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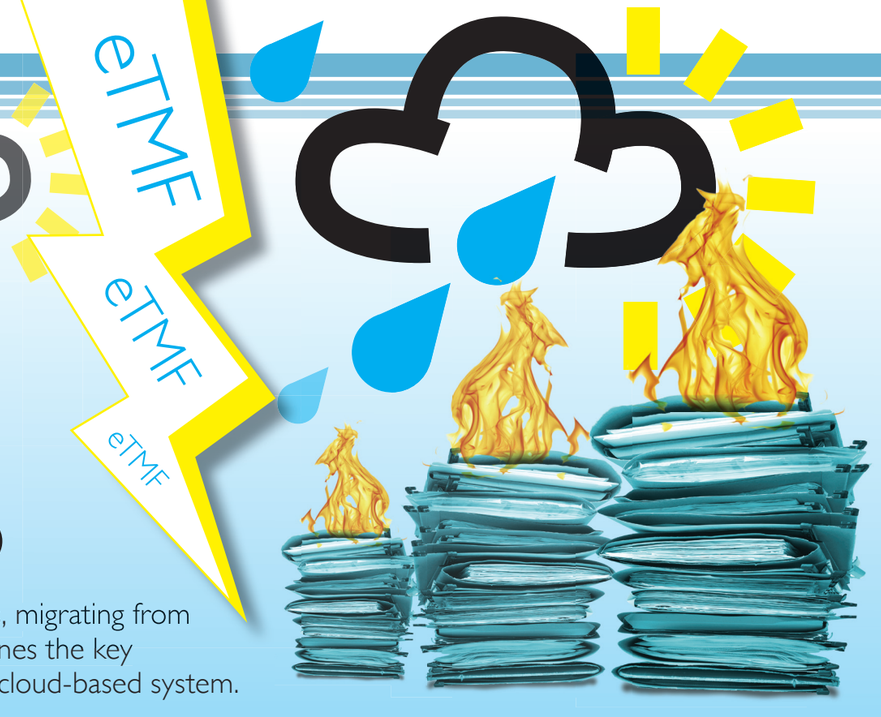
Changing conditions



With regulatory pressure mounting on pharma companies, migrating from paper to trial master files is a no brainer. Rik van Mol outlines the key considerations for making the transition to a fully-fledged, cloud-based system.

Time is money, and never has the cliché been more apt. With biotech pioneers spending an average of 10 years and more than $1.2 billion on bringing a new therapy to market, in recent years there has been a particular focus on applying technology - particularly cloud-based tools - to the challenge of cost and time-efficient trial processes.

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 $2bn in lost revenue for a blockbuster therapy. Bearing these staggering figures in mind, it is little surprise that technology which promises to bend both the time and cost curves downward is an attractive alternative for a cash-strapped and time-impoverished industry.

Despite these economics, a recent study of trial master file owners across the pharma, biotech and life sciences industries found that just 13% of drug developers have adopted purpose-built electronic trial master files (eTMFs). The study - carried out by Veeva Systems - sought to understand the barriers preventing drug developers from taking advantage of the eTMF applications that would streamline many of the inefficient processes that can so often slow down 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.

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

Everyone on board

According to Veeva's study, 69% 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 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," he said.

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

Due to all parties having 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 have visibility of current 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.

Managing a successful process change is critical for gaining many of the benefits associated with using an eTMF. Therefore, 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 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 artefacts are called 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.

Standardising a common terminology drives better communication by harmonising the filing efforts of diverse stakeholders. When multiple parties refer to items by different names, filing and tracking inevitably becomes confusing, increasing the chance of error. The language 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 naming, the TMF reference model introduces standards for content, structure, and metadata.

Additional elements of the repeatable framework include operationalising standard operating procedures (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 in the process. By comparison, a paper-based TMF or eArchive relies on people remembering and following written SOPs.

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 organisations 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 Veeva's research, which finds that companies with full eTMFs are twice as likely to report audit-readiness as those 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 rectify the situation.

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

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% and 29%, respectively), audit readiness (56% and 25%), and increased SOP compliance (49% and 16%).

eTMFs allow TMF owners to define standard 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.

Veeva's research finds that even 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, ensuring that the systems they choose have been designed to align with both the letter and the spirit of electronic filing regulations.

Act now – save time and money

The urgent need for greater transparency and the economic incentive to speed up trial times are driving the pharma industry's growing use of new tech.

Notwithstanding the staggering costs of failing to maximise 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 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

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