Look to the Cloud to Save Time and Money

With regulatory pressure mounting, pharma companies may decide to migrate to paperless trial master files. Rik van Mol outlines the key considerations for making the transition to a fully-fledged, cloud-based eTMF.

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In recent years there has been a particular focus on applying technology (particularly cloud-based tools) to the challenge of running costs and time-efficient trial processes.

So what are the issues that waste time and leak value from the drug development process? In 2010, McKinsey & Company published a report that found mismanagement of the trial master file (TMF) was responsible for slowing down trials by an average of 12 months, costing providers up to $2 bn in lost revenue for a blockbuster therapy. Bearing these staggering figures in mind, it is little surprise that technology promising to bend both the time and cost curves down is an attractive alternative for a cash-strapped and time-poor industry.

Despite these economics,

a recent study of trial master file owners across the pharma, biotech, and life sciences industries finds that just 13 percent of drug developers have adopted purpose-built electronic trial master files (eTMFs).

The study by Veeva Systems sought to understand the barriers preventing drug developers from taking advantage of eTMF applications that would streamline many of the inefficient processes that can slow clinical trials.

The results highlight some of the common challenges companies face when undergoing major transformations in their business-critical technology, but also illuminate the long-term benefits pharma and biopharma companies stand to gain from making strategic investments in paperless TMF.

However, recognizing the efficiencies that an eTMF application offers an organization is one thing. Transforming an eTMF into a truly strategic asset capable of improving the bottom line is another matter. To extract the full potential of an eTMF, a life sciences organization must take a few important steps with the partner, the application itself, and their own organization. These include:

Getting everyone on board

According to the study, 69 percent of respondents say they rely on email to exchange trial documents with sponsors or CRO partners. The biggest hurdles companies face when making the transition to paperless TMFs is the creation of a collaborative system that all stakeholders in the drug development process can access easily and securely.

Even when the sponsor and/or CRO maintain an eTMF on their own network, access to outsiders is blocked. In this scenario, stakeholders send documents via paper shipments or email and maintain separate copies of TMF documents, which need to be reconciled at the conclusion of the trial.

Alternately, a cloud-based eTMF is, by its very nature, easily and securely accessible to all parties. Sponsors can define new processes that are more efficient upfront, maintain visibility throughout the trial, and help ensure that the TMF remains inspection ready at all times. This type of collaborative and open process begins by uploading a document into a cloud eTMF in real time.

Eldin Rammell, a clinical records management expert and managing director at Rammell Consulting, says the research confirms that not all eTMFs are created equal. "Many eTMFs are simple file shares that perpetuate manual processes."

According to our research, firms using mature technologies, specifically process-driven eTMF applications and content management systems, report good or major improvement in misfiled documents, compared to 62 percent of local file system users. Yet, today approximately only one in 10 respondents (13 percent) use eTMF applications to manage their TMFs. Moving from "simple file share" to a repeatable, cloud-based eTMF framework improves quality and decreases non-compliance.

Because all parties have direct access, physical distribution of content becomes obsolete, eliminating the need to email copies of documents as attachments. Managing collaborative processes within the eTMF combines information exchange and tracking into a single system. Not only does collecting TMF documents become more efficient, but all parties gain visibility into status and outstanding tasks.

When developing a CRO-sponsor shared eTMF, both parties must establish time frames for completing management milestones, as well as roles and responsibilities for execution. In many cases, the responsibility for filing TMF documents and other content will shift from a records management function to the author/owner of the TMF.

Processes That Would Shorten Clinical Development Times if Paperless

Process	Percentage
Study/Site Start-up	64%
TMF Filing	54%
Study Planning/Protocol Authoring	43%
Country Start-up	31%
Country/Site Feasibility	30%
Site Close-out	28%
Study Close-out	26%
Drug Accountability	25%
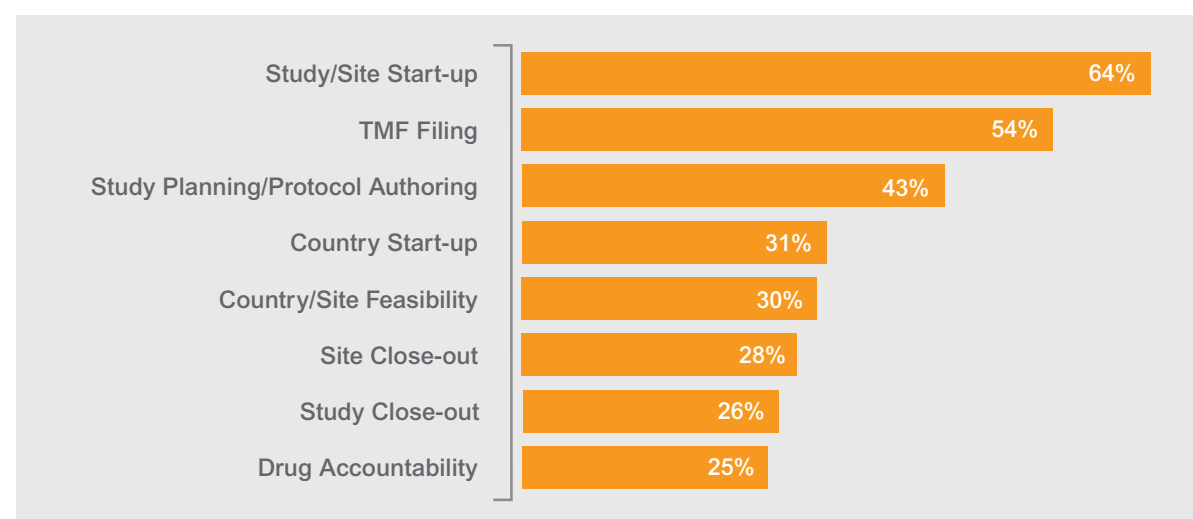
*Source: Veeva Systems, The Paperless TMF, An Industry Benchmark 2014

Managing a successful process change is critical for gaining many of the benefits associated with using an eTMF. Because of this, establishing a repeatable framework is an important part of the change management process.

Defining each stakeholder's role is also critical to successful outsourcing, finds an Avoca Group survey of 237 respondents. Collaborative relationships "require absolute clarity in roles and responsibilities and upfront planning assumptions," Avoca states. Typical clinical collaborations have lacked this clarity, sometimes resulting in difficulties and disappointment in the relationship.

Building a stable and replicable model

Building a repeatable TMF framework involves defining expectations upfront to ensure that all TMF participants are aligned and in agreement on what the TMF artifacts are called, when they are due, and who is responsible for filing them. In order to know what content is missing or late, all contributors must first understand what is expected. A repeatable framework sets expectations at the outset, reinforces the collaborative process, and improves overall efficiency.

Standardizing a common nomenclature drives better communication by harmonizing the filing efforts of diverse stakeholders. When multiple parties refer to items by different names, filing and tracking become confusing, increasing the chance for error.

The nomenclature defined by the Drug Information Association's (DIA's) TMF Reference Model represents input from hundreds of pharmaceutical companies, CROs, regulatory agencies, and vendors from across the globe. In addition to standardized naming, the TMF Reference Model introduces standards for content, structure, and metadata. For these reasons, more and more clinical trial sponsors, including Kythera, are leveraging this model to build their own repeatable frameworks.

Additional elements of the repeatable framework include operationalizing SOPs by configuring them within the eTMF application, essentially codifying them into system workflows. The eTMF application orchestrates task completion across companies and stakeholders, in keeping with company SOPs. A common workflow automates many manual steps, improving productivity and trial efficiency.

By comparison, a paper-based TMF or eArchive relies on people remembering and following written SOPs and then documenting them.

When collaborative processes are coupled with a repeatable framework, the foundation is in place to begin defining and leveraging performance metrics.

Avoiding non-compliance

To meet the audit expectations of health authorities globally, more organizations are considering adopting eTMF applications. The trend can be likened to the industry's move from paper case report forms (CRFs) to electronic

data capture (EDC) a decade ago. The growth trend here is reflected in our research, which finds that companies with full eTMFs are twice as likely to report audit-readiness as their peers relying on manual or paper-based TMF systems.

eTMF reports such as study site document status, site acknowledgement of investigators' brochures, and document expiration can all help inspection readiness by providing greater visibility into what stages of the trial process are being inefficiently run, and what the trial owner can do to course correct.

These common, trial-specific metrics — efficiency and completeness — establish a baseline for improvement, allowing managers to look at metrics in an organized way, as opposed to extrapolating from paper-based processes. However, as more data is collected over time and across multiple trials, it also becomes possible to identify trends.

These benefits are being realized by eTMF operators in Veeva's study. Those companies that extensively leverage metrics to improve the execution and/or design of trial processes are more than twice as likely to report business improvements from their eTMFs as those not using metrics.

These advantages include better TMF document quality (63 percent and 29 percent, respectively), audit readiness (56 percent and 25 percent, respectively), and increased SOP compliance (49 percent and 16 percent, respectively).

eTMFs allow TMF owners to define standard operating procedures (SOPs) for how any clinical document is managed, and therefore flag any mismanagement early. By creating rules and definitions for SOPs, the eTMF creates ways to track application workflows and identify noncompliant processes before the TMF is put before regulators for approval.

Our research finds that even particularly in the early stages of clinical trials, TMF owners with cloud-based eTMF applications are already improving the

DIA and EMA's submission processes.

This is unsurprising when one considers that e-submission protocol was developed in conjunction with the DIA and EMA. Companies making the transition to paperless can speed up the submission and approval process by researching potential eTMF providers to ensure that the systems they choose have been designed to align to both the letter and the spirit of electronic filing regulations.

Act now — save time and money

The urgent need for greater visibility into study conduct and the economic incentive to speed up trial times are driving the pharma industry's growing use of new technology.

Setting aside the staggering costs of failing to maximize sales opportunities as regulators set the bar higher for SOP compliance and prepare their own systems for electronic submissions, the actual costs associated with maintaining a

paper-based clinical TMF are steadily rising.

Early adopters of eTMF technologies experience greater inspection readiness, visibility, SOP compliance, and cost savings from their eTMFs than those using local or cloud-file systems.

As CROs work to demonstrate their value and keep their contracts, they have the opportunity to influence study design and prove their fees by helping sponsors eliminate excess secondary elements.

No matter what complex protocols sponsors put into place, CROs, as objective service providers, can help sponsors move toward more efficient and effective trial designs, and they will have the data to demonstrate the risks of poor trial design.

About the Author

Rik van Mol is Vice President of R&D Strategy at Veeva Systems.