The Key to Inspection Readiness: Using Your eTMF as a Process Tool

Any clinical team for a sponsor or contract research organisation (CRO) can relate to the long hours and sleepless nights leading up to the inspection of a trial master file (TMF). Paper-based processes, still prevalent in many clinical operations, result in inefficiencies and errors in exchanging and storing accurate trial documentation. It’s not surprising, then, that more life sciences companies are adopting electronic TMF applications to improve inspection readiness.

Drug makers have further incentive from the Medicines and Healthcare Products Regulatory Agency (MHRA) to find a solution to the longstanding problem of maintaining accurate, audit-ready clinical trial documentation. With more than one-third of TMF inspections experiencing unnecessary delays due to incomplete or inaccessible files, the MHRA has issued updated guidance that clarifies regulatory expectations for accessibility, availability, and completeness of TMFs.

The good news is that there are measurable advances in the industry’s move away from paper and the number of companies adopting eTMF systems, according to the Veeva 2015 Paperless TMF Survey. Speeding study start-up (56%), cost savings (53%), and improved audit and inspection readiness (45%) are cited as key drivers for eTMF adoption this year, which is consistent with last year’s survey findings.

Paper and Digital Process Maturity
This year’s survey charts the industry’s continued progress towards removing paper from TMF processes – a critical step toward improving accuracy, efficiency, and inspection readiness. Today just 31% of respondents report that their clinical operations departments are managing “most or all” of their TMF documents on paper, down from 43% last year.

Email remains the dominant method of exchanging TMF documents between sponsors and CROs (70%). However, the least efficient means of exchanging documents – paper and faxing – saw the greatest declines in their usage compared with 2014. Only 13% of respondents report using faxing (down from 25% in 2014), and 47% use paper (down from 57% in 2014). On the other end of the spectrum, use of eTMF applications to exchange documents between sponsors and CROs has increased by 24% of respondents, compared with 15% in 2014.

The survey shows a shift to adopt more paperless processes, with more than half of respondents (59%) reporting that they “mostly or always” archive TMF documents electronically. Although this is a good start, fewer organisations are performing other key processes electronically, including e-signatures (21%), source document creation (25%), and external collaboration (30%).

However, the majority of respondents see benefits in moving to paperless processes. For instance, more than 63% of those surveyed say they believe managing TMF filing in an eTMF would shorten clinical development time, while 57% believe managing study/site start-up in an eTMF would shorten development time. Respondents also cite audit response (39%) and inspection preparedness (38%) among the processes that would benefit if they were managed with an eTMF.

Success Factors of Next-generation eTMFs
The motivation to move towards electronic-based processes is clear, yet the survey illustrates that life sciences companies have considerable variation in eTMF technology adoption. Many well-intentioned companies are moving their paper TMF systems onto simple file shares or document management systems that are little more than electronic archives or were previously paper-based documents. So although companies may be moving to electronic systems, the process for managing and exchanging TMF documentation is still managed through traditional paper-based processes, which doesn’t unlock the full potential of an eTMF.

It is clear that not all eTMFs deliver the same level of business and operational benefit. This year’s survey shows that eTMF adoption remains distributed across the maturity spectrum. In fact, 55% of respondents report that their TMFs are little more than archives (file share, local file systems, paper), and nearly 28% report using content management systems. Of the respondents, 18% use eTMF applications, which goes beyond archiving to manage business processes.

When we look at the key reasons survey respondents are moving to purpose-built eTMF applications, the benefits fall into the following categories:

Improved audit and inspection readiness. The majority (61%) of respondents that use purpose-built eTMF applications report improved inspection readiness. Unlike purpose-built eTMF applications, other types of eTMFs lack the robust functionality and built-in controls that support workflows throughout the study. Only eTMFs can automate workflows to ensure standard operating procedure (SOP) adherence at all times during a study, plus provide robust reporting for deeper insight into trial activity.
Comprehensive trial documentation, with fewer incomplete or missing documents. Going a layer deeper into inspection readiness, survey respondents report that eTMF applications offer significant improvements in most areas, eliminating misfiled (65%) and duplicate documents (60%). This issue is not specific to companies reliant on paper. It also applies to those that use early eTMF systems. Few cloud file-share users have achieved significant inspection-area improvements. For example, only 13% of respondents using cloud file shares report significant improvement in eliminating duplicate documents. Inspectors report finding documents stored in multiple repositories and different formats, with little version control. Purpose-built eTMF applications enable a single source of truth across all parties to ensure that all documents are up to date and in one location.

Improved central/remote monitoring. By an almost two-to-one margin (48%), respondents using purpose-built eTMF applications have seen improved central/remote monitoring compared to other types of eTMFs. For example, only 13% of respondents using cloud file shares report significant improvement in eliminating duplicate documents. Inspectors report finding documents stored in multiple repositories and different formats, with little version control. Purpose-built eTMF applications enable a single source of truth across all parties to ensure that all documents are up to date and in one location.

Better visibility into performance. In total, 42% of survey respondents cite better visibility into performance as a benefit of adopting an eTMF. Performance metrics play an important role in helping auditors ensure that sites adhere to study protocols and SOPs. Simple file shares and generic content management systems cannot provide critical insight into the clinical development process. In contrast, purpose-built eTMF applications offer better visibility into performance metrics, with real-time reporting and dashboards that provide in-process views of the trial.

Finally, forward-thinking organisations are unlocking the benefits of TMF metrics to improve trial processes. Respondents that report extensive use of performance data have seen markedly more benefits from their eTMF systems than those that did not collect metrics. For example, these organisations note greater audit and inspection readiness (82% versus 25%), easier collaboration with sites (41% versus 25%), and faster study start-up (41% versus 8%). Access to trial data at the click of a button means sponsor company auditors and inspectors benefit hugely from paperless eTMFs. According to Veeva’s most recent survey, over half (53%) of companies using next-generation eTMFs consider improved central or remote reporting a major business benefit.

Leveraging the Latest eTMF Technology to Improve Inspection Readiness and Clinical Processes

Sponsors are calling out for improved communication and document exchange between sites and with their CROs. The result is that more and more CROs are including some form of modern eTMF support in their proposals. Investing in a robust, accessible eTMF solution to support clients across continents is business critical for CROs to remain relevant in a competitive marketplace. CROs that have migrated to next-generation eTMFs are...
realising the cost and time savings that come from a streamlined, automated system for sharing and storing all trial documents. Rather than spending weeks working with a client to prepare the TMF for inspection, CROs can use this time to analyse trial data and gain new insight to share with sponsors.

Cloud-based eTMFs are well suited to support this type of paperless environment, as they offer the highest level of collaboration across a diverse set of participants. Sponsors ensure consistency and adherence to process controls by creating documents directly in the eTMF system. With multiple parties submitting information to the TMF remotely throughout the lifecycle of the trial, automated standards are in place to ensure quality up front. Missing documents are brought to sponsors’ attention throughout the trial, and incomplete documentation is identified early in the process and sent back to the study team for immediate correction. A sponsor’s ability to quickly identify and rectify errors means that quality control is built into the process. The result is a TMF that is always inspection ready. Renee Fate is a senior manager responsible for document management at Kythera Biopharmaceuticals, a clinical-stage biopharmaceutical company that develops therapies for the aesthetic medicine market. Fate said that Kythera’s new eTMF system provided the rapidly growing company with a single platform on which to collaborate with partners efficiently and ensure inspection readiness at all times. “Since adopting a cloud eTMF, we’ve been able to shave at least 40% off the time needed to reconcile TMF documents at the conclusion of a trial. Now we have full visibility and can track the status of the TMF in real time for the duration of the study.”

One of the biggest challenges that sponsors and CROs have faced when implementing eTMFs has been getting people to use them. Typically, eTMF and content management systems have proven overly complex and cumbersome to navigate. Over the last year, more sponsors have started implementing improved eTMF systems with simplified operations to satisfy inspectors’ ease-of-use requirements.

The opportunity is for an eTMF to become an integral part of the clinical trial process workflow, ensuring that study findings are reported in real time and status reporting is more accurate and effortless. Real-time insight into trial progress allows the entire team to use data to make better decisions. Over time, trials that are more real-time data-driven will result in more efficient trials and faster time to market. Kythera’s eTMF solution allows the internal auditor to regularly run a full range of standard and ad hoc reports, giving a more accurate view of trial progress. According to Fate, “When everyone has visibility into the reports, it removes a lot of questions at team meetings and time spent on the phone with our CRO. We are all spending less time meeting and more time working.”

Automated filing and accessible data-sharing systems mean that internal auditors have the opportunity to redefine their roles and do more with less. Cloud eTMF solutions allow auditors to manage the quality of TMFs remotely and in real time, ensuring compliance without the need to visit multiple sites and spend weeks at a time on the road.

“In the past, our auditors were used to waiting 48 hours or longer for a box to arrive from off-site storage, only to find that it didn’t contain the desired document,” Fate said. “Today, the correct documents are retrieved in seconds. With our cloud eTMF, my audit teams are travelling less, and spending more time ensuring quality and analysing trial effectiveness. Having immediate, remote access to the appropriate documents is transforming our audit team’s role from compliance managers to insight gatherers.”

Looking Forward to Inspection Ready eTMFs

Regulatory expectation for accessibility, availability, and completeness of TMFs motivates sponsors and CROs to evolve beyond paper-based processes. Yet, the shift from paper to eTMFs also delivers measureable benefits to the entirety of clinical operations. The Veeva 2015 Paperless TMF Survey demonstrates wide variation in the technologies used to manage TMF documents and processes, and in how the type of eTMF that is used impacts the benefits that are achieved. Those using eTMF applications are more likely to see improved inspection readiness, centralised monitoring, and better visibility into performance. This shows that the transition involves more than moving paper-based processes from a manual system to an electronic system. It means moving to a purpose-built eTMF application that will deliver the most benefits and shorten clinical development time. Fully unlocked, next-generation eTMFs are strategic assets.

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