ABSTRACT

Beckham, Amber, Benefits, Challenges, and Future Directions: Making the Case for eTMF in Clinical Research. Master of Science (Clinical Research Management), November, 2016. 87pp., 14 tables, 8 figures, survey, internship summary, journal entries, bibliography, 16 titles.

In clinical research there are many documents that must be retained in order to evaluate a trial, known as essential documents and collectively held in a trial master file. A trial master file can show if a trial was conducted according to regulatory standards. Traditionally this file has contained all paper documents, but with the advancement of technology, an electronic trial master file is now available. Although the technology of electronic trial master files exists, some organizations are still reluctant to make the switch from paper to electronic.

This practicum aims to measure current opinions about the use of an electronic trial master file, as well as determine what benefits and challenges are associated with using an electronic trial master file. Finally, this project aims to show the promising future and usefulness of an electronic trial master file in order to make the case for using an electronic trial master file in clinical research. This project will use a survey of clinical research professionals working at a CRO and an illustrative comparison in order to support the hypothesis that the benefits of using an electronic trial master file compared to a paper trial master file outweigh the challenges.

Participants of this project are generally in favor of using an electronic trial master file over a paper one, and they believe that using and electronic trial master file has positively impacted the role they have in clinical research. Although respondents view electronic trial master files as a good investment, they are also aware that there is room for improvement and have used their industry knowledge and experience to suggest future directions for the continued adoption and use of electronic trial master files.

BENEFITS, CHALLENGES, AND FUTURE DIRECTIONS: MAKING THE CASE FOR eTMF IN CLINICAL RESEARCH

INTERNSHIP PRACTICUM REPORT

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MASTER OF SCIENCE

IN CLINICAL RESEARCH MANAGEMENT

By

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I would lastly like to thank all my family and friends who have helped support me throughout my education. I would like to give special thanks to my parents and grandmother who have always believed in me and were always there to encourage me. I would especially like to thank my husband who despite being not being in the U.S. during my internship, was still able to love and support me every day.

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CHAPTER I

INTRODUCTION

The following practicum report was conducted and written during a six-month internship at a Contract Research Organization (CRO). Dr. Patricia Gwirtz from the University of North Texas Health Science center (UNHSC) served as the major professor for this project. The other members of the committee consist of Dr. Stephen Mathew from the UNTHSC, and from the CRO, Chief Executive Officer Lynn Van Dermark and Senior Compliance Specialist, Learning and Development, Bridget Browder. This practicum report was approved for exempt review by the UNTHSC IRB, submission information is located in appendix C.

Trial master files are a collection of essential documents that are critical to conducting a clinical trial. The documents that are found within a trial master file (TMF) reflect how a clinical trial is conducted and can help determine if a trial was conducted ethically. A list of essential documents can be seen in table 1 and in International conference on Harmonization (ICH) E6 guidelines (1). Many individuals contribute to the documents housed in a TMF. Regulations regarding the responsibilities of the sponsor and investigator can be found in title 21 of the Food and Drug Administration's (FDA) Code of Federal Regulations (CFR). A sponsor is the entity who initiates and takes responsibility for financial management of a clinical investigation. The investigator conducts the research at a site, and is responsible for ensuring that the research is conducted according to the investigators statement, investigational plan, and any regulations (2). Both the sponsor and the investigator are responsible for keeping required documents in their respective TMFs. In some cases, an organization may hire a Contract Research Organization (CRO) and delegate to them the responsibility of maintaining the TMF. A CRO is an organization that can be contracted to perform various aspects of a clinical trial.

Table 1: Essential Documents

Before Trial	During Trial	After Trial
1. Investigators brochure 2. Signed protocol and amendments 3. Information given to trial subject 4. Informed Consent 5. Advertisements 6. Financial agreements 7. Insurance statements 8. Signed agreement between involved parties 9. Dated and documented IRB approval 10. IRB/ethics committee composition 11. Regulatory authority's authorization/notification of protocol 12. CV and other relevant documents of PI and Sub-Investigators 13. Normative lab values 14. Medicals/laboratory procedures 15. Sample of labels attached to IP 16. Instructions for handling IP 17. Shipping records for IP and related materials 18. Certificate of analysis of IP shipped 19. Decoding procedures for blinded trials 20. Master randomization list 21. Pre-monitoring report 22. Trial initiation monitoring report	1. Investigators brochure 2. Revisions to: protocol, CRF, informed consent, written/provided information, advertisements 3. Dated and documented IRB approval of any revisions 4. Regulatory authority notification of amendments 5. CV for new PI or Sub-Investigators 6. Updated normative lab ranges 7. Updated medical/laboratory procedures 8. Updated medical/laboratory techniques 9. Documentation of IP and related materials shipment 10. Certificate of analysis for new batches of IP 11. Monitoring visit reports 12. Relevant communications 13. Signed informed consent forms 14. Source documents 15. Signed, dated, & completed CRFs 16. Documentation of CRF corrections 17. Notification by PI to Sponsor of any SAE 18. Notification by Sponsor to regulatory authorities of ay SAE 19. Notification by sponsor to PI of any new safety information 20. Interim reports to IRB and authorities 21. Subject screening log 22. Subject identification code list 23. Subject enrolment log 24. IP accountability 25. Signature sheet 26. Record of retained body fluids/tissue samples	1. IP Accountability 2. Documentation of IP destruction 3. Completed subject identification code list 4. Audit certificate 5. Final trial close-out monitoring report 6. Treatment allocations and decoding document 7. Final report by investigator to IRB/IEC, or regulatory authorities 8. Clinical study report

Auditors and inspectors use the TMF to help in determing if a trial was conducted in accordance with the laws and guidelines that govern clinical trials (3). A TMF will include all documentation that the personnel responsible for conducting a clinical trial are qualified by training, education and experience, so it can be used to determine if the individuals conducting the trials are qualified and have fulfilled their roles and responsibilities as outlined in ICH guidelines and CFR. By viewing data in documents within a TMF, data collected can be more critically evaluated to determine the quality (3). The accuracy and completeness of a TMF can help auditors/inspectors decide if there are significant findings that may delay or shut down a clinical trial. Having a well-developed TMF is essential to conducting a trial that is ethical and contains high quality data.

The use of an eTMF over a paper TMF has recently been increasing in clinical research. An eTMF has great potential to maximize quality while reducing costs of clinical research. There are, however, challenges to overcome when adopting new technology. This practicum highlights the benefits and addresses the challenges of an eTMF while also providing potential future directions for continued advancements. A survey administered to CRO employees in technical departments was used to illustrate how a purpose built eTMF is being used in a CRO. It also illuminates real life experiences seen with implementation and use of an eTMF.

CHAPTER II

BACKGROUND AND LITERATURE REVIEW

A Trial Master File is an important part of conducting a clinical trial. There are many documents that the sponsors and investigators of a clinical trial are required to complete in order to fulfill their obligations to the regulatory requirements and guidelines related to conducting clinical trials. A robust TMF allows clinical research professionals to organize essential documents and ensure compliance with CFR and GCP guidelines. A well maintained TMF can also help ensure good quality data is being recorded and it contains documentation that key individuals such as the investigator and sub-investigators are qualified to conduct clinical research for a particular study.

The eTMF with which the respondents of this practicum are familiar with follows the structure outlined by the Drug Information Association (DIA) reference model (4). This model includes the nomenclature that should be used to organize documents in an eTMF, as well as common names documents may be listed as in other systems. It also includes definitions as well as specifies whether a document is required or recommended by regulations and guidelines. Also presented is the ICH code with which a user can use to look up the guidance for a document in ICH GCP. Also the reference model describes whether the document is contained in the sponsor or investigator trial master file. The eTMF used by clinical research professional surveyed in this practicum also uses metadata to organize documents into the TMF. Metadata is information about data that is structured in a way that makes locating, retrieving and managing data easier (5). In a purpose built eTMF metadata is used to help organize documents into specific sections or groups so that those documents can be located easily without knowing exactly where to look. This feature directly ties into searchability in an eTMF because with metadata individuals can

search for descriptive information pertaining to a document such as a specific site, the investigator, the title of a document and even a combination of characteristics and are still able to find the document they are looking for, assuming the document was uploaded into the system with the correct metadata. In a purpose built system the metadata can be determined as needed and individuals can be instructed on the proper metadata to use for each document.

Trial Master Files have traditionally been organized into a paper system where are all of the documents are printed and filed into a physical filing cabinet. They can, however, be organized into an electronic system or a hybrid of paper and electronic. Documents can be organized into a system such as a file share system or a local file system where documents may be created and edited electronically and then shared through email or sent through the mail. Similarly, to a local share, a cloud based system can be used where documents are stored in the cloud and users can access them directly (6). Alternatively, documents can be organized into a purpose build electronic TMF. A purpose built eTMF is what participants of this practicum are familiar with and is the model which will be used to make the case for using eTMF throughout this practicum. In a purpose built system, documents can be created, edited, and shared through the system and the system can be customized to the specific needs of the user or organization.

A purpose built eTMF provides additional features such as the use of workflows, version control and a clear audit trail which may not be available in other electronic or paper based systems. A workflow is an automated sequence of events in an electronic system that is initiated by the user once they have created a document. Workflows allow for documents to be easily sent, edited, and approved between multiple individuals. Workflows also allow documents to be assigned to a specific person or a groups of people, and documents can be dispersed in a desired order, for example, to ensure that the approver sees the document last. For a TMF this can be

particularly helpful in creating an audit trial where the life of a document can be followed by an auditor or inspector. Having a clear audit trail allows an organization to be better prepared for an audit or inspection thus increasing overall inspection readiness. Version control refers to the purpose built eTMFs ability to have an effective version and superseded versions of a document, but only have the effective version be viewable to individuals who are accessing that document. The eTMF system can also keep track of the changes that have been made and who made those changes.

The differences between a paper TMF and an eTMF are not in the content of the files, because the regulations governing all forms of TMFs are the same, but rather in the efficiency of the overall process. Veeva, a cloud based computing company, has conducted a survey every year for the last three years on the adoption and use of eTMFs. Since 2014 Veeva survey participants have reported that the use and implementation of more advanced eTMFs has doubled (7). In the 2015 Veeva paperless survey, two thirds of representative CRO respondents cited easier document searches as one of the main benefits to eTMF (8). Also cited were improved inspection readiness, automated tracking of documents, and easier external collaboration as direct benefits of using an eTMF system (8). In the 2016 Veeva survey the most cited benefits were improved inspection readiness, followed by faster study start up and improved trial oversight (7). The benefits reported from respondents in the Veeva survey are a direct result of using an eTMF which shows that clinical research professionals in industry are noticing that using an eTMF instead of a paper TMF can improve the overall quality of a trial and make the process easier for individuals conducting research.

In a paper system for a study with multiple research sites at various locations, each site would have its own collection of required TMF documents and copies would have to be sent to

the study sponsor. In an electronic system, each site still has its own document collection, but there are additional features that can help streamline the maintenance of an eTMF. In an eTMF documents are searchable and readable through the electronic system instead of using physical paper folders and filing cabinets. The eTMF also allows for the creation of templates which can easily be updated and shared allowing the process of generating new documents to be more efficient. Also, since access can be granted directly to documents within the eTMF, the sponsor can be given direct access. The proprietary nature of the templates can be better persevered in an eTMF because permissions must be given to view documents, which may not be easily achieved in a paper, file share, or local system.

The eTMF also improves accessibility, making it easier for anyone involved in a clinical trial to access the system from a remote location, provided they are given specific permissions, and edit or approve documents quickly (9). In any system, there must be a way to control who is handling essential documents. In a paper system, this is traditionally done through a central file room which is accessed with a key. In this system, documents must be checked out and signed for as needed. In a purpose built eTMF, documents can be checked out electronically and individuals must be given permission to see documents with in the TMF. In a purpose built system when a document is checked out, others are able to open and read the document electronically but are unable to edit that document until it can be checked out again.

Storage and archiving are also improved with the use of an eTMF. In a paper system, when a trial is completed there may be thousands of documents which need to be boxed up and archived. The documents must be kept by the sponsor for two years after the last marketing application. This requires a large amount of space which must be climate controlled and have some protections again disasters. If an organization such as a CRO is delegated the

responsibility of managing the TMF for a sponsor, the documents will need to be shipped to the sponsor at the end of the trial. This process is very time consuming and can be very costly due to the material such as paper, ink, shipping supplies, and postage needed to get the documents to a sponsor. The process of storage and archiving in an eTMF is much less time consuming because the documents can be saved on to a flash drive or disk and sent to the sponsor, and because no paper is being shipped the cost of sending the TMF is also reduced.

The features that can be used in a purpose built eTMF can lead greater efficiency in creating, editing, and sharing essential documents. It is predicted that the time savings that using an eTMF creates will translate into cost savings and it will help to create more meaningful roles for the individuals who are involved in conducting those trials (10). Being able to spend less time on creating and formatting a document or waiting to review a document, translates to more time being spent on ensuring the quality of the information being recorded.

While the benefits of using an electronic TMF seem promising, some organizations are still reluctant to make the switch. It is important to address the challenges associated with implementation and continued use of an eTMF that are often deterrents for those who are not yet using an eTMF. In the 2015 Veeva paperless survey, 85% of CRO responders stated that they are still not using an eTMF (8). The top reasons given for not adopting eTMF were: cost of implementation, regulatory requirements, lack of tools or knowledge to support an eTMF, and the impact of organizational change. In 2016 the number of responders not using an eTMF went down to 74%. In a survey by Nextdocs of companies managing clinical trials, the major reason that companies are not adopting eTMF is that they are not convinced that eTMF will positively impact their business (11). It is hard to get concrete proof that an eTMF is going to save a company time and money over a paper TMF because every trial is unique.

This project aims to address all of these concerns and show that they do not outweigh the benefits associated with adopting an eTMF and show that it does make good business sense to adopt this technology. This project will accomplish these goals through the use of a survey designed to look at the benefits and challenges of an eTMF system. It will also look at trials that have adopted eTMF and those who have not by comparing the processes involved with creating, editing, and archiving essential documents. The table comparison of paper vs electronic TMF will be used to show the efficiency of an eTMF in managing essential documents in a tangible way that can be used to make the case for clinical research businesses to adopt eTMF.

One of the most pressing issues surrounding clinical trials today is the time and money it takes to complete them. An article written in 2014 by the U.S. Department of Health and Human Services states that the cost of bringing a new drug to the market through clinical trials costs anywhere from $161 million to $2 billion dollars (12). This number continues to grow every year and is, in part, associated with the increased time for conducting clinical trials. There is a need to decrease the time and cost of clinical research associated with bringing new drugs to market and ensure profits for the stakeholders involved in conducting research. Also there are individuals who are in need of new treatments, diagnostics, and preventative medicines, and decreasing the time and cost of clinical trials will get products to them sooner and hopefully at a lower cost. One of the ways industry leaders are trying to accomplish this goal is through the use of technology. FDA has already set guidelines for the use of electronic data capture (EDC), electronic health records (EHR), and electronic source documents (13). The push towards the use of technology by the FDA seems to suggest that guidelines on the use of eTMF in clinical research are not far off, and those companies who are already adopting this technology may end up being “ahead of the game” if and when regulatory requirements are released.

This project will also discuss potential improvements to the current state of eTMF. Changes such as the integration of Clinical Trial Management Systems (CTMS) and eTMF, using more of the features already available in eTMFs, and the use of mobile devices and tablets will be discussed. Innovations could be used to decrease the total amount of time and money spent on an individual clinical trial. Continuing to grow through the adoption of new technologies can also help companies like CROs gain a competitive advantage and increase their overall efficiency. In clinical research today, CROs strive to stay on top of the industry by adopting new technologies, such as an eTMF. CROs do this in order to show clients that they are industry leaders and that they have the means keep up with their clients increasing demands for conducting faster trials at lower costs. Research professionals in industry also adopt new technologies to continuously improve the clinical trial process in order to get new drugs and devices on the market faster for individuals in need.

SPECIFIC AIMS

Hypothesis: The benefits of using an electronic trial master file compared to a paper trial master file outweigh the challenges.

Aim 1: Measure current opinions on the usefulness and challenges associated with the use of eTMF in a CRO.

Aim 2: Address the benefits and the challenges of using an eTMF as compared to a paper TMF in clinical research.

Aim 3: Assert the promising future of eTMF and its continued usefulness in the conduct of clinical trials.

SIGNIFICANCE

The development of new life saving drugs, biologics, and devices are fueled by the clinical research industry. Without clinical trials there would be no new treatments, but the cost and time it takes to go from the start of a trial to when the product can go on the market is a major limitation (14). The use of an eTMF may help to reduce the cost and length of clinical trials, thus allowing for important new discoveries to benefit the public in a timelier manner. The adoption of new technologies, like eTMF, could also give a distinct competitive advantage to companies that choose to take advantage of all technology has to offer. This project aims to directly show how an eTMF can provide competitive advantages while enabling faster, more cost efficient clinical trials resulting in benefits for all parties involved.

MATERIALS AND METHODS

Data Collection

Data was collected via an optional online survey of the employees at a CRO. The survey was administered through Survey Monkey, a secure online service that allows the composition and distribution of surveys. The survey included questions specifically worded to limit the amount of biased responses and mainly focused on the overall benefits and challenges to using an eTMF. The survey was optional and anonymous to encourage honest answers. The survey participants were not asked to give any personal or identifiable information about themselves.

Methods

The respondents of the survey were CRO employees at least 18 and older in all technical departments at all locations. Participation was voluntary and all participants were informed of the survey via company email. The email contained a link to the survey upon which participants

clicked if they wished to participate. The email also had a brief description of the contents of the survey and the risks associated with participation. The survey was hosted by an online website, Survey Monkey, and was open for two weeks, with an email sent out once a week to request participation. Results from all questions were used in the subsequent practicum report to either support or refute the proposed hypothesis. No calculations were used to determine sample size, as the pool of participants was limited to employees of the CRO where this internship takes place.

RESULTS AND DISCUSSION

Results

The survey used consisted of 20 questions designed to measure current opinions of eTMF from clinical research professionals working in industry. Questions were designed to determine what participants believed to be the benefits and challenges of their current eTMF and what they thought needed to change. The survey was open to all personnel in all technical departments at a CRO for a two-week period starting on August 30, 2016. There was a total of 26 respondents to the survey. A table of general processes and how they are carried out in a paper TMF and an eTMF is included to aid in the illustration of the benefits of using an electronic trial master file (Table 2).

Table 2: Comparison of Paper TMF and eTMF

Process	Paper TMF	Electronic TMF
Collaboration	• Progress reports must be scheduled when all investors are available • Documents need to be located and sent via mail or email	• Use of workflows shows project status in real time • Documents are accessible through esystem with internet access
Access control	• Human control, documents are physically printed out or taken from file cabinet and sent via mail or email as requested	• Individuals can be given permissions to allow real time access for specific documents and projects in the esystem
Creating/editing documents	• Create new document or template • Documents emailed or mailed back and forth for edits	• Stored/controlled template • Real time updates to documents in a workflow that can be electronically sent back and forth
Storing/archiving documents	• Paper documents are physically stored in file cabinets	• Electronic documents stored on a server or in the cloud
Organization	• Filing based on specified system that depends on employees to uphold	• Filing based on structured metadata and automated filing of electronic documents
Inspection readiness	• Paper files have to be located and copied • Compliance depends on human filing system to be accurate	• Instant access to up-to-date documents in system • Electronic systems are easily searchable without knowing where documents are located

Respondent background

The industry background and experience with clinical research was determined at the beginning of the survey. Table 3 describes the various technical departments in which CRO employees work. Of those who responded, about 85% of were from the Clinical Operations department, about 12% from the Quality Assurance and Training Department, and about 4% from the Informatics department. Table 4 presents the length of time that respondents have

worked in clinical research. About half of respondents have worked in clinical research for more than 10 years, and 80% have worked in clinical research for six years or more.

Table 3: Respondent Department

What area/department do you work in?		
Answer Options	**Response Percent**	**Response Count**
Clinical Operations	84.6%	22
Informatics	3.8%	1
Quality Assurance and Training	11.5%	3
	answered question	**26**

Table 4: Years Worked in Clinical Research

How long have you worked in the clinical research industry?		
Answer Options	**Response Percent**	**Response Count**
5 years or less	19.2%	5
6-10 years	34.6%	9
11-15 years	15.4%	4
16 years or more	30.8%	8
	answered question	**26**

Current uses

The uses of the current eTMF by employees at the internship site was determined through three survey questions. Table 5 shows the results of how often employees use/interact with their current eTMF. The majority of participants stated that they use their current eTMF multiple times a day. The data presented in Table 6 describes where employees are most likely to access

the eTMF for work related activities. Most respondents reported accessing the eTMF outside of a company office, with 88% stating that they use their home office. Table 7 shows how employees use their current eTMF. Most respondents (80%) cited "viewing regulatory documents" as the main reason to access the eTMF vault. Equally cited were using the eTMF for creating and editing regulatory documents and sending or uploading regulatory documents.

Table 5: Frequency of Responders Use of eTMF

How often do you use/interact with the current eTMF system?		
Answer Options	**Response Percent**	**Response Count**
Once a day	8.0%	2
Multiple times a day	56.0%	14
A few times a week	12.0%	3
A few times a month	16.0%	4
Rarely to never	8.0%	2
	answered question	**25**

Table 6: Location Responders Access eTMF

Where do you normally access the MedTrials eTMF? (select all that apply)		
Answer Options	**Response Percent**	**Response Count**
At your home office	88.0%	22
At an investigational site	40.0%	10
At a company office	24.0%	6
In a hotel room	44.0%	11
At an airport	32.0%	8
At a restaurant	0.0%	0
Other (please specify)	4.0%	1
	answered question	**25**

Table 7: Employee Use of Current eTMF

For which activities do you currently use your curent eTMF? (select all that apply)		
Answer Options	**Response Percent**	**Response Count**
Regulatory document viewing	80.0%	20
Creating or editing regulatory documents	28.0%	7
Sending and uploading regulatory documents to or from clients	28.0%	7
Other (please specify)	20.0%	5
	answered question	**25**

Effects of eTMF: Benefits and Challenges

The overall effects of the current eTMF were determined through three survey questions. Respondents were asked if the use of an eTMF positively or negatively impacted their role in clinical research. The results of this question are presented in Figure 1. The majority of individuals polled stated that their role in clinical research was positively impacted by the use of an eTMF.

The benefits of using of eTMF can be seen in Figure 2. Respondents were given a list of common benefits that have been associated with using an eTMF and asked to rank them from 1 to 5 in order of how beneficial they believe the benefits to be, with 1 being the most beneficial and 5 being the least beneficial. The average score of each answer choice is displayed in Figure 1. Searchability of documents had the lowest average score, which correlates to the greatest benefit as seen by respondent's experience using an eTMF. Completeness of study files and document quality also had lower scores, correlating with direct benefits experienced with the use of an eTMF. External collaboration and audit trails had the highest scores, meaning that responders viewed these categories as less beneficial.

Subjects were also given a list of common challenges associated with using an eTMF and asked to rank the challenges, with 1 being the most challenging and 5 being the least challenging. The results of this question are shown in Figure 3. The average scores for all of the challenges were very similar with the greatest difference between any two scores being 0.35. Respondents chose "training of personnel" as the most common challenge, followed by organization/searchability, client hesitation, accessibility and cost of implementation and maintenance.

Figure 1: Impact of eTMF on Respondent Role

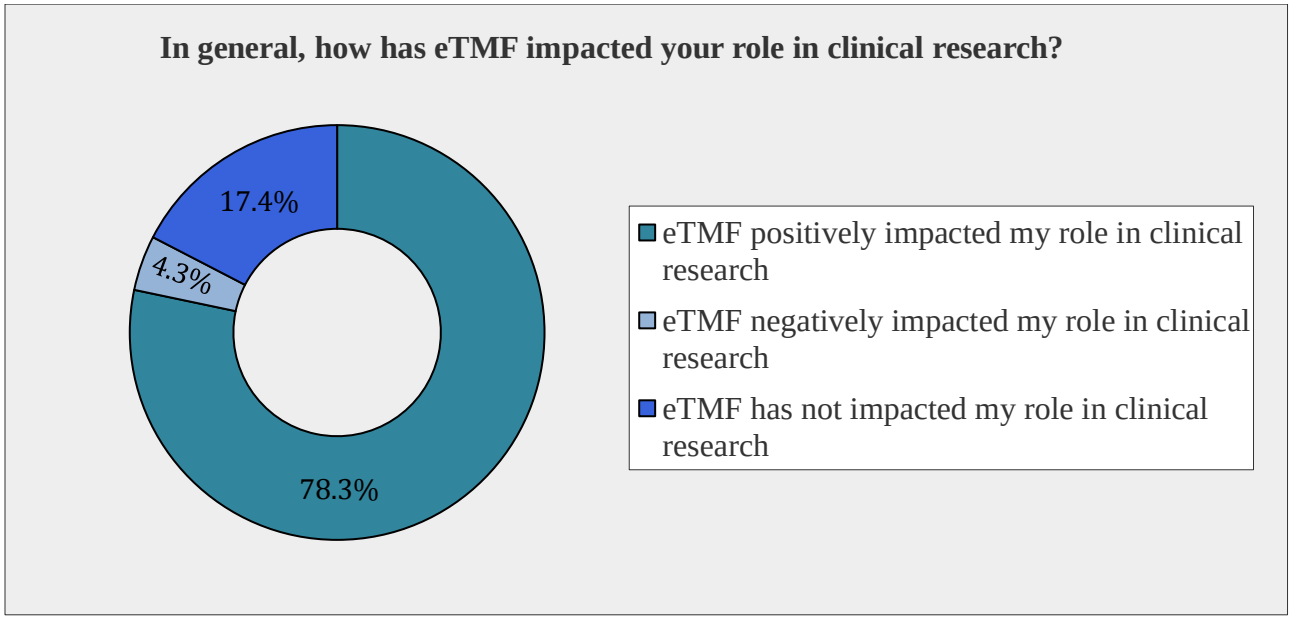


Figure 2: Benefits of eTMF

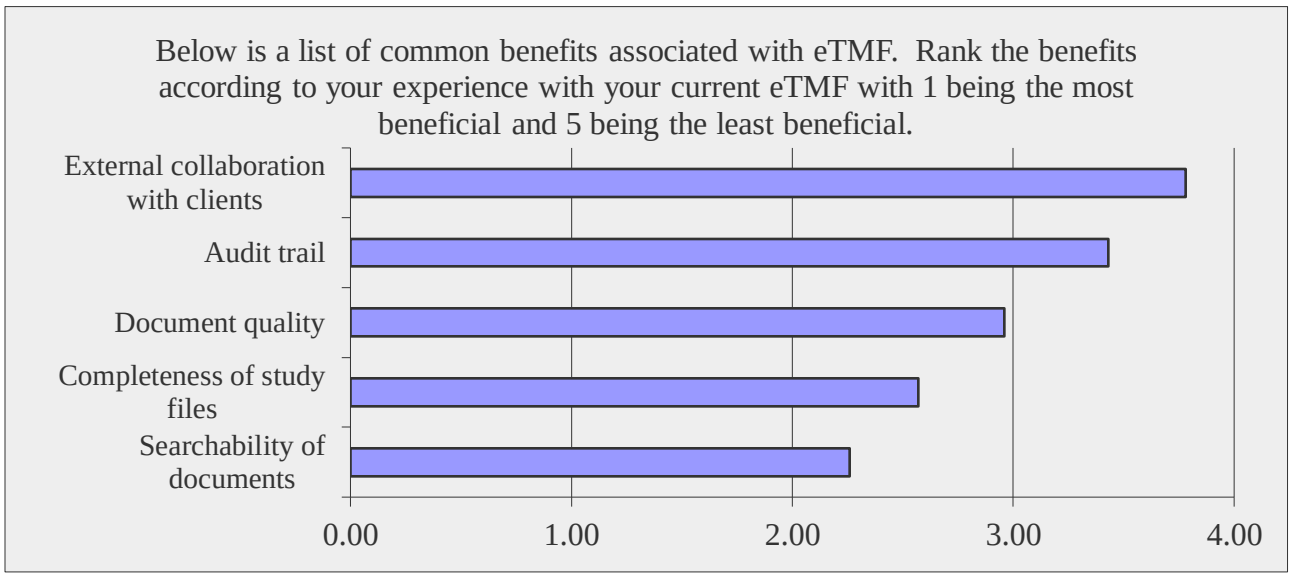
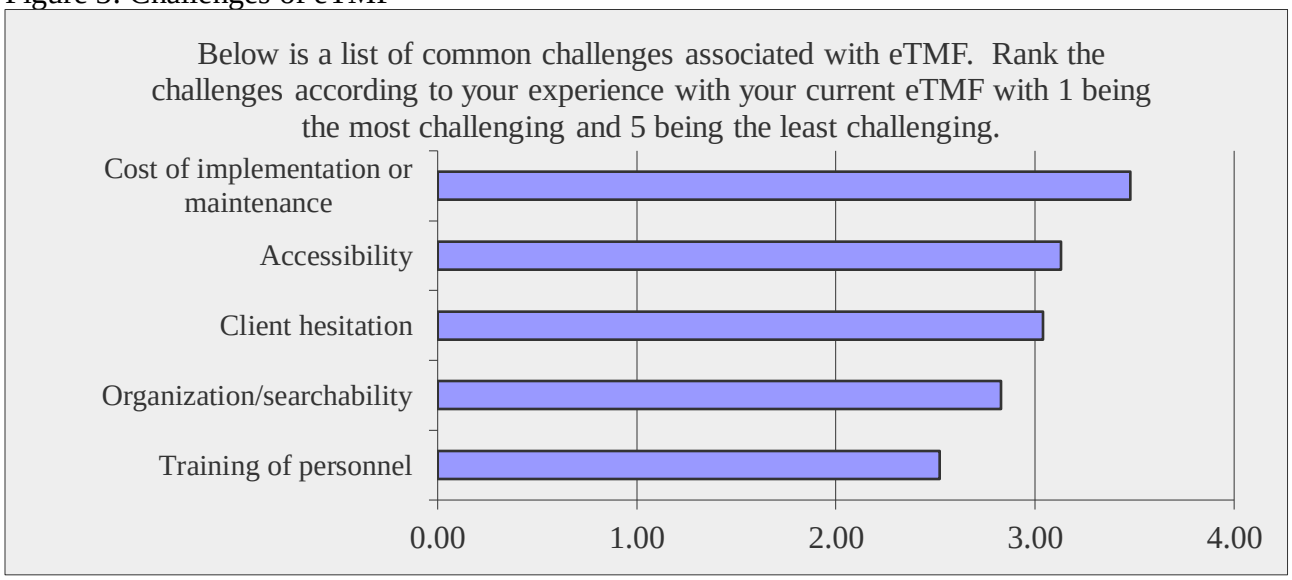


Figure 3: Challenges of eTMF



Effects of eTMF: Cost

Three survey questions were used to acertain the general opinions of the effect using an eTMF has on the cost of running a clinical trial. The first question directly asked respondents if they thought using an eTMF increased or decreased cost (Figure 4 and Table 8). The results of this question show that about 35% of those polled believe that using an eTMF would increase the cost of running a clinical trial and about 48% believe using an eTMF decreases the cost of running a clinical trial. The other 18% believe that an eTMF does not impact the cost of running a clinical trial.

The second question, directed at individuals who stated that an eTMF would increase the cost of running a clinical trial, asked participants to state the factors which they believed contribute to an increased cost (Table 9). The majority stated that implementation and maintenance of an eTMF are the main factors that contribute to an increased cost. Half of the responders also listed "training of personnel" to be a contributor for increased cost associated with the use of an eTMF.

Alternatively, the third question asked participants who stated that eTMF decreases the cost of running a clinical trial to state what factors contribute to a decreased cost; these results can be seen in Table 10. According to the survey, the greatest contributor to a decreased cost was "increased overall efficiency" with 82% of respondents selecting this choice. The next highest contributor to decreased cost associated with using an eTMF was streamlining of the overall process (73%), followed by decreased time to create, edit and share documents (64%), and speeding up external collaboration (55%).

Table 8: Effect of eTMF on Cost

In your opinion, what effect does eTMF have on the cost of running a clinical trial?		
Answer Options	**Response Percent**	**Response Count**
Increases cost significantly	13.0%	3
Increases cost slightly	21.7%	5
Does not impact cost	17.4%	4
Decreases cost slightly	26.1%	6
Decreases cost significantly	21.7%	5
	answered question	**23**

Figure 4: Effect of eTMF on Cost

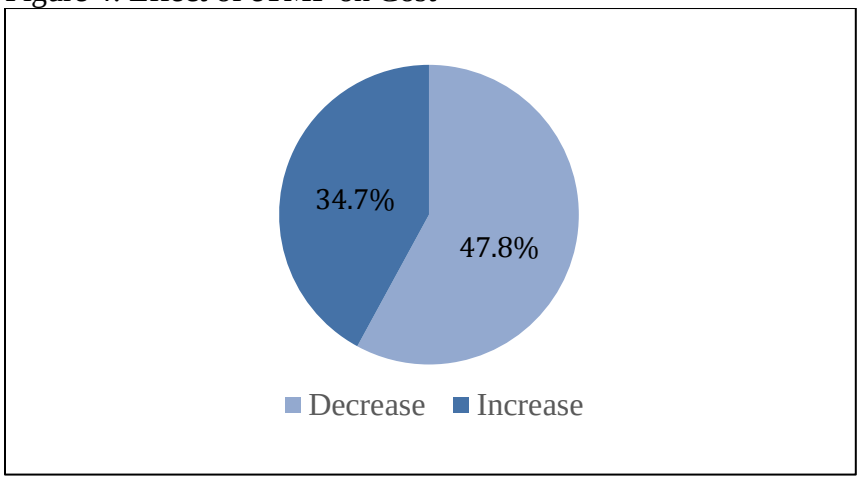


Table 9: Contributors to Increased Cost

In your opinion, what contributes to an increased cost? (select all that apply)		
Answer Options	**Response Percent**	**Response Count**
Implementation of eTMF	75.0%	6
Maintenance of eTMF	87.5%	7
Training of Personnel	50.0%	4
Other (please specify)	12.5%	1
answered question		**8**

Table 10: Contributors to Decreased Cost

In your opinion, what contributes to a decreased cost? (select all that apply)		
Answer Options	**Response Percent**	**Response Count**
Decreased time to create, edit and share documents	63.6%	7
Streamlining the overall process	72.7%	8
Speeding up external collaboration	54.5%	6
Increased overall efficiency	81.8%	9
Other (please specify)	9.1%	1
answered question		**11**

Effects of eTMF: Efficiency

The impact of an eTMF on the efficiency of clinical trials was measured by three survey questions. Figure 5 represents results from the first question which asked whether using an eTMF increases or decreased the overall efficiency of conducting a clinical trial. Of those who responded, all except one individual stated that using an eTMF increases efficiency when

working with project-related documents. The respondents were then instructed to state what they believe contributes to the increased efficiency; these results are shown in Figure 6. Participants then ranked several answer choices on a scale of 1 to 5 in order of how they increase efficiency with 1 being the greatest increase to efficiency. Respondents listed "organization" and "searchability" to be the greatest factors increasing efficiency. "Ease of use and the use of workflows" had the same average score as the third greatest factor influencing increased efficiency followed by the use of templates for creating documents.

Figure 5: Effect of eTMF of Efficiency

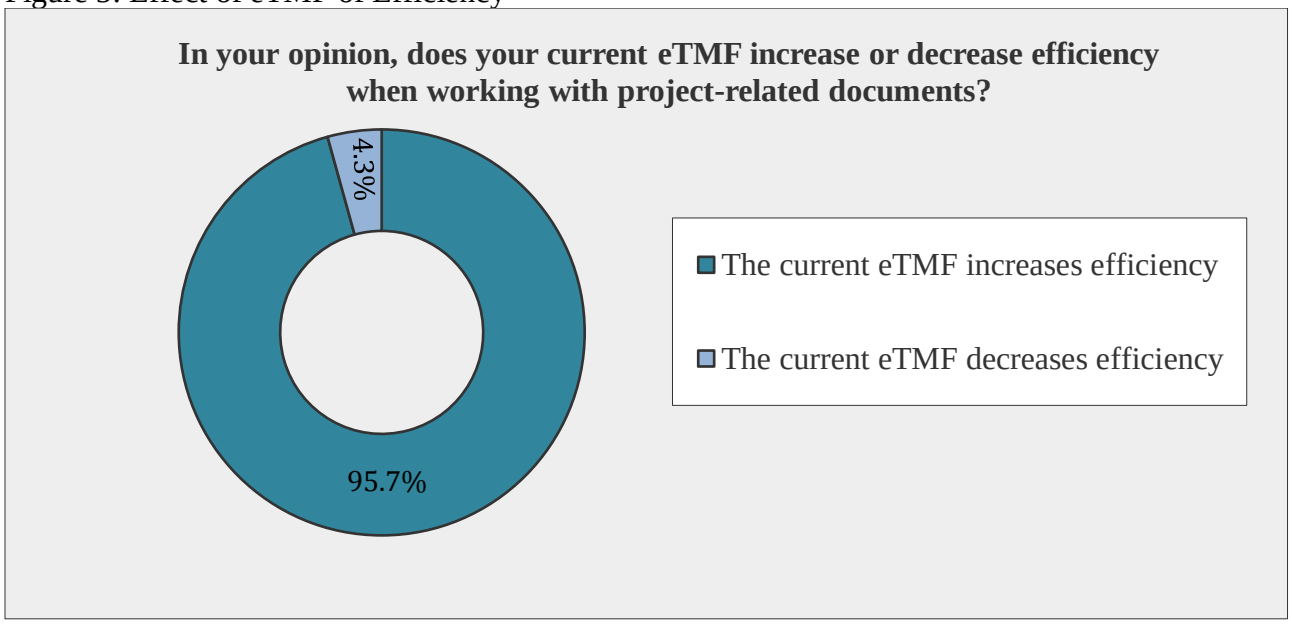
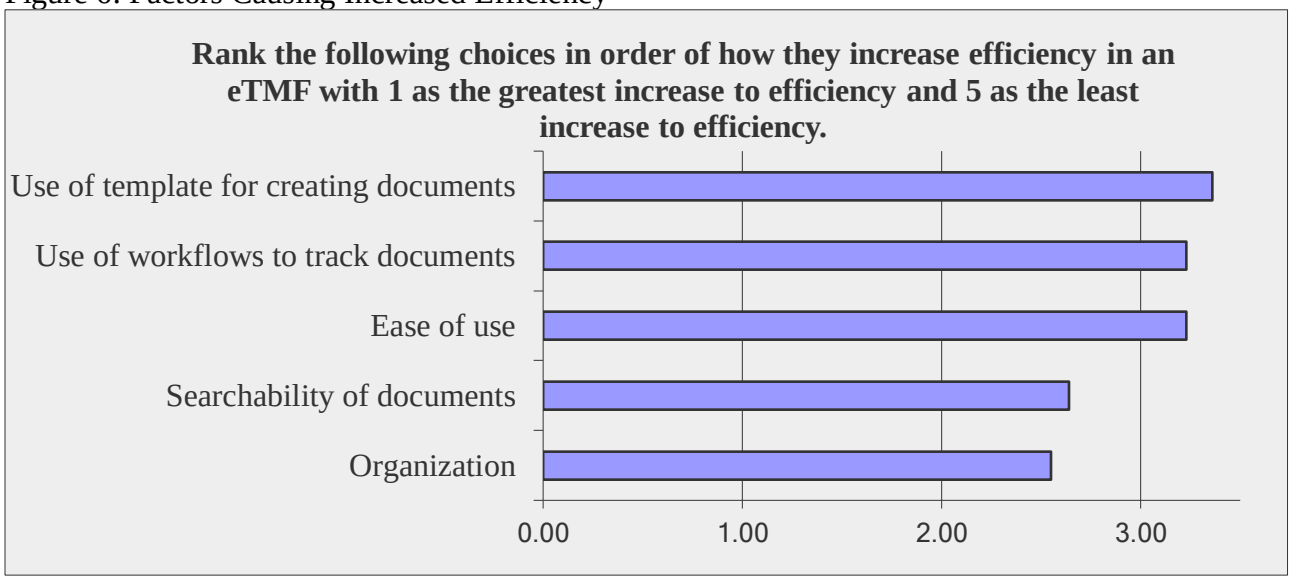


Figure 6: Factors Causing Increased Efficiency



Functionality of eTMF

Four questions addressed the respondent's opinion of the functionality of their current eTMF. Figure 7 represents results related to the difficulty of locating documents in the eTMF. About 83% of respondents stated that documents were not difficult or were a little difficult to locate. About 13% stated that documents were somewhat difficult to locate. Only one respondent stated that documents were very difficult to locate and no one responded that documents were extremely difficult to locate. Figure 8 shows the results of how the use of metadata affects the searchability of documents in an eTMF. About 83% of respondents stated metadata makes searching for documents easier and 13% stated that metadata makes searching for documents slightly more difficult.

The results in Table 11 represent opinions regarding the quality and completeness of documents located in the current eTMF. Survey responders were asked to determine the quality and completeness of documents they encountered in the eTMF from 1-5 with 1 representing the highest quality documents, meaning that documents are rarely or never missing. About 87% of

respondents gave their eTMF a rating of 1, 2 or 3. The majority (39%) gave the eTMF a score of 3, and no one gave a score of 5. Participants opinions on the general security of their eTMF was determined with one question (Table 12). All individuals who answered stated that they believed their current eTMF was at least somewhat secure, and 61% of responders stated the eTMF is very secure.

Figure 7: Difficulty of Locating Documents in Current eTMF

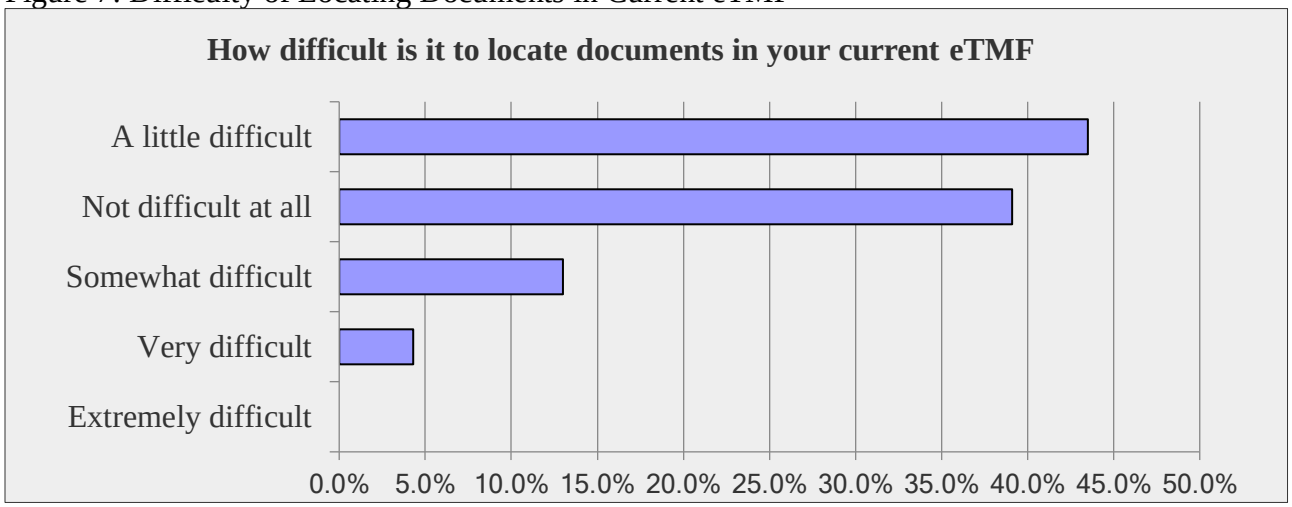


Figure 8: Use of Metadata in eTMF

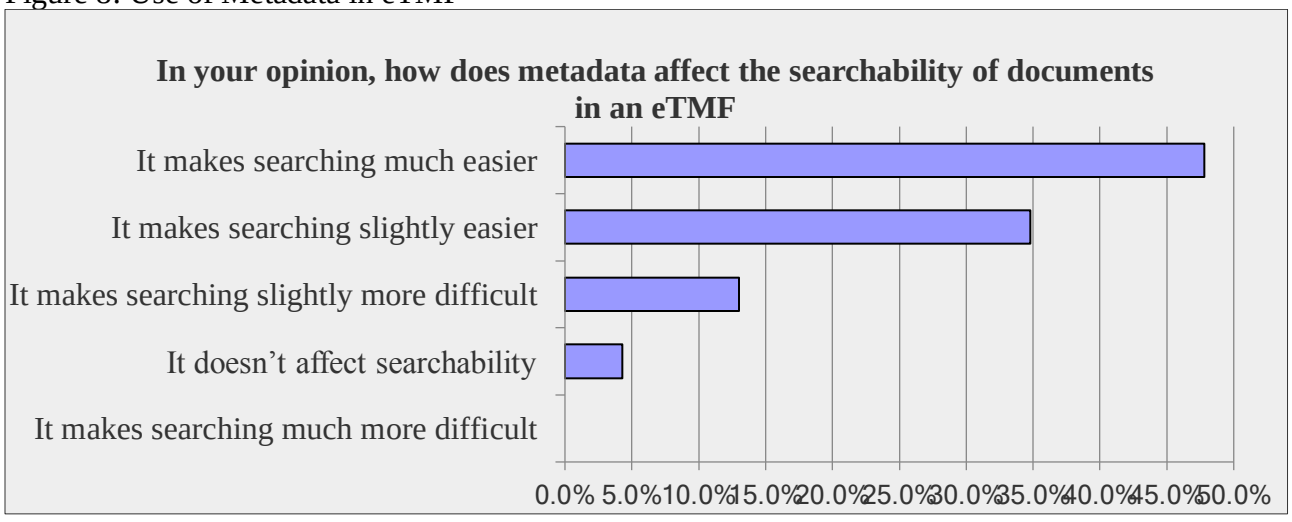


Table 11: Quality and Completeness of Documents in eTMF

On a scale of 1-5, describe the quality and completeness of documents you access in your current eTMF. 1 represents the highest quality: there are rarely (or never) missing, inaccurate, or incomplete documents. 5 represents the lowest quality: the documents are often missing, inaccurate, or incomplete.		
Answer Options	**Response Percent**	**Response Count**
1	13.0%	3
2	34.8%	8
3	39.1%	9
4	13.0%	3
5	0.0%	0
answered question		**23**

Table 12: Security of eTMF

How secure do you believe your current eTMF is?		
Answer Options	**Response Percent**	**Response Count**
Extremely secure	13.0%	3
Very secure	60.9%	14
Somewhat secure	26.1%	6
Not very secure	0.0%	0
Not at all secure	0.0%	0
answered question		**23**

Future Directions

Respondents were asked two questions to determine what changes they believed should be implemented in order to improve their current eTMF. The results shown in Table 13 represent the features which respondents view as underutilized with their current eTMF. Users identified the use of a mobile device application, electronic signatures, and the use of fillable forms as the features which have been the most underutilized. A small number of individuals also stated that

document sharing through workflows is an underutilized feature in their current eTMF. Responders were given an open ended question which asked what employees believed should be changed or imporved in their current eTMF. The responses given are listed in Table 14. The most common changes suggested involved improving searchability and customizability of the system, improved naming conventions, and increased utilization of the features available.

Table 13: Underutilized Features of eTMF

Which feature(s) do you believe are underutilized in your current eTMF? (select all that apply)		
Answer Options	**Response Percent**	**Response Count**
Electronic signatures	47.8%	11
Document Sharing through workflows	17.4%	4
Fillable forms	39.1%	9
Use of mobile device application	52.2%	12
Other (please specify)	8.7%	2
	answered question	**23**

Table 14: Future Changes to eTMF

	What Changes do you believe should be made to the current eTMF to improve the system?
1	More user friendly
2	More customized views for users
3	Ability to create site/individual specific reports for tracking of documents. Use of standardized summary reports for contents of Regulatory documents
4	Permission defaults
5	Currently there are too many "numbering" issues. I would like to see an easier way to actually get to a document, without having to go thru multiple steps
6	The search function is too broad and sometimes the naming conventions make items difficult to search for.
7	More detailed training so all documents are labeled correctly which in turn makes them more searchable
8	Password protect files to avoid accidental opening of documents
9	Make clear legend of what button symbols mean
10	The speed of the search feature should be faster.
11	Standard naming convention of document types across the board, handheld scanners for CRAs to scan the documents to in-house while onsite instead of taking hard copies to scan after the visit
12	Increase in workflow and assignment use; further integration and clarification of item location with non CTMS/eTMF vaults (DMS, QMS)
13	The metadata structure is a bit difficult to understand - traditional files would be nice.
14	Utilize the system more across all studies.
15	Implement more automated services: workflows, assignments, overdue assignments notifications, unauthorized access attempts reporting
16	Everything should be on 1 platform with a simple search to find docs.

Discussion

The purpose of this survey was to uncover how individuals who work in the clinical research industry felt about the use of eTMFs. The survey was designed to collect information from clinical research professionals who have experience working with a purpose built eTMF in the clinical research industry in order to determine the benefits and challenges associated with an eTMF. This survey also assessed industry opinions regarding which aspects of an eTMF should be changed or utilized more.

Respondent Background

The background information gathered on CRO employees who were surveyed showed that most had an extensive background in clinical research, with at least six years of experience working in the industry. Also, there were a large number of individuals who have 16 or more years of experience, which makes them uniquely qualified to assess benefits and challenges to using an eTMF as they have worked with both paper and electronic trial master files.

Current uses of eTMF

The majority of respondents access their current eTMF multiple times a day. Some only access the eTMF a few times a week or month. Most employees surveyed were able to make good use of their eTMF by accessing files remotely from their home office, at their investigator sites, or other public areas. Regulatory document viewing is the most common reason cited for accessing the eTMF. Clinical research professional must constantly access essential documents. The ability to view, created, edit, and share these documents remotely is very beneficial and allows research professionals the flexibility to work outside a traditional

office setting. It may even increase productivity since individuals are able access essentials documents from anywhere, not just when they are in the office.

Impact of eTMFs: Benefits and Challenges

Respondents generally believe that their role is positively impacted by the use of an eTMF in conducting a clinical trial. Through the use of an eTMF, survey participants also have experience with the benefits and challenges associated with using an eTMF. Document Searchability was the highest ranked benefit using an eTMF. Other benefits that respondent ranked highly were better document quality, audit trails, and external collaboration with clients. Individuals believe that previous TMF management solutions need to be improved, and that embracing new technology such as a purpose built eTMF can help make improvements to important areas such as searchability, document quality, inspection readiness, and collaboration.

Challenges associated with using an eTMF were also expressed by survey participants. Training of personnel on the use and management of an eTMF was reported as a difficult challenge when working with an eTMF. Interestingly, searchability also seems to be a large area that respondents find challenging even though they also believe that an eTMF improves searchability of documents. Another concern associated with using an eTMF is that the system may be difficult to access or that sponsors may be hesitant to accept an eTMF. Cost, however, seems to be the least challenging hurdle to using eTMFs. The challenges listed had very similar average scores, suggesting that individual participants differ on what is perceived as a challenge when using an eTMF. The results of this question also suggest that even though, in general, individuals believe using and eTMF improves management and quality of essential

documents, it is not perfect and there is still room for improvement. The opinions on what needs to be improved, however, seemed to be customized to the individual user.

Impact of eTMFs: Cost

When asked about cost, survey Reponses were almost evenly split between an eTMF increasing the cost of a clinical trial and an eTMF decreasing the cost. It would seem that research professionals in the industry are unsure of the potential cost benefits of using an eTMF. As seen in the challenges section, industry professionals also do not believe cost is a challenge associated with using an eTMF. Those who believed that an eTMF increases the cost of a clinical trial felt that the implementation and maintenance of an eTMF were the greatest factors which increase the cost of running a clinical trial. Half of the respondents also answered that training personnel increases cost, which fits with their response that training personnel is the greatest challenge associated with the use of an eTMF.

Respondents who stated that using an eTMF decreases the cost of running a clinical trial felt that increased efficiency and streamlining of study processes were the greatest cost reducers associated with using an eTMF. They also responded that their eTMF decreases the time to create, edit, and share documents which, to them, relates to a decrease in the cost of a clinical trial. This suggests that industry professionals see a monitary value associated with being able to decrease time spent conducting a clinical trial. Since the greatest benefit of using an eTMF was reported to be searchability followed by the completeness and quality of essential documents, it fits that respondents would also view increased efficiency and streamlining of study processes as ways eTMF decreases the cost of conducting a clinical trial.

Impact of eTMF: Efficiency

When asked about efficiency, an overwhelming majority stated that their current eTMF increases productivity when working with project-related documents. Individuals also postulated that the reason for the increased efficiency lies in the eTMFs organization and searchability. The overall ease of use and especially the utilization of workflows and templates to create and track documents are also credited with increasing overall efficiency of managing project-related documents. Although the majority of survey participants consider the use of an eTMF to increase efficiency, only half of individuals credited the increased efficiency with also decreasing the cost of a clinical trial suggesting that some individual may not see efficiency as a way to reduce cost.

Functionality of eTMF

It was generally accepted by survey participants that their eTMF makes it easier to locate study-related documents, and since searchability was reported as the greatest benefit to using an eTMF, individuals especially like the use of metadata as a way to organize and search for documents. It was also reported that documents stored and used within the current eTMF were considered to be of high quality with very little missing, inaccurate, or incomplete information. Survey participants using an eTMF also trust that the current eTMF in use is secure and can be used to store confidential information.

Future Directions

Individuals polled in this survey consider some features available in their current eTMF to be underutilized. Use of a mobile device application and electronic signatures were regarded as features that should be used more often going forward. Also participants believe there should be more fillable forms used and that workflows for document sharing should be utilized more. Changes suggested by survey participants involve features that could be used to

increase accessibility of essential documents which is important for research professionals who are retrieving documents outside of a traditional office which most responders are doing.

Respondents generally conclude that functionality of an eTMF can be improved by enhancing the searchability of documents, not just in how documents are organized in the eTMF but also in the speed at which documents are retrieved. The naming conventions of documents was reported as another element to improve in the current eTMF. A more "traditional" naming convention was suggested as a way to improve the current conventions. Respondents also believe the eTMF should be more user friendly, customizable, and that the underutilized features should be utilized more often. Viewing the customizability and user friendliness of an eTMF as ways to improve the system going forward fits with responses to common challenges seen with the use of an eTMF because responses given were specific to the individual particpants.

SUMMARY AND CONCLUSIONS

The first two aims of this practicum report are to measure current opinions regarding the benefits and challenges of using an eTMF as well as to compare the benefits and challenges of a paper TMF to an electronic TMF in an effort to support the hypothesis that the benefits of using an electronic trial master file instead of a paper trial master file outweigh the challenges. The responses from individuals polled as well as industry literature suggest strong evidence supporting the hypothesis. The current opinions regarding eTMFs are generally positive, even though those interviewed believe that there is room for improvement.

Current opinions of eTMF

The majority of clinical research professionals surveyed agree that using an eTMF positively impacts their role in clinical research, which can be partially attributed to the many benefits created by the use of an eTMF. Participants are more prepared for audits and inspections as a result of using an eTMF, which will contribute to time savings as well as relieve stress, create better working environments and allow for a better overall product. Clinical research professionals are seeing time savings due to increased searchability, as well as more complete and better quality documents. High quality study files allow individuals to view content more critically and, in turn, further elevate the quality of essential documents housed in a TMF.

In a purpose-built eTMF, essential documents are tracked from the time a document is created to when it is approved. Since documents are tracked, features such as version control and document history can be used during audits and inspections. The most recent version of a document can be shown to an auditor or inspector in real time, also previous versions and information about who edited a document and when it was edited can be obtained. Version control and document history may contribute to faster audits and inspections. Another benefit associated with the use of an eTMF is fewer audit/inspection findings related to missing, incomplete, or inaccurate study documents. A paper system relies on individuals to "check out/in" documents and if individuals are irresponsible with document handling it may lead to missing documents in the TMF which could lead to findings during an audit or inspection.

Although survey participants generally agree that using an eTMF increases the overall value of their role as well as the final research product, participants are also aware that there are some challenges to overcome. Training of personnel was the greatest challenge associated with using an eTMF. When any new technology is implemented, all users must be trained on how to use that system, and transitioning to an eTMF is no different. According to 21 CFR part 11,

individuals who will be using or maintaining an electronic system must have proof that they have the education, training, and experience to conduct their assigned tasks. The regulations apply to new systems, and also to system updates.

In a paper system, users are still required to be trained on organization and nomenclature, but in a paper system there is no search feature for assistance. In an electronic TMF, users are able to search for a document, and if metadata is used, they can search any of the parameters used to file a document. Metadata was viewed by research professionals as a feature that greatly increase searchability in an eTMF, this feature is not available in a paper system. In a cloud sharing or local electronic file share system, again individuals still need to be trained on how to use the system, and there still may not be a search feature and metadata may not be utilized. The cloud and local share system relies on people uploading and sharing documents as needed and the organization, and document control may not be as robust as is experienced with a purpose built eTMF.

Organization and searchability were challenges reported with the use of an eTMF. Opinions which seems to contradict earlier Reponses that searchability is one of an eTMF's greatest benefits. Contradictory responses could be indicative of areas respondents believe should be improved. For example, the searchability feature is not as effective as respondents would like it to be. Also consistency with naming conventions and customizability to user needs are viewed as features that need to be improved. It is unclear how many survey participants have looked at and are aware of the DIA reference model used to structure their eTMF. Not being familiar with the DIA model may contribute to a lack of understanding of the overall organization of the eTMF, which may have contributed to the results. A lack of understanding of the reference model could be rectified through more training on the DIA model directed at

employees who are learning to use or having difficulties operating within the current eTMF. Overall, Searchability was still seen as a benefit as it allows eTMF users to find documents in a manner that would not be possible in a paper system or even in a cloud or local file share systems. This is especially important with individuals who work outside of a corporate based office or travel often for work, which is how most of the eTMF users who were surveyed report using their current system.

In terms of accessibility, respondents previous reported being able to access their eTMF from virtually anywhere as long as there was internet connectivity. When reporting on challenges to eTMF, however, accessibility was reported as an issue. The challenge associated with accessibility lies in the speed of the system and permissions associated with retrieving documents. As a security feature, permissions must be given to an individual before they are able to view or edit specific documents. Permissions can be given to an entire department, project team, or to a specific individual as needed by anyone with the authority to give document access. Obtaining access to a document requires communications between employees but access can be given in real time. Restriction of documents is necessary to protect information related to trial specific documents and to assure the confidentiality of the protected information. Confidentiality and proprietary information may be more difficult to protect with the use of a paper system which may not have a rigorous document control process in place. The added protection from the use of permissions should be considered a benefit when using an eTMF, especially when marketing an eTMF service to a potential sponsor or investigator. The use of permission is also important when validating that a system is secure and accomplishes the confidentiality it promises.

When asked to describe the impact of an eTMF on efficiency when working with project-specific documents, about 96% stated that efficiency is increased. Organization and searchability were the main factors believed to be driving an increase in efficiency. The factors driving increased efficiency also support conclusions given above which state that, although there is room for improvement, individuals believe that organization and searchability are important factors that help make the case for using an eTMF over a paper system. workflows and templates were also credited with increasing efficiency; utilization of these features should increase going forward.

Cost was a topic that participants were divided on which seems contradictory since the options on efficiency were that efficiency is increased with the use of an eTMF. Inconsistent responses may suggest a lack of understanding among individuals regarding efficiency and cost. The pool of individuals surveyed may account for divided responses related to cost and efficiency. From a business prospective, increased efficiency translates to a decrease in the time it takes to get to the final product, and thus a lowered cost. Personnel in clinical departments are less likely to deal with the business side of clinical research and may therefore be less likely to think of efficiency in terms of cost savings. Since most respondents reported that they were from clinical departments they may have not been thinking about clinical research as a business when answering questions. In fact, business operations was not one of the departments consulted on this survey. It is imperative for research teams to understand the business aspect when discussing the idea of adopting and using an eTMF, especially considering the Nextdocs survey, which found that 44% of respondents had not adopted an eTMF because they were not convinced of the business benefits. Personnel from Business Operations are more likely to view benefits and

challenges from a business perspective, and, therefore, should be included when discussing the adoption and use of an eTMF.

All of the benefits and challenges that are associated with implementation and continued use of an eTMF also affect the business of research. When determining if a new technology such as a purpose built eTMF is worth an organizations investment, decision makers will weigh advantages and disadvantages. Advantages elicited by an eTMF, such as increased inspection readiness, increased efficiency, and better collaboration should be considered by both individuals evaluating their own roles, but also in the larger context of the effects advantages can have on the final product, for example lowering cost or decreasing time to market. Stakeholders who are investing their money in clinical trials should view increased inspection readiness as a way to cut down on costs that would be incurred by trial delays or even closure from inspection findings. A clear audit trail also allows for better overall document quality. Improved document quality and inspection readiness can translate into products that are more likely to be approved for use in the general public, which will allow investors to recoup invested money and to get products to those in need sooner.

As discussed above, increased efficiency associated with an eTMF will contribute to decreased study start up and thus less time overall to get a product to market. Better collaboration and consistency through the use of workflows and permissions can also contribute to increasing overall efficiency and decreasing the length of a trial. Being able to give specific individuals access to documents in real time allows for a quicker turnaround of important documents necessary to move a trial forward. Being able to use workflows to create and edit documents in real time from any location helps to decrease the time it takes to finalize essential documents which can decrease the total time for conducting a trial.

Paper vs eTMF

Several comparisons between paper and electronic master files have already been discussed. Among those discussed are: increased efficiency seen with an eTMF, the use of metadata and document searches to easily locate important documents, better collaboration with other stakeholders, increased security, and inspection readiness. Additional connections should be made in order to truly make the case for using an eTMF in clinical research. As seen in the illustrative comparison in Table 13, there are many processes which differ in an eTMF and a paper TMF. One process that should be considered when deciding if eTMF is a good investment is storage and archival of documents. In a paper system, all documents are stored in file cabinets and those cabinets have to be stored and secured with limited access given to individuals who need to access essential documents. Documents may also be accessed in the event of an audit or inspection which is more difficult for a paper system if documents are not housed at the location of the audit or inspection.

The amount of space required to house paper documents is enormous, and with the additional space comes higher rent and electric bills, which are going to increase the overall cost of conducting a trial. Also increased cost may be accrued due to fire and water proofing. File cabinets used to hold essential trial documents should be fire and water resistant in order to protect trial documents. Estimates show that fire and water-resistant file cabinets can cost upwards of $500 each, with some totaling over $8,000 each. The file room and cabinets must be locked, with limited access which may require close tracking of individuals who use the room, usually through the use of a key to enter and a sign in sheet to mark when documents have been checked out. Monitoring of this process would be done by a person and internal audits may only be done a few times a year.

A paper system can leave room for error with regards to keeping documents confidential and even perhaps remaining in the secured area. If someone needs to use a document for a prolonged period of time, they would need to make a copy and there is no way of knowing how many copies of a document have been made. In an electronic system, individuals can print out a document but they would not need to since they can access it any time which leaves less room for human errors such as leaving or misplacing a paper document. Also outside of scheduled audits it may not be clear which documents have not been returned when using a paper system, if for example and individual did not properly check out a document and they also did not put it back then that document would be missing. In the event of an audit this may be cause for audit findings that could shut down or delay a clinical trial.

Reviewing, editing, and finalizing documents is very time consuming with a paper system since documents must be viewed during business hours at the location where the documents are being housed. In an electronic system, documents can be accessed at any time and from anywhere as long as internet access is available. Being able to access documents outside of a traditional work schedule allows for greater flexibility within a company to work in other locations, even those outside of parent country without the added cost of having facilities in trial locations.

Disasters are another example of how an eTMF can be beneficial. With a paper system if there is a disaster, such as a fire, documents that are destroyed may not be able to be recovered. With an eTMF, disasters can still occur. The network being down, not have access to files and cyberattacks are examples of issues that could occur in an electronic system. Ensuring proper validation of the system, and the use of a disaster recovery plan and document backup are ways to ensure essential information is not lost due to a disaster. A good disaster recovery plan helps

ensure that essential documents are backed up and can be recovered with limited interruptions normal business operations. Disaster recovery plans are not unique to electronic systems, but recovery of information is more easily achieved in an electronic system. Once a piece of paper is destroyed, it cannot be recovered unless a copy was made. In an electronic system documents can be backed up regularly and automatically so that in the event of a disaster those documents are not lost. In a purpose build eTMF system where documents are accessed through the internet, a computer or entire office may not be operational, but the information in the TMF is still accessible.

In 2015 cyber hacking of health and medical records was identified as the second highest type of data hacked in the U.S. (15). In order to protect human subjects, medical and health records in clinical research must be kept confidential. It is also important to protect proprietary information related to the investors in research products. Any electronic system runs the risk of being hacked, but there are effective steps that can be put in place to protect confidential information from being stolen. When employing an eTMF, it is important to perform proper validation to identify any potential issues. Taking protective measure such as encrypting data, employing strict password policies such as changing passwords every few months and having password complexity requirements, and monitoring for failed login attempts can help to ensure the overall security on an electronic system (16). Also training personnel to good practices such as not writing down passwords, not using public unsecured wireless internet to view sensitive documents, and strict adherence to access control policies can help to prevent protected information from being exposed (16).

The current opinions on the use of eTMFs by industry professional are genrally positive. Participants believe that eTMFs help to increase tiral efficiency and thus decrease the length of clinical trials. In general, the use of an eTMF can increased the quality of the data being recorded in essential documents by making it easier to create, edit, share, and located important documents. Although there are some areas that need to be imporved such as the eTMFs ability to meet specific personalized needs, responders believe that the benefits of using and eTMF outweight the challenges, and that the use of eTMFs should continue to grown in clnical research. As the use of eTMFs increases, it is important to ensure that all individuals who will use a new system are properly trained on their responsibilities within the system. Also FDA guidance should help to ensure that research professional use eTMFs in accordance with all guidances and regulations governing clinical trials.

LIMITATIONS

The largest limitation of this project is the short amount of time from start to finish. With only a six months available in which to conceive, plan, submit, conduct, and write, it is difficult to gather much measureable data to support a hypothesis. The use of a comparison between electronic and paper TMFs is included to add support for the hypothesis along with the survey results. Another limitation is the small sample size. The survey was open to all willing participants at the CRO in all technical departments, but that is still a limited sample of individuals who, for the most part, are experienced in working with the same eTMF.

The employees surveyed have robust background of experience in clinical research from the current CRO as well as other companies where they have worked. This wealth of industry knowledge was harnessed through the survey in order to collect well rounded and precise

answers. It is also important to note that some answers may be biased towards eTMF since there is already an eTMF system in use at this CRO. Survey questions were intentionally formatted to avoid asking questions about paper TMF versus eTMF, but instead focused on what the benefits and challenges were to using an eTMF. There is also a great deal of variety within the CRO in regards to how eTMF is used on each project and which employees use the eTMF most often. Projects and individuals who utilize the system more often may be biased towards the use of an eTMF.

FUTURE DIRECTIONS

Finally, this practicum project aims to assert the promising future of eTMF and the continued usefulness of eTMFs in the conduct of clinical trials. The respondents of this survey have noted that future eTMFs should be more user friendly and customizable to individual needs. Clinical research professionals also believe that increasing the use of electronic signatures, fillable forms, and workflows will increase the usefulness of an eTMF. Many participants also commented on the structure of their current eTMF, which is modeled after the DIA reference model, suggesting that in the future, employees should be more familiar with this model before learning how to use the current eTMF.

As eTMF systems continue to change and grow, the overall processes of essential document creation, editing, and sharing should continue to become more streamlined. Also the integration of eTMFs with other systems such as clinical trial management systems, institutional review board systems, and site systems such as EDC and EHR are not far off. The ultimate goal of integration is the ability to complete all trial tasks is one system. However, the implementation of systems coming together is a slow process and includes many steps such as technological development and system validation before new or upgraded systems can be used.

The use of mobile device applications also continues to grow and can be seen as an avenue for the improvement of eTMF. Many systems already have mobile device capabilities but, as reported in the survey, these capabilities are not being utilized.

Industry needs guidance from the FDA to help ensure compliance when adopting new technology, including eTMF solutions. FDA has widely accepted the use of new technologies in clinical research in the past few years, made evident with their guidance's on the use of EDC, EHR, electronic records, and electronic signatures. With FDA's increasing interest in electronic systems, it is becoming more clear that the future of clinical research lies in the use of new electronic technologies, such as eTMF, in order to increase the timeliness of clinical trials and to create better quality products for the individuals who rely on research products for improved health and wellness.

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CHAPTER III

INTERNSHIP SITE

This internship practicum was conducted at MedTrials Incorporated in Dallas Texas under the direct supervision of Bridger Browder and Lynn Van Dermark. MedTrials is a Contract Research Organization that is hired to manage various aspects of clinical trials.

INTERNSHIP EXPERIENCE

During my time as an intern, I was able to work on a variety of projects including those related to Quality Assurance, Learning and Development, and Clinical Operations. Below are detailed descriptions of the work done in each area.

Quality Assurance

While interning, I learned and performed many tasks with the members of the Quality Assurance (QA) department. I received hands-on training from the Senior Manager of QA, the Senior Compliance Specialist, Learning and Development, and the QA Compliance Specialist on a regular basis. I also assisted with conducting audits on the quality management system (QMS) and with system validation related to upgrading the current internet portal used at MedTrials. I was also able to create and manage portals for internal use and for project-specific content. In managing portals, part of my role was helping with user issues as they arose. My duties in QA also entailed keeping employee training files updated, which included uploading documentation of attended courses to the QMS, as well as listing courses on employee training records. In this role I also recorded employee attendance for various in house and project-specific training and uploaded the records into the QMS.

Learning and Development

In my role as an intern, I was able to work closely with the Senior Compliance Specialist, Learning and Development. This gave me an opportunity to help research and develop course materials for internal and external training events. I co-presented a presentation on study subject recruitment at a research hospital. During the time of my internship, MedTrials transitioned to a new continuing education (CE) providership organization. I was able to assist with the transition from the previous organization to the new one. During the transition, I helped with developing new Standard Operating Procedures and Work Place Guidances to reflect processes required with the new CE providership. In addition, I collaborated with the QA team to help create templates for CE courses such as the sign in sheet, evaluation form, and certificate of completion. Internal training support was also part of my role in learning and development, by helping to develop quizzes for Clinical Research Associates (CRA), and assisting with a survey to get ideas about future training events from current employees.

Clinical operations

In the Clinical Operations departments, I was assigned to do non-billable work on various ongoing projects. I was able to help create source documents, project-related meeting flyers, and recruitment materials for an ongoing phase 4 study. For that same study I also created and manage a Google AdWords campaign for the purpose of study subject recruitment. In addition to the AdWords campaign, I also helped create a Facebook ad campaign for the same phase 4 study. I read protocols in order to develope protocol quizzes for clinical project protocol training for various ongoing studies. I spent a lot of time with the Dallas office team, and worked closely with the In-House CRAs to learn more about their duties. The in-house CRAs allowed me to observe how forms such as a monitoring visit report is completed by a CRA and see how it is

filed into an electronic clinical trial management system. I worked through a source data verification training binder with one of the In-house CRAs to see what common errors would look like. I was also able to sit in on various clinical project team meetings and listen to topics that were discussed.

JOURNAL SUMMARY

The internship journal located in appendix B lists the daily activities during the six-month internship used to compose this practicum report. The actives listed include specific projects assigned to me, meetings, and trainings I attended while participating in the internship. The journal represents the experiences and learning opportunities I engaged in during my time as an intern at MedTrials.

APPENDIX A

COVER LETTER AND SURVEY

Research statement – survey cover letter:

Benefits, Challenges, and Future Directions: Making the Case for eTMF in Clinical Research

Principal Investigator: Patricia A. Gwirtz, Ph.D., FACC

Student Investigator: Amber C Beckham

Institution: University of North Texas Health Science Center

Introduction/overview:

This research practicum project aims to get current industry opinions on the use of eTMF in clinical research. The current eTMF used at MedTrials is M-Files CTMS/eTMF and will be used

as the basis for the questions asked. If you choose to participate, you will complete the following:

A brief online survey that will ask questions about the current eTMF in use at MedTrials. It should take about 20 minutes to complete and is entirely anonymous.

Participation in the study:

Participation in this study is entirely voluntary and anonymous. Completion of the survey counts as consent to participate in this study. You may choose to leave the study at any point without penalty.

Confidentiality:

The only identifiable information in this study is your email. Your company email will be used only to send out a reminder to take the survey, and will not be stored or used to identify you in any way. Your email will also not be linked to your responses.

Risk/Benefit:

The risks involved with this survey-based research are minimal. They include the risks associated with your time investment and the use of your email address. The survey is designed to take only minimal time to complete, and every effort will be made to maintain confidentiality in regards to your email address provided. There is no foreseeable or direct benefit to you associated with your participation in the research study. This study is designed to increase the knowledge and understanding of eTMF and make the case for their use in clinical research.

Questions/Concerns:

If you have any questions regarding this project, please Believe free to contact:

Student investigator: Amber Beckham: Abeckham@medtrials.com

If you have any questions about your rights as a research subject, please contact the UNT Health Science Center Institutional Review Board at (817)-735-0409.

Survey Questions:

1. What area/department do you work in?

a. Quality assurance and training

b. Clinical operations

c. Informatics

2. How long have you worked in the clinical research industry?

a. Less than 5 years

b. 5-10 years

c. 10-15 years

d. Over 15 years

3. How often do you use/interact with the M-files eTMF/CTMS system?

a. Multiple times a day

b. Once a day

c. A few times a week

d. A few times a month

e. Rarely or never

4. What do you currently use M-Files eTMF for? (select all that apply)

a. Regulatory document viewing

b. Creating or editing regulatory documents

c. Sending and uploading regulatory documents to or from clients

d. Other: please specify

5. Where do you normally access M-Files eTMF? (select all that apply)

a. At your home office

b. At an investigational site

c. In the Dallas or Media office

d. Other: please specify

6. Below is a list of common **benefits** associated with eTMF, please rank them according to your experience with M-files eTMF. 1 would be the most beneficial and five would be the least beneficial.

a. Searchability of documents

b. Clear audit trail

c. Better document quality

d. External collaboration with clients

e. Completeness of study files

7. Below is a list of common **challenges** associated with eTMF, please rank them according to your experience with M-files eTMF. 1 would be the most challenging and 5 would be the least challenging.

a. Training of personnel

b. Organization/searchability

c. Accessibility

d. Client hesitation

e. Cost of implementation or maintenance

8. In your opinion, what effect does eTMF have on the cost of running a clinical trial?

a. Increases cost

b. Decreases cost

c. No effect

9. If they answered increased cost above: In your opinion, what contributes to an increased cost? (select all that apply)

a. Implementation of eTMF

b. maintenance of eTMF

c. Training employees

d. Other please specify

10. If they answered decreased cost above: In your opinion what contributes to a decreased cost? (select all that apply)

a. Decreased time to create, edit and share documents

b. Streamlining the overall process

c. Speeding up external collaboration

d. Increased overall efficiency

e. Other, please specify

11. In your opinion does M-Files eTMF increase efficiency when working with project related documents?

a. Yes

b. No

12. If they answered yes to Q11: Rank the following in order of how they **increase** efficiency. 1 would be the greatest increase to efficiency and 5 would be the least increase to efficiency.

a. Ease of use

b. Organization

c. Use of template for creating documents

d. Use of workflows to track documents

e. Searchability of documents

13. If they answered No to Q11: Rank the following in order of how they **decrease** efficiency: 1 would be the greatest decrease to efficiency and 4 would be the lowest decrease to efficiency.

a. Too many options/documents to look trough

b. Organization

c. Search parameters are not intuitive

d. Difficulty of use

14. When using M-Files eTMF, how often do you find missing, inaccurate, or incomplete documents?

a. Always

b. Sometimes

c. Rarely

d. Never

e. Other, please specify

15. How secure do you believe M-Files eTMF is?

a. Extremely secure

b. Very secure

c. Somewhat secure

d. Not very secure

e. Not secure at all

16. What changes, if any would you like to see with M-Files eTMF? (select all that apply)

a. Use of the cloud for storage and archiving

b. Integration with other systems (EDC or HER)

c. Industry standardization among different companies using different eTMFs

d. The use of mobile devices to upload and view eTMF documents

e. Other, please specify

17. What feature/s do you believe are under-utilized in M-Files eTMF? (select all that apply)

a. Electronic signatures

b. Document Sharing through workflows

c. Fillable forms

d. Use of mobile device application

e. Other, please specify

18. How has M-Files eTMF impacted your role in clinical research?

a. Positively

b. Negatively

c. Not at all

19. Please explain your answer to Q18

a. _____

APPENDIX B

INTERNSHIP JOURNAL

Internship Journal:

Tuesday May 31st:

- 8 hours: orientation
    - Learned company goals and standards, learned how to use various systems utilized by MedTrials such as M-Files, MT-connect, mobile VPN
    - Went over day to day procedures and how to communicate with other employees: learned how to use timecard, email, and skype

Wednesday June 1st:

- Worked with M-files uploading documents. Uploaded training files, CE information, certification updates, and new hire information on various current employees of MedTrials.
- Skype meeting with CEO and Senior Compliance Specialist, Learning and Development about the roles I would undertake as an intern and about expectations of my time here. Discussed general information about degree related tasks such as my daily journal and thesis requirements.
- Met the QA team over Skype interview
- Worked on created a training document for new employees to use when navigating M-Files, specifically working in the training records sections.
    - Worked on creating an updated PowerPoint slide template for MedTrials employees.
- Worked on CORE training
    - GCP training.

Thursday June 2nd:

- Uploaded training documents into M-Files
- Worked on assigned QMS vault readings. Readings included information on Quality policy, Project Management, Business Continuity, and Conflict of interest.
- Went to a local hospital in Dallas with Senior Compliance Specialist, Learning and Development (SCS) to give a lecture on GCP updates. Discussed changes to current regulations, specifically the common rule and BIMO.
- Scanned and uploaded attendance and surveys from GCP update at a local hospital, created completion certificates to send to participants of the lecture.
- Looked at training documents in QMS vault, started Inspection readiness training in CORE
- Completed certificates for GCP lecture given on May 18th 2016 by SCS.

Monday June 6th:

- Started working on CORE training
    - Inspection readiness: what to expect during and FDA inspection, including what they look for and how to conduct yourself.
- Webinar: turning around slow enrollment, reasons for low enrollment and ways to approach fixing it.
- CORE training on electronic records
- QMS vault assignments
    - Retention records: what documents need to be retained and for how long
    - Computer systems validation
    - Protecting the Confidentiality of Clinical Research Subject
    - Inspection policy

Tuesday June 7th:

- Worked on Journal
- Read protocol for Pediatric Safety and PK Study
- Training on CORE admin, how to create and edit courses with SCS
- Entered files into training records
- Sexual harassment training
- QMS vault training:
    - Protecting the Confidentiality of Company Proprietary Information
    - Email Archiving and Retention
    - Staff Qualification
- Practiced editing CORE to make changes to courses. Added sections to my internship course page and uploaded my training documents. Changed theme, fonts, colors, etc.
- QMS Vault training:
    - EDC Development SOP
    - Development and Approval of SOPs
    - Research Personnel Training
- Continued to read protocol document for Pediatric Safety and PK study.

Wednesday June 8th:

- Continued reading Protocol for Pediatric Safety and PK study.
- CORE training
    - Understanding the Significance of Routine Diagnostic Tests: Dr. Van Dermark discussed various lab values, what they meant and how they may be relevant in a clinical research setting. Also discussed things to look for when monitoring a study in regards to lab values.
- Edited CORE course page to learn more about the system
- 12:45pm: QMS vault training:
    - Exporting Electronic Clinical Data
    - Data Storage, Backup and Recovery
    - Conducting Quality Audits
    - Employee Training File Management
- Continued reading pediatric Safety and PK study protocol
- Met with Sr. Administrative Assistant to go over office related tasks such as FedEX.

- Finished reviewing Pediatric Safety and PK study protocol.
- CORE training:
    - Introduction and Review of CTMS/eTMF System (did not finish at this time)
- Reviewed the informed consent form for the Pediatric Safety and PK study.

Thursday June 9th:

- Reviews advertising materials for Pediatric Safety and PK study. Looked at general guidelines for writing a radio and webpage advertisement.
- Worked on creating a Certificate for the completion of training to be given out after training courses delivered by MedTrials.
- Had my weekly internship meeting with SCS and CEO to discuss how my internship was progressing. Discussed current tasks and ideas for my Internship Practicum project.
    - Went through how to add materials from courses taught by MedTrials employees into M-Files.
- Helped SCS get materials ready for CE course on Practical Implications of GCP. Read over the Department of Health and Human Services guidelines for unanticipated problems involving risks and AE in clinical trials.
- Skype call with one of the Project Mangers working for MedTrials. Discussed what the role of a Project Manager is and how they deal with problems that may arise during a clinical trial.
- Continued to read HHS guidelines on unanticipated problems involving risks and AE in clinical trials.

Friday June 10th:

- Accompanied SCS to a 4 hour training seminar at a local hospital in Temple TX. Lecture discussed practical application of GCP and the topic of AE and when to report them to the IRB.
    - Helped prepare lecture handouts and materials, and assisted throughout the lecture.

Monday June 13th:

- Worked on creating a new CE certificate for CE courses offered by MedTrials.
- First Committee advisory meeting with all committee members
    - Discussed my role as an intern and the ideas for practicum project
    - Went through timeline of internship and when my project needed to be completed
- Worked on creating advertisement materials for a pediatric safety and PK study.
- Continued QMS vault assignments:
    - Network and Systems Security
    - Importing Electronic Clinical Data
- Worked on creating a staff spreadsheet for pediatric study.
- Complied background research on a specific therapeutic area in the U.S., UK, and Australia for an upcoming trial as tasked by SCS
- Created certificates for Practical Applications of GCP lecture given by SCS to give to those who attended for CE

Tuesday June 14th:

- Continued to research current studies on a specific therapeutic area as tasked by SCS.
- Skype meeting with Compliance specialist about systems validation. Discussed how to determine if a system needs to be validated and if so how much validation is required. Went through the overall process of how systems including M-Files and CORE are validated, and discussed the possibility of me helping on the upcoming upgrades to current MedTrials systems.
- Research on current studies on a specific therapeutic area.
- Entered training courses into training records for current MedTrials employees.
- QMS Vault Training:
    - Quality Oversight of Approved Contracts
    - Quality Oversight of Approved Service Vendors
- CORE training:
    - Introduction and Review of CTMS/eTMF System
- Research on eTMF to better my understanding of its purpose and contents, as well as what the federal requirements are for the contents of the TMF. Saw the direct role of a CRO in compiling and maintaining a TMF system.
- QMS Vault Training:
    - CE Application Processing and Management
    - Contractor Qualification and Approval
    - Protecting Client Confidential Information
- Reviewed guidelines set by the California Board of Nursing in preparation for obtaining a CE provider number to offer courses approved through this organization. New guidelines were reviewed to be able to compare current SOPs with new requirements and change them as well as other CE related documents such as course evaluations.

Wednesday June 15th:

- Worked on creating a new course evaluation for training CE courses offered by MedTrials. New evaluation will be used for courses approved by the California Board of Nursing once they have approved MedTrials as a CE provider.
- QMS vault assignments:
    - Document Change Control
- Worked with SCS to create a google AdWords campaign for study to aid with recruitment of trial subjects.
- Sat in on skype meeting to review audit agenda and prep for an upcoming audit on a current study being conducted at MedTrials.
- Discussed with SCS some questions concerning how audits are done and who is involved. Discussed the role of in-house CRAs and regular CRA's and scheduled a skype meeting to discuss this further with a current MedTrials CRA.
- Updated CE certificates for SCS, worked in M-Files learning about what files go where and how they are organized.
- QMS vault assignments:
    - Contractor Management
    - Business Continuity and Disaster Recovery
    - Clinical Documents and Project File Management

    - Corrective and Preventive Action (CAPA)
    - Installation and Operational Qualification of IT Hardware and Software
- CORE training assignments
    - 2014 GCP updates
    - Monitoring Medical Devices
- Worked on demo page from the CORE website to see what new features would be included in an update to CORE. Compared old features to new features that will be offered with an upgrade.

Thursday June 16th:

- Worked in CORE and researched CORE upgrades to determine what would be different if MedTrials did an upgrade to the CORE training system
- Read a study protocol as tasked by SCS in order to create quiz questions that could be given to site staff to assess their comprehension of the study protocol.
- Worked on creating quiz questions on a study protocol.
- Worked with SCS to create an electronic sign in sheet that could be used during training courses given by MedTrials.
- Continued to work on creating questions for the a study
- Worked on creating a Save the Date invitation tasked by Clinical Project Manager for an investigator meeting.

Friday June 17th:

- Worked on Save the Date invitation for an investigator meeting in order to get a working draft to the Clinical Project Manager on the study.
- Research on eTMF specifically on how it is used by a CRO. I wanted to better understand implementation and challenges to eTMF. I also wanted to better understand M-Files which is the eTMF used at MedTrials. This information could be useful in creating a testable hypothesis for the practicum project.
- Worked with In-house CRA. She showed me what the CTMS vault looks like and walked me through different reports that are done on a project. I got to see an MVR, IVR, SQV, reports from PM on project status update, and what the QC documents look like. She also gave me some insight on what the in-house CRA does compared to the regular CRAs and what the different roles of MedTrials can be in trials (i.e., full service or partial).
- Read through a Monitoring Plan from a current study that MedTrials is contracted to do work for in order to see what all it entails.
- Weekly internship meeting with CEO and SCS. Discussed current projects that I have been working on as well as some opportunities coming up. CEO stated that I should be able to help with some QC related work on a study that is ending. We discussed how to write effective quiz questions for my current project. Discussed topics that I may choose for my practicum report including standardization of eTMF, benefits and challenges to using eTMF, and other areas of technological advancements such as EDC that have already been standardized.
- Read through another protocol for a current study at MedTrials as tasked by the SCS. For this protocol I am also helping to create quiz questions make sure that study personnel understands the protocol.
- Began familiarizing myself with a current multi-center, randomized, double-masked,

positive controlled, phase 3 clinical trial. In the next few weeks I may be helping out with some recruitment related tasks. I may also be helping to develop an agenda, invitation, PowerPoint slides, and other materials related to this study.

Monday June 20th:

- Continued to read through protocol of a current study, created more quiz questions
- Continued to familiarize myself with a study that I will be helping with in the next few weeks. Read through the protocol, case report form template, agenda, monitoring plan, project plan, and other relevant templates/documents in order to better understand the aims and procedures of this study.
- Worked on editing quiz questions that the SCS and I wrote on a study in order to get an overall list together to submit to project manager. Read through all questions for grammar and spelling, and added answer choices to all questions.
- Watched webinar on 21 CFR Part 11: Vendor and Sponsor Responsibilities
- Read through the TMF reference model that the eTMF used and MedTrials uses for the TMF structure

Tuesday June 21st:

- Assisted SCS in preparing for a course on Meeting Patient Need on Learning in the Digital World, which will be given later today at a local hospital.
- Attended webinar titled Reinventing Remote Monitoring: The Implications of Innovation
- Continued to work on assignments in the QMS vault
    - Project Specific Training
- Went to a local hospital with SCS to deliver a CE course on Meeting Patient Needs for Learning in the Digital World.
- Created CE certificates and scanned in sign in sheets from course on Meeting Patient Needs for Learning in the Digital world. Added all relevant materials to M-Files.
- Started looking at source documents for various projects to familiarize myself with the formatting so that I could help create new source documents for a current study that I have been helping with.

Wednesday June 22nd:

- Read several source documents to familiarize myself with what their general format is. Read through the final CRF that SCS and I will be using to create source documents for a current trial.
- Continued QMS training assignments
    - Internal Quality Systems Audits
    - Internal IT Operational Procedures Manual
    - Handling Sponsor SOPs
    - Monitoring the Informed Consent Processes
    - Internal IT Server Room Environmental Monitoring
- CORE training
    - Risk Based Monitoring
- Reviewed a monitoring plan as well as templates for site visits and communication letters between the CRAs at MedTrials and the sponsors for companies that have hired MedTrials. I wanted to get a better understanding of all the things a CRA might do during

a monitoring visit and get a list of questions to ask a CRA that I am scheduled to meet with later today.
- CORE Training
    - Monitoring Visit Reports
- Attended skype meeting with CRA at MedTrials. We went through day to day what a CRA does. Talked about monitoring visits and what the CRAs do in between visits. Talked about timelines for submitting different documents and the chain of command on submitting them. Talked about general characteristics of the job like travel requirements and differences in job responsibilities depending on if someone is a CRA I, II, III or if someone is a lead CRA on a project.
- Added training certificates from the Meeting Patients Needs for Learning in the Digital World course to M-Files.
- Read FDA website guidelines on using standardized clinical research data.
- Watched FDA webinar on Source Data Capture from Electronic Health Records Using Standardized Clinical Research Data

Thursday June 23rd:
- Finished my outline for practicum project and sent it to CEO and SCS for review, then continued to research source documents to get a better understanding of what they look like. Read through the provided source document information to see what the project manager already had for the project. Looked though some example source documents to get an idea of what a real one looks like.
- Spent the remainder of the day drafting source documents for a study. Drafted documents while working through the protocol and the source document information provided. Drafted source documents and sent them to SCS for editing and finalization.

Friday June 24th:
- Continued drafting source documents for a study.
- Attended webinar given by MedTrials on Clinical Trial Risk Management for Registered Nurses and Clinical Research Professionals.
- Continued to create source documents for a study
- Weekly intern meeting. Went through my rough outline and discussed points I wanted to make for my practicum project.

Monday June 27th:
- Checked in with CEO and Sr. Compliance manager regarding my practicum project progress over the weekend.
- Continued QMS Vault assignments
    - Software Development Process and Lifecycle
    - Filed Monitoring of Adverse Events for Devices
    - Regulatory Review
    - Internal IT Audits
    - Requirements for Computer System Validation
- CORE training
    - Managing Investigational Product Accountability
- eTMF research

- Continued QMS Vault assignments
    - Field Monitoring of Adverse Events for Drugs and Biologics
    - Data Center Qualification
    - Handling Deviations
- Spent some time looking at the active projects in the MedTrials vault to see what types of documents are stored there.
- Started therapeutic training PowerPoint slides for a current project as tasked by the project manager.

Tuesday June 28th:

- Continued to edit PowerPoint slides. Received feedback and editing suggestions for the drafted source documents and spent some time editing them.
- Continued QMS vault assignments
    - Validated Computer System Decommissioning
    - Development and Approval of WPG's
    - Preparing for and Hosting Regulatory Audits and Inspections
    - Change Control Requirements for Validated Computerized Systems
    - Management of Controlled Documents
    - Escalation Procedure
    - Detecting and Handling Fraud and/or Research Misconduct
    - Good Documentation Practices
- Went online to do some research on the use of eTMF compared to paper for my practicum project. Also researched looking at clinical research as a business to better understand the benefits of eTMF from that prospective.
- CORE training
    - Dealing with difficult personalities
- Finished making edits on source documents and sent them back to SCS for review.

Wednesday June 29th:

- Read through some articles on the business aspect of clinical research.
- Worked on QMS Vault assignments:
    - Development of Approval of Work Instructions
    - Monitoring Investigator Regulatory Files
    - Development, Approval and Maintenance of Audit Plans
    - Development, Approval and Handling of Audit Reports
    - Protecting Subject Confidentiality
    - Complaint Handling
    - Regulatory Inspection Preparation
- Spent the rest of the day working on creating protocol quiz questions for several studies that MedTrials is contracted to manage.

Thursday June 30th:

- Continued to draft protocol quiz questions
- Watched a webinar on Bridging the Gap: Managing and Maintaining CTMS and eTMF. The webinar discussed the benefits of an integrated system
- Helped SCS add users onto the study portal for a study that MedTrials is contracted with

- Talked with several MedTrials employees about the use of eTMF and how the eTMF servers are hosted.
- Continued to work on protocol quiz questions
- Spoke with in-house CRA II about the use of eTMF and electronic systems. We discussed the various benefits to using an eTMF. We also discussed some measurable outcomes for comparing eTMF to paper TMF

Friday July 1st:

- Researched information about the cost and time of a clinical trial to relate that to how eTMF would be useful. Used some of the information from my conversation yesterday with the in-house CRA II in order to shape the background section of my practicum project.
- QMS Vault assignments
    - Non-Local Institutional Review Board Assessment
    - Management of Financial Disclosure Information
    - Development, Management, and Use of the QSM Matrix
    - Clinical Project File Management
    - Development, Management, and Use of the PST Matrix
    - CE Application Processing and Administration
- Watched webinar on Case Studies: Why Clinical Organizations are Going Beyond EDC and Embracing Clinical Data Management
- Went into M-Files to see what the procedure was for managing TMFs. I looked at several TMF management plans and Project management plans. I am trying to find a measurable way to confirm efficiency of eTMF.
- Prepared for weekly intern meeting with CEO to discuss my internship
- Weekly intern meeting
- Worked on creating quiz questions for current protocols.

Tuesday July 5th:

- Went through my email and answered any outstanding emails from Friday after I left. Sent emails to committee members to find out which guidelines I should follow for my practicum report as there are two sets of instructions and they are different from each other.
- QMS Vault assignments
    - MedTrials CV Development and Management
    - Computer System Validation Process
    - Use and Completion of the Employee Review Record and Employee Training
    - Deviation Reporting
    - CLINPLUS Database Testing
    - Computer System Validation Risk Assessment Worksheet Instructions
    - Formatting Guidelines for SOPs
    - Formatting Guidelines for WPGs
    - Best Practices for Handwritten Entries and Corrections
- Worked on creating protocol quiz questions
- Continued research on eTMF for my practicum project. Looked at the validation protocols in M-Files to see what the procedure for validation is.

- Watched webinar "When Does Validation Start?"

Wednesday July 6th:

- Checked/replied to emails. Logged into CORE to work with various themes and make sure that I understand how to edit and change layouts. Updated internship CORE page with current projects as well as added a training record.
- QMS vault assignments
    - Review and Revision of SOPs
    - Review and Revision of WPGs
    - Initiating and Processing a DCCR in M-Files QMS
    - Conducting a Root Cause Analysis
    - Clinical Document Management-TrialWorks
    - Field Monitoring Electronic Trial Data
    - Review and Oversight of Delegation of Authority
    - Clinical regulatory Documents-Project File Quality Control
- Worked on creating polling questions in Survey Monkey for my practicum report
- Read/studied ICH guidelines for clinical trials.
- Worked on creating protocol quiz questions for the rest of the day.

Thursday July 7th:

- CORE training
    - Therapeutic Training: Ophthalmology & AMD
- Skype call with CEO to discuss first draft of my practicum proposal.
- CORE training
    - Continued Therapeutic Training: Ophthalmology & AMD
    - Therapeutic Training: Acne Vulgaris
    - Therapeutic Training: Congestive Heart Failure
- Read/studied ICH guidelines for clinical trials
- Went through current issues of Applied Clinical Trials and The Clinical Researcher to read on current issues involving the use of eTMF and electronic systems.

Friday July 8th:

- Research the use of Smartphones for a training presentation being given by the CEO later today
- Went through PowerPoint slides for the mobile device training. Edited and added a few slides and sent back to CEO for presentation today at 12pm.
- Webinar with CEO on the use of Smartphones and Mobile devices
- Continued working on differences that would be seen by upgrading to CORE 3.1 from the version that MedTrials has now.
- Weekly intern meeting with CEO to discuss internship. Discussed an FDA inspection readiness training session that is coming up and how I could help with updating the presentation.
- Started reading FDA inspection manual and taking notes with the specific focus of what they look for when conducting inspections of CROs and Investigators.

Monday July 11th:

- Continued reading the FDA inspection manual and taking notes.
- Helped organize a way to record an investigator meeting so that the audio could be transcribed into notes for attendees.
- Spent the rest of the rest of the afternoon reading the FDA inspection manual. Started to put together a list of what the FDA requires from a CRO. Looked up 2016 warning letters that have been issued so far.

Tuesday July 12th:

- Continued to compile research and sources for FDA inspections as tasked by CEO
- Research eTMF vs paper TMF and did some rough sketches of what my illustrative comparisons will be for my practicum project
- Explored the FDA website, looked up information about inspections, compliance, and regulatory information. Looked at differences between drugs and cosmetics. Read a few articles from ACRP regarding the National Academies of Science request that the FDA hold of any changes to the Common Rule. Looked at the FDA website and read information about their unapproved drugs initiative.
- Read current SOP on FDA inspections. Read WPG on Clinical Project Management in order to review the process for creating, editing, transferring, and storing important project documents both on paper and in the eTMF. I hope to use this information to create an illustrative comparison between the two systems. Looked up other helpful SOPs and WPGs for creating an illustrative comparison of eTMF and paper TMF.
- Added attendance for an in house training webinar to employee files. The training was: Monitoring Considerations for the Use of Mobile Health Technology in Clinical Trials.
- Updated my daily journal and current projects section of CORE.

Wednesday July 13th:

- Read through current articles from ACRP, began working on a table comparing paper TMF to eTMF for my practicum project, did additional research for my practicum project
- Began a CORE training audit to ensure that the training records of the MedTrials employees reflected the current training they have completed through CORE
- Updated daily internship journal to reflect the changes that SCS suggested and uploaded new version to CORE

Thursday July 14th:

- Continued and completed CORE training audit
- Started uploading protocol quiz questions to CORE for a current study
- Attended and online investigator meeting for a current study. Assisted with attendance record and compiling questions that were asked by trial personnel who were also attending the meeting.
- Continued to upload protocol questions to CORE

Monday July 18th:

- Continued uploading protocol questions to CORE
- Started an audit to make sure that all courses for TNA have the required/completed documents in M-Files
- Started working on IRB approval forms for my practicum project

- Continued and completed TNA audit tracker
- Transferred online attendance for a training even to a word document so that it can be added to M-Files

Tuesday July 19th:

- Added training course to employee training files
- Continued research on google AdWords to see how to run a campaign. This information will be used to run an ad for recruitment of a current study
- Meeting with SCS, Learning and Development regarding the survey for my practicum project and to do some M-Files training.
- Continued working on my IRB submission documents as well as my survey materials for my practicum project.

Wednesday July 20th:

- Started going through paper documents from CE training to find what was missing from TNA audit computer files. Scanned and added missing files to M-Files.
- Finished putting together my IRB submission for my practicum project
- Continued to research how to use google AdWords

Thursday July 21st:

- Logged on to CORE and M-Files, checked emails, and made sure all of my IRB paperwork was ready to go
- Meeting at UNTHSC with Major Professor/PI on my practicum project to get signatures on IRB paperwork.
- Attended conference call for a recruitment kick off meeting for a current study
- Attended Skype meeting with Sr. Manager Quality Assurance to discuss file quality control and the difference between file QC and File auditing.
- Began project assigned by Sr. Manager Quality Assurance. I compared the current released copies of SOPs and WPGs to the QC index provided. Checked to make sure that the correct version was available, that the effective date was corrects, and that the correct document was displayed.

Friday July 22nd:

- Checked/responded to emails, set up weekly intern meeting for every Friday until the end of my internship. Updated Journal and time sheet to include yesterday.
- Continued and completed file QC as tasked by Sr. Manager Quality Assurance
- Webinar on Risk Based Validation Considerations when Implementing Clinical Research Systems
- Started ACRP Course for Introduction to Clinical Research as tasked by SCS, Learning and Development.
- Weekly intern meeting with CEO and SCS
- Formatted sources for Inspection Readiness research that was done on July 8th-11th as tasked by CEO so that sources could be added to the training slides where the information was used.
- Continued ACRP course on Introduction to Clinical Trials.

- Updated CORE internship page and daily internship journal. Complete time clock for today and yesterday.

Monday July 25th:

- Uploaded study related documents to the CORE portal for a current study
- Meeting with Sr. Manager Quality Assurance, discussed regulatory requirements for quality assurance, the differences between quality control, quality assurance, and a quality control system. She gave me some insight into what all the quality assurance team does.
- Started editing my survey for practicum project based on advice from CEO
- Added more documents to CORE portal for current study, Skype meeting with SCS on how to add labels in CORE.
- Worked on creating an Adverse Event source document for a current study
- Finished editing my survey for practicum project and sent it to SCS for final review and updating in Survey Monkey.
- Updated daily journal and CORE page
- Looked at different CORE themes to try and decide which would work best for a current study that needs a CORE portal.

Tuesday July 26th:

- Worked on creating a more appropriate attendance form for online CE courses
- Began reading assignments given by Sr. Manager Quality Assurance. Read through the MT Quality Policy, and ICH E6 section 5
- Received finalized survey to add to IRB submission, emailed a list of questions on readings to SCS
- Continued ACRP course on Introduction to Clinical Trials
- Read 21 CFR part 820 Quality Systems Management
- Updated daily internship journal, CORE page, and time clock

Wednesday July 27th:

- Uploaded documents to CORE study portal for current study
- Meeting on campus to turn in IRB submission and intent to graduate form
- Finished uploading documents to CORE portal for current study
- Started and completed approved forms audit. Compared version number, effective date and title with index provided by Sr. Manager Quality Assurance. Compared documents that were in QMS to those listed in DMS to make sure they matched.
- Started work instruction audit. Compared documents that were in QMS to those listed in DMS to make sure they matched.
- Made corrections to uploaded documents on CORE portal

Thursday July 28th:

- Continued editing documents for CORE portal
- Continued work instruction audit
- Skype meeting with Sr. Manager Quality Assurance. Talked about reading from last week over ICH E6 section 5 and Title 21 CFR part 820. Talked about the quality policy and the different parts. Talked about vendors and validation of electronic systems. Went

over the differences between class I, II, and III vendors
- Meeting with SCS about general internship activities
- Updated internship CORE page with current projects and activities
- Finished ACRP course on Introduction to Clinical Trials
- Meeting with SCS to go over and begin AdWords campaign for a current study, talked about upcoming tasks she would also like me to help with
- Worked on adding missing documents to WI index after review from Compliance Specialist
- Updated CORE page and recorded time on time clock

Friday July 29th:
- Meeting with project manager on a current study to discuss using AdWords campaign for recruitment of subjects. Typed up notes for what we discussed and sent them to project manager and SCS.
- Continued and finished adding missing documents to WI index and sent new finding to Compliance specialist and Sr. Manager of Quality Assurance
- Scanned and uploaded continuing education (CE) evaluations for a current training course into the online course file
- Weekly Intern meeting with CEO and SCS to discuss my internship activities and project
- Read over SOPs and WPGs related to recording training files to prepare for QA meeting
- QA meeting to discuss how employee training is currently recorded and how it could be improved. Talked about recoding web based internal training on the new form created by myself and SCS, and how we could improve the process for external courses submitted by employees.
- Started looking up CE courses to evaluate pricing and cost as tasked by SCS
- Looked up course requirements and application information for courses for the California Board of Nursing. MT needs a new form/WPG for when a new course is developed to ensure that the trainer has every that is required and that all courses are created uniformly.

Monday August 1st:
- Continued look up other CE courses and working on the application information for California Board of Nursing courses
- Started Working on the QSM 3 year review to ensure that employees have reviewed current required documents within the last three years.
- Researched ways to take attendance directly from Skype meetings to try to improve the way attendance is recorded for online trainings.
- Continued Working on QSM 3 year review.
- Updated time clock

Wednesday August 3rd:
- Uploaded documents to the CORE page for a current study
- Created quiz questions related to a protocol for a current study
- Updated internship CORE page
- Started reading ICH Q10 and slides provided by Sr. Manager of Quality Assurance that was assigned at our last meeting.

- Continued working on approved form for CE courses
- Completed 3 year QSM audit
- Updated internship journal and recorded time on time clock.

Thursday August 4th:

- Finished 3 year QSM review
- Continued working on approved form for CE courses
- Webinar: "Drive Value and make the Patient-Centric Trial a Reality"
- Uploaded documents to CORE portal for a current study
- Read PowerPoint slides provided by Sr. Manager of Quality Assurance from out last meeting in order to prepare for out next meeting
- Finished and submitted rough draft of approved form for CE courses to SCS.
- Uploaded more documents to CORE page for current study
- Continued to research other providers of CE and how much they charge for their courses as tasked by the SCS
- Updated CORE internship page and recorded time on time clock

Friday August 5th:

- Attended inspection readiness training
- Started recruitment and retention research for upcoming training course
- Meeting with CRA on current study to discuss her general opinion of the protocol quiz that she recently took for a current study
- Recruitment and retention research for upcoming training course
- Weekly Intern meeting with CEO and SCS to discuss my internship activities and project
- Reviewed California Board of Nursing requirements for courses so that a form can be made to determine what qualifies as a CE course
- Read through current SOPs and WPGs on creating CE courses
- Updated CORE internship page and recorded time on time clock

Monday August 8th:

- Reviewed and made corrections to QSM 3 year review records as requested by SCS.
- Responded to emails and sent out reminders to committee member of UNTHSC about when my thesis defense date was. Downloaded documents sent by Major Professor and went through requirements for practicum paper
- Continued to research other providers of CE and how much they charge for their courses as tasked by the SCS
- Meeting to plan/discuss courses that MT will be giving next month. Went over objectives and content outlines
- Started doing focused recruitment and retention research after discussing general objectives with SCS and CEO
- Updated internship CORE page and recorded time on time clock

Tuesday August 9th:

- Continued recruitment research
- Started working on suggestions for the requirements listed on the UFRS form for the CORE upgrade
- Meeting with SCS on the specifics of what content topics we would be using for an upcoming training hosted by MT
- Continued recruitment research which new sources given by SCS
- Updated CORE internship page and recorded time on time clock

Wednesday August 10th (Half Day):

- Continued to read resources given to me by SCS for a current course I am helping with
- Started going through quizzes in M-Files from other courses in order to find questions that would be appropriate for an a GCP CORE quiz
- Meeting with Sr. Manager of Quality Assurance, went over escalation of issues and deviations during a clinical trial and when a CAPA would be used

Thursday August 11th:

- Continued to look through quizzes from other courses to find appropriate GCP questions.
- Read through ICH GCP E6 guide and ACRP prep quiz to increase my understanding of GCP and clinical trial ethics
- Weekly intern meeting with CEO and SCS
- Uploaded training documents to employee training record
- Went through PowerPoint slides from training with Sr. Manager of Quality Assurance and read through all of the documents in M-Files as assigned
    - POL-0000-001: Quality Policy
    - SOP-0000-011: Handling Deviations
    - SOP-3100-019: Escalation Procedure
    - SOP-3100-020: Detecting and Handling Fraud and/or Research Misconduct
    - SOP-3100-027: Complaint Handling
    - SOP-3100-005: Corrective and Preventive Action
- Continued working on the suggestions for the requirements for CORE upgrade UFRS form
- Updated CORE internship page and recorded time on time clock

Friday August 12th:

- Continued working on CORE UFRS from
- In house webinar: “Clinical Training: Managing Queries”
- Continued working on CORE UFRS form
- Uploaded attendance from webinar and collected in office signatures for attendance and uploaded it to M-Files. Added webinar to training records of all attendees.
- Continued working on CORE UFRS form and sent what I have done to Compliance Specialist so that she can see my work before our meeting on Monday
- Updated CORE intern page, recorded time on time sheet

Monday August 15th:

- Read feedback from Compliance Specialist on CORE update and began filling out and editing the official form for the CORE system upgrade. Used the provider website to determine specific features that would be available with an update and added them to the list. Sent final form to SCS to get final input before submitting final form.
- Continued Recruitment research to prepare for upcoming course
- Looked through edits made to CORE upgrade UFRS form and did some more research to answer some of the comments given by Compliance Specialist. Edited/made changes to document and sent it back to Compliance Specialist
- Continued recruitment research
- Updated CORE internship page and recorded time on time clock

Tuesday August 16th:

- Continued recruitment research, updated some of the sources that were in the sources sent to me by SCS.
- Worked on thesis template for practicum project
- Continued recruitment research
- Continued researching current providers of CE to determine what their costs are and what kind of courses they offer, sent what I had to SCS for feedback
- Read through relevant SOPs and WPGs on CAPAs to prepare for training with Sr. Manager of Quality Assurance
- Uploaded CORE intern page and recorded time on time clock

Wednesday August 17th:

- Continued to read relevant documents for training meeting today:
    - SOP-3100-005
    - SOP-3100-006
    - ICH E6: 5.1
    - U.S. 21 CFR 820
- Meeting with Sr. Manager of Quality Assurance to discuss CAPA procedures. Discussed how CAPAs are created and closed and who has access.
- Continued to research CE providers with feedback from Compliance Specialist
- Read over and took notes the 2016 Veeva Paperless TMF Survey that was just released for my practicum project
- Continued recruitment research with resources given to me by SCS
- Updated daily internship Journal, CORE intern page, and recorded time on time clock

Thursday August 18th:

- Went through PowerPoint slides and documents given by Sr. Manager of Quality Assurance from our Skype discussion.
    - APP FRM-3100-020
    - APP FRM-3100-042
    - APP FRM-3100-054
    - APP FRM-3100-055
    - APP FRM-3100-062

- Started updating metadata for training documents that were moved from DMS to QMS as tasked by SCS
- Updated CORE Intern page and recorded time on time clock

Friday August 19th:
- Continued reorganizing training files that have been moved to QMS
- Clinical operations meeting and clinical training on Identifying and Ensuring Technical Requirements for Unblinded Monitoring
- Continued Reorganizing training files in QMS
- Updated CORE internship page and recorded time on time clock

Week of 08/22/2016-08/26/2016: out of the office

Monday August 29th:
- Continued reorganization of training documents in QMS
- Worked on rough outline for a training course I will be assisting SCS, Learning and Development with. Set meeting for tomorrow to go over our outlines and get a formal plan together for training course
- Continued reorganization of training documents in QMS
- Started uploading quiz questions for a new CORE quiz
- Updated CORE internship page and recorded time on time clock

Tuesday August 30th:
- Finished uploading quiz questions on CORE for new quiz
- Continued outline and research for training course I will be assisting with
- Meeting with SCS to discuss outline and plan course content and to discuss my practicum project survey.
- Continued reorganization of training documents in QMS
- Updated CORE internship page and recorded time on time clock

Wednesday August 31st:
- Worked on PowerPoint slides and presentation for upcoming training event.
- Continued reorganization of training documents in QMS
- Updated CORE internship page and recorded time on time clock

Thursday September 1st:
- Continued working on upcoming training course, found examples from clinicaltrials.gov to use as an interactive exercise
- Meeting with Sr. Manager of Quality Assurance to continue our discussion of the CAPA process and go over all of the relevant forms used in the process
- Continued working on examples for upcoming training course
- Started doing research on a new software that MT will be trying out for designing online courses
- Updated CORE internship page and recorded time on time clock

Friday September 2nd:

- Edited slides for upcoming training course
- Weekly intern meeting to discuss my current projects and my thesis
- Attended a training webinar for a new software that MT may use to develop online training courses
- Practiced presenting my portion of the training course for next week
- Updated CORE intern page and recorded time on time clock

Tuesday September 6th:

- Practiced presenting PowerPoint slides for upcoming course
- Attended live demo of software that MT might use for online training courses
- Meeting with SCS to run through PowerPoint slides for course
- Continued reorganizing training files in QMS
- Updated CORE intern page and recorded time on time clock

Wednesday September 7th:

- Added content and slides to PowerPoint presentation for upcoming course, practice presentation with new slides
- Continued reorganizing training files in QMS
- Printed out documents for training course being given tomorrow at a nearby hospital

Thursday September 8th:

- Accompanied CEO for a 4 hour training course at a nearby hospital
- Finished prepping for presentation tomorrow

Friday September 9th:

- Traveled to Central Texas for training course that I co-presented with SCS

Monday September 12th:

- Scanned and uploaded documents from last week's training courses into QMS
- Generated certificates for the participants of the training courses from last week
- Attended orientation meetings for new hires on GCP and FDA guidelines for clinical research and business continuity and ethics regarding clinical research
- Continued working on training certificates
- Updated CORE internship page and recorded time on time clock

Tuesday September 13th:

- Finished uploading documents from last week's training courses into QMS
- Filled out and collected signatures from MT committee members for my intent to defend paperwork for my practicum project
- Attended new hire orientation meetings for MT tools and systems, review of policies and procedures, and GCP training
- Created social media advertisements for a current study
- Looked through a demo regulatory binder to see what it contained and what the different forms looked like.

- Updated CORE intern page and recorded time on time clock

Wednesday September 14th:
- Assisted SCS work through an issue with the CORE system
- Continued reorganizing training files in QMS
- Attended orientation meetings regarding travel policies and safety procedures
- Meeting on campus with Dr. Mathew since he took over as program director, had intent to defend signed and submitted

Thursday September 15th:
- Updated Intern CORE page and time clock
- Created training records in QMS for new employees
- Attended orientation training on Professional Development
- Continued to reorganize training files into QMS
- Updated CORE intern page and recorded time on time clock

Friday September 16th:
- Continued reorganizing training documents in QMS
- Attended monthly clinical meeting
- Weekly intern meeting with CEO and SCS to discuss my internship activities and project
- Went through eTMF tracker that is used at MT to get an idea of how regulatory documents are tracked for different projects
- Looked through practicum survey results
- Continued reorganizing training documents in QMS

Monday September 19th:
- Updated CORE intern page and time clock from last week
- Meeting with SCS to go over forms that needed to be created from the new hire orientation last week
- Created attendance forms and completion certificates for activities done during new hire orientation
- Read through current SOP on Writing a Monitoring Visit Report
- Read ICH E6 and ISO guidelines on monitoring
- Read through current results from eTMF survey
- Continued reorganizing training documents in QMS
- Updated CORE intern page and time clock

Tuesday September 20th:
- Prepared for meeting with CRA I to discuss monitoring visit report (MVR) submission
- Meeting with CRA I to discuss how MVRs are created, edited, approved, and stored
- Meeting with in house CRA I to discuss her role with MVR compliance and to look at CTMS
- Continued reorganizing training documents in QMS
- Continued reading ICH guidelines reference for ACRP certification

Wednesday September 21st:

- Added documents to CORE page for a current study
- Continued reorganizing training documents in QMS
- Read through FDA regulations binder that SCS put together so I can help add documents that need to be added
- Watched demo videos for a new software that may be used for training events.
- Went through eTMF survey results and made notes
- Updated CORE intern page and time clock

Thursday September 22nd:

- Read articles on efficiency and cost savings in a business
- Updated AdWords bids for current study
- Continued reorganizing training files in QMS
- Continued reading ICH reference guidelines for ACRP certification
- Talked briefly with SCS about launching a Facebook campaign we have been working on for a current study
- Watched videos on how to use new training software that MT may start using
- Updated CORE intern page and time clock

Friday September 23rd: ½ day, 4hrs

- Updated Google AdWords campaign for current study
- Continued reorganizing training files in QMS
- Continued reading ICH reference guidelines for ACRP certification
- Meeting with SCS about a Facebook ad campaign for a current study
- Continued reading ICH reference guidelines for ACRP certification
- Updated CORE intern page and time clock

Monday September 26th:

- Updated Google AdWords campaign and changed bidding strategy
- Launched Facebook ad campaign for current study
- Continued reorganizing training files in QMS
- Continued finding FDA guidance documents to improve the FDA guidance reference binder
- Formatted tables for practicum results section
- Checked AdWords and Facebook ad campaigns again, did some troubleshooting for issues with the Facebook campaign
- Updated CORE intern page and time clock

Tuesday September 27th:

- Updated Google AdWords Campaign bids. Check status of FB help question, no response
- Uploaded documents on CORE portal page for current study
- Checked status of FB help question, no response
- Continued reorganizing training files in QMS
- Continued reading ICH reference guidelines for ACRP certification

- Printed Documents to be added to FDA Guidance Binder, created cover page and contents page for binder.
- Updated references for Practicum Thesis
- Updated training records for current employees with new trainings
- Updated CORE intern page and time clock

Wednesday September 28th:

- Updated Google AdWords bids for current study
- Continued working on QMS training file reorganization
- Continued reading ICH reference guidelines for ACRP certification
- Meeting with SCS to discuss Facebook ad campaign issues for a current study
- Started working with demo of new learning software
- Updated CORE intern page and time clock

Thursday September 29th:

- Updated Google AdWords bids for current study
- Finished first run through of QMS training documents, sent list of documents that I do not have access to edit to SCS so the permissions could be changed
- Started working with demo creating an online course from an existing course
- Checked in with Google AdWords campaign and adjusted bids
- Updated CORE intern page and time clock

Friday September 30th:

- Updated Google AdWords bids for current study
- Worked with new software to update a current course
- Weekly intern meeting with CEO and Senior Compliance Specialist to discuss internship activities
- Continued working with new learning software
- Updated CORE intern page and time clock

Monday October 3rd:

- Updated Google AdWords bids for current study
- Started a QSM matrix audit where I compare the current matrix with the previous to see which review documents have changed depending on individual roles.
- Worked with new software to continue updating a current course
- Continued QSM Matrix audit
- Updated time clock and Google AdWords bids

Tuesday October 4th:

- Updated Google AdWords bids for current study
- Worked with new software to continue updating a current course
- Continued QSM Matrix audit
- Updated CORE intern page, time clock, and Google AdWords bids

Wednesday October 5th:

- Updated Google AdWords campaign for current study, discussed current strategies with SCS to determine if we should alter it.
- Attended Webinar: "What Effect Does ICH E6 R2 Have on Risk-Based Monitoring and Overall Quality Risk Management?"
- Finished QSM matrix audit and emailed results to QA team
- Continued to work with new software to develop and update online courses
- Updated CORE intern page and time clock

Thursday October 6th:

- Updated Google AdWords campaign for current study
- Created a new ad for a current study to be used as a Facebook post
- Continued working with new software to create online courses
- Meeting with CEO, SCS, and Manager of Information Technology to discussing moving forward with the training software we have been testing.
- Updated time clock

Friday October 7th:

- Updated Google AdWords bids and added some keywords to the current campaign
- Read through several articles about the types of campaigns and keywords to use for Facebook and Google AdWords campaigns
- Weekly intern meeting with SCS to discuss projects I have been working on, also discussed changes to the ad campaigns we are running and how to optimize the results we are seeing
- Read through Research Practitioner article on changes to the common rule written by staff members at my internship site
- Started preliminary research on ophthalmology equipment tasked by SCS to help with therapeutic training
- Read Article from Clinical Researcher: "Monitoring of Clinical Trials—Are Remote Activities Helpful in Controlling Quality?"
- Updated CORE intern journal and time clock

Monday October 10th:

- Updated Google AdWords bids for current study
- Did research on common ophthalmology instrument as tasked by SCS
- Worked with new software to create online courses
- Sat with in-house CRA while she filled out IMV to see how it was done
- Continued working with new software creating online courses
- Updated CORE intern page and time clock

Tuesday October 11th:

- Updated Google AdWords bids for current study, paused some of the keywords that were not doing very well
- Continued research on ophthalmology instruments

- Meeting with CEO and SCS to discuss how files would be handled with upcoming upgrade to online portal system. Discussed which documents would be moved and which would be taken down and how we would ensure that compliance will be upheld.
- Continued working with online course building software
- Updated CORE intern page and time clock

Wednesday October 12th:

- Updated Google AdWords bids for current study
- Continued research on ophthalmology instruments
- Weekly Intern meeting with CEO to discuss current projects and my thesis
- Started downloading and saving CORE content that would not be transferred once the system is updated
    - GCP Fundamentals
    - Risk Management for Clinical Trials
- Updated CORE intern page and time clock

Thursday October 13th:

- Updated Google AdWords bids for current study
- Continued research on ophthalmology instruments
- Webinar: "What you need to know about EDC, SAEs, E2B, and Pharmacovigilance Systems"
- Meeting with in-house CRA to discuss clinical data source materials and what types of things you look for when monitoring and some examples of mistakes you may find while reviewing source data.
- Helped employee with CORE portal issue
- Meeting with Manager of Clinical Operations to discuss my internship and what my goals are for after I graduate.
- Updated Google AdWords bids for current study
- Updated CORE intern page and time clock

Friday October 14th:

- Updated Google AdWords bids for current study
- Continued research on ophthalmology instruments
- Meeting with Sr. Manager of Quality Assurance for continuation of QA training. Discussed internal and external audits, looked at some of the audit tools used to conduct audits, and went through the form that audit findings are listed on
- Read BIMO manual for investigators and sponsors as assigned by Sr. Manager of Quality Assurance.
- Updated CORE intern page and time clock

Monday October 17th:

- Updated Google AdWords bids for current study
- Read relevant SOPs related to quality audits as assigned by Sr. Manager of Quality Assurance
    - SOP 3100-002

    - SOP 3100-006
- Attended project meeting for current study related to lab testing and best recruitment practices
- Continued Ophthalmology research
- Meeting with SCS and CEO related to planning ACRP fall symposium.
- Updated CORE intern journal and time clock

Tuesday October 18th:

- Updated Google AdWords bids for current study
- Continued Ophthalmology research
- Continued downloading and saving CORE content that would not be transferred once the system is updated
    - Completed all Public courses and started on the MT Employee courses
- Began research on emergency IND pathways and emergency use authorization for emergencies in order to help develop content for a presentation being delivered by CEO during ACRP fall symposium.
- Updated intern CORE page and time clock

Wednesday October 19th:

- Updated Google AdWords bids for current study
- Continued research to help develop content for a presentation being delivered by CEO during ACRP fall symposium
- Scanned, uploaded, and organized training binders, discussed with VP of Clinical Operations how the documents could be organized into the CTMS for future training needs
- Updated CORE page and time clock

Thursday October 20th:

- Updated Google AdWords bids for current study
- Worked on edits for my practicum thesis
- Accompanied SCS while doing system validation test scripts for the upgrade of M-Files in order to learn more about the process of validation
- Continued downloading and saving CORE content that would not be transferred once the system is updated, completed General MT training courses and started working on project specific portals
- Started going through MT connect library to see if the course materials that have been uploaded are all in M-Files
- Updated CORE intern page and time clock

Friday October 21st:

- Created CE evaluation for ACRP fall symposium
- Weekly intern meeting with CEO and SCS to discuss internship activities, preparation for tomorrow's symposium, and practicum project
- Edited CE evaluation for symposium and created electronic CE sign in sheet
- Formatted sources for presentation being given at tomorrow's symposium

- Edited and updated internship journal

Monday October 24th:

- Updated AdWords bids for current study
- Created CE certificate from ACRP fall symposium
- Emailed CE certificates to attendees of the symposium
- Uploaded necessary CE documentation to QMS in compliance with CE provider ship
- Read articles on breaches of security related to medical and health records
- Edited research practicum paper
- Updated CORE intern page and time clock

Tuesday October 25th:

- Updated AdWords bids for current study
- Edited CE certificates from ACRP fall symposium
- Edited research practicum report
- Read article on dietary supplements
- Research google AdWords to prepare for consultation with AdWords specialist
- Continued going through MT connect PowerPoints to ensure all training presentations are saved in the QMS
- Updated CORE intern page and time clock

Wednesday October 26th:

- Updated AdWords bids for current study
- Continued AdWords research for possible questions to address during consultation
- Continued auditing MT Connect presentations to ensure training materials are saved into QMS
- Worked on practicum presentation slides
- Updated CORE intern page and time clock

APPENDIX C
IRB SUBMISSION

UNT HEALTH SCIENCE CENTER

Institutional Review Board

DATE: 2 August 2016

TO: Patricia Gwirtz, PhD CRM Program
(with Amber Beckham)

FROM: Brian A. Gladue, PhD, CIP
Executive Director, Office of Research Compliance

SUBJECT: PROTOCOL **2016-104**
Benefits, Challenges and Future Directions: Making the Case for eTMF in Clinical Research

NOTICE OF DETERMINATION / APPROVAL

The Office of Research Compliance, on behalf of the Institutional Review Board (IRB) of the University of North Texas Health Science Center (UNTHSC) has reviewed your protocol and has determined this protocol to meet criteria for **EXEMPT** status (as specified in Federal Regulations 45 CFR 46 101(b) in one or more of the following categories, as initialed below:

____ (1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of... instructional techniques, curricula, or classroom management methods.

____ (2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless: (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

____ (3) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (2) of this section, if: (i) the human subjects are elected or appointed public officials or candidates for public office...

____ (4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

____ (5) Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine: (i) Public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs...

____ (6) Taste and food quality evaluation and consumer acceptance studies...

You are responsible for complying with all UNTHSC policies, decisions, conditions and requirements regarding projects involving human subjects. You are responsible for insuring that the research is implemented as specified in the protocol. In addition, you are required to use ONLY the reviewed and approved documents, materials and/or procedures designated for this protocol that were acknowledged by the Office of Research Compliance.

You must report to the Office of Research Compliance any changes affecting the protocol upon which this certification is based. **No changes may be made without prior approval by the Office of Research Compliance** except those necessary to eliminate immediate hazards.

If you have any questions, please contact the Office of Research Compliance at (817) 735-0409

Texas College of Osteopathic Medicine • Graduate School of Biomedical Sciences • School of Public Health
School of Health Professions • UNT System College of Pharmacy • Health Institutes of Texas • UNT Health
3500 Camp Bowie Boulevard, Fort Worth, Texas 76107 • 817-735-0409 • Fax 817-735-0124 • www.unthsc.edu
An EEO/Affirmative Action Institution

EXEMPT Approval Letter May 2013 excl Subpart B/C

University of North Texas Health Science Center
Office for the Protection of Human Subjects (OPHS) / Institutional Review Board (IRB)

2016-104

ALL research involving human subjects requires review and consideration by the UNTHSC Office for the Protection of Human Subjects (OPHS) and the Institutional Review Board (IRB). Some research projects may be "exempt" from IRB Review and thus qualify as "Exempt Category" research. To determine if your research project is in this category, provide information using the following form. Note that proof or declaration of Human Subjects Research Training for all study personnel must accompany this form. Also, incomplete applications and supporting documentation will delay OPHS-IRB review and approval of this project. If it is determined that your research project is NOT Exempt category research, you will need to re-submit a full protocol and a completed Expedited IRB Application Form. Attach page if more space is needed for any of the below. Go to website for guidance on what is NOT Exempt.

PROJECT INFORMATION

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Faculty Research ☐ **Student Research:** ☒ **Masters** ☐ **Doctoral**

Title of Research Activity:
Benefits, Challenges, and Future Directions: Making the Case for eTMF in Clinical Research

Name of Principal Investigator (Faculty Member): Dr. Patricia Gwirtz

Contact Information- Telephone: 817-735-2979 *Email Address:* Patricia.Gwirtz@unthsc.edu

Name of Student Investigator: Amber C. Beckham

Contact Information- Telephone: 214-727-0874 *Email Address:* amber.beckham@my.unthsc.edu

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Department/Program: Clinical Research Management

Name(s) of each Co-Investigator (Study Personnel):

Project Description: Briefly state the objective(s) and procedures associated with this project. *Recall that incomplete or unclear information will delay OPHS-IRB review and approval* **(attach page if needed):**

See attached survey, protocol, and recruitment documents

Educational Practices and Strategies: Yes ☐ **No** ☒ (If Yes, please answer **all** questions below)

Will research involve normal educational practices such as (check appropriate box)?

☐ Regular instructional strategies including those commonly used in a classroom
☐ Special education instructional strategies such as the use of a device for performing skills or exercise
☐ Effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods
☐ Other __
☐ The study does not involve research in educational practices and strategies

Will research be conducted in an established or commonly accepted educational setting (university or teaching hospital)?

Yes ☐ **No** ☒ **[If yes, please answer the question below]**

Where will it be conducted? Clinical Research Organization

Is the educational activity itself part of your research or will the educational activity occur regardless of research?

☐ **Yes, it is part of research**
☒ **No, the practices are normal educational practices that will occur regardless of this research project**

Survey or Interview Study: Yes ☒ **No** ☐ (If Yes, please answer all questions AND attach copy of survey instruments and procedures)

Source of subject population: MedTrials Employees

Age Range of subjects to be included in the survey or interview: 18-99 years

Where will the survey/interview occur? (Location of activity): Survey will be accessed online thorugh their home or work computer

Date(s) survey/interview to be conducted? (Include month and year) From 08/2016 To 11/2016

Will subjects be identified? **Yes** ☐ **No** ☒ Will subject responses be audio, video or digitally recorded? **Yes** ☐ **No** ☑

OPHS Form EX-1 (rev. 02/12)
Request for Review EXEMPT Category Project

Request for Review of EXEMPT Category Research Project **IRB #**

Will your subjects include children (under age 18)? **Yes** ☐ **No** ☒ **[If Yes, STOP. Project does not qualify as EXEMPT]**

Retrospective Record or Chart Review: Yes __ **No** ☒ (If 'Yes', Please check all that apply)

☐ Retrospective review of medical records: Name of hospital or institution from which records will be obtained:
☐ Employment records ☐ Student records ☐ Other records: _____

Name of institution or agency from which records will be obtained:

If a non-UNTHSC unit will provide records, attach letter from that agency/clinic.

The data were collected during Time Period (month and year): From _____ To _____

Will the investigators have access to subject identifiers? **Yes** ☐ **No** ☐

Will a "master list" of subject identifiers for this data set be kept? **Yes** ☐ **No** ☐ If yes, for how long?
If your protocol calls for a "master list" of identifiers then this may NOT qualify for Exempt. Contact OPHS staff for assistance

Use of existing biological specimens: **Yes** ☐ **No** ☒ If "Yes", Source of specimens (contact name, entity name and address) and attach description of specimens and origin

Secondary Data Set Study: **Yes** ☐ **No** ☒ If 'Yes', Answer all questions

Source of data:

Were the data originally collected for research purposes: **Yes** __ **No** ☐ If yes, by UNTHSC researchers? **Yes** ☐ **No** ☐

Is the Source "publicly available"? **Yes** ☐ **No** ☐

Note that "Publicly available" means that the general public can obtain the data. Sources are not considered "publicly available" if access is limited ONLY to researchers. ***NOTE: You must attach a copy of the catalog page/ website page indicating where the dataset can be obtained or located.***

Does the secondary dataset contain personal identifiers? Yes ☐ **No** ☐

Type of identifier (i.e., name, SSN, address, medical record number, etc.):

Public Benefit or Services Programs

Is the study conducted or subject to approval by the federal department or agency head? ☐ **Yes** ☐ **No**

Is the aim to study, evaluate, or otherwise examine one or more of the following [check appropriate box(es)]?

☐ Public Benefit or Service Programs (i.e. Social Security Services, Medicaid, welfare)
☐ Procedures for obtaining benefits or services under those programs
☐ Possible changes in or alternatives to those programs or procedures
☐ Possible changes in methods or levels of payment for benefits or services under those programs

Taste and Food Evaluation

Will this study involve taste evaluation and/or food quality assessment? ☐ **Yes** ☒ **No**

Is the food approved by the Food and Drug Administration (FDA)? ☐ **Yes** ☐ **No [If No, STOP. This does NOT qualify as Exempt]**

Will wholesome (no additives) food be consumed? ☐ **Yes** ☐ **No**

Are the food ingredients at or below the level found to be safe by the FDA? ☐ **Yes** ☐ **No**

Do you ever intend to publish or present (oral, poster or written) the results of this project? Yes ☒ No ☐

Is an informed consent needed for this research? Yes ☐ **No** ☒

If yes, this project may NOT be Exempt from Full Board or Expedited IRB review and consideration. Please attach a complete protocol form and synopsis along with this application for further review (see OPHS website for Protocol Form and Summary Format guidelines).

ATTACH TO THIS FORM:

- *Certificate of Human Subjects Training* for all study personnel. If such documentation is already on file for all key personnel, initial here: _____ [Note that inaccurately claiming that such documentation is on file will

significantly delay Review]
(If applicable)

Copy of Secondary Data documentation (examples include: website address or reference information for public use data files; letters of agreement from owners of the dataset, etc.)

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PHS-IRB Faculty
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Amber Beckham 7 1

Copy of Survey or Interview questions and any research statement or cover letters to be used (if applicable)

Any other documentation that will assist in a timely review of your project.

SIGNATURES AND ASSURANCE Signature certifies that the Principal Investigator understands and accepts responsibility to ensure that this research and the actions of all project personnel involved in conducting the study will conform to the OPHS-IRB approved protocol, OPHS-IRB requirements/policies and procedures, and all applicable federal regulations.

Patricia A. Gwirtz 7/21/2016

PRINCIPAL INVESTIGATOR Signature Print Name Date

NOTE: If this is a "Student Project", the Principal Investigator signing above agrees to be fully responsible for all aspects of this project Ordinarily this person will also serve as the Faculty Advisor for the Student on this project. The Faculty Sponsor / Advisor may designate an alternate Faculty Sponsor / Advisor who will assume responsibilities on a temporary basis, and will notify the OPHS-IRB of any change in the Faculty Sponsor / Advisor for this project.

Student Investigator's Assurance: By my signature as student investigator, I certify the above applicable assurances and that I will meet with my Faculty Sponsor / Advisor on a regular basis to monitor study progress. If my Faculty Sponsor / Advisor is unavailable, I will meet with his/her designated alternate Faculty Sponsor / Advisor who will assume his/her responsibilities. I also agree to notify the O of any change in Sponsor / Advisor

ST NT INVESTIGATOR Signature Print Name 12/ 2014 Date

UNIVERSITY *of* NORTH TEXAS HEALTH SCIENCE CENTER
OFFICE *for the* PROTECTION *of* HUMAN SUBJECTS
INSTITUTIONAL REVIEW BOARD

Request for Waiver of Documentation of Informed Consent
Form A

IRB #

Investigator's Name: Patricia A Gwirtz, PhD. FACC. Student Investigator: Amber C Beckham

Title of Project: Benefits, Challenges, and Future Directions: Making the Case for eIMF in Clinical Research

Documentation of consent means that participants are required to sign a consent form, thereby documenting their consent. A waiver of documentation means that the UNTHSC IRB is waiving the requirement to obtain the participant's signature. Even if this waiver is granted, a consent process must still be in place. The consent process must contain all the required elements of consent and usually consists of a consent form/verbal script that is read aloud to them.

For the UNTHSC IRB to grant this waiver, your research project must meet one of the following conditions. ***Please initial the line next to the appropriate condition and explain why your research meets the condition in the space provided.***

_____ *(initial)* **Condition 1-** The only record linking the participant and the research would be the consent document and the principal risk would be the potential harm resulting from the breach of confidentiality. This refers to instances where participants could be seriously harmed if it became known that they were participants in the research.

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OR

DCK *(initial)* **Condition 2-** The research presents no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required outside of the research context.

Explanation: Research data will be collected through a brief online survery. The probability and magnitude of harm anticipated for this project is no greater than what is encountered in every day life or during the performance of routine surveys. Because of this, it meets the definition of "minimal risk"

Investigator's Signature Patricia A Gwirtz **Date** 7/21/2016

IRB Chair's Signature [signature] **Date** 8/2/16
Exec Dir ORC

2016-104

UNIVERSITY of NORTH TEXAS HEALTH SCIENCE CENTER at Fort Worth
Office for the Protection of Human Subjects
Institutional Review Board

Application for Waiver of HIPAA Authorization for Research Purposes

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IRB #: 2016-104

PROJECT INFORMATION

Title of Project: Benefits, Challenges, and Future Directions: Making the Case for eTMF in Clinical Research

Name of Principal Investigator: Dr. Patricia Gaines

Department: Clinical Research Management

Name of Each Co-Investigator (Study Personnel): Student Investigator: Rubel C Berakhai

Name, Address, and Phone Number of Study Sponsor (if any): None

PURPOSE OF THE STUDY/OBJECTIVE OF THE RESEARCH: TO SHOW THAT ELECTRONIC TRIAL MASTERS ARE SUPERIOR TO PAPER TRIAL MASTER FILES, AND THAT THE BENEFITS FROM USING AN ELECTRONIC TRIAL MASTER FILES OUTWEIGH THE CHALLENGES IN CLINICAL RESEARCH.

1. PROTOCOL/PLAN

a) How, and or from where, do you plan to gather the information? Data will be generated from an online survey sent out through email to current employess to relevant departments.

b) What is the source(s) of PHI (choose all that apply):

- ☐ Medical Records
- ☐ Billing system records
- ☐ Laboratory results
- ☐ Pathology results
- ☐ Radiology results
- ☒ Interviews/surveys/questionnaires
- ☐ Databases or tissue repositories that were created for operational (i.e. non-research) purposes
- ☐ Other (describe) _____

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c) Describe the health information that you will collect (attach a copy of your data collection sheet if applicable): None

Not needed No PHI involved 8/2/16

d) State the anticipated beginning and end dates of the research (or approximate length of data gathering activities): 08/2016-11/2016

e) Give an estimate of the number of records that will be involved in the project: 0

f) Necessity of PHI:

☐ **This research could not practicably be conducted without access to and use of the Protected Health Information (PHI)** *(i.e. Basically, you are unable to do the research without the PHI. For Example, the health information in the medical record is necessary for the case report or retrospective chart review).*

Please explain why the PHI is necessary for the proposed research related activity:

g) Is this a retrospective chart review? ☐ **Yes** ☒ **No***

***If you answered no, can you get Authorization from the research subjects?** ☒ **Yes** ☐ **No**

*** If you answered no, explain why it is not feasible to get authorization for this research:** _____

h) Is the risk to individuals whose information you are using minimal? *(i.e. the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests)*

OR

More than minimal?

☒ **Minimal risk** ☐ **More than minimal risk***

***If you answered more than minimal, please explain what the risk is:** _____

2. PROTECTION OF DATA

HIPAA requires that there be an adequate plan to protect the identifiers from improper use and disclosure, that there be an adequate plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research, and that there be adequate written assurances that the PHI will not be reused or disclosed to any other person or entity, unless required by law or by oversight of the research by a regulatory agency.

a) What security measures will you take to protect the PHI from improper use or disclosure or reuse? *(e.g. they are kept in a locked file cabinet only available to researchers, or they are maintained in a password-protected database and only the researchers have access to the password.)* **Please Note: List all of the entities that might have access to the study's PHI such as UNTHSC, sponsors, FDA, data**	No personal information will be collected or stored during this research. The survey is anonymous and will not require any identifyable information to participate.

monitoring boards, any others given authority by law.	
h) When and how do you plan to destroy the PHI? If you do not plan to destroy the PHI, please give your rationale. *(e.g. there is a plan to break any links to identifiable information, unless links need to be maintained, in which case a reason should be given.)*	N/A
e) What security measures will you take to assure that the PHI will not be reused? *(e.g. "The information will not be used or disclosed for any purpose other than this specific research project.")*	N/A

INVESTIGATOR'S CERTIFICATION/ASSURANCE

I certify that the information provided in this request for Alteration to/Waiver of Individual Authorization is complete and correct. I understand that I have the ultimate responsibility for protecting the confidential information of individuals and ensuring the privacy of their protected health information.

Patricia A. Gwartz — 7/21/2016

Signature of Principal Investigator **Date**

PG **(please initial) I agree that subjects will not be identified by name in any presentation or publication related to this research project.**

INSTITUTIONAL REVIEW BOARD ACTION (FOR IRB USE ONLY)

The University of North Texas Health Science Center Institutional Review Board (IRB) is established in accordance with 21 CFR 56.107 and 45 CFR 46.107.

Based upon the information provided above, the University of North Texas Health Science Center Institutional Review Board (IRB) finds that this waiver request meets all the legal requirements for a Waiver of Individual Authorization under HIPAA pursuant to 45 CFR 164.512 (i)(2)(i)-(v) and approves the request under:

_____ **Exempt status as specified in 45 CFR 46.101 (b)**

_____ **Expedited Review Procedures (21 CFR 56.110 and 45 CFR 46.110)**

_____ **Full board review procedures (21 CFR 56.108 (b) and 45 CFR 46.108 (h)**

_____ _____

Chair, Institutional Review Board **Date**

Recruitment email 2: Marks the beginning of the two week survey period

Good Morning,

My name is Amber Beckham, and I am a Clinical Research Management Masters student at the University of North Texas Health Science Center at Fort Worth. As part of my internship, I am conducting research on the use of eTMF in clinical research and would like your participation. Your participation is voluntary. Please see the attached research statement for details about the study and your rights as a study participant.

Dr. Patricia Gwirtz at UNTHSC will be serving as the Principal Investigator for this research study. If you agree to participate, the study will being by analyzing your response to an online survey, for which the link is provided below. Please complete the survey within two weeks

"Survey Link"

In this survey, you will not be asked to give out any personal information and your participation will be completely anonymous. If you have any questions regarding this study please email the student investigator, Amber Beckham, at Abeckham@medtrials.com.

Your participation consists of completing a brief survey that should take about 20 minutes. This survey may be completed at this time and must be done within two weeks

Thank you for your time and consideration,

Sincerely,

Amber Beckham

Abeckham@medtrials.com

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Reminder email for survey: to be sent one week after the first email

Good Morning,

My name is Amber Beckham, and I am a Clinical Research Management Masters student at the University of North Texas Health Science Center at Fort Worth. As part of my Internship, I am conducting research on the use of eTMF in clinical research and would like your participation. Your participation is voluntary. Please see the attached research statement for details about the study and your rights as a study participant.

Dr. Patricia Gwirtz at UNTHSC will be serving as the Principal Investigator for this research study. If you agree to participate, the study will being by analyzing your response to an online survey, for which the link is provided below. Please complete the survey within one week

"Survey Link"

In this survey, you will not be asked to give out any personal information and your participation will be completely anonymous. If you have any questions regarding this study please email the student investigator, Amber Beckham, _____.

Your participation consists of completing a brief survey that should take about 20 minutes. This survey may be completed at this time and must be done within one week.

Thank you for your time and consideration,

Sincerely,

Amber Beckham

Abeckham@medtrials.com

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at Abeckham@medtrials.com

UNTHSC Research Survey

RESEARCH STATEMENT – Survey Cover Letter

Benefits, Challenges, and Future Directions: Making the Case for eTMF in Clinical Research
Principal Investigator: Patricia A. Gwirtz, Ph.D., FACC
Student Investigator: Amber C Beckham
Institution: University of North Texas Health Science Center

Introduction/overview:

This research practicum project aims to get current industry opinions on the use of eTMF in clinical research. The current eTMF used at MedTrials will be used as the basis for the questions asked. If you choose to participate, you will complete the following:

-A brief online survey that will ask questions about the current eTMF in use at MedTrials. It should take about 20 minutes to complete and is entirely anonymous.

Participation in the study:

Participation in this study is entirely voluntary and anonymous. Completion of the survey counts as consent to participate in this study. You may choose to leave the study at any point without penalty.

Confidentiality:

The only identifiable information in this study is your email. Your company email will be used only to send out a reminder to take the survey, and will not be stored or used to identify you in any way. Your email will also not be linked to your responses.

Risk/Benefit:

The risks involved with this survey-based research are minimal. They include the risks associated with your time investment and the use of your email address. The survey is designed to take only minimal time to complete, and every effort will be made to maintain confidentiality in regards to your email address provided. There is no foreseeable or direct benefit to you associated with your participation in the research study. This study is designed to increase the knowledge and understanding of eTMF and make the case for their use in clinical research.

Questions/Concerns:

If you have any questions regarding this project, please feel free to contact:

Student investigator: Amber Beckham: Abeckham@medtrials.com

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If you have any questions about your rights as a research subject, please contact the UNT Health Science Center Institutional Review Board at (817)-735-0409.

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UNTHSC Research Survey

Introduction

Thank you for your participation in this research study. Your participation will consist of a brief survey which may be completed at this time. The survey should take around 20 minutes to complete.

You can choose to leave this study at any point without penalty or loss of benefits that you are otherwise entitled. If a problem should occur during the survey, or if you have any questions at any time about the study, you may contact Amber Beckham, student investigator, at abeckham@medtrials.com. If you have questions about your rights as a research participant in this study, you may contact the UNT Health Science Center Institutional Review Board at (817)-735-0499.

* Do you consent to participate in this research project?

- ◯ Yes, I indicate that I understand and choose to participate in this research project.
- ◯ No, I decline to participate.

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UNTHSC Research Survey

Demographics

* What area/department do you work in?

- ◯ Clinical Operations
- ◯ Informatics
- ◯ Quality Assurance and Training

* How long have you worked in the clinical research industry?

- ◯ 5 years or less
- ◯ 6-10 years
- ◯ 11-15 years
- ◯ 16 years or more

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UNTHSC Research Survey

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eTMF

* How often do you use/interact with the current eTMF system?

* Where do you normally access the MedTrials eTMF? (select all that apply)

* For which activities do you currently use your curent eTMF? (select all that apply)

- [ ] Regulatory document viewing

Once a day

Multiple times a day

A few times a week

A few times a month

Rarely to never

At your home office

At an investigational site

At a company office

In a hotel room

At an airport

At a restaurant

Other (please specify)

Creating or editing regulatory documents ☐

Sending and uploading regulatory documents to or from clients ☐

Other (please specify) ☐

UNTHSC Research Survey

eTMF Benefits

* Below is a list of common benefits associated with eTMF. Rank the benefits according to your experience with your current eTMF with 1 being the most beneficial and 5 being the least beneficial.

- [ ] Searchability of documents
- [ ] Audit trail
- [ ] Document quality
- [ ] External collaboration with clients
- [ ] Completeness of study files

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UNTHSC Research Survey

eTMF Challenges

* Below is a list of common challenges associated with eTMF. Rank the challenges according to your experience with your current eTMF with 1 being the most challenging and 5 being the least challenging.

- [ ]
- [ ]
- [ ] Accessibility
- [ ]
- [ ]

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Training of personnel

Organization/searchability

Client hesitation

Cost of implementation or maintenance

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eTMF

* In your opinion, what effect does eTMF have on the cost of running a clinical trial?

- Increases cost significantly
- Increases cost slightly
- Does not impact cost
- Decreases cost slightly
- Decreases cost significantly

UNTHSC Research Survey

eTMF Increases Cost

* In your opinion, what contributes to an increased cost? (select all that apply)

- [ ] Implementation of eTMF
- [ ] Maintenance of eTMF
- [ ] Training of Personnel
- [ ] Other (please specify)

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UNTHSC Research Survey

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eTMF Decreases Cost

* In your opinion, what contributes to a decreased cost? (select all that apply)

- [ ] Decreased time to create, edit and share documents
- [ ] Streamlining the overall process
- [ ] Speeding up external collaboration
- [ ] Increased overall efficiency
- [ ] Other (please specify)

UNTHSC Research Survey

eTMF

* In your opinion, does your current eTMF increase or decrease efficiency when working with project-related documents?

- ◯ The current eTMF increases efficiency
- ◯ The current eTMF decreases efficiency

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☐ Ease of use

☐

☐

☐

APPROVED AS
EXEMPT

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eTMF Increases Efficiency

* Rank the following choices in order of how they increase efficiency in an eTMF with 1 as the greatest increase to efficiency and 5 as the least increase to efficiency.

Organization

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Use of workflows to track documents

Use of template for creating documents

Searchability of documents

UNTHSC Research Survey

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eTMF Decreases Efficiency

* Rank the following choices in order of how they decrease efficiency in an eTMF with 1 as the greatest decrease to efficiency and 4 as the least decrease to efficiency.

Too many options/documents to look through

Organization

Search parameters are not intuitive

Use of workflows to track documents

Difficulty of use

UNTHSC Research Survey

eTMF

* How difficult is it to locate documents in your current eTMF

- ◯ Extremely difficult
- ◯ Very difficult
- ◯ Somewhat difficult
- ◯ A little difficult
- ◯ Not difficult at all

* In your opinion, how does metadata affect the searchability of documents in an eTMF

- ◯ [illegible]
- ◯ [illegible]
- ◯ [illegible]
- ◯ [illegible]
- ◯ [illegible]

* On a scale of 1-5, describe the quality and completeness of documents you access in your current eTMF.

1 represents the highest quality: there are rarely (or never) missing, inaccurate, or incomplete documents.
5 represents the lowest quality: the documents are often missing, inaccurate, or incomplete.

- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5

It makes searching much more difficult

It makes searching slightly more difficult

It doesn't affect searchability

It makes searching slightly easier

It makes searching much easier

* How secure do you believe your current eTMF is?

- ◯ Extremely secure
- ◯ Very secure
- ◯ Somewhat secure
- ◯ Not very secure
- ◯ Not at all secure

* What changes do you believe should be made to the current eTMF to improve the system?

* Which feature(s) do you believe are underutilized in your current eTMF? (select all that apply)

- ☐ Electronic signatures
- ☐ Document Sharing through workflows
- ☐ Fillable forms
- ☐ Use of mobile device application
- ☐ Other (please specify)

* In general, how has eTMF impacted your role in clinical research? Please explain in the text box provided.

- ◯ eTMF positively impacted my role in clinical research
- ◯ eTMF negatively impacted my role in clinical research
- ◯ eTMF has not impacted my role in clinical research

Please explain your answer:

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End of Survey

End of Survey

Thank you for participating in this research study.

If you would like to review the results of this survey, please email Amber Beckham at: Abeckham@medtrials.com.

By clicking "Done", this window will close.

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