Regulatory Compliance and Efficiency Savings Key Drivers of eTMF Adoption

Each year, Veeva surveys the pharmaceutical industry on its use of trial master file (TMF) processes. Our 2016 survey is our third, providing us with a great view of the progress made by the life sciences industry in its move towards paperless processes.

The *Veeva 2016 Paperless TMF Survey*[1] features feedback from 217 TMF managers worldwide. It shows a significant change is underway as the industry shifts from passive to active TMF management and adopts advanced electronic TMF (eTMF) applications. The key drivers for TMF managers are to improve inspection readiness and shorten clinical trial times.

We also observe a widening gap between those organisations that use data to drive productivity efficiencies and those that do not have the ability to access critical trial information due to outdated systems and practices.

Here, I will outline key findings from the survey and what they mean for the life sciences industry. We will see how active eTMFs are making life science organisations inspection-ready and learn how users currently using eTMF processes are benefitting.

We will also explore the key benefits of active eTMFs and look at how increased access to data improves trial efficiencies. Finally, we will cover the practical steps that life sciences executives can take to adopt successful active eTMF models.

Before we start, it's key to recognise why TMF processes are so critical in the current environment. First, regulatory agencies demand higher levels of access to TMF processes. Also, life sciences organisations are seeking ways to make the TMF process more efficient.

Both these challenges help build a strong business case for deploying eTMF processes. By using an active eTMF, life sciences organisations can enable regulators to access up-to-date trial data to assess good clinical practices (GCP) compliance. They can also improve productivity and access valuable performance insight on which they can base strategic decisions.

Let's be clear on what we mean by passive TMFs. These involve antiquated, paper-based processes. Even if documents are saved in electronic format, they can often be saved loosely in multiple locations so users cannot track the trial's progress.

Active TMF management, on the other hand, involves the use of purpose-built eTMF applications to manage documents and processes in real time as the TMF is being generated. This way, study partners can create, access, review and act upon documents in one single system.

What's the State of TMFs in 2016?

Our survey finds that organisations' ability to respond to regulatory requirements is improving, but as an industry we still have a lot of work to do. According to our survey, four out of five (80 %) sponsors using eTMF applications are providing remote access to regulators, or plan to do so in the coming 12 months. Improving inspection readiness (67 %) was the most cited business benefit driving sponsors' adoption of eTMF processes, followed by speeding study start-up (53 %). Nearly half (49 %) of sponsors report that integrating their eTMF applications with their clinical trial systems (CTMS) is key.

What's clear is that the industry is going through a period of maturation, in which the old paper-based practices are being phased out and replaced over time with digitised practices. The level of maturity of TMF processes varies greatly from passive TMF management to more advanced active TMF processes.

Our survey found that sponsors are a driving force in the adoption of eTMF processes. Sponsors' adoption of advanced eTMF applications nearly doubled in the last two years to 24 %. At the same time, sponsors using local file systems as their eTMFs dropped from 26 % in 2014 to just 8 % today.

During this two-year period, clinical operations departments cut the use of paper for most or all TMF documents from 41 % to 28 %. Since our initial survey in 2014, we have also seen declines in the use of paper in regulatory processes (down 12 %), drug safety (down 11 %), and data management (down 6 %).

We observe that nearly a quarter (23 %) of sponsors now use their eTMF applications to share documents with contract research organisations (CROs). This is up from 14 % in 2014, demonstrating steady progress in digital collaboration.

While paper is steadily being taken out of the process, a challenge exists when it comes to using digital/electronic signatures. Nearly two-thirds (61 %) of respondents report that digital/electronic signatures are currently missing from their processes.

Data Drives Efficiencies

The pharma industry benefits from the increased access to data, making strategic decisions based on data. Our study finds that organisations that have already

moved to eTMF applications are seeing better visibility into performance metrics (55 %). In addition, those organisations using metrics to improve trial processes see far greater benefits compared to those not currently collecting data. These include:

- Improved audit and inspection readiness (67 % compared to 29 %)
- Better visibility into performance metrics (53 % compared to 14 %)
- Cost savings (47 % compared to 10 %)

Metrics also play a vital role in accelerating time to market during the trial process. Respondents using eTMFs and metrics productively experience other advantages over those who do not collect data at all, such as faster study start-up time (20 % compared to 5 %) and shortened clinical trial time (23 % compared to 5 %).

There is an opportunity to use data even more effectively in eTMF processes. Despite the demonstrable benefits provided by increased access to data, we find that TMF owners' use of operational metrics remains largely static. The number of respondents who are "extensively using data" grew from 14 % to 18 % in the last year.

An eTMF is becoming an integral piece of the clinical trial process workflow, which ensures that study findings are recorded as they happen and status reporting is more accurate and effortless. Real-time insight into trial progress allows the entire team to gather data throughout studies and use that data to make better decisions about commercial strategy and therapy effectiveness.

Benefits of Active eTMF

As the *Veeva 2016 Paperless TMF Survey* indicates, deploying an active eTMF process enables organisations to meet regulatory requirements and efficiency objectives. The four biggest benefits include:

1. Inspection readiness and accessibility at all times

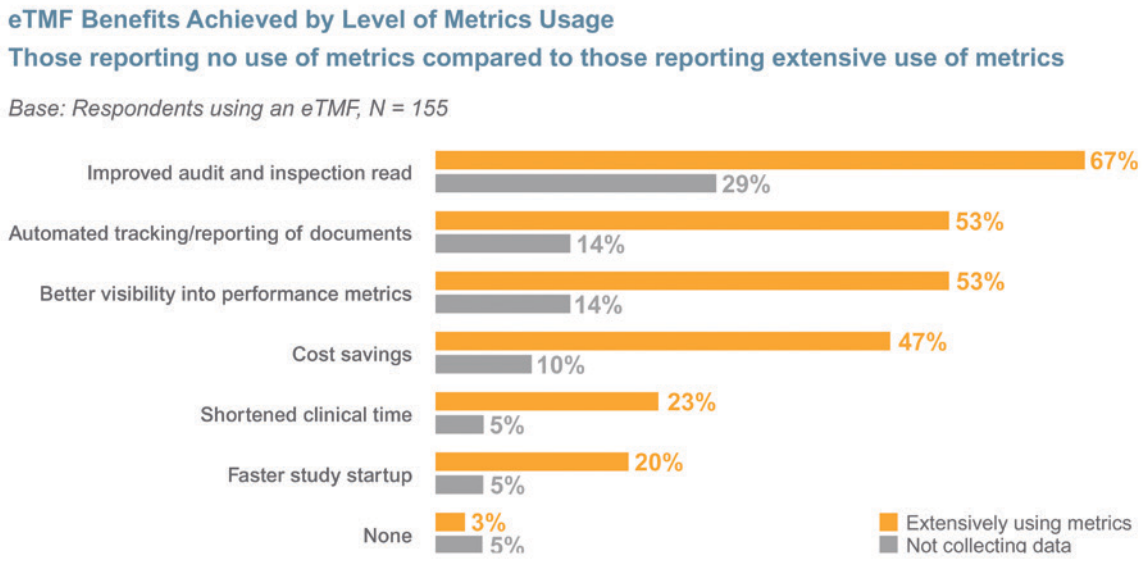
Regulators such as the European Medicines Agency and Medicines & Healthcare Products Regulatory Agency (MHRA) expect, at a minimum, that an organisation's TMF accurately reconstructs how a clinical trial was conducted to demonstrate effective sponsor oversight, support decisions made, and comply with GCP guidelines.

The MHRA also raised the minimum expectation to have the TMF readily available at all times, and it must be accessible and complete. This is proving a struggle for many organisations, despite the technology choices open to them.

MHRA data states that 35 % of 2014 site inspections were delayed due to incomplete or unavailable TMFs[2]. Its latest report[3] cites two organisations as producing inadequate TMFs, and in one case, "there was no single system that was designed to be the eTMF with the appropriate functionality."

2. Comprehensive trial documentation

eTMFs remove the challenge of incomplete or missing documents, a major quality-control frustration for the MHRA. Purpose-built eTMFs enable a single source of truth across all parties to ensure all documents are up-to-date and stored in a single location.



What benefits were achieved with your organization's implementation of the eTMF solution specified in question 9? Select all that apply. (Q.10) What type of eTMF solution do you currently use? (Q.9) To what extent is your organization leveraging TMF operational data (e.g., time from initial review to approval) to improve trial processes? (Q.13)

3. Simple navigation with intuitive user interfaces
Regulatory agencies typically recommend that their inspectors are able to navigate a sponsor's eTMF after no more than one hour of training. A familiar, consumer-style web user interface allows for quick training and easy navigation.

4. Rich insight to improve operational efficiency
Purpose-built eTMF systems capture process- and quality-specific data as the trial is being conducted. Real-time reporting and dashboards use this information to provide organisations with an in-process view of the trial.

Active eTMFs enable life sciences organisations to take advantage of these capabilities, so let's hear from an organisation that is successfully implementing eTMF processes.

Active eTMF: A Success Story
As we observe above, survey respondents using eTMFs and metrics experience advantages over those who do not collect data, such as faster study start-up time (20 % compared to 5 %) and reduced clinical trial time (23 % compared to 5 %).

Exom Group, a CRO that combines strong medical, regulatory, and operational expertise with the most disruptive digital technological solutions to improve quality and performance of clinical trials, is an example of a CRO using improved access to data provided by an eTMF environment to streamline the startup process.

Luigi Visani, CEO of Exom Group, says: "First, the eTMF enables a quicker and more accurate collection of documents during the pre-study phase. These can be filed in real time and shared remotely with the relevant parties as required. Additionally, the presence of dashboard reports gives the study manager an 'at-a-glance' view of documentation completeness per site."

According to Visani, the study start-up phase ends once the regulatory package has been approved, as the clinical monitor can then perform the study initiation visit. The eTMF significantly reduces the review and approval time by giving the central reviewer simple and complete access to any study document. Even requests for additional information and/or documents can be handled faster.

Visani continues: "Using the eTMF means that we have full and secure control of all steps during the approval process, across multiple recipients, saving considerable time overall. Even when delays occur due to local bureaucratic complications, the availability of an online document management system such as Veeva Vault eTMF can help to more efficiently manage poorly responding clinical sites. Our experience shows that using the eTMF has significantly simplified and accelerated every part of the document management process."

Remaining Agile in a Competitive World
As our survey demonstrates, the industry is moving away from paper and seeking a competitive advantage through active eTMF processes. In particular, cloud-based solutions support the paperless environment, as they provide access and collaboration for multiple stakeholders, wherever they are, whenever they need it during the lifecycle of the trial.

The business case for adopting active eTMF processes is apparent: Businesses that move to eTMFs report smoother regulatory compliance and improved operational efficiencies. The challenge for pharmaceutical executives is how to transition their organisations, and it starts with buy-in from the C-suite. It's not an IT issue; it's a business decision. There must be willingness to transition to a cloud-based eTMF environment.

Over time, data-driven trial optimisation will result in more efficient trials and faster time to market. If your organisation is yet to transition to active eTMF processes, now is the perfect time to start. The life sciences industry is changing; don't fall behind.

References
1. Veeva 2016 Paperless TMF Survey by Veeva Systems, June 2016.
2. Viglya, as posted on the UK MHRA web site. For more: http://viglya.com/uk-mhra-updated-definition-of-a-critical-gcp-inspection-finding/
3. GCP Inspections Report (April 2016) https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/517483/GCP_INSPECTIONS_METRICS_2014-2015__final_11-04-16_.pdf

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