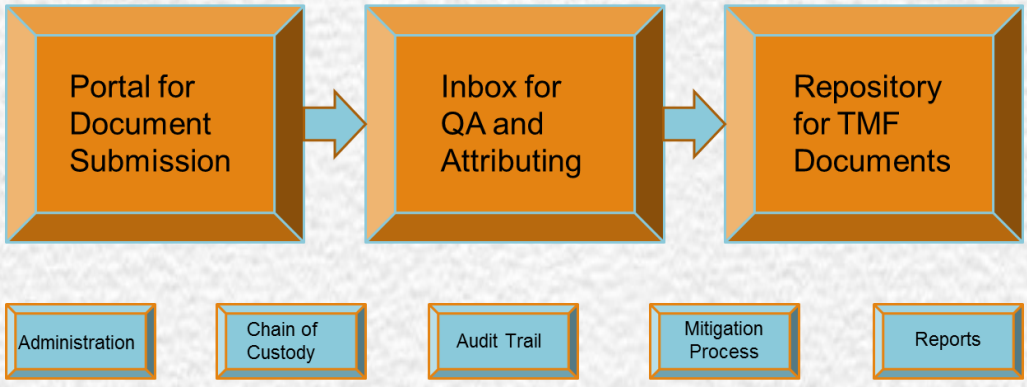
DRS eTMF
Designed **to deliver document collection accuracy.**
Developed **to ensure 24/7 inspection readiness.**

Lest We Forget...

During regulatory agency inspections, including those conducted by the FDA...

"The Agency intends to exercise enforcement discretion with regard to specific part 11 requirements for generating copies of records in each case, we recommend that the copying process used produces copies that preserve the content and meaning of the record. If you have the ability to search, sort, or trend part 11 records, copies given to the Agency should provide the same capability if it is reasonable and technically feasible. You should allow inspection, review, and copying of records in a human readable form at your site using your hardware and following your established procedures and techniques for accessing records."

www.fda.gov/downloads/regulatoryinformation/guidances/ucm126953.pdf - 89k - 2013-07-15



Reportable Document Status -- Present and Missing

Current **Centralized** **Mitigated**

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DRS DATA REDUCTION SYSTEMS
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