



A 15-MINUTE GUIDE TO CLINICAL TRIAL DOCUMENT MANAGEMENT AND THE eTMF

FOREWORD

For you as an executive in the life sciences industry, time is a precious commodity. When you need to know something, you need that knowledge in a form that can be assimilated quickly—forget the mind-numbing detail and get to the point.

With that in mind, we've developed our series of 15-minute guides to essential topics in information technology. This guide focuses on the challenges presented to pharmaceutical companies that need to plan, collect, track, assemble, distribute, secure, and archive clinical trial documentation: the trial master file (TMF). The fact that most companies outsource a significant number of trials to contract research organizations (CROs)—a trend that's been growing for more than a decade—simply adds another layer of complexity to the task.

In this guide, we'll take about 15 minutes to examine the benefits of managing the TMF electronically (eTMF), looking at the impact of an eTMF before, during, and after the trial. We think you'll agree that it will be 15 minutes well spent.

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TMF STANDARDIZATION AND ETMF SOLUTIONS

At the Drug Industry Association's (DIA) annual meeting held in June 2012, the TMF Reference Model Working Group released TMF reference model 2.0, which included significant updates from the group's 2010, 1.0 release. The reference model is not mandatory, but it is gaining wide acceptance in the industry. And the working group made clear from the outset that this effort is purely about standardization. It does not endorse any technology or application, and the model can be applied equally well to an electronic or paper-based TMF.¹

Nevertheless, many trial sponsors are considering eTMF solutions for the same reasons that organizations eschew paper-based information management in other domains. Well designed digital document management can be cheaper, faster, more secure, and more accessible, as well as easier to automate. Although no standard exists for eTMF offerings, EMC believes that a sensible approach to eTMF solution design rests on the TMF reference model.

SETTING EXPECTATIONS—WHAT ETMF SOLUTIONS CANNOT DO

Eager to jump on the eTMF bandwagon, software vendors tend to exaggerate the scope and power of eTMF technology. For example, it's often claimed that an eTMF solution can track "trial status" and inform go/no go decisions about drug development. No, it can't.

Trial status concerns trial data and an eTMF doesn't touch the actual trial data. It's not a trial data analytics platform. What an eTMF solution can do is communicate the status of trial documentation, which is vital and necessary. Likewise, eTMF evangelists assert that eTMFs can reduce trial risks—identifying and stopping ineffective or harmful trials early. Again, no. That's another job for trial data analysis, not trial documentation management.

MANAGING TRIAL DOCUMENTS FROM START TO FINISH

The foregoing while true does not negate the tremendous value eTMF solutions can provide to trial sponsors and other stakeholders. In fact, a well designed eTMF can accelerate trial set up, deliver comprehensive document visibility during the trial, and streamline access to trial documents at the conclusion of the trial.

BEFORE THE TRIAL: ACCELERATING TRIAL START UP

Since a clinical trial cannot begin until the pharmaceutical company sponsoring the trial receives Institutional Review Board (IRB) approval of essential trial documents, it's important to speed the collection, completion, and review of those documents. An eTMF can support this process by

- Providing templates based on the TMF reference model that define a logical document structure and create placeholders for required documents
- Identifying missing documents and alerting the responsible parties
- Simplifying document review and approval via automated workflows

¹ http://www.contractpharma.com/issues/2011-05/view_features/cros-and-the-tmf-reference-model/

DURING THE TRIAL: IMPROVING TRIAL DOCUMENT VISIBILITY

During the trial, an eTMF enables the trial manager to synchronize documents across investigational sites and provide role-based access and visibility to sponsors, CRO staff, and IRB members. It can also track inspection readiness and trial status against defined milestones. For example, when changes are made to the trial protocol, an eTMF can vastly simplify the effort required to route the protocol amendment and supporting documents for IRB approval. Such changes can stall a trial for weeks or months. Eliminating a “paper chase” minimizes the delay, saving time and money. In addition, eTMF solutions with a standards-based integration layer can be connected to clinical trial management systems (CTMS), which contain site and investigator information, trial metadata, and milestones.

AFTER THE TRIAL: SIMPLIFYING ACCESS AND RETRIEVAL OF TRIAL DOCUMENTS

The trial master file lives on long after the trial is completed. Some documents from the TMF must be sent to regulators as soon as the trial is completed and also linked with future submissions to obtain marketing authorization. When the CRO transfers the TMF to the sponsor, the sponsor must retain it for a minimum of five years and make it available for regulatory agency inspections.

Of course, an eTMF makes transferring the file and responding to subsequent requests for documents much simpler. A paper TMF can be massive and brings with it ongoing costs for storage and handling. Moreover, agencies are starting to request direct access to the TMF for on-site and remote inspections.

An eTMF provides rapid document search and retrieval, especially when the eTMF structure adheres to the TMF reference model. Access and retention policies can be set and enforced automatically.

AN ETMF SOLUTION CAPABILITIES MODEL

As no eTMF solution standard exists, what capabilities should an eTMF offer? We believe an enterprise-class eTMF should enable clinical trial teams to easily and effectively track progress in trial documentation, control and synchronize study artifacts, and deliver fast, secure access during and after the trial. To do that, it should provide governance, tools, document control functionality, and embedded industry models for consistent document handling across the entire life sciences product lifecycle. These capabilities will fall into several categories.

FUNCTION-SPECIFIC INTERFACES

Trial managers, clinical document authors, trial librarians, and clinical investigators should have function-specific interfaces to the eTMF. In addition, mobile clients for laptops, tablets, and smart phones will soon become basic requirements in eTMF solutions.

VISIBILITY INTO TRIAL DOCUMENTATION STATUS AND RISK MANAGEMENT

CROs need the ability to set up trials quickly by reusing configuration templates, and maintain trial, country, and site-level artifacts with recommended, required, or optional classifications. The solution needs to provide tools that support trial management across multiple stages, using milestones and automated progress tracking and notification against first-patient-in/last-patient-out planning.

These tools help trial managers assess and avoid the risk of trials delayed by lack of documentation or documentation that does not comply with regulatory guidelines. They provide automated risk assessment of documentation progress and notification of status changes.

AUTHORING AND CONTENT MANAGEMENT

Clinical document authors and trial librarians require a full range of content management features to quickly search for and identify missing or redundant content, replace placeholders with documents, mark recommended content as omitted, and capture audit-worthy justifications for those omissions.

SECURITY AND ACCESS CONTROL

In addition to function-specific user interfaces, the eTMF security and access control protocols should restrict access to documents by function and individual authorization level. Read-only views reduce access control maintenance overhead. Agency inspectors can be allowed controlled access to the eTMF so they may review it for completeness and compliance with GCP.

MANAGEMENT REPORTING

Reporting is an important part of what trial managers do. The need for reports includes document status/missing documents, trial progress, and summary of trial status by country and site. Managers need the ability to add reports, automate production and distribution, and control style, layout, and output format.

INTEGRATION

A services layer that supports integration of the eTMF with a sponsor's or CRO's CTMS can solve certain issues more effectively than either system in isolation. For example, data concerning the trial, sites, and milestones can be consolidated in one system and then shared with another.

DOCUMENT CAPTURE

Since the source of many trial documents will be paper or electronic file systems, the eTMF should provide for bulk electronic capture, validation, and ingestion of file system documents.

THE BENEFITS OF A BROAD APPROACH TO DOCUMENT MANAGEMENT FOR LIFE SCIENCES

Of course, life sciences companies face stiff controlled document management challenges in areas other than clinical trials, such as research, manufacturing, quality control, submissions, drug safety disclosure, and promotional materials. EMC believes the technology and processes that create the foundations for solid document management must span the extended, virtual enterprise and the product lifecycle. And that requires a broad approach that can accommodate a range of narrower, domain specific solutions.

We also believe that this approach will help life sciences organizations reduce the overall cost of compliance, simplify collaboration with external partners and inside their own organizations, and improve the organization's ability to meet regulatory demands. A broad approach, built around emerging DIA standards known as the electronic document management (EDM) and TMF reference models, is the most effective way to deliver the control and ease of use that ensures consistent, ubiquitous compliance with document handling requirements and regulations across the document lifecycle within every part of the organization regardless of domain. As the reference model is extended, a standards-based, extensible platform can be configured to support additional applications.

EMC DOCUMENTUM FOR THE LIFE SCIENCES

EMC has many years of experience in the life sciences industry. The EMC Documentum-based life sciences solutions deliver a unified, configurable document control platform for compliance with industry regulations. The foundation of these solutions includes the Documentum enterprise content management platform, Documentum D2 for configuration and intuitive user interfaces, and implementation and migration services. The D2 configuration technology enables auditing, reporting and e-signature support for compliance, lifecycle management and document control services, and industry-specific modeling capabilities all designed for life sciences.

About EMC

EMC Corporation (NYSE: EMC) is the world's leading developer and provider of information infrastructure technology and solutions that enable organizations of all sizes to transform the way they compete and create value from their information. Information about EMC's products and services can be found at www.EMC.com.

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