Wearing Thin

Organisations that have already leveraged purpose-built electronic trial master files are enjoying a host of advantages over their peers – from improved operational efficiency to being permanently inspection-ready. The barriers that once held life sciences companies back are now being seen for what they really are: paper thin

Rik van Mol at Veeva Systems

With biotechnology pioneers spending an average of 10 years and over $1.2 billion bringing a new therapeutic to market, there has been an understandable industry focus on cutting running costs and improving the efficiency of trials.

So what are the core issues that waste time and leak value from the drug development process? Is it recruiting patients? Or gaining ethical approval for the study? Although these are undoubtedly significant factors, there are bottlenecks in other, more unexpected areas, especially given the state of technology today. According to a 2010 report by McKinsey & Company, mismanagement of the trial master file (TMF) was responsible for slowing down trials by an average of 12 months, costing providers up to $2 billion in lost revenue for a blockbuster therapy.

Bearing these staggering figures in mind, it is little surprise that technologies offering an opportunity to cut cost and time to approval are attractive to a cash-strapped and time-poor industry. With regulatory and competitive pressures mounting, life sciences companies are on the cusp of evolving from what have been largely manual TMF processes and simple file shares to new, advanced electronic TMF (eTMF) technologies that enable paperless trials.

A recently published Veeva survey examines the current state of eTMF adoption, as well as the benefits, drivers and barriers to implementing electronic processes. The in-depth study of more than 250 TMF owners demonstrates that eTMFs deliver deep operational efficiencies and high quality.

In fact, 1 in 10 respondents (13%) is already leveraging modern, purpose-built eTMF applications that include process-driven workflows and capabilities for managing trial documents and data electronically. Furthermore, the number of TMF owners actively building or evaluating eTMF applications to support efficient collaboration throughout a clinical study is up from 17% in 2010 to 33.6% today, according to the 2014 DIA TMF Reference Model survey.

However, given the potential benefits, what is preventing more drug developers from taking advantage of eTMF applications that would streamline many of the inefficient processes that can slow clinical trials?

According to the Veeva survey, the most frequently cited barrier to going paperless is cost, in terms of both new technologies (38%) and the implementation and services (33%). Concern over regulatory requirements for wet ink signatures (28%) are also noted.

Secure Access

The ability to grant secure access to their TMFs was one of the chief concerns of respondents to Veeva's study – but, in fact, this fear is largely unwarranted. Modern cloud technologies already provide secure access to systems over the internet, enabling all parties in the study to collaborate efficiently. Gone are the challenges of distributing laptops, accessing a virtual private network, and trying to circumvent the organisation's information security policies or get around a corporate firewall.

Cloud eTMF systems allow approved collaborators to access clinical trial documents in real-time with a secure log-in. This permits document exchange on demand, wherever authorised users can access the web. Sponsors, CROs and site personnel can quickly access cloud eTMFs from any device, anywhere in the world, and then make necessary changes to documents and save them back to the central repository in the cloud for an up-to-date, single source of the truth.

Eldin Rammell, a clinical records management expert and Managing Director at Rammell Consulting, contends that the research confirms not all eTMFs are created equal: "Many eTMFs are simple file shares that perpetuate manual processes", he says. And, according to Veeva's survey, only 13% of respondents use electronic applications to manage their TMFs. Moving from a simple file share to a repeatable, cloud-based eTMF framework improves quality and decreases non-compliance.

Regulatory Barriers

Life sciences companies have long believed that health authorities' requirements for wet ink signatures would hinder the use of electronic systems for their TMFs. And while it is acknowledged that there are still challenges with legal contractual documentation – the industry is looking forward to a unified and clearer position from local European governments in this area – health authorities today are broadly accepting the use of electronic or digital signatures and, in many instances, no longer require signatures at all.

As far back as 2003, the FDA stated in 21 CFR 11: "These regulations [21 CFR 11], which apply to all FDA program areas, were intended to permit the widest possible use of electronic technology, compatible with FDA's responsibility to protect the public health." In fact, no major health authority globally mandates wet ink signatures on TMF documents anymore; all accept signatures electronically when they are required.

"Despite industry perceptions, today there are only seven documents requiring signatures as mandated by ICH GCP Section 8. Most do not require signatures, as audit trails can be used in their place", remarks Lisa Mulcahy, Owner and Principal of Mulcahy Consulting, and Co-Chair of the DIA TMF Reference Model group. Many life sciences companies waste time chasing people for wet ink signatures – often on documents where they are not required. Even companies with eTMFs often unnecessarily deliver, sign and scan documents – steps no longer needed with most eTMF applications.

Purpose-built eTMF applications typically include e-signature capabilities that meet the 21 CFR 11 requirements, making it easier to collect electronic signatures where needed, without regulatory concern. In the Veeva survey, 66% of respondents indicated the need for e-signature capabilities in order to go paperless, showing that the barrier here may not just be concern over regulatory requirements, but rather the lack of adoption of necessary technology.

With increasing regulatory pressure demanding monitoring of TMFs, organisations are seeking new ways to improve inspection readiness and make TMFs accessible to auditors on demand. Most recently, the UK's Medicines and Healthcare Products Regulatory Agency tightened its guidelines to include ready TMF accessibility – a difficult objective to meet using a local paper-based system.

To meet the growing expectations of health authorities globally, organisations are rapidly adopting eTMF applications in the same way that they once moved from paper case report forms to electronic data capture. The growth trend here is tremendous. By automating standard operating procedures (SOPs), the eTMF is streamlining the practice, and creating ways to track application workflows and identify non-compliant processes before the file is put before regulators for approval.

Cloud-Based Savings

Although some voice concern over the expenses of transitioning to electronic applications, the truth is that costs are likely to be reduced with cloud-based eTMFs. The improvements in tracking the state of key documents and the ability to respond easily to regulatory enquiries – allowing easy access to records and an overall increase in efficiency across the entire process – drives down the cost of managing TMFs. However, there are even greater benefits to a cloud-based service. Before the current generation of eTMF applications, many life sciences companies built custom software on top of existing platforms in order to manage content. These required huge financial investments and, as such, companies continue to leverage the systems today, despite their ageing capabilities.

Currently, purpose-built eTMF applications are designed with applicable functionality built in for use right off the shelf, with only minor configuration – eliminating the expense associated with custom design. In addition, with multitenant eTMF applications in the cloud, there are even more cost savings, as a company only pays for what it needs, without the intimidating upfront cost of traditional systems. With true cloud applications, there is no infrastructure to purchase, install or maintain. The provider manages the software and all updates are delivered automatically behind the scenes, with little or no disruption to users. This ensures that users are always working on current technology and eliminates the massive expense of updates.

Interestingly, despite the fact that 38% of respondents in the Veeva survey see cost as a significant barrier to going paperless, an equal number report cost savings as a substantial benefit of their eTMFs. This balance seems to imply that the industry is still evolving in its knowledge of newer technologies. According to a report published by Nucleus Research: "Companies continue to invest in cloud applications because of low upfront cost and faster time to deployment, but those are not the only reasons to move to the cloud. Beyond their initial payback, cloud applications deliver 1.7 times more [return on investment] than on-premise software."

Electronic Future

Early adopters of more sophisticated eTMF technologies experience greater inspection readiness, visibility, automated SOPs and cost savings 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 provide the data to demonstrate the risks of poor trial design.

About the author

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