Support System

CROs are under increasing pressure to provide higher levels of collaboration and transparency, yet 80% still use outdated methods to exchange critical clinical study documents. Upgrading from paper-based systems to cloud-based eTMF technologies can provide stakeholders with greater visibility and control over the trial process

Rik Van Mol at Veeva Systems

For CROs, the outlook for 2015 brings both good and bad news. On the positive side, according to recent research, one-third of trial sponsors expect their spending next year to increase by 10%, and most anticipate spending to be the same or slightly higher (1). Less good is that 43% of those companies also said they have reduced, or plan to reduce, their number of outsourced partners (2).

In a climate where sponsors are looking to streamline their operations and simplify their outsourcing relationships, what do CROs need to do to become – or remain – a valued partner, rather than surplus to requirements?

The answer is that CROs need to critically review their operational processes. Are they using technology to provide better insight and improve collaboration with sponsors, partners, regulators and review boards? Or are they still reliant on outmoded ways of information sharing that complicate relationships and, critically, increase time-to-market?

In many cases, it seems to be the latter. A new survey, the *Veeva 2014 Paperless TMF Survey: The State of CRO TMFs*, found that only one-in-five CROs is currently using a purpose-built electronic trial master file (eTMF) application to manage the mass of documentation in clinical trials (3). This means that the great majority of CROs are still using paper-based and simple file-share systems to manage and assimilate clinical data and documents. These outdated technologies arguably hinder collaboration, and limit sponsors' visibility and control over the clinical process.

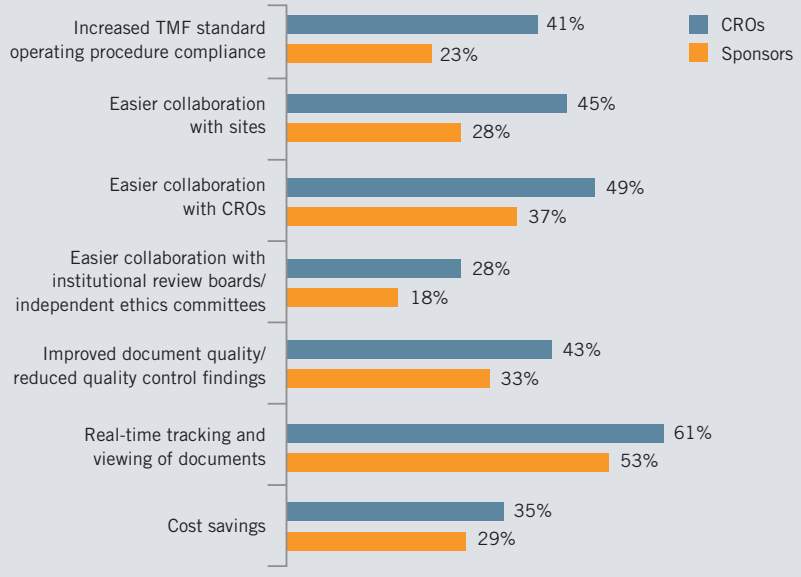
For those forward-looking CROs that have already implemented them, cloud-based eTMF systems deliver significantly improved efficiency, visibility and compliance, and provide the technology backbone necessary to build sustainable and truly collaborative relationships with sponsors. The survey shows that CROs using eTMF solutions have experienced major benefits, including increased inspection-readiness, higher quality trial master files (TMFs) and improved collaboration with external partners (see Figure 1).

Turn to Technology

Traditional paper or file-share systems are time-consuming and resource-intensive, requiring an inordinate amount of manual effort to maintain TMF quality and completeness. Documents can be stored in both paper and electronic format (making version control difficult) and are often siloed by functional area or organisational boundary. This inevitably leads to process redundancies and duplicate documents, not to mention unnecessary compliance risk – all of which requires time and effort to reconcile.

Figure 1: Benefits attributed to an eTMF solution

Base: sponsor and CRO respondents, N=161



When a typical Phase 3 study can generate many thousands of documents, this is no trivial matter. Add to this the increasing complexity of study protocols, the global nature of clinical development and the growing number of trial stakeholders (CROs, sites, agencies, committees, etc), it is no wonder the act of simply compiling multiple trial documents into a coherent and readily accessible TMF has become a massive organisational headache for CROs and sponsors alike.

Yet technology exists that can radically improve this process. For example, using a shared eTMF system in the cloud can provide a single source of truth during the entire study. All stakeholders – whether investigators, monitors and even inspectors – can access the same documents and associated workflows. This helps to increase visibility, compliance and efficiency, ultimately encouraging a trusted and lasting partnership between CRO and sponsor.

Going Paperless

Paperless TMF systems – easily and securely accessible by all – remove barriers between sponsors and CROs. This fosters trust and creates an environment conducive to real-time information sharing throughout the entire trial process. Strategic collaboration also improves dramatically when technology removes internal and external silos. According to the survey, CROs using purpose-built eTMF systems report significant improvements in collaboration with sponsors, while almost half of the organisations surveyed report easier collaboration with sites (45%) and other CROs (49%).

In addition, the results demonstrate that many CROs can gain improvements in real-time tracking and viewing of documents (61%), as well as increased document quality (43%). Jessica Vicari, Director of Regulatory Support Services and Document Management at global CRO, Advanced Clinical, explains: "The survey results are eye-opening, yet point towards a clear-cut way for all CROs to step up their level of support to sponsors. We invested in a cloud eTMF 12 months ago and almost immediately began collaborating more efficiently with sponsors."

Total Transparency

Using an eTMF application provides a single point of access for both CROs and sponsors throughout the clinical trial – from site feasibility to study start-up and through database lock – so everyone is always working with the most up-to-date versions of documents. With better visibility, sponsors have more control over content and grow more secure in the relationship.

Sponsors can collaborate with CROs in real-time and still maintain a single source of the truth. "With a cloud-based eTMF, we can provide sponsors with total transparency of trial data and enable a richer, more collaborative partnership for improved trial results, including faster time-to-market," says Gregg Dearhammer, Chief Operating Officer at top eight CRO, inVentiv Health Clinical.

PharmaStart, another global CRO, has been able to provide increased visibility and control to its clients since implementing a cloud-based eTMF globally across more than 75 investigator sites. Rebecca Moraris, its Director of Clinical Operations, comments: "Securely accessible in the cloud and as easy to use as Amazon, our new eTMF ensures both external and internal teams can fully leverage the system. Everyone can work in parallel so we do not wait, for example, while documents are shipped to sites or a wet signature is captured via courier from locations all around the globe. It also provides total transparency and a better vantage point for sponsors, sites and internal groups to identify problems early and fix them quickly."

Regulatory Best Practice

Paperless technology enables inspection-readiness too – a top concern of life sciences companies. CROs using advanced eTMF applications report improvements in many inspection areas, including reduction of missing (76%), misfiled (76%), duplicate (72%), incomplete (65%) and expired (62%) documents (see Figure 2, page 60).

Furthermore, a cloud-based eTMF provides a convenient window for health authorities, which are increasingly seeking electronic access to the TMF. In April 2014, the UK's Medicines and Healthcare Products Regulatory Agency (MHRA) updated its definition of a critical Good Clinical Practice finding to include TMFs that are incomplete and inaccessible – difficult objectives to meet with a TMF system dependent on paper. The MHRA tightened its parameters on the TMF after repeated inspection delays. In 2013, 33% of sponsor inspections required extra days due to an incomplete TMF or lack of accessibility. With other regulatory authorities likely to follow the precedent set by the MHRA, TMFs worldwide will come under ever-increasing pressure to address these issues.

Cloud-based eTMFs can mitigate this challenge and greatly improve inspection-readiness because they are always available and accessible. Eldin Rammell, a clinical records management expert and Managing Director at Rammell Consulting, notes: "In the face of MHRA's updated definition for critical findings, it is encouraging that organisations utilising eTMF applications are experiencing significant benefits in inspection-readiness and business efficiency gains."

Breaking the Paper Chain

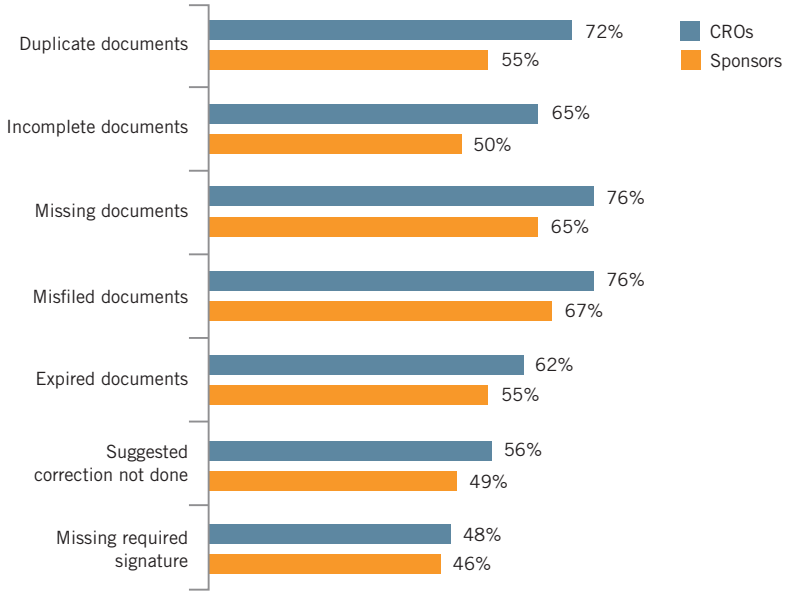
According to the survey data, CROs are swamped in paper, using more than their sponsors across all functional areas. Contracts and clinical operations teams were the most

paper-dependent, with 59% of all contracts (52% for sponsors) and 47% of all clinical operations documents (41% for sponsors) still in paper format.

In addition, 80% of CRO survey respondents reported using email, and 65% still rely on paper-based methods, to share TMF documentation, whereas the number of sponsors exchanging TMF documents via email (64%) and paper (52%) was lower. While email is technically electronic, it offers few advantages over manual paper exchange methods. It is faster, but still an unstructured communication that is highly insecure and not integrated with the TMF, which inevitably creates version control issues.

Figure 2: Percentage rating improvements in inspection area as good or major after implementing an eTMF

Base: sponsor and CRO respondents, N=161



One explanation for CROs' continued reliance on paper is an outdated perception that institutional review boards and ethics committees require wet ink signatures on physical documents. However, since all major health authorities now accept electronic signatures, this is a perception that quickly needs to change.

Going paperless enables CROs to eliminate slow, risk-prone manual hand-offs, and create new efficiencies they can pass on to their cost-conscious sponsors. Any CRO that can demonstrate improvements here – swapping one type of paper for the kind that pays for new research – provides a tremendous competitive advantage. Unsurprisingly, 63% of CROs surveyed said that cost savings were a top driver of eTMF adoption. Another significant advantage is that, once defined, they can easily be reused from study to study, speeding start-up on future trials.

Agents of Change

While both sponsors and CROs stand to benefit from driving industry-wide transformation with new eTMF technology, CROs have the greatest opportunity to positively impact the most number of products in development. One CRO can be involved with many different studies and their corresponding sponsors, whereas a sponsor generally affects just its own products. In an industry where the top eight CROs account for more than 66% of all clinical trials, their position as agents of change is a considerable one.

As sponsors increasingly outsource clinical operations, including TMF management and oversight, it is CROs that can gain the most from more automated and streamlined clinical processes. While sponsors benefit from real-time status updates, improved trial quality and inspection-readiness, CROs benefit from a more efficient, scalable model which enables them to leverage technology across hundreds of trials and thousands of sites. The survey shows that CROs report large improvements in standard operating procedure compliance (41%) and improved document quality, with fewer quality control findings with their eTMF applications than their sponsors (23% and 43%, respectively).

IDDI, a biostatistical and eClinical services provider headquartered in Belgium, has not looked back since it transitioned to a cloud-based eTMF application. "We were looking to move from our hybrid system [part paper and part online file-share] to a single, digital solution for improved quality, efficiency and control, while allowing our colleagues and clients to easily access data through the cloud," explains Chief Operating Officer, Linda Danielson. The company migrated most of its active studies to a cloud eTMF in 2013 followed by 40 new studies in 2014, and reports improved partnerships. "Our eTMF enables effective collaboration since sponsors can review, edit and approve documents in real-time."

Long-Term Survival

Life sciences companies are evolving away from what have been largely manual TMF processes and simple file-shares, towards advanced eTMF technologies to enable paperless trials. In fact, the number of TMF owners actively building or evaluating eTMF applications to support more efficient collaboration throughout clinical trials is up from 17% in 2010 to 34% today, according to a 2014 Drug Information Association TMF Reference Model survey. In the industry's big push forward, CROs cannot

afford to lag behind. There is too much to lose and much more to gain by embracing e-collaboration.

"CROs have a tremendous opportunity to distinguish themselves from the pack and position their organisations as long-term partners," says Ken Getz, Director of Sponsored Research Programs and Professor at Tufts Center for the Study of Drug Development. "There is a lot at stake for all parties, so it is vital that CROs urgently build the modern infrastructure, top talent and compliant processes that will lead to efficient and safe drug development."

Sponsors may be embracing cloud-based collaboration, but CROs still have a major opportunity to drive wider industry acceptance and use. Early adopters have already reaped significant benefits, including streamlined operations, increased visibility and access, and improved collaboration across the clinical ecosystem. These forward-looking CROs are well-positioned to survive the streamlining cull and establish themselves as long-term partners, critical to the success of sponsors.

The Veeva 2014 Paperless TMF Survey: The State of CRO TMFs *examines the current state of eTMF adoption among sponsors and CROs, as well as the benefits, drivers and barriers to implementing electronic processes. It is available at* www.veeva.com/cro-report

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About the author

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