

Veeva 2016 Paperless TMF Survey

The *Veeva 2016 Paperless TMF Survey* explores the life sciences industry's progress in streamlining clinical trials and unifying clinical operations. It represents the experiences and opinions of 217 trial master file (TMF) owners from around the globe. The goal of the research is to understand the impact of electronic trial master file (eTMF) adoption on broader clinical processes as well as the drivers, benefits, and expectations of eTMF solutions. This is the third annual *Veeva Paperless TMF Survey*, and while a wide variety of methods for TMF management remain, adoption of advanced, purpose-built eTMF applications has accelerated amid an industry-wide drive to improve inspection readiness and shorten clinical trial times.

Key Findings

- Adoption of advanced eTMF applications has doubled since 2014. One in four (24%) sponsors now use a purpose-built eTMF application (up from 13%) while the use of local file systems as an eTMF dropped from 26% to 8%.
- Over the same period, clinical operations departments at sponsor organizations have cut the use of paper for most/all TMF documents from 41% in 2014 to 28% today.
- Electronic collaboration with partners has increased and a quarter (23%) of sponsors now use their eTMF application to share TMF documents with CROs, up from 14% in 2014.
- Most (80%) with an eTMF application now provide remote access to inspectors/auditors.
- Consistent with the growing demand to unify clinical processes, half (49%) of sponsors say integrating their eTMF application with their clinical trial management system (CTMS) is a key need in an effort to go paperless.
- The top business drivers motivating sponsors to move to eTMFs are improving inspection readiness (67%), speeding study startup (53%), and remote oversight of the TMF (48%).
- Those who have adopted eTMF applications in particular, report improved audit and inspection readiness (61%), improved central and remote monitoring (59%), and better visibility into performance metrics (55%). Those using other types of eTMF systems are significantly less likely to see these benefits.

- In addition to the overall benefits cited, nearly all (98%) also see specific improvements in key inspection areas after implementing an eTMF application including duplicate, missing, and incomplete documents.
- Organizations using metrics to improve trial processes see far greater benefits as compared to those not collecting data such as, improved audit and inspection readiness (67% vs. 29%), faster study startup (20% vs. 5%), and shortened clinical time (23% vs. 5%).

Types of eTMF and Use of Paper

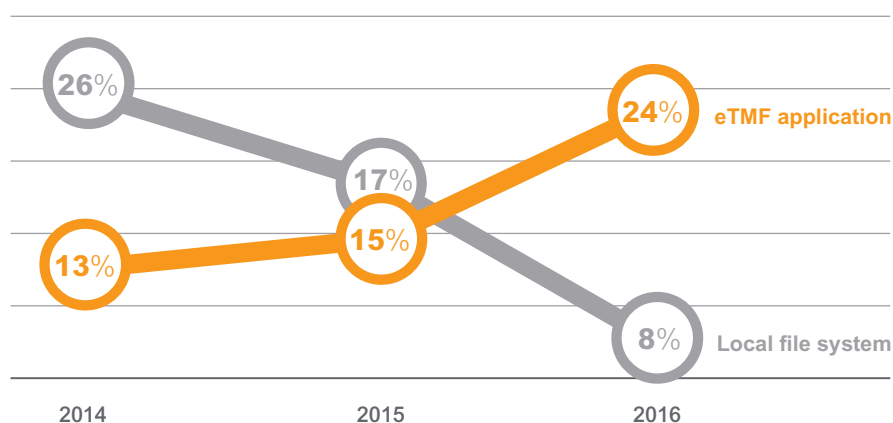
This research tracks the type of eTMF solutions in use, which vary widely in their capabilities and fit for the purpose of managing a TMF. The least mature solutions, such as local file systems, cloud file shares, and static repositories, provide simple storage and archival of TMF documents and are typically referred to as 'passive' TMFs. Content management systems are often slightly more mature providing capabilities like search, versioning, and some workflow. However, general content management systems have limited accessibility and are not designed for TMF processes. The most mature solutions are purpose-built eTMF applications. Designed specifically to manage TMF documents and end-to-end processes, these 'active' solutions manage documents and processes in real-time as the TMF is being generated.

There has been a significant shift to 'active' from 'passive' TMFs since 2014. In that time, sponsors' use of advanced eTMF applications increased nearly twofold to 24% today while the use of local files systems as an eTMF dropped from 26% to 8%. Use of cloud file shares, content management systems, and paper-based TMFs remained flat over the same period.

eTMF System Used, 2014 to 2016

Percent using a local file system or eTMF application

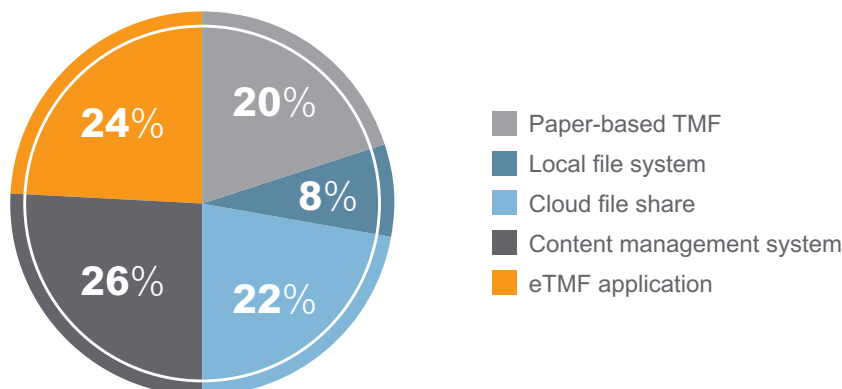
Base: Sponsor respondents, 2016 N = 137, 2015 N = 124, 2014 N = 135



What type of eTMF solution do you currently use? (Q.9)

eTMF System Used

Base: Sponsor respondents, N = 137

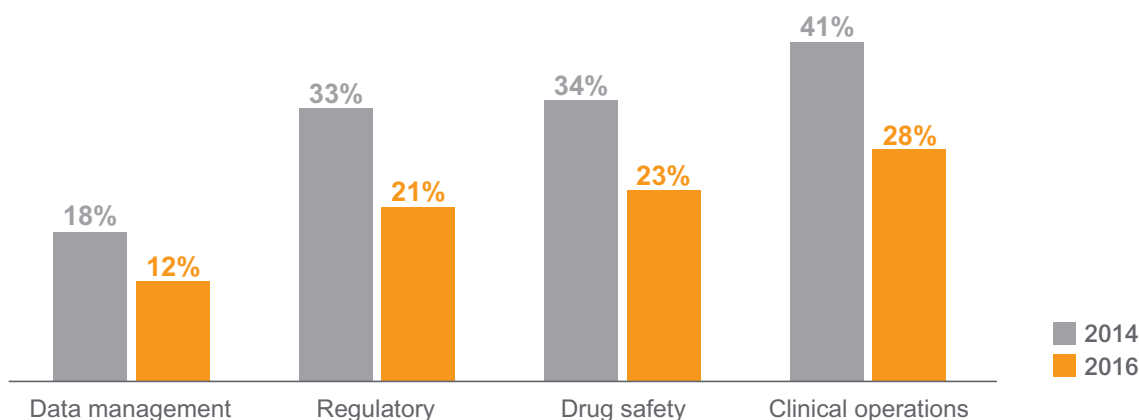


What type of eTMF solution do you currently use? (Q.9)

The use of paper has declined across all functional areas over the last three years. Clinical operations departments at sponsor organizations cut the use of paper for most/all TMF documents from 41% in 2014 to 28% today. Large declines were also seen in other key areas measured including: regulatory (down 12 percentage points), drug safety (down 11 percentage points), and data management (down six percentage points).

Most or All Documents Managed on Paper at Some Point in Their Lifecycle

Base: Sponsor respondents, 2014 N = 135, 2016 N = 137



In each area, how many of your company's TMF documents are managed on paper at any point in their lifecycle? (Q.3)

Digital Collaboration and Access

The most common processes sponsors conduct electronically are the archival of documents (56%), creation of source documents (46%), and collaboration with external partners (44%).

Consistent with the move to more active TMFs, there has been a marked increase in the use of electronic means to manage the TMF and work with trial partners. Sponsors 'mostly' or 'always' creating TMF source documents and collaborating with partners electronically has grown significantly from just one year ago (up 21 percentage points and 14 percentage points respectively).

Less than a quarter of sponsors (22%) use electronic signature of documents, despite broad acceptance of electronic signatures on almost all TMF documents by regulatory agencies worldwide.¹

TMF Document Activities Mostly or Always Done Electronically

Base: Sponsor respondents, N = 137



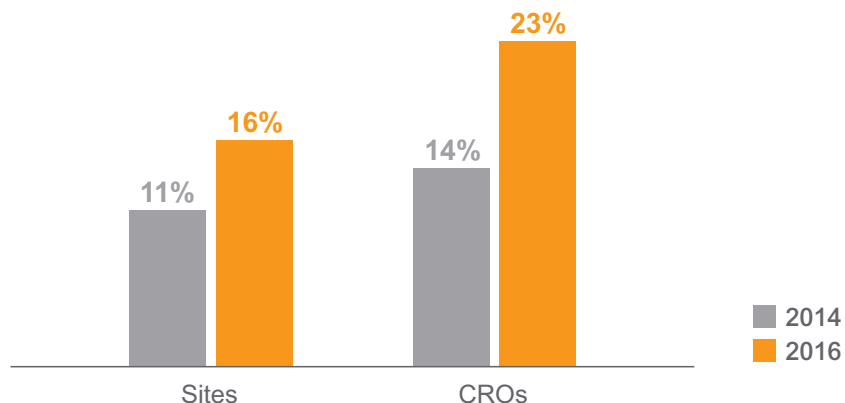
To what extent is your company currently doing the following (electronically) with TMF documents? (Q.8)

Sponsors are increasingly exchanging TMF documents with external parties in a single system accessed by all study partners. Almost a quarter (23%) of all sponsors now report using an eTMF application to exchange documents with CROs, up from 14% in 2014. Similar growth was seen in the use of eTMF applications by sponsors to exchange TMF documents with sites. Today, roughly one in six (16%) sponsors use an eTMF application to exchange documents with sites, up from 11% in 2014.

Email remains the dominant means for sponsors to exchange TMF documents with external parties. More than two-thirds of sponsors use email to exchange documents with CROs (70%) and sites (68%).

Sponsors Using an eTMF Application to Exchange TMF Documents with Sites/CROs

Base: Sponsor respondents, 2014 N = 135, 2016 N = 137



What methods does your team use to exchange TMF documents with external parties? Select all that apply (Q.2)

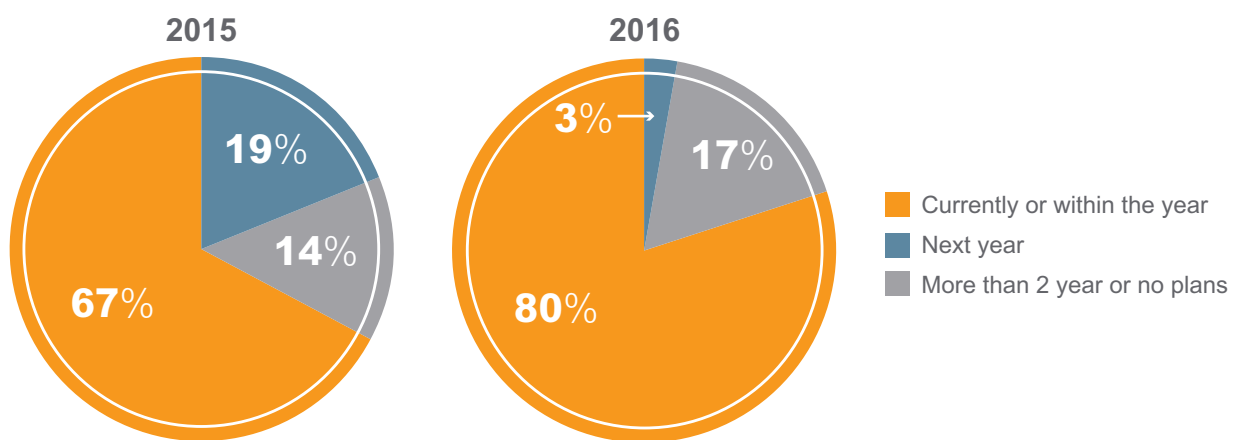
¹ European Medicines Agency, Good Clinical Practice Working Group. *Reflection Paper on GCP Compliance in Relation to Trial Master Files (Paper and/or Electronic) for Management, Audit and Inspection of Clinical Trials*. June 15, 2015.
 United States Food and Drug Administration. *Code of Federal Regulations, Title 21, Part 11, Electronic Records; Electronic Signatures*.

The 2014 MHRA update² that incomplete or inaccessible TMFs could be a critical good clinical practice (GCP) finding intensified an already growing focus on TMF accessibility and inspection readiness, and likely hastened a move to provide auditors/inspectors with remote access.

Most (80%) respondents using an eTMF application currently provide remote access to auditors and inspectors or plan to do so within the next year, a 13 percentage point increase from 2015. There was a corresponding 16 percentage point drop in respondents who either have no plans to provide access or plan to provide access in more than two years (down from 19% in 2015 to 3% in 2016).

Currently Providing Remote TMF Access to Auditors/Inspectors

Base: Respondents using an eTMF application, 2015 N = 21, 2016 N = 45



When, if ever, does your organization plan to provide auditors/inspectors with remote access to trial master file documents? (Q. 12) What type of eTMF solution do you currently use? (Q.9)

Drivers and Barriers to Going Paperless

Improving inspection readiness (67%), speeding study startup (53%), and providing remote oversight of the TMF (48%) are the most cited business benefits driving eTMF adoption among sponsors.

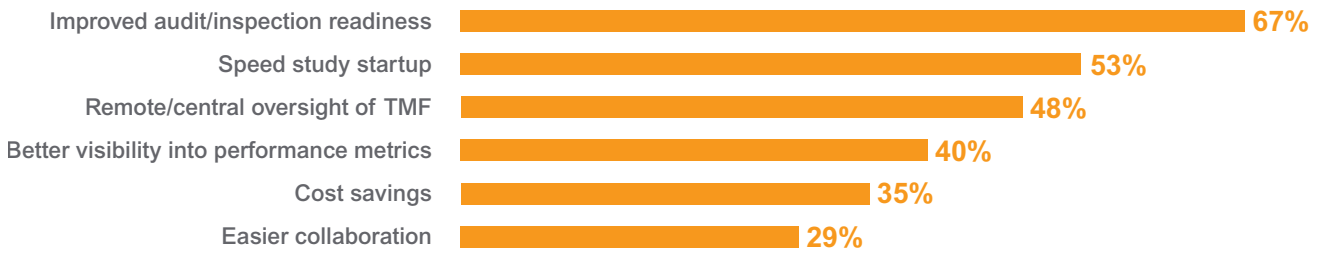
Improved inspection readiness remains the number one driver for sponsors and is up 16 percentage points from 51% in 2014. This heightened priority may also be motivated, in part, by the MHRA's 2014 mandate.

Study startup continues to be a key process life sciences organizations are looking to improve, consistently cited as a top driver for eTMF adoption by half of sponsors (53% and 50% in 2016 and 2014 respectively). Better visibility into performance metrics (40%) also rated highly.

² United Kingdom Medicines and Healthcare products Regulatory Agency. *Good Clinical Practice for Clinical Trials*. December 18, 2014.

Top Drivers of eTMF Adoption

Base: Sponsor respondents, N = 137



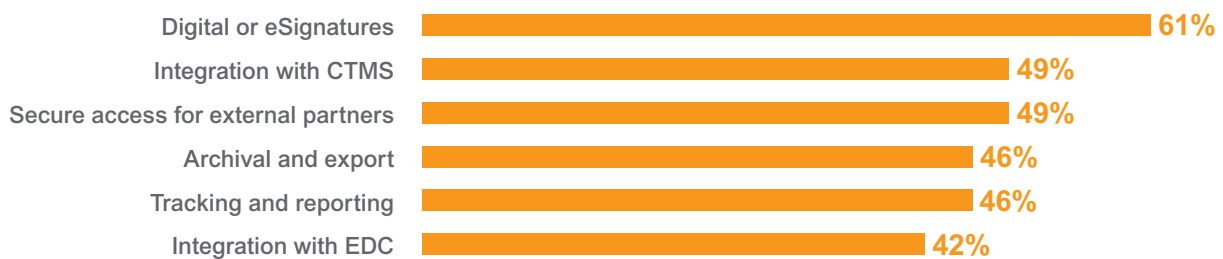
Which of the following business benefits are the most important in motivating your organization's adoption of an eTMF? Please select the top three benefits? (Q.7)

When asked which capabilities their organization needs to move to a fully paperless TMF, 61% of sponsors with an eTMF application report digital/esignature, consistent with the modest numbers of sponsors who say they are currently using electronic signature for TMF documents (22%).

Second most cited, by half of sponsors (49%), is the need to integrate their eTMF application and CTMS system. Half (49%) also say secure access is a required capability and 46% say they need TMF tracking and reporting. These findings confirm the trend to unify clinical operations systems, processes, and stakeholders for increased visibility, improved inspection readiness, and shorter clinical trials.

Capabilities Missing and Required

Base: Sponsor respondents using an eTMF application, N = 33



Which capability(ies) listed is your organization currently missing and would be required by your organization in order to move to paperless TMFs? Select all that apply. (Q.5)

Benefits of an eTMF Application

Respondents were asked to indicate which, if any, benefits they are achieving with the adoption of an eTMF. Those using a purpose-built eTMF application see the greatest impact on improving TMF audit and inspection readiness. Three in five (61%) of those using an eTMF application report improved audit and inspection readiness, up 14 percentage points from 2014 (47%). Those with all other types of eTMFs are less likely to cite audit and inspection readiness as a benefit.

Improved Audit and Inspection Readiness

Base: Respondents using an eTMF, N varies



What benefits were achieved with your organization's implementation of the eTMF solution specified in question 9? Select all that apply. (Q.10) Which type of eTMF solution did you use most recently? (Q.9)

When drilling deeper into improvements in specific inspection finding categories, nearly all (98%) respondents with an eTMF application report significant improvements in at least one category, and half (51%) report significant improvements in all categories asked about. Sponsors say using an eTMF application is significantly improving inspection issues related to duplicate documents (50%), missing documents (43%), and documents that are incomplete and missing required signature (43%).

Significant Improvements in Inspection Finding Categories

Base: Respondents using an eTMF application, N = 45



How much improvement, if any, did you observe in the following inspection finding categories after your organization implemented the eTMF solution specified in question 9? (Q.11)

By an almost two-to-one margin, those using an eTMF application are more likely to see improvements in central and remote monitoring as compared to users of other types of eTMFs. This benefit was reported by 59% of eTMF application users as compared to roughly a third of respondents using a local file system (37%), content management system (36%), or file share (31%). Nearly half (48%) say central/remote oversight is a top driver for eTMF adoption likely due to its ability to significantly reduce the number of onsite visits required by a monitor, allowing sites to focus on research and reducing study costs.

Improved Central and Remote Monitoring

Base: Respondents using an eTMF, N varies



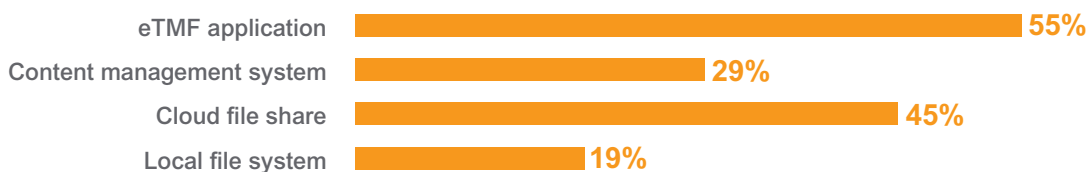
What benefits were achieved with your organization's implementation of the eTMF solution specified in question 9? Select all that apply. (Q.10) Which type of eTMF solution did you use most recently? (Q.9)

Across a number of areas, respondents frequently cite the importance of greater visibility, as it plays a key role in improving operational efficiency and TMF quality. Roughly half (55%) of eTMF application users and cloud file share users (45%) report better visibility into performance metrics through the use of these systems.

Significantly fewer report their content management system (29%) or local file system (19%) provides visibility into performance metrics. Historically, content management systems have limited access for external parties and local file systems typically provide no access, which may be a contributing factor as these systems only provide a portion of TMF documents and data needed for better visibility.

Better Visibility into Performance Metrics

Base: Respondents using an eTMF, N varies



What benefits were achieved with your organization's implementation of the eTMF solution specified in question 9? Select all that apply. (Q.10) Which type of eTMF solution did you use most recently? (Q.9)

Use of Metrics and Impact on eTMF Benefits

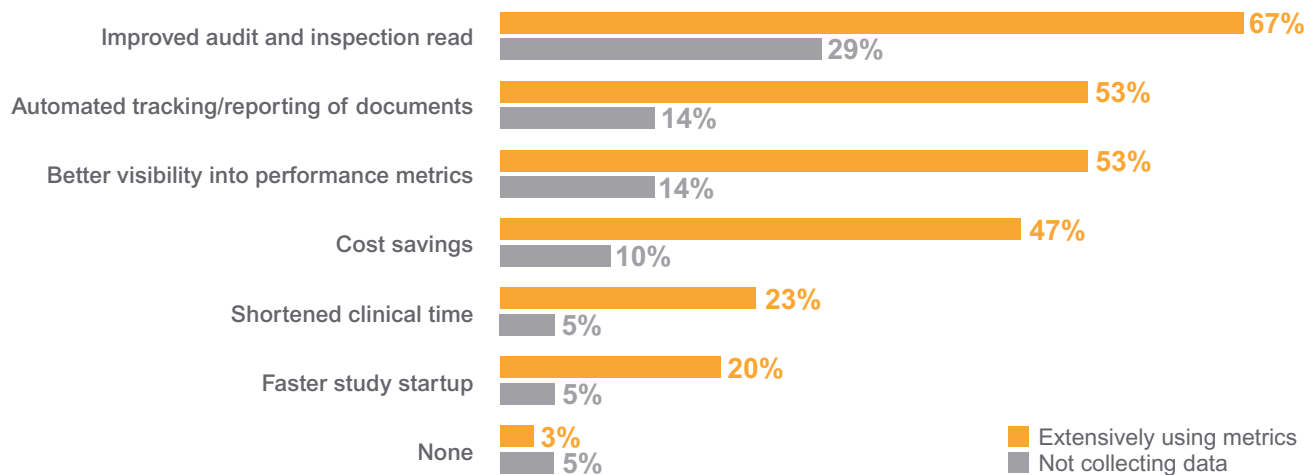
Organizations that use metrics to improve trial processes see more benefits than those who do not, including improved audit and inspection readiness (67% vs. 29%), better visibility into performance metrics (53% vs. 14%), and cost savings (47% vs. 10%).

Metrics also play an important part in speeding time to market. Respondents using an eTMF and extensively collecting data experienced faster study startup (20% vs. 5%) and shortened clinical time (23% vs. 5%) than those not collecting data.

eTMF Benefits Achieved by Level of Metrics Usage

Those reporting no use of metrics compared to those reporting extensive use of metrics

Base: Respondents using an eTMF, N = 155

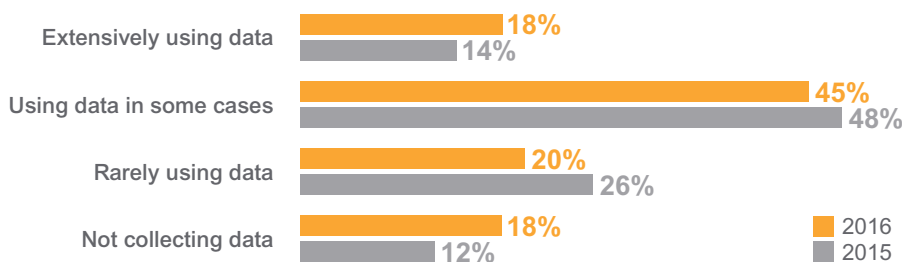


What benefits were achieved with your organization's implementation of the eTMF solution specified in question 9? Select all that apply. (Q.10) What type of eTMF solution do you currently use? (Q.9) To what extent is your organization leveraging TMF operational data (e.g., time from initial review to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

The number of TMF owners leveraging TMF operational data to improve trial processes remains relatively flat, with a majority (63%) sometimes or extensively using TMF data for process improvement. The number of respondents not collecting TMF operational data remains low (12%), declining slightly since 2015.

Organizations using TMF Metrics to Improve Clinical Processes

Base: Total respondents excluding "I don't know," 2015 N = 155, 2016 N = 184



To what extent is your organization leveraging TMF operational data (e.g., time from initial review to approval) to improve trial processes? Select one of the following. (Q.14)

Conclusion

Since the first annual *Veeva Paperless TMF Survey* in 2014, sponsors have made great strides in maturing their TMF technology and processes. Active TMF management is a direct result of this evolution, and sponsors are now actively managing TMF documents, data, and processes in one system and achieving greater benefits, including improved inspection readiness and shortened clinical trial time. Access for external collaborators is also on the rise, removing barriers, providing new insights, and improving TMF quality and timeliness.

The Shift to Active TMF – The 2016 survey indicates that organizations are maturing towards active TMF management by adopting advanced technologies, such as purpose-built eTMF applications. Compliance and shortened clinical trial time are the primary drivers of this shift, and improving inspection readiness and speeding study startup are the most cited benefits of adopting a purpose-built eTMF application.

Unifying Clinical Operations – Organizations continue the trend towards unifying clinical systems and processes. Direct access to sponsor systems for CROs and investigators continues to grow. Remote access for auditors and inspectors is now an expectation, and half of sponsors would like to integrate their eTMF application with a CTMS.

Process Improvement and Removal of Paper – The use of paper in clinical operations continues to drop significantly year over year, as does the exchange of paper documents between sponsors and CROs, and sponsors and sites. There remains much opportunity, however, as the majority of processes remain manual and leverage uncontrolled systems such as email.

Inspection Readiness and Visibility – Survey respondents using a purpose-built eTMF application continue to report the greatest improvements in inspection readiness, as well as central and remote monitoring. With a single source of truth there are no version control issues and monitors can proactively engage with sites to ensure SOP adherence.

The eTMF has become an integral component of daily clinical operations. When documents are created, reviewed, and acted upon in a unified manner it provides full visibility and enormous operational efficiencies. Organizations that use purpose-built eTMF applications are already expanding the scope of its use to help execute critical TMF activities and to plan and manage their overall clinical development strategy.

Survey Methods

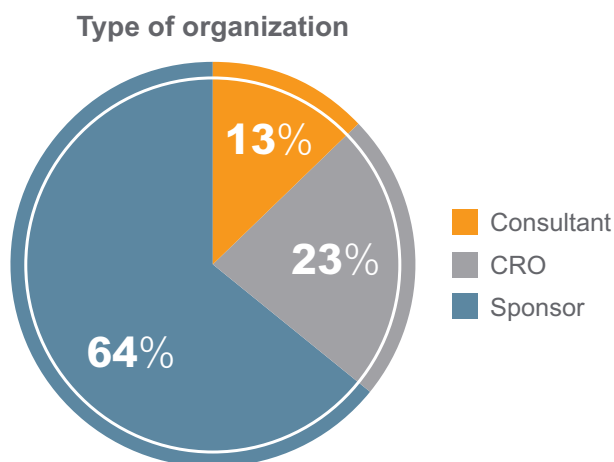
The survey consisted of 13 questions, many of which included sub-questions with response matrices. Survey questions were designed for individuals with knowledge of TMF document processes and with partial or full responsibility for a TMF within their organization. The survey was commissioned by Veeva Systems and conducted by Fierce Markets. Completion of the survey was voluntary, and a \$5 donation was made to Doctors Without Borders for each valid completion of the full survey. All respondents were offered a summary of the survey results. No other compensation was offered or provided.

Survey Respondents

Of the approximately 300,000 individuals invited to take the survey, a total of 1,804 surveys were initiated, the majority of which were terminated based on a qualification question gauging the level of responsibility for a TMF in their organization. More than 190 unverified responses were eliminated, yielding 217 qualified survey responses. More than half of the respondents were from sponsor companies in the United States.

Survey Respondent Demographics

Base: Total respondents, N = 217



Contact

For more information about this study, please contact us at eTMFsurvey@veeva.com.