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Perceptions of clinical research coordinators about the quality of monitoring and major failings/ concerns in the monitoring process

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Perceptions of Clinical Research Coordinators about the Quality of Monitoring and Major Failings/Concerns in the Monitoring Process

by

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THESIS

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Dedication

This thesis is dedicated to God, who gave me the strength and patience to complete this study.

I lovingly dedicate this thesis to my wife, Sushma, who supported me each step of the way.

I also dedicate this thesis to my parents and my grandfather who introduced me to the joy of reading from birth, enabling such a study to take place today.

Also, this thesis is dedicated to my committee members, Focus group members, IRB committee members, Clinical Research Coordinators for their endless support and encouragement.

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Abstract

The primary goals of clinical research monitoring are to assure adequate protection of the rights of human subjects, and the safety of all subjects involved in clinical investigations or clinical trials, and the quality and integrity of the data generated from clinical trials. Adequate monitoring of clinical trials can prevent the occurrence of significant problems, which may affect the entire process of bringing a new drug to market. The proper monitoring of clinical trials is a challenge. In spite of well established regulations and guidance, there remain many monitoring related concerns in clinical trials (e.g. protocol deviations and violations, IRB violations, improper adverse event reporting, etc). The survey results indicate that clinical research coordinators believe that there are concerns in the monitoring process, and that the quality of monitoring varies from monitor to monitor. Results also suggest that some monitors are exceptional, where as some monitors are abysmal.

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Chapter 1: Introduction

Clinical Research is a fast-growing, knowledge-based industry with a diverse pool of clinical research professionals (Gudadhe, 2001). Among the many professionals who play an important role in clinical research is the *clinical monitor or clinical research associate (CRA).* According to ICH GCP (1996), "Monitoring is the act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, standard operating procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirement(s)." The monitor is the "first line of communication between the sponsor and the investigational site" (Nylen, 2000). According to ICH GCP (1996), the monitor is responsible for various activities such as:

- Site selection.
- Training the site staff.
- Ensuring that the investigator and site staff are knowledgeable about the protocol and trial procedures.
- Protecting the rights, safety, and well-being of human study subjects.
- Checking the investigational product accountability.
- Ensuring that the site is following the protocol properly.
- Reviewing the CRFs, source documents, and informed consent documents.
- Reviewing of serious adverse event reporting.
- Helping the site staff in solving the generated queries.
- Checking whether the investigator has essential documents for the conduct of a trial (i.e., review of proper documentation at the site).

- Informing the investigator about the deviations from protocol, SOPs, and GCP guidelines and taking appropriate action.

Monitors should have scientific as well as clinical knowledge, and they should be trained adequately concerning the specifics of protocol which they are monitoring (ICH GCP, 1996). The quality of the clinical trial depends on the monitoring visit reports. Lack of proper monitoring may lead to many problems. Mihajlovic – Madzarevic (2010) identified the following problems which can result from inadequately performed monitoring:

- Inability to determine whether there has been non – compliance, fraud or misconduct in the trial.
- Failure to determine the CRF issues, protocol deviations, and violations.
- Improper monitoring affecting subject safety and quality of data recorded in the trial.

The monitor is appointed by a sponsor or a contract research organization to determine all the inconsistencies (e.g. Protocol deviations, CRF issues etc) in clinical trials (ICH GCP, 1996). According to Nylen (2000), ensuring proper and accurate adverse event reporting is one of the major responsibilities of the monitor. However, common findings from FDA inspections include improper adverse event reporting and failure to report adverse events to the FDA. Warning letters were issued to clinical investigators, sponsors, and contract research organizations for inadequate monitoring of clinical trials (Mihajlovic – Madzarevic, 2010).

Why are there inconsistencies, if there is a qualified, well-trained, knowledgeable, and experienced clinical monitor? (Inspection Observations, 2012). Why, then, are clinical monitors not able to determine the problems and facilitate their solution before the FDA identifies them?

"The clinical research coordinator (CRC) is a specialized research professional working with, and under the direction of, the clinical investigator" (Woodin, 2009) and the responsibilities of clinical research coordinator are:

- Reviewing and evaluating the protocol.
- Screening and enrolling the study subjects.
- Obtaining participant informed consent.
- Protecting the rights, safety, and well-being of study subjects.
- Ensuring that study medication was received by eligible subjects.
- Completing all study documents at the study site properly.
- Ensuring proper documentation at study site (e.g. Documenting signed informed consent forms).
- Submitting all the essentials documents for IRB review.
- Checking source documents and CRFs thoroughly.
- Resolving data queries generated by monitor.
- Proper scheduling of the study subject and monitor visits.

The clinical research coordinator (CRC) plays an important role in study conduct. I have chosen clinical coordinators for this study, because the CRC is the person at the site who most frequently interacts with the monitor and will be able to comment most reliably

about the monitoring process (Wanna Be a Clinical Research Associate(CRA)? First Become a CRC!, n.d.).

The current study focuses on the perceptions of clinical coordinators about the quality of monitoring. The information from this study will inform the identification of the major inadequacies in the monitoring process and the reasons underlying these inadequacies. These steps are crucial in developing strategies to improve the monitoring process and thereby improving the safety as well as the ethical and scientific quality of clinical research.

Chapter 2: Background

According to the Bioresearch Monitoring Program report of 2011, a total of 127 cases with inconsistencies were reported in Sponsor/Monitor/CRO inspections (Bioresearch Monitoring (BIMO) Metrics – FY'11, 2011). The most common deficiencies found were:

- Failure to report the protocol deviations in monitoring reports from one or more study sites.
- Failure to report the informed consent violations in monitoring reports from one or more study sites.
- Failure to report the IRB reporting violations in monitoring reports.
- Continuous non-compliance regarding CRFs completion, review, and submission was determined by the sponsor through other means of communication, but monitoring reports does not include any of the issues regarding CRFs.
- Failure to bring the investigators into compliance:
    - According to ICH GCP (1996), the monitor is responsible for ensuring that the investigator follows approved protocol and amendments (if any). If the investigator is not adhering to protocol, then it is (initially) the responsibility of the monitor to bring the investigator into compliance. However, warning letters were issued to investigators regarding non-compliance in clinical trials.
- Inadequate accountability for the investigational product (Bertram, 2002):
    - The monitor is responsible for ensuring accurate drug accountability at the investigational site i.e., monitors should review, documentation regarding drug accountability, ensure proper drug storage, and log maintenance during

monitoring visits. However, findings from the FDA include warning letters related to drug accountability (Drug Accountability at the Investigative site, http://www.appliedclinicaltrialsonline.com/appliedclinicaltrials/article/articleDetail.jsp?id=87219).

- Failure to obtain FDA and IRB approval prior to study initiation:
    - According to ICH GCP (1996), the monitor is responsible for ensuring that the site has all required approvals before initiation of the study. However, there are FDA warning letters which cite that the monitor failed in determining non-compliance.

All of the above are responsibilities of the monitor. In spite of well established regulations and guidance for monitoring, there are many concerns in clinical trials (e.g. protocol deviations and violations, IRB violations, improper adverse event reporting, etc).

Chapter 3: Thesis Statement

Purpose of the Study

The purpose of the study is to determine the perceptions of clinical research coordinators about quality of monitoring and major inadequacies/concerns in the monitoring process. Hopefully, data collected will help the sponsors and monitors to develop solutions for the major concerns relating to the monitoring process.

Research Questions

Question 1:

What are the perceptions of clinical research coordinators about the quality of monitoring?

Question 2:

What are the major concerns/failings in the monitoring process?

Chapter 4: Research Design and Methodology

Target Population

Target population refers to the entire group of people or objects or individuals to which the researcher generalizes the conclusions or study findings (Populations and Sampling, n.d.). It is also defined as a possible group of respondents to the survey questions. The target population for this study includes clinical research coordinators.

Sample Population

Sample population (Actual people or respondents selected for survey) is the subset of a target population and is also called a study population or sample size for the study (Populations and Sampling, n.d.). The sample population for this study includes 2177 clinical research coordinators from different clinical research sites.

Selection of Sample Size for Survey

Sample size is determined by degree of precision (confidence interval) and accuracy (confidence level) required for the responses to the survey questions. For this study, confidence level is 95% and confidence interval is ±10%. Percentages below and above 50% would have the least amount of variance. Therefore, the sample for this study is based on a 50% point estimate for any question. Sample size needed to obtain the desired precision and accuracy is approximately 100 (Macorr research solutions, Sample size formula, http://www.macorr.com/sample-size-methodology.htm). Anticipating a 4% to 5% response rate, the survey was sent to 2177 research coordinators (Zoomerang

online surveys and polls, calculate survey sample size, http://www.zoomerang.com/sample-size/).

Development of Survey Instrument or Questionnaire

I performed the literature review and summarized the established concerns related to monitoring. Then I constituted a focus group with three members (Dr. Ronald Maio, Terry VandenBosch, and Ted Hamilton) at the University of Michigan and conducted focus group interactions. Then I developed the final questionnaire or survey instrument by using the suggestions from focus group participants.

The questionnaire or survey questions include six general demographic questions (e.g. Academic degree, experience level), which provided the demographic information about coordinators and 15 questions related to monitoring practices (e.g. quality of monitoring, concerns in monitoring, importance of quality monitoring).

General demographic questions are closed ended (multiple choice questions). Questions related to monitoring practices include both open ended and closed ended. I have used the five-point Likert rating scale for closed ended questions related to monitoring practices and open ended questions are to determine "what is at the tip of the respondent's mind" (Brace, 2008).

Human Subjects Protection

Prior to conducting the research or study or survey, I submitted an application for Review and Approval to conduct research or a survey involving human subjects (Clinical Research Coordinators) to the College of Health and Human Services Human Subjects

Review Committee (CHHS-HSRC) at Eastern Michigan University. The CHHS-HSRC approved the study to conduct the survey on November 7, 2012. (Appendix A: College of Health and Human Services Human Subjects Review Committee Approval Letter).

All of the potential participants were informed clearly about the purpose of the study, procedure for responding to the survey, voluntariness and withdrawal, protecting the rights of the participant, and contact information by means of Online Survey Consent Form. (Appendix B: Survey Completion Request or Online Survey Consent Form or Email Survey).

An Informed consent form or Online Survey Consent Form was mailed electronically along with the survey. By filling out the survey, the participant agreed to the conditions of Online Survey Consent Form. If the potential participants decided to participate, they were told that they could withdraw at anytime, and their participation was purely voluntary. There are no direct benefits or risks associated with their participation, and all the responses to the survey are anonymous and confidential.

Method of Data Collection

Finally, with the approval of the Human Subjects Review Committee (HSRC), I conducted the computer-based survey using Google docs.

I (Investigator) emailed the survey instrument (Appendix C: Survey) including the email survey consent form to the potential participants following the approval of CHHS-HSRC. The survey instrument included the consent form and three mandatory questions to be answered before they take the short online survey. The purpose of three mandatory questions is to ensure that the potential participant has read the consent form, voluntarily

agrees to take the survey, and participant is a clinical research coordinator (Survey should be taken only by the clinical research coordinators). Then, it directs the participant to the survey (Appendix C: Survey). After completing the six demographic questions and 15 questions related to monitoring practices, the participant was directed to click the "submit" button, which submits their anonymous answers to the investigator.

Chapter 5: Analysis and Presentation of Data

This chapter is dedicated to presentation of the results of the study which were obtained by analyzing the data of the responses received.

The basis of this study is quantitative research acquired by collecting the perceptions of clinical research coordinators about the quality of monitoring through an electronic survey. The survey was emailed to 2177 potential participants along with a consent form stating that the survey was completely voluntary and their participation would remain anonymous. Out of the 2177 potential participants invited to participate in the study, 92 participants successfully completed the survey and submitted to the investigator, which represents a 4.23% response rate. Five participants did not meet the eligibility criteria because they are not clinical research coordinators, and their data or results were excluded from analysis. Therefore, 87 completed surveys were used in the final analysis of data.

The electronic survey for this study evaluated the perceptions of clinical research coordinators about the quality of monitoring and major inadequacies or concerns in the monitoring process.

Overview of Demographics

The respondents were asked to answer six optional demographic questions before answering the monitoring practice questions. Demographic questions include their level of education, educational background, work setting, working pattern, experience as a clinical research coordinator, and experience in interacting with the monitors. Tables 1 to 6 present the tabulations of the demographic responses.

Question 1:

What is the highest degree (or) level of education you have completed?

Survey respondents were asked to select from the following options: (a) High School Graduate, (b) Associate degree, (c) Bachelor's degree, (d) Post-baccalaureate certificate, (e) Master's degree, (f) Doctorate degree, (g) Other (Please Specify).

The objective of this question was to evaluate whether a majority of the clinical research coordinators hold a master's degree.

As shown in Table 1, 42.5% of respondents hold a master's degree, 41.4% of respondents hold a bachelor's degree, 5.7% of respondents hold a doctorate degree, 5.7% of respondents hold a post baccalaureate certificate, 1.2% of respondents hold an associate degree, and 3.5% of respondents hold another degree like CFA.

Question 2:

Which of the following best describes your educational background?

Survey respondents were asked to select from the following options: (a) Nursing degree, (b) Life Science degree (e.g. Pharmacy, Biochemistry, and Biology), (c) Health Science degree (e.g. Clinical Laboratory Science, Physical Therapy), (d) Clinical Research degree, (e) Other (Please Specify).

The objective of this question was to evaluate whether a majority of the clinical research coordinators hold a clinical research degree.

As shown in Table 2, 28.7% of respondents have a life science degree like pharmacy, biochemistry, and biology, 21.8% of respondents have a health science degree like clinical laboratory science, and physical therapy, 23% of respondents have a nursing degree, 9.2% of respondents have a clinical research degree, and 17.3% of respondents have degrees in other fields like economics, social work, public health, statistics, psychology, and clinical social work.

Question 3:

Which of the following best describes your current work setting?

Survey respondents were asked to select from the following options: (a) Private Practice site, (b) Academic site (University or Teaching Hospitals), (c) Community Hospital (Not Academically affiliated), (d) Site management organization (organizing a group of sites centrally to do studies), (e) Contract research organization (company or organization contracted by a pharmaceutical, medical device or biotechnology company to conduct clinical trials), (f) Other (please specify).

The objective of this question was to evaluate in what kind of work setting or organization a majority of the clinical research coordinators are working.

As shown in Table 3, 90.8% of respondents work at academic sites like university or teaching hospitals, 6.9% of respondents work at private practice sites, and 2.3% of respondents work at other work settings like non-profit genetic institutes, and community hospitals affiliated with an academic setting.

Question 4:

Which of the following describes your current working pattern? (Select all that apply)

Survey respondents were asked to select from the following options: (a) Medical device clinical trials, (b) Pharmaceutical clinical trials, (c) Investigator—initiated clinical trials, (d) Government (or) Foundation—sponsored clinical trials, (e) Other (please specify).

The objective of this question was to evaluate whether a majority of the clinical research coordinators work on pharmaceutical clinical trials.

As shown in Table 4, 37.1% of respondents work on investigator—initiated clinical trials, 26.9% of respondents work on government or foundation sponsored clinical trials, 24.6% of respondents work on pharmaceutical clinical trials, and 11.4% of respondents work on medical device clinical trials.

Question 5:

About how long have you been working as a clinical research coordinator?

Survey respondents were asked to select from the following options: (a) ≤ 2 years, (b) > 2 to 5 years, (c) > 5 to 10 years, (d) > 10 years.

The objective of this question was to evaluate the experience of clinical research coordinators.

As shown in Table 5, 27.9% of respondents have more than 10 years of experience as a clinical research coordinator, 27.9% of respondents have 5 to 10 years,

27.9% of respondents have 2 to 5 years, and 16.3% of respondents have 0 to 2 years of experience as a clinical research coordinator.

Question 6:

How many clinical trials have you participated in where you have interacted with a monitor?

Survey respondents were asked to select from the following options: (a) 1 to 5, (b) 6 to 10, (c) 11 to 20, (d) > 20.

The objective of this question was to evaluate the experience of clinical research coordinators with the clinical monitors.

As shown in Table 6, 47.1% of respondents have participated in 1 to 5 trials where they interacted with the monitor, 23.5% of respondents have participated in more than 20 trials where they interacted with the monitor, 17.6% of respondents have participated in 6 to 10 clinical trials where they interacted with the monitor, and 11.8% of respondents have participated in 11 to 20 clinical trials where they interacted with the monitor.

Overview of Responses or Reflections based on Monitoring Practice Questions

The respondents were asked to answer 15 questions related to monitoring practices to evaluate the experiences of clinical research coordinators in relation to clinical monitoring. Tables 7 to 21 represent the reflections of clinical research coordinators about the monitoring process or practices.

Question 7:

In general, how satisfied are you with the skill and competency of the monitors with whom you have interacted?

Survey respondents were asked to select from the following options: (a) Very satisfied, (b) Satisfied, (c) Not sure, (d) Dissatisfied, (e) Very dissatisfied.

The objective of this question was to evaluate what percentage of clinical monitors are knowledgeable to monitor the clinical trials.

As shown in Table 7, 59.5% of respondents are satisfied with the skill and competency of monitors, 19.1% of respondents are not sure, 14.3% of respondents are very satisfied, and 7.1% of respondents are dissatisfied.

Question 8:

In general, how satisfied are you with the monitor's level of understanding of the protocol and its requirements?

Survey respondents were asked to select from the following options: (a) Very satisfied, (b) Satisfied, (c) Not sure, (d) Dissatisfied, (e) Very dissatisfied.

The objective of this question was to evaluate what percentage of monitors are familiar with the clinical trial protocol and protocol amendments because protocol is the most important document which is the basis for clinical trial monitoring.

As shown in Table 8, 60.7% of respondents were satisfied with the monitors understanding of protocol and its requirements, 21.4% of respondents were very satisfied, 11.9 % of respondents were not sure, and 6.0% of respondents were dissatisfied.

Question 9:

In general, how satisfied are you with the review of the informed consent process conducted by the monitors with whom you have interacted?

Survey respondents were asked to select from the following options: (a) Very satisfied, (b) Satisfied, (c) Not sure, (d) Dissatisfied, (e) Very dissatisfied.

The objective of this question was to evaluate to what extent the monitors are reviewing proper completion and documentation of informed consent process because informed consent process is the keystone for conducting the research or clinical trial or clinical study ethically.

As shown in Table 9, 54.8% of respondents were satisfied with the monitors review of informed consent process, 22.6% of respondents were very satisfied, 19.0% of respondents were not sure, and 3.6% of respondents were dissatisfied.

Question 10:

In general, how satisfied are you with the review for protocol deviations conducted by the monitors with whom you have interacted?

Survey respondents were asked to select from the following options: (a) Very satisfied, (b) Satisfied, (c) Not sure, (d) Dissatisfied, (e) Very dissatisfied.

The objective of this question was to evaluate whether the monitors are properly reviewing the protocol deviations in their monitoring visits and discussing about the issues with the clinical research or trial coordinators for remedial action. Protocol deviations may affect the patient safety, and quality of data recorded during the trial.

As shown in Table 10, 52.4% of respondents were satisfied with the monitors review for protocol deviations, 17.9% of respondents were very satisfied, 19.0% of respondents were not sure, and 10.7% of respondents were dissatisfied.

Question 11:

In general, how satisfied are you with the review for accuracy and completeness of CRF entries and source documents against each other conducted by the monitors with whom you have interacted?

Survey respondents were asked to select from the following options: (a) Very satisfied, (b) Satisfied, (c) Not sure, (d) Dissatisfied, (e) Very dissatisfied.

The objective of this question was to evaluate what percentage of monitors are detail oriented and comparing the data in the CRF's with the source documents properly. This process is very important because it investigates whether reliable, and accurate information is being reported in the study or not.

As shown in Table 11, 55.9% of respondents were satisfied with the monitors review for accuracy and completeness of CRF's against source documents, 22.6% of respondents were very satisfied, 14.3% of respondents were not sure, 6.0% of respondents were dissatisfied, and1.2 % of respondents were very dissatisfied.

Question 12:

In general, how satisfied are you with the review for reporting of adverse events conducted by the monitors with whom you have interacted?

Survey respondents were asked to select from the following options: (a) Very satisfied, (b) Satisfied, (c) Not sure, (d) Dissatisfied, (e) Very dissatisfied.

The objective of this question was to evaluate whether monitors are checking the proper reporting of adverse events and assisting the trial coordinators in correctly reporting the adverse events. Proper reporting of adverse events is very important in ensuring the patient safety.

As shown in Table 12, 60.2% of respondents were satisfied with the monitors review of adverse events, 19.3% of respondents were very satisfied, 12.1% of respondents were not sure, and 8.4% of respondents were dissatisfied.

Question 13:

In general, how satisfied are you with the review for accuracy of drug accountability records conducted by the monitors with whom you have interacted?

Survey respondents were asked to select from the following options: (a) Very satisfied, (b) Satisfied, (c) Not sure, (d) Dissatisfied, (e) Very dissatisfied.

The objective of this question was to evaluate whether monitors are properly reviewing the drug accountability records to ensure the quality and accuracy of drug accountability during the course of a trial. Improper drug accountability may affect the outcome of a clinical trial.

As shown in Table 13, 53.8% of respondents were satisfied with the monitors review for accuracy of drug accountability records, 23.7% of respondents were very satisfied, and 22.5% of respondents were not sure.

Question 14:

In general, how likely are the monitors with whom you have interacted to fail to review FDA and IRB approvals prior to study initiation?

Survey respondents were asked to select from the following options: (a) Very Likely, (b) Likely, (c) Not sure, (d) Unlikely, (e) Very Unlikely.

The objective of this question was to evaluate whether monitors are reviewing required approvals for study initiation because protection of patients is very important in clinical trials.

As shown in Table 14, 32.2% of respondents indicate that very unlikely monitor's fail to review the FDA and IRB approvals prior to study initiation, 29.8% of respondents indicate unlikely, 22.6% of respondents are not sure, 8.3% of respondents indicate likely, and 7.1% of respondents indicate very likely.

Question 15:

In general, how likely are the monitors with whom you have interacted to provide adequate technical support to the site staff about the study?

Survey respondents were asked to select from the following options: (a) Very Likely, (b) Likely, (c) Not sure, (d) Unlikely, (e) Very Unlikely.

The objective of this question was to evaluate whether monitors are supporting and helping the site staff during the course of a clinical trial.

As shown in Table 15, 47.6 % of respondents indicate that the monitors likely provide the technical support, 20.7% of respondents indicate very likely, 17.1% of respondents were not sure, 12.2% of respondents indicate unlikely, and 2.4% of respondents indicate very unlikely.

Question 16:

In general, how likely are the monitors with whom you have interacted to help the site staff in resolving the generated queries?

Survey respondents were asked to select from the following options: (a) Very Likely, (b) Likely, (c) Not sure, (d) Unlikely, (e) Very Unlikely.

The objective of this question was to evaluate whether monitors are helping the site staff in addressing the queries properly and resolving them.

As shown in Table 16, 50.0% of respondents believe that monitors likely help the site staff in resolving the queries, 32.1% of respondents believe that very likely monitors help the site staff in resolving queries, 10.7% of respondents believe that unlikely monitors help the site staff in resolving the queries, and 7.2% of respondents were not sure.

Question 17:

In general, how likely are the monitors with whom you have interacted to provide site monitoring reports in a short time frame after completing a monitoring visit?

Survey respondents were asked to select from the following options: (a) Very Likely, (b) Likely, (c) Not sure, (d) Unlikely, (e) Very Unlikely.

The objective of this question was to evaluate whether the monitors are providing the monitoring reports within the time frame stating any issues that were observed during monitoring inspection. Monitoring reports are very helpful in addressing the issues during the study and ensure the progress of a clinical trial.

As shown in Table 17, 54.9% of respondents believe that monitors likely provide the monitoring report within short time frame, 18.3% of respondents believe very likely to provide the monitoring report within short time frame, 14.6% of respondents were not sure, 11.0% of respondents indicate that monitors unlikely provide the monitoring report within the short time frame, and 1.2% of respondents indicate that very unlikely monitors provide the monitoring report within the short time frame.

Question 18:

In general, how likely is it that there is an increase in work load following the completion of a monitoring visit?

Survey respondents were asked to select from the following options: (a) Very Likely, (b) Likely, (c) Not sure, (d) Unlikely, (e) Very Unlikely.

The objective of this question was to evaluate whether the monitors are increasing the workload of the site staff due monitoring visit or helping the site staff in addressing the issues properly in turn decreasing the workload of clinical research coordinators.

As shown in Table 18, 42.2% of respondents reveal that monitors likely increase the work load after the monitoring visit, 36.1% indicate very likely, 12.0% represent unlikely, and 9.7% of respondents are not sure.

Question 19:

In general, in a clinical study, how much do you believe the quality of the data at your site reflects upon the monitors with whom you have interacted?

Survey respondents were asked to select from the following options: (a) Very much, (b) Moderately, (c) Not sure, (d) Minimally, (e) Does not reflect.

The objective of this question was to evaluate whether the quality of data and success of a clinical trial will depend on the monitor or not.

As shown in Table 19, 39.8% of respondents believe quality of data depends moderately upon monitor, 27.7% of respondents believe that quality of data depends very much upon monitor, 16.9% of respondents are not sure, and15.6 % of respondents believe that quality of data minimally depends upon monitor.

Question 20:

Has your site been audited or inspected in the past 3 years? If so, has the monitor been helpful in preparation for the audit or inspection?

Survey respondents were asked to select from the following options: (a) Very much, (b) Moderately, (c) Not sure, (d) Minimally, (e) Not at all.

The objective of this question was to evaluate whether the monitor is helping the site staff in reporting the accurate data according to the protocol, SOP's, GCP's and applicable regulatory requirements. A clinical trial audit is necessary to protect the subjects and to ensure that the trail is conducted according to the required regulations.

As shown in Table 20, 37.5% of respondents are not sure about the monitors help in the preparation of audit or inspection, 27.8% of respondents believe that monitor was helpful moderately in the preparation for the audit, 13.9% of respondents indicate that monitor was not at all helpful in the preparation for the audit or inspection, 12.5% of respondents reveal that monitor was very much helpful, and 8.3% of respondents believe that monitor was minimally helpful.

Question 21:

In general, what is your opinion about the quality of monitoring in clinical trials today as compared to 5-10 years ago?

The objective of this question was to evaluate whether the quality monitoring was increasing day by day or decreasing.

This is an open ended question, and respondents were allowed to write their own comments about the quality of monitoring. The responses to this question were tabulated in Table 21.

Summary of Results/Findings based on the Data Collected

- 42.5% of the clinical research coordinators who responded hold a master's degree.

- 9.2% of clinical research coordinators who responded have a clinical research degree and that the majority of the clinical research coordinators have a degree in a life science, e.g. pharmacy, bio-chemistry and biology.
- 90.8% of the clinical research coordinators who responded work at sites which are affiliated with a university or teaching hospital.
- 37.1% of the clinical research coordinators who responded are working on investigator-initiated clinical trials.
- 83.7% of respondents have more than two years of experience as a clinical research coordinator.
- 47.1% of the clinical research coordinators who responded have participated in at least one clinical trial where they have interacted with a monitor.
- Only 14.3% of the clinical research coordinators who responded were very satisfied with the monitors who visited them, but most (59.5%) of the clinical research coordinators were satisfied with the skill and competency of the monitors with whom they have interacted.
- Only 21.4% of clinical research coordinators who responded were very satisfied, and most (60.7%) of the clinical research coordinators were satisfied with the monitor's level of understanding of the protocol and its requirements.
- 22.6% of the clinical research coordinators who responded were very satisfied, and 54.8% of the clinical research coordinators were satisfied with the review of the informed consent process conducted by the monitors with whom they have interacted.

- 17.9% of the clinical research coordinators who responded were very satisfied, and more than half (52.4%) of the clinical research coordinators were satisfied with the review for protocol deviations conducted by the monitors with whom they have interacted.
- 22.6% of the clinical research coordinators who responded were very satisfied, whereas 55.9% of clinical research coordinators were satisfied with the monitors review for the accuracy and completeness of CRF's and source documents.
- Only 19.3% of the clinical research coordinators who responded were very satisfied, and 60.2% of the clinical research coordinators were satisfied with the monitors review for reporting of adverse events.
- 23.7% of the clinical research coordinators who responded were very satisfied, and 53.8% were satisfied with the monitors review for accuracy of drug accountability records.
- 29.8% of the clinical research coordinators who responded indicated unlikely, whereas 32.2% of clinical research coordinators indicate that it is very unlikely that monitors fail to review the FDA and IRB approvals prior to study initiation.
- 20.7 % of the clinical research coordinators who responded indicated that the monitor is very likely to provide the technical support (e.g. helping site staff in resolving the enrollment barrier, training the site staff, and helping the site staff in resolving the issues encountered during the conduct of the study), and 47.6% of respondents indicate that the monitors likely provide the technical support.
- 50.0% of the clinical research coordinators who responded indicated that the monitors are likely to help the site staff in resolving the generated queries,

whereas 32.1% of clinical research coordinators indicated that it is very likely that monitors help the site staff in resolving queries.

- 54.9% of the clinical research coordinators who responded indicated that the monitors are likely to provide the monitoring report within a short time after the visit, and 18.3% of clinical research coordinators indicated that the monitors are very likely to provide the monitoring report within a short time after the visit.
- 88.0% of the clinical research coordinators who responded indicated that the monitors are likely to increase the work load after the completion of a monitoring visit.
- 27.7% of the clinical research coordinators who responded believe that the quality of trial data depends very much upon the monitor, and 39.8% of the clinical research coordinators believe that the quality of trial data depends moderately upon the monitor.
- 12.5% of respondents indicated that the monitor was very much helpful, and 27.8% of respondents believe that monitor was moderately helpful in the preparation for an audit or inspection of the site.

Chapter 6: Summary, Conclusion, and Inferences

The objective of this study was to determine the perceptions of the clinical research coordinators about the quality of clinical monitoring. The author of this report thinks that there are some problems in the monitoring of clinical trials based on the warning letters issued to clinical investigators, sponsors, and CROs for inadequate monitoring of clinical trials. Therefore, he is interested in finding the reasons for improper monitoring and major concerns in the monitoring process as well as perceptions of clinical research coordinators about the quality of monitoring.

The data from this study suggest that there are issues or problems in the monitoring of clinical trials based on the perceptions of clinical research coordinators.

This study found that majority of the clinical research coordinators participating in the study have either a master's degree or bachelor's degree in life science (pharmacy, biology, and bio-chemistry) or nursing, majority are working at academic sites like university or teaching hospitals, and the majority participated in all kinds of clinical trials like medical device clinical trials, pharmaceutical clinical trials, investigator-initiated clinical trials, and government or foundation sponsored clinical trials. Also, a majority of the clinical research coordinators participating in this study have more than 2 years of experience in clinical trials and have interacted with the monitor in at least one clinical trial. Results also indicate that very few of the clinical research coordinators have a clinical research degree.

Based on the responses to the monitoring practice questions, majority of the clinical research coordinators are satisfied with the skill and competency of monitors, the

monitor's level of understanding of the protocol and its requirements, the monitor's review for the informed consent process violations, the monitor's review for the protocol deviations, the monitor's review for accuracy and completeness of CRF's (case report form) as well as source documents, the monitor's review for proper reporting of adverse events, and the monitor's review for accuracy of drug accountability records. They also indicate that the monitors review the IRB and FDA approvals before the study initiation, provide adequate technical support to the site staff about the study and also the monitoring reports within a short time frame, and help the site staff in resolving the generated queries and also in the preparation of the site for audits or inspections. Results also reveal that most of the clinical research coordinators believe that the quality of data in a clinical trial depends upon the monitor.

On the other hand, a majority of the clinical research coordinators participated in this study stated that the monitors are increasing the workload after the completion of a monitoring visit. Although a majority of the coordinators are satisfied with the work done by the monitors, some of the clinical research coordinators are not satisfied with the skill of monitors, the monitor's protocol knowledge, and the monitor's review for the problems in the informed consent process as well as with the monitor's review for protocol deviations. Also, they are not satisfied with the monitor's review for accuracy and completeness of CRF's as well as the source documents review, review for proper reporting of adverse events. They also state that the monitors fail to review the required approvals before the study initiation, do not provide the adequate technical support for the study, do not help the site staff in resolving the generated queries as well as in the preparation of the site for audits or inspections, and will not provide the monitoring visit

report quickly or within the time frame. Very few clinical research coordinators believe that the quality of data minimally depends upon the monitor.

Major Concerns or Problems in the Monitoring Process

Following are the major concerns or problems in the monitoring process based on the percent of response by the clinical research coordinators:

- Monitors are increasing the work load on clinical research coordinators after the monitoring visit.
- Monitors failed to review the required approvals like FDA and IRB approvals prior to the study initiation.
- Monitors failed to provide the technical support to the site staff during the course of a clinical trial.
- Monitors are not providing the support to the site staff in the preparation of the site for the inspection or audit.
- Monitors are not providing the monitoring visit reports within a short time frame.
- Monitors failed to review the protocol deviations properly.
- Monitors are not supporting or helping the site staff properly in the process of solving the generated queries.
- Monitors failed to review the proper reporting of adverse events.
- Monitors failed to review the accuracy as well as the completeness of CRF's and source documents.
- Some monitors do not have the required skills and knowledge.
- Monitors do not have the required protocol knowledge.

- Monitors failed to review the informed consent process properly.

Clinical Research Coordinators Perceptions about the Quality of Monitoring

Perceptions of clinical research coordinators about the quality of monitoring are quite variable. Based on the responses given to the open-ended question about quality of monitoring, some clinical research coordinators believe that the quality of monitoring has increased compared to the monitoring five to ten years ago. Some clinical research coordinators believe that there is minimal improvement in monitoring and some other coordinators believe that there is no significant change in the quality of monitoring. But the majority of the clinical research coordinators conclude that the overall quality of the clinical monitoring has decreased.

Perhaps the study coordinator's perceived quality of monitoring varies from monitor to monitor because some clinical research associates are trained well and they have good knowledge about the study as well as about the applicable regulations. Also, perhaps perceptions could be affected by the fact that some clinical research coordinators have positive experience with the monitors, whereas some clinical research coordinators have a hard time in working with the monitors.

Reasons for Decreased Quality of Monitoring

Based on the findings of this study, the author suggests the following:

- Monitors are not trained or mentored well.
- Monitors have inadequate knowledge.
- Monitors have a lack of adequate experience as a clinical research associate.

- Monitors were changed during the course of the study.
- Monitors are overwhelmed with too many sites or too many studies.

How Can we Improve the Quality of Monitoring?

The quality of monitoring can be improved by training the clinical research associates adequately according to the industry standards, which in turn depends on the CROs, sponsors, or monitoring company for which the monitors are working. Skills of the clinical trial monitors can also be improved by encouraging them to attend the conferences related to clinical monitoring.

Clinical monitors should be trained in such a way that the monitors have a good understanding of the protocol as well as the SOPs related to the study on which they will be working (SPONSOR, n.d). Clinical monitors need to have the appropriate and adequate clinical knowledge as well as scientific knowledge required to monitor the clinical trials adequately (ICH GCP, 1996). Proper planning by the monitors can also help in reflecting quality data (The art and science of monitoring, 2001).

Decrease the workload of the clinical monitors, which can be done by decreasing the number of protocols or studies or sites they are responsible for monitoring and also by increasing the number of clinical monitors for the purpose of monitoring the studies (Kenneth, 2012). Have the same monitor for the study until the study closes. If the monitors change frequently during the study, it disturbs the way the study is done and the quality of monitoring decreases. It also decreases the proper communication between the site staff and monitors. Improve the communication power or capability of clinical

monitors with other the monitors, sponsors, investigators as well as with the site staff during the conduct of the clinical trial (The art and science of monitoring, 2001).

Implementation of the correct monitoring procedures increases quality of monitoring. The quality of monitoring can also be increased by hiring the monitors with required qualifications as well as with the adequate experience in the monitoring or as a clinical research coordinator. Prior experience as a clinical research coordinator enables the monitors to efficiently find and help in correcting the problems (Wanna Be a Clinical Research Associate [CRA]? First Become a CRC!, n.d.).

Finally, through excellent coordination and team work we can improve the quality of monitoring as well as quality of data reflected in the clinical trials, which paves a path for the success of a clinical trial.

Conclusion

This research study suggests that there are still concerns about the monitoring process, which affect the quality of monitoring, which in turn which may have impact on the quality of data reflected in the study as well as on the success of a clinical trial. Effective monitoring can be achieved by addressing the issues in the process of monitoring through which we can protect the subjects as well as improve the health of subjects.

Effective clinical monitoring ensures that the clinical trial is conducted, recorded, and reported in accordance with the protocol's standard operating procedures (SOPs), good clinical practice (GCP), and the applicable regulatory requirement(s), which dictates that the clinical trials should be conducted according to the ethical principles necessary

for the proper conduct of a clinical trial. This can be achieved through qualified, competent, and knowledgeable monitors.

Monitors should be trained effectively, as they are ultimately responsible for the success of a clinical trial. Monitors should be knowledgeable about the trial documents, clinical or study protocol, Good Clinical Practice (GCP), Standard Operating Procedures (SOPs), local and state laws and other applicable regulations, research ethics and study conduct issues, and the ethical issues that they may encounter during conduct of a clinical trial.

Monitors should be proficient in finding the concerns related to the approved protocol, informed consent documents as well as the process, SOPs, reporting of adverse events, participant's inclusion criteria for the study, clinical trial documentation, and site facilities. Also monitors have to check whether the investigators and the study team are qualified and knowledgeable. The monitor is also responsible for ensuring whether participant confidentiality is maintained.

Responsible clinical monitoring ensures the protection of participants and their rights while meeting the GCP standards and regulations and properly following the protocol and SOPs. An effective clinical monitor is responsible for finding the problems in the study as well as with the data recorded in the trial and ensuring the compliance as well as the progress of a clinical trial. Success of the research project or clinical trial or study depends on choosing the right trained, knowledgeable, and experienced monitoring team.

In summary, the monitor is responsible for the successful execution of a clinical study. By strengthening the communication between the site staff and the monitor, clean and quality data can be acquired by following the applicable regulations as well as protecting the rights and safety of participants or subjects. Monitors' roles are very valuable because they help in guiding the new medications to the market and directly affect the health of the participants around the country as well as at the global level.

Limitations and Recommendations for Future Research

There are some limitations for this study. First, the overall response rate was only 4.23%. Second, the sample of this study is limited to clinical research coordinators, and most of the respondents were working at sites which are affiliated with a university or a teaching hospital. Also, the respondents are primarily working on the investigator-initiated clinical trials. Therefore, my responding sample may not be representative, and the results of this study are limited to the perceptions and experiences of the sample group.

Through this study, the author has provided evidence to suggest that there are still concerns in clinical monitoring despite the presence of the well established regulations for monitoring practice. A similar study can be done or replicated with a larger sample, which would enhance the validity and reliability of the conclusions reached. This study captured and examined only the perceptions of clinical research coordinators, which is a select population. A more broad population of clinical research professionals would likely provide wide range of monitoring practice concerns as well as wide range of perceptions about the quality of monitoring.

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Demographic Profile of Clinical Research Coordinators

Table 1

Survey Respondents by the Level of Education they have completed

Response or Answer	Frequency	Percent (%)	Cumulative Frequency	Cumulative Percent (%)
High School Graduate	0	0%	0	0%
Associate degree	1	1.2%	1	1.2%
Bachelor's degree	36	41.4%	37	42.6%
Post-baccalaureate certificate	5	5.7%	42	48.3%
Master's degree	37	42.5%	79	90.8%
Doctorate degree	5	5.7%	84	96.5%
Other	3	3.5%	87	100.0%
TOTAL	**87**	**100%**		

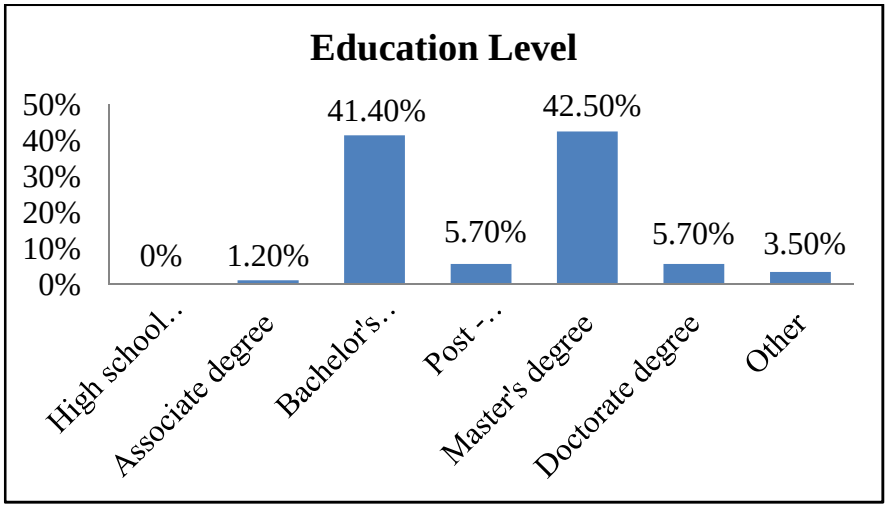


Figure 1. Highest Degree or Level of Education Completed by Clinical Research Coordinators

Table 2

Survey Respondents based on their Educational Background

Response or Answer	Frequency	Percent (%)	Cumulative Frequency	Cumulative Percent (%)
Nursing degree	20	23%	20	23%
Life Science degree (e.g. Pharmacy, Biochemistry, Biology)	25	28.7%	45	51.7%
Health Science degree (e.g. Clinical Laboratory Science, Physical Therapy)	19	21.8%	64	73.5%
Clinical Research degree	8	9.2%	72	82.7%
Other	15	17.3%	87	100.0%
TOTAL	**87**	**100%**		

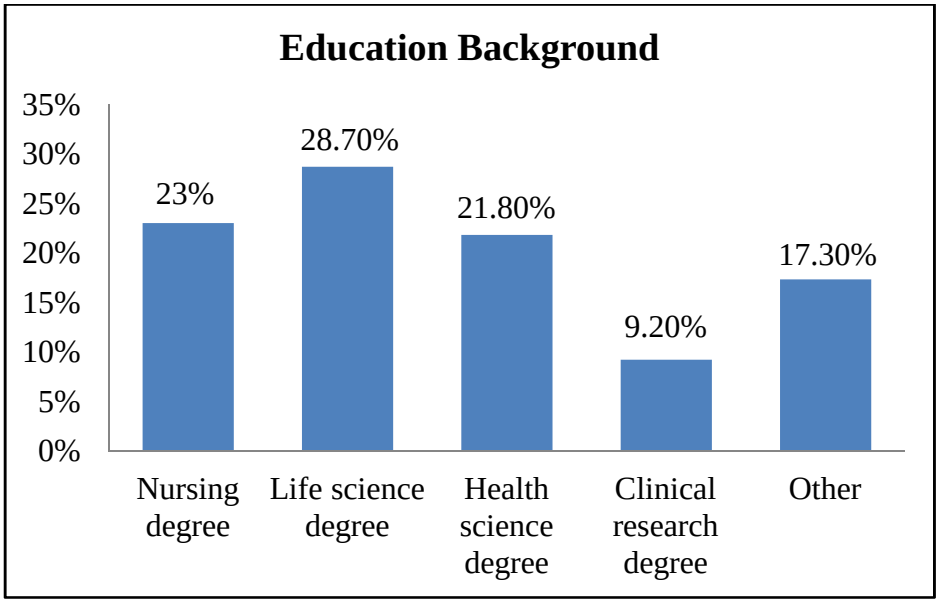


Figure 2. Educational Background of Clinical Research Coordinators

Table 3

Survey Respondents based on their Current Work Setting

Response or Answer	Frequency	Percent (%)	Cumulative Frequency	Cumulative Percent (%)
Private Practice site	6	6.9%	6	6.9%
Academic site (University or Teaching Hospitals)	79	90.8%	85	97.7%
Community Hospital (Not Academically affiliated)	0	0%	85	97.7%
Site management organization	0	0%	85	97.7%
Contract research organization	0	0%	85	97.7%
Other	2	2.3%	87	100.0%
TOTAL	**87**	**100%**		

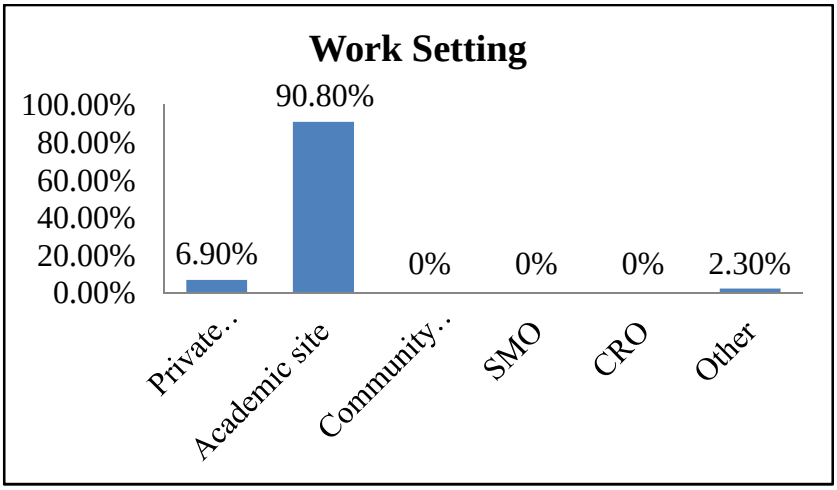


Figure 3. Work Setting of the Clinical Research Coordinators

Table 4

Survey Respondents based on their Current Working Pattern

Response or Answer	Frequency	Percent (%)	Cumulative Frequency	Cumulative Percent (%)
Medical device clinical trials	19	11.4%	19	11.4%
Pharmaceutical clinical trials	41	24.6%	60	36.0%
Investigator - initiated clinical trials	62	37.1%	122	73.1%
Government (or) Foundation – sponsored clinical trials	45	26.9%	167	100.0%
Other	0	0%	167	100.0%
TOTAL	**167**	**100%**		

People may select more than one check box or response, that's why respondents number (N=167) is more than 87 (number of people actually responded).

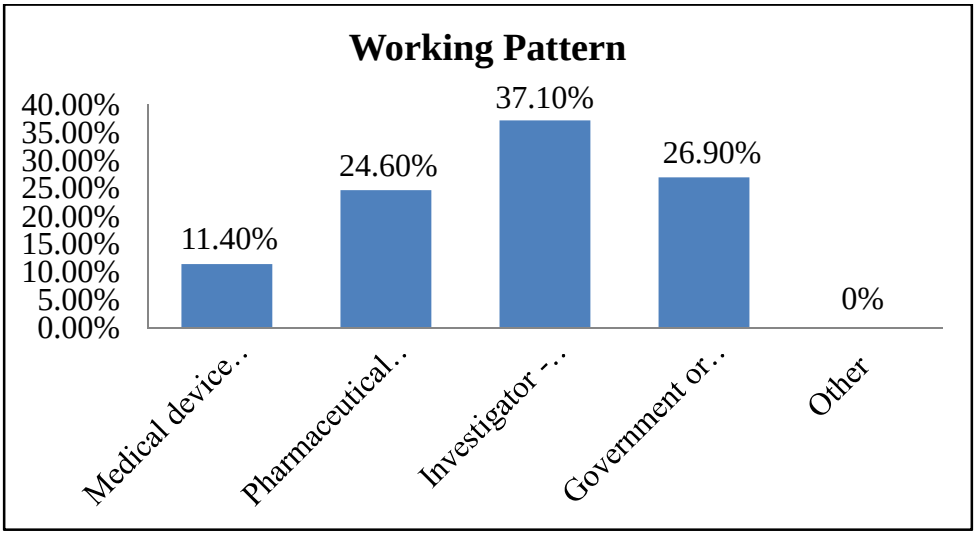


Figure 4. Working Pattern of Clinical Research Coordinators

Table 5

Survey Respondents based on their Experience as a Clinical Research Coordinator

Response or Answer	Frequency	Percent (%)	Cumulative Frequency	Cumulative Percent (%)
≤ 2 years	14	16.3%	14	16.3%
> 2 to 5 years	24	27.9%	38	44.2%
> 5 to 10 years	24	27.9%	62	72.1%
> 10 years	24	27.9%	86	100.0%
TOTAL	**86**	**100%**		

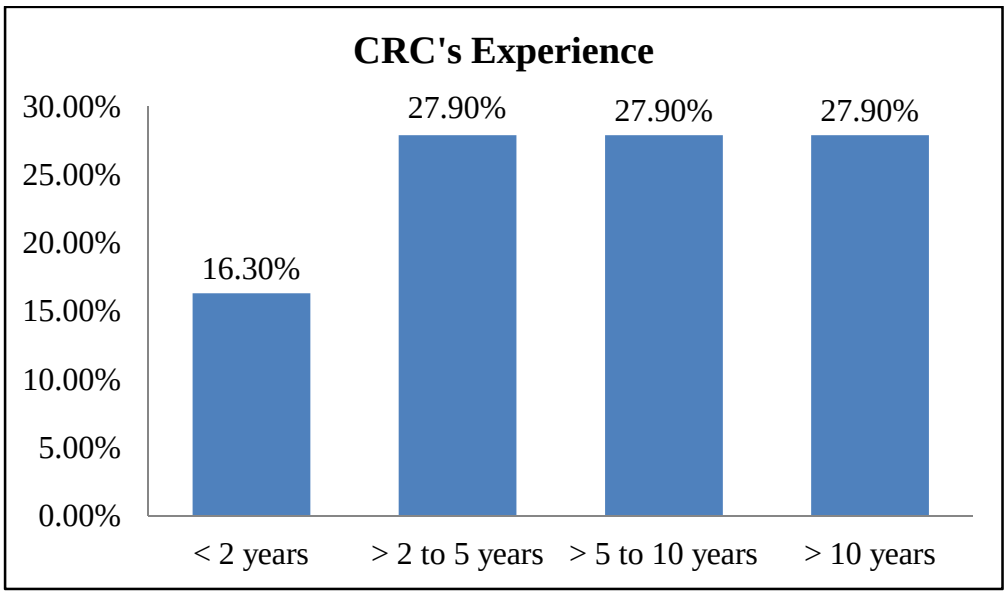


Figure 5. Experience of Clinical Research Coordinators

Table 6

Survey Respondents based on their Experience with the Clinical Monitor

Response or Answer	Frequency	Percent (%)	Cumulative Frequency	Cumulative Percent (%)
1 to 5	40	47.1%	40	47.1%
6 to 10	15	17.6%	55	64.7%
11 to 20	10	11.8%	65	76.5%
> 20	20	23.5%	85	100.0%
TOTAL	**85**	**100%**		

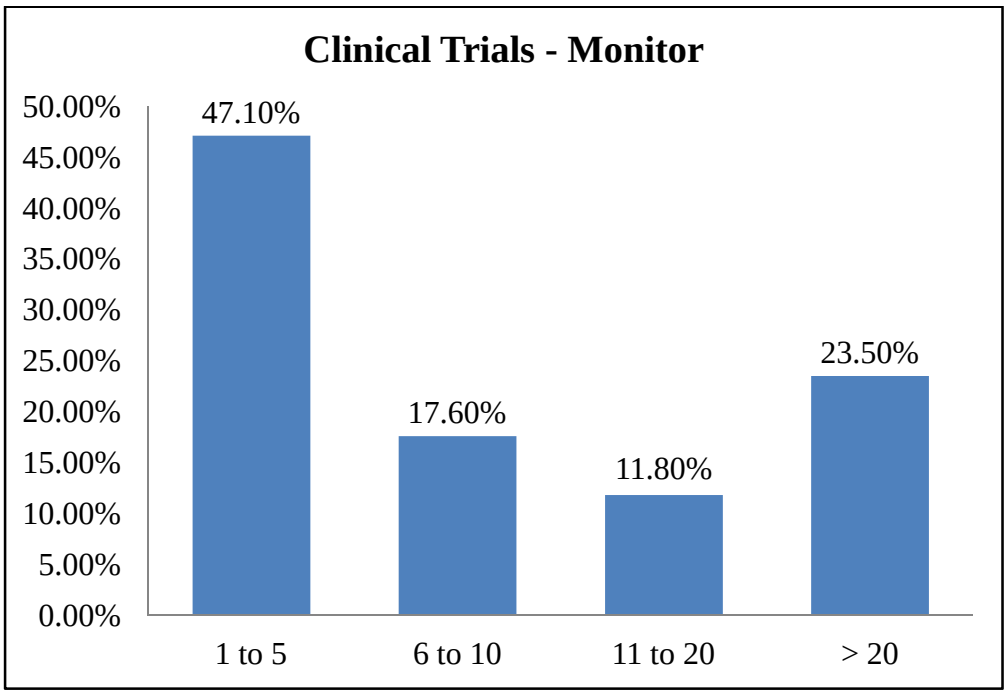


Figure 6. Number of Clinical Trials Interacted With Monitor

Presentation of Responses to Monitoring Practice Questions

Table 7

Survey Respondents based on their Satisfaction with the Skill as well as Competency of the Monitors

Response or Answer	Frequency	Percent (%)	Cumulative Frequency	Cumulative Percent (%)
Very satisfied	12	14.3%	12	14.3%
Satisfied	50	59.5%	62	73.8%
Not sure	16	19.1%	78	92.9%
Dissatisfied	6	7.1%	84	100.0%
Very dissatisfied	0	0%	84	100.0%
TOTAL	**84**	**100%**		

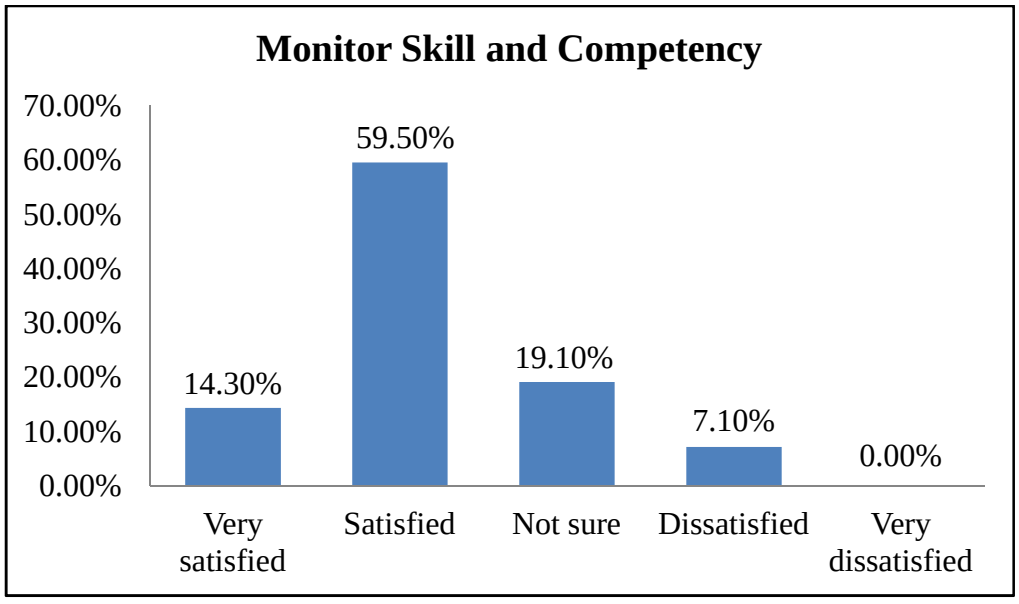


Figure 7. Satisfaction of Clinical Research Coordinators with the Skill and Competency of Monitors

Table 8

Survey Respondents based on their Satisfaction with the Monitor's Knowledge about Protocol and Its Requirements

Response or Answer	Frequency	Percent (%)	Cumulative Frequency	Cumulative Percent (%)
Very satisfied	18	21.4%	18	21.4%
Satisfied	51	60.7%	69	82.1%
Not sure	10	11.9%	79	94.0%
Dissatisfied	5	6.0%	84	100.0%
Very dissatisfied	0	0%	84	100.0%
TOTAL	**84**	**100%**		

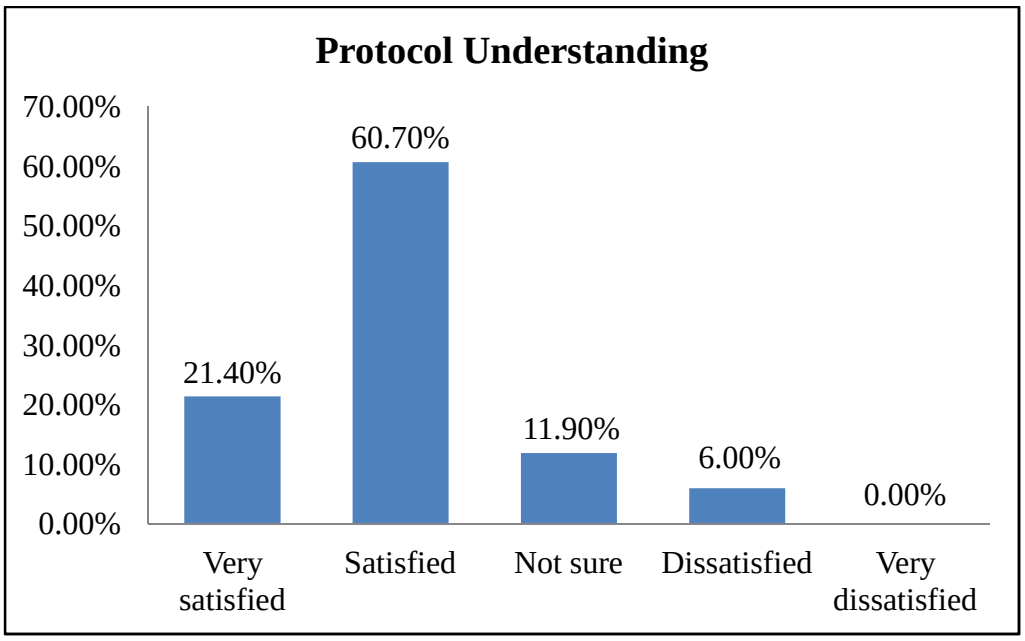


Figure 8. Satisfaction of Clinical Research Coordinators with the Monitor's Understanding of Protocol and Its Requirements

Table 9

Survey Respondents based on their Satisfaction with the Review for Informed Violations by the Monitors

Response or Answer	Frequency	Percent (%)	Cumulative Frequency	Cumulative Percent (%)
Very satisfied	19	22.6%	19	22.6%
Satisfied	46	54.8%	65	77.4%
Not sure	16	19.0%	81	96.4%
Dissatisfied	3	3.6%	84	100.0%
Very dissatisfied	0	0%	84	100.0%
TOTAL				

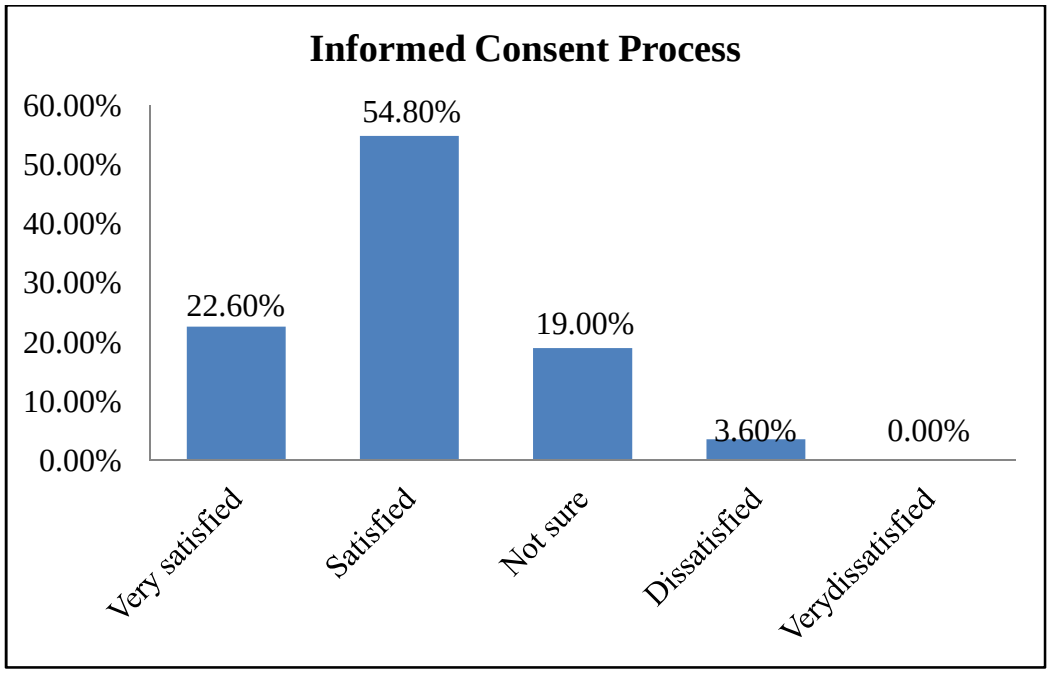


Figure 9. Satisfaction of Clinical Research Coordinators with the Monitor's Review of Informed Consent Process

Table 10

Survey Respondents based on the Satisfaction with the Review for Protocol Deviations by the Monitors

Response or Answer	**Frequency**	**Percent (%)**	**Cumulative Frequency**	**Cumulative Percent (%)**
Very satisfied	15	17.9%	15	17.9%
Satisfied	44	52.4%	59	70.3%
Not sure	16	19.0%	75	89.3%
Dissatisfied	9	10.7%	84	100.0%
Very dissatisfied	0	0.0%	84	100.0%
TOTAL	**84**	**100%**		

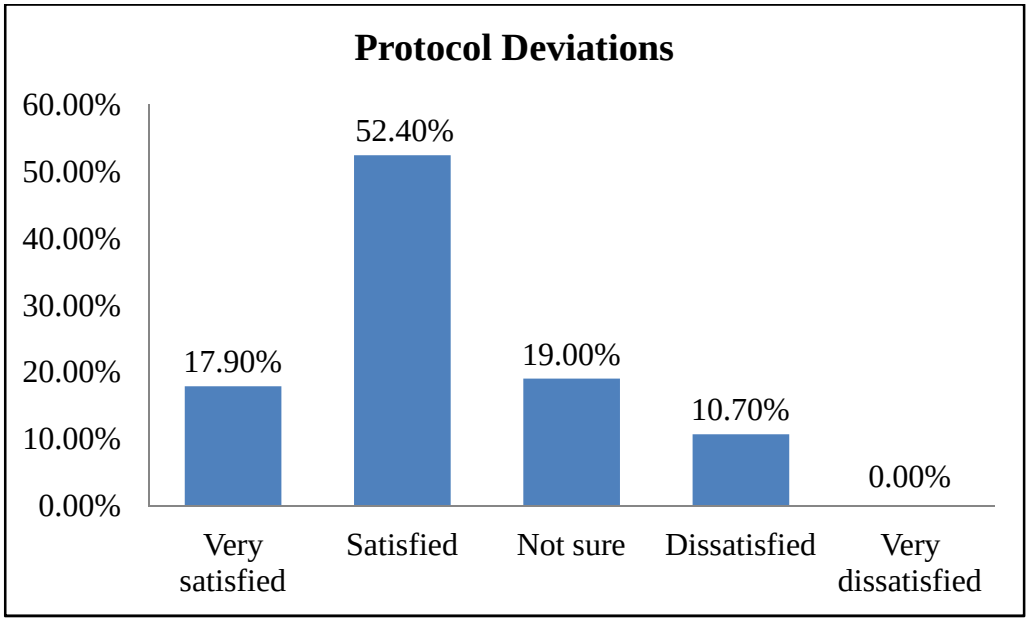


Figure 10. Satisfaction of Clinical Research Coordinators with the Monitor's Review for Protocol Deviations

Table 11

Survey Respondents based on their Satisfaction with the Review for Accuracy of CRF's and Source Documents by the Monitors

Response or Answer	Frequency	Percent (%)	Cumulative Frequency	Cumulative Percent (%)
Very satisfied	19	22.6%	19	22.6%
Satisfied	47	55.9%	66	78.5%
Not sure	12	14.3%	78	92.8%
Dissatisfied	5	6.0%	83	98.8%
Very dissatisfied	1	1.2%	84	100.0%
TOTAL	**84**	**100%**		

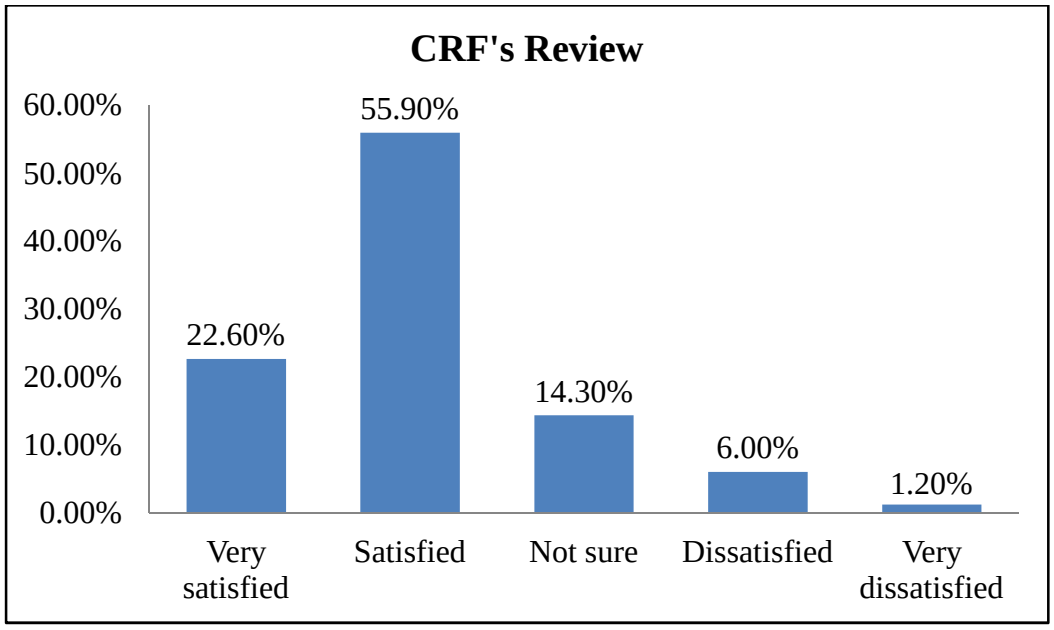


Figure 11. Satisfaction of Clinical Research Coordinators with the Monitor's Review for Accuracy and Completeness of CRF's, Source Documents and against Each Other

Table 12

Survey Respondents based on their Satisfaction with the Review for Reporting of Adverse Events by the Monitors

Response or Answer	Frequency	Percent (%)	Cumulative Frequency	Cumulative Percent (%)
Very satisfied	16	19.3%	16	19.3%
Satisfied	50	60.2%	66	79.5%
Not sure	10	12.1%	76	91.6%
Dissatisfied	7	8.4%	83	100.0%
Very dissatisfied	0	0.0%	83	100.0%
TOTAL	**83**	**100%**		

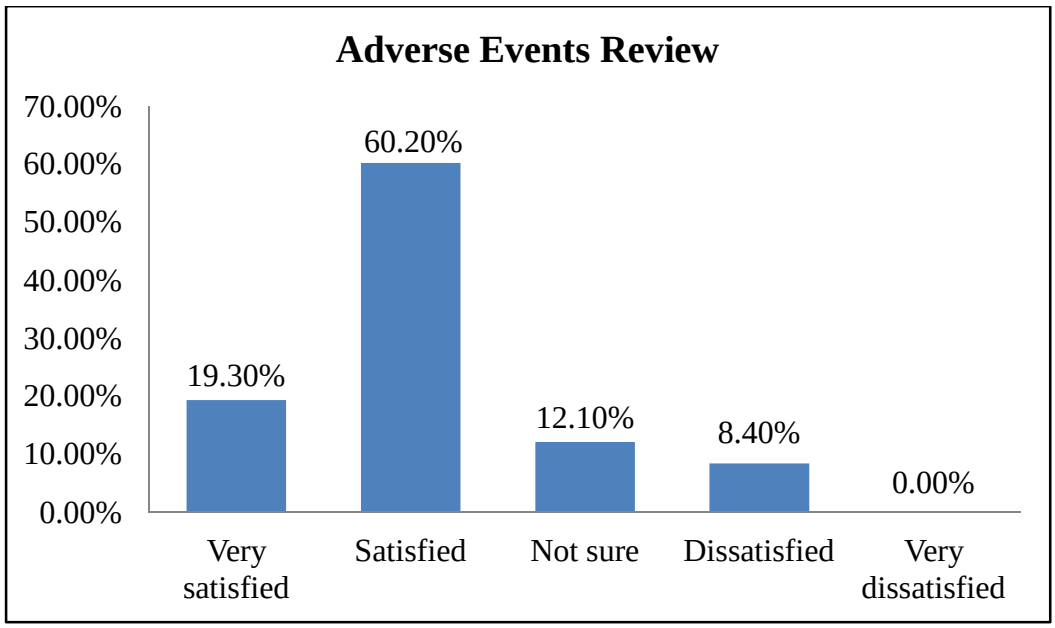


Figure 12. Satisfaction of Clinical Research Coordinators with the Monitor's Review of Adverse Events

Table 13

Survey Respondents based on their Satisfaction with the Review for Accuracy of Drug Accountability Records by the Monitors

Response or Answer	Frequency	Percent (%)	Cumulative Frequency	Cumulative Percent (%)
Very satisfied	19	23.7%	19	23.7%
Satisfied	43	53.8%	62	77.5%
Not sure	18	22.5%	80	100.0%
Dissatisfied	0	0.0%	80	100.0%
Very dissatisfied	0	0.0%	80	100.0%
TOTAL	**80**	**100%**		

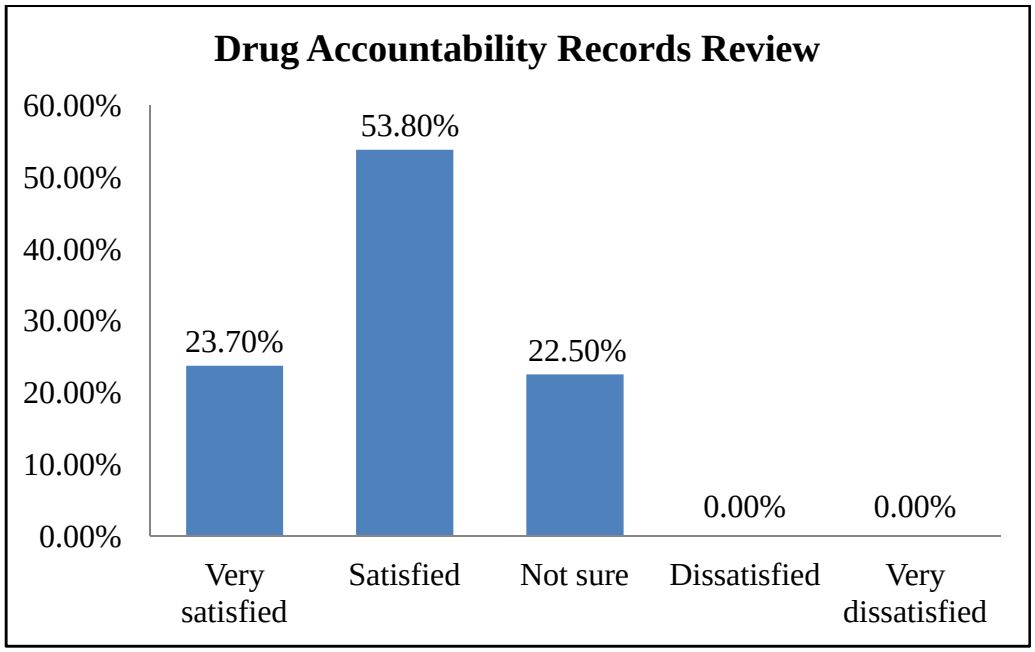


Figure 13. Satisfaction of Clinical Research Coordinators with the Monitor's Review of Drug Accountability Records for Accuracy

Table 14

Survey Respondents based on their Opinion about the Likeliness of Monitors Failing to Review the Required Approvals Prior to Study Initiation

Response or Answer	**Frequency**	**Percent (%)**	**Cumulative Frequency**	**Cumulative Percent (%)**
Very Likely	6	7.1%	6	7.1%
Likely	7	8.3%	13	15.4%
Not sure	19	22.6%	32	38.0%
Unlikely	25	29.8%	57	67.8%
Very Unlikely	27	32.2%	84	100.0%
TOTAL	**84**	**100%**		

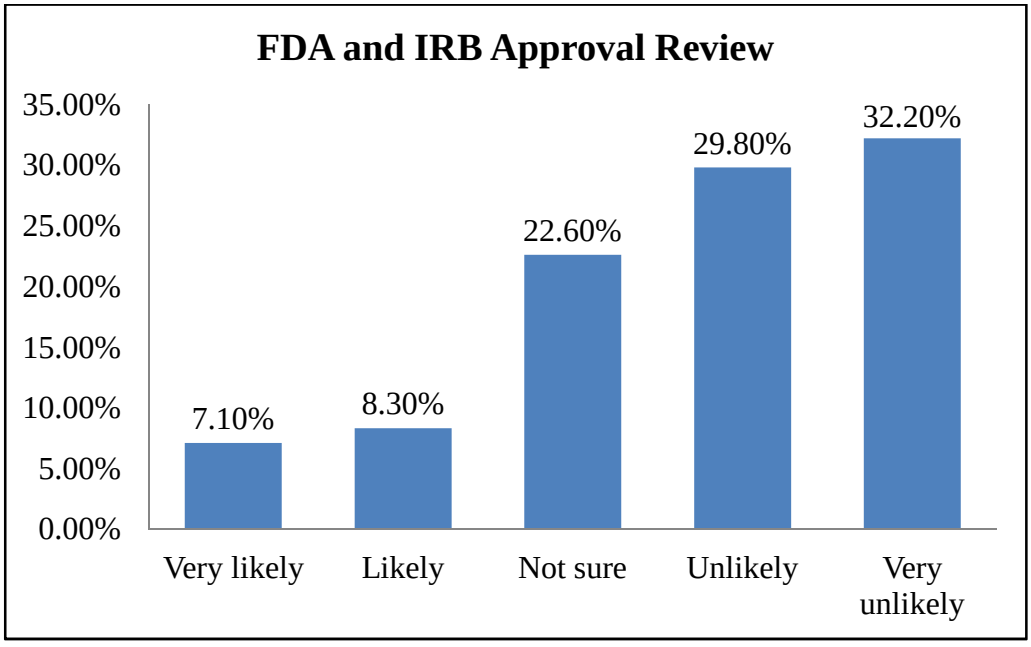


Figure 14. Likeliness of Monitor Fails To Review IRB and FDA Approvals

Table 15

Survey Respondents based on their Judgment about the Likeliness of Monitors Providing Required Technical Support to the Site Staff

Response or Answer	Frequency	Percent (%)	Cumulative Frequency	Cumulative Percent (%)
Very Likely	17	20.7%	17	20.7%
Likely	39	47.6%	56	68.3%
Not sure	14	17.1%	70	85.4%
Unlikely	10	12.2%	80	97.6%
Very Unlikely	2	2.4%	82	100.0%
TOTAL	**82**	**100%**		

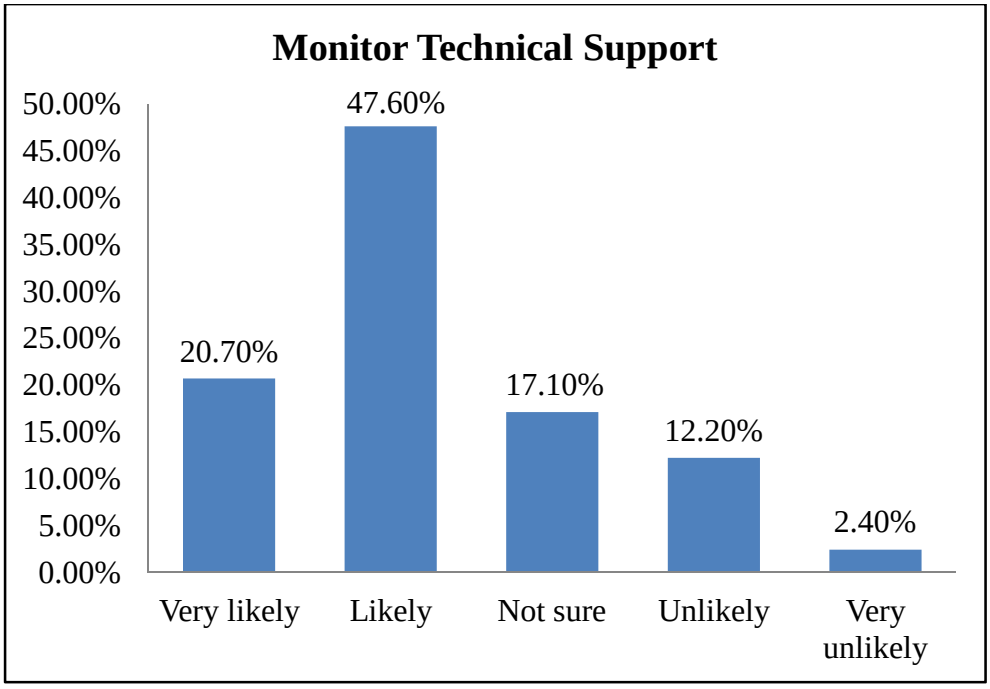


Figure 15. Likeliness of Technical Support Provided by Monitor's to Clinical Research Coordinators

Table 16

Survey Respondents based on their View about the Likeliness of Monitors Helping the Site Staff in Resolving the Generated Queries

Response or Answer	Frequency	Percent (%)	Cumulative Frequency	Cumulative Percent (%)
Very Likely	27	32.1%	27	32.1%
Likely	42	50.0%	69	82.1%
Not sure	6	7.2%	75	89.3%
Unlikely	9	10.7%	84	100.0%
Very Unlikely	0	0.0%	84	100.0%
TOTAL	**84**	**100%**		

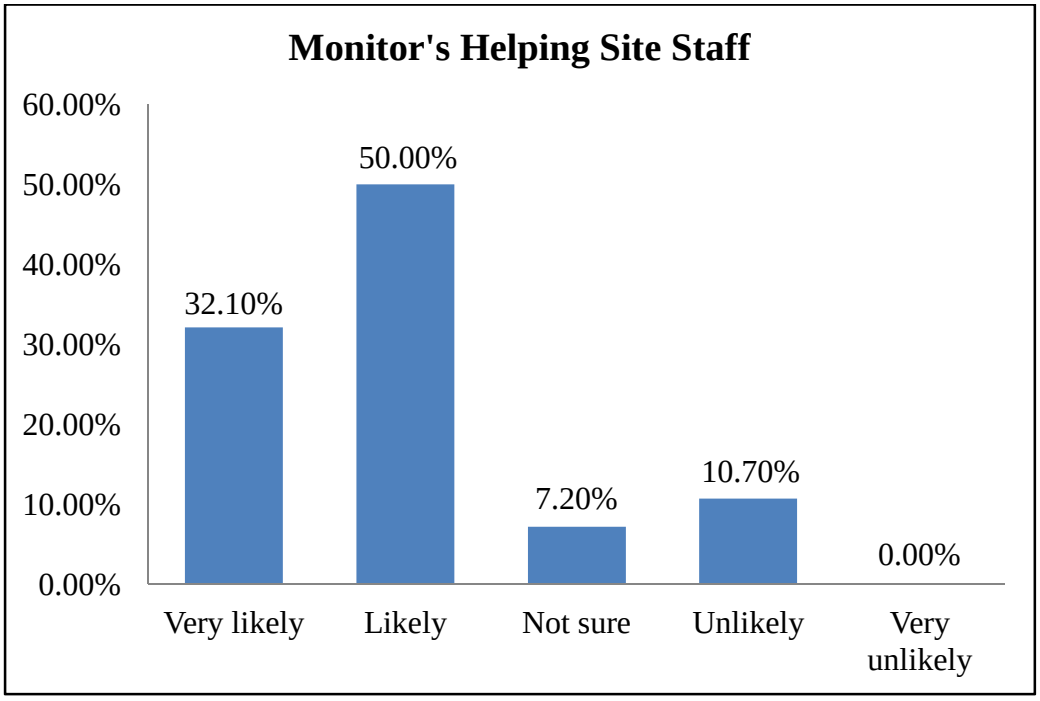


Figure 16. Likeliness of Monitors Helping Site Staff

Table 17

Survey Respondents based on their Opinion about the Likeness of the Monitors Providing the Monitoring Visit Reports within a Short Time Frame

Response or Answer	**Frequency**	**Percent (%)**	**Cumulative Frequency**	**Cumulative Percent (%)**
Very Likely	15	18.3%	15	18.3%
Likely	45	54.9%	60	73.2%
Not sure	12	14.6%	72	87.8%
Unlikely	9	11.0%	81	98.8%
Very Unlikely	1	1.2%	82	100.0%
TOTAL	**82**	**100%**		

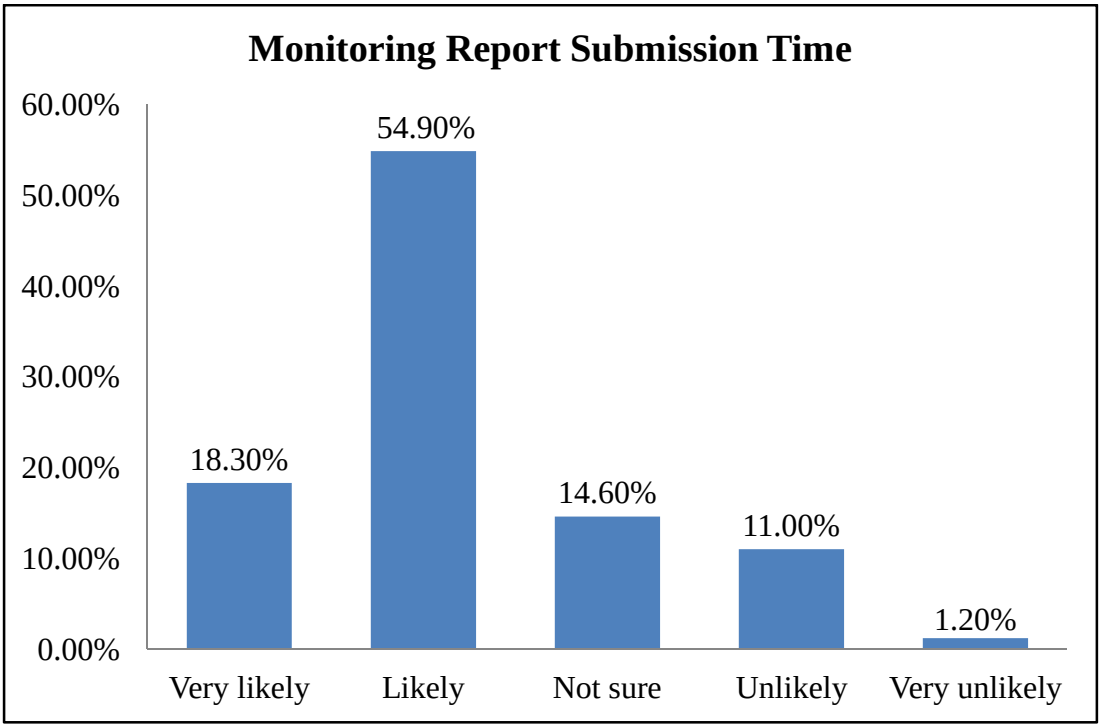


Figure 17. Likeliness of Monitor Submitting the Monitoring Report within a Short Frame of Time

Table 18

Survey Respondents referring to their Assessment about the Likeliness of Monitors Increasing the Work Load after the Completion of a Monitoring Visit

Response or Answer	Frequency	Percent (%)	Cumulative Frequency	Cumulative Percent (%)
Very Likely	30	36.1%	30	36.1%
Likely	35	42.2%	65	78.3%
Not sure	8	9.7%	73	88.0%
Unlikely	10	12.0%	83	100.0%
Very Unlikely	0	0.0%	83	100.0%
TOTAL	**83**	**100%**		

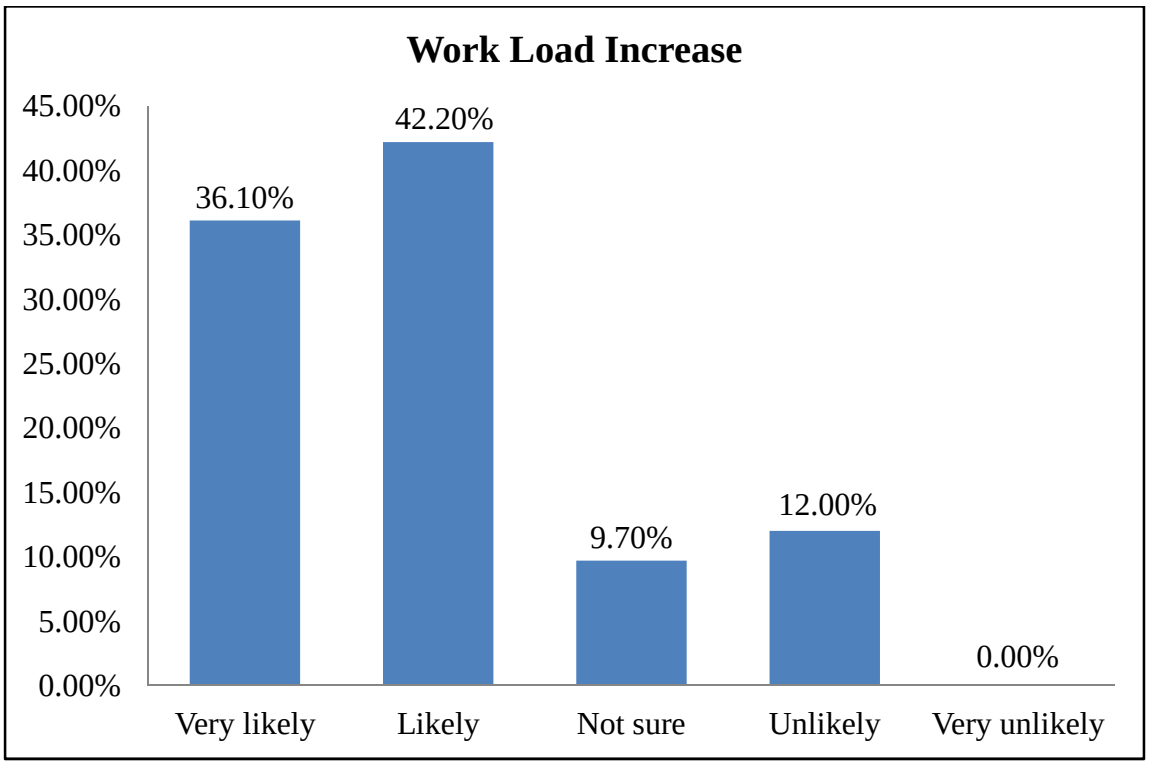


Figure 18. Likeliness of Monitor Increasing the Work Load after a Monitoring Visit

Table 19

Survey Respondents based on their Judgment, Whether or Not the Quality of Data at the Site Depends upon the Monitor

Response or Answer	Frequency	Percent (%)	Cumulative Frequency	Cumulative Percent (%)
Very much	23	27.7%	23	27.7%
Moderately	33	39.8%	56	67.5%
Not sure	14	16.9%	70	84.4%
Minimally	13	15.6%	83	100.0%
Does not reflect	0	0.0%	83	100.0%
TOTAL	**83**	**100%**		

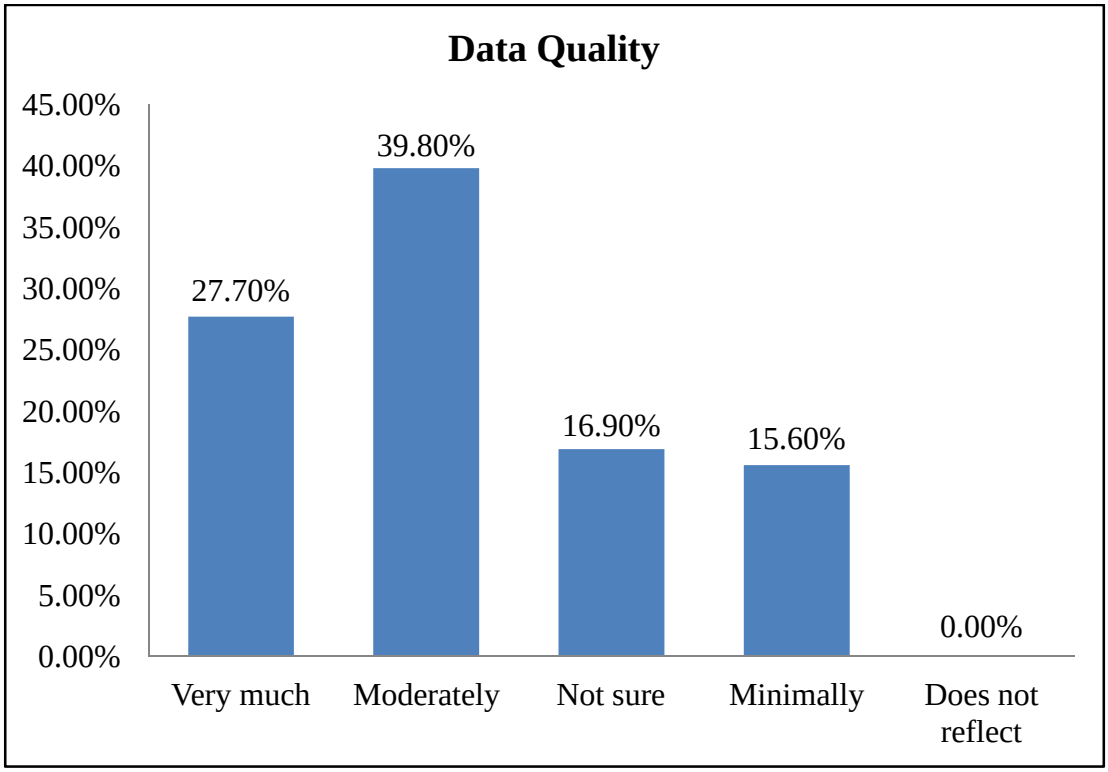


Figure 19. How Much the Quality Of Depends Upon Monitor

Table 20

Survey Respondents based on their Assessment about the Helpfulness of Monitor in the Preparation of the Site for Audit or Inspection

Response or Answer	Frequency	Percent (%)	Cumulative Frequency	Cumulative Percent (%)
Very much	9	12.5%	9	12.5%
Moderately	20	27.8%	29	40.3%
Not sure	27	37.5%	56	77.8%
Minimally	6	8.3%	62	86.1%
Not at all	10	13.9%	72	100.0%
TOTAL	**72**	**100%**		

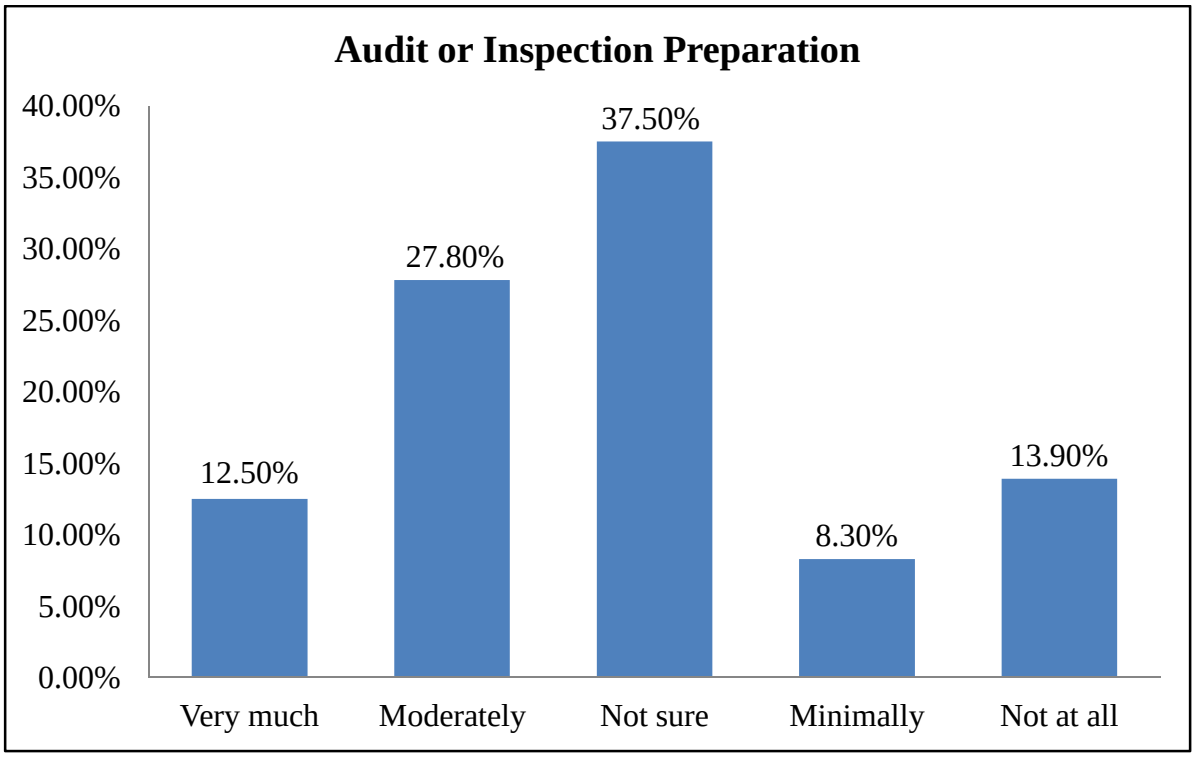


Figure 20. Helpfulness of Monitor in the Preparation of Audit or Inspection

Table 21

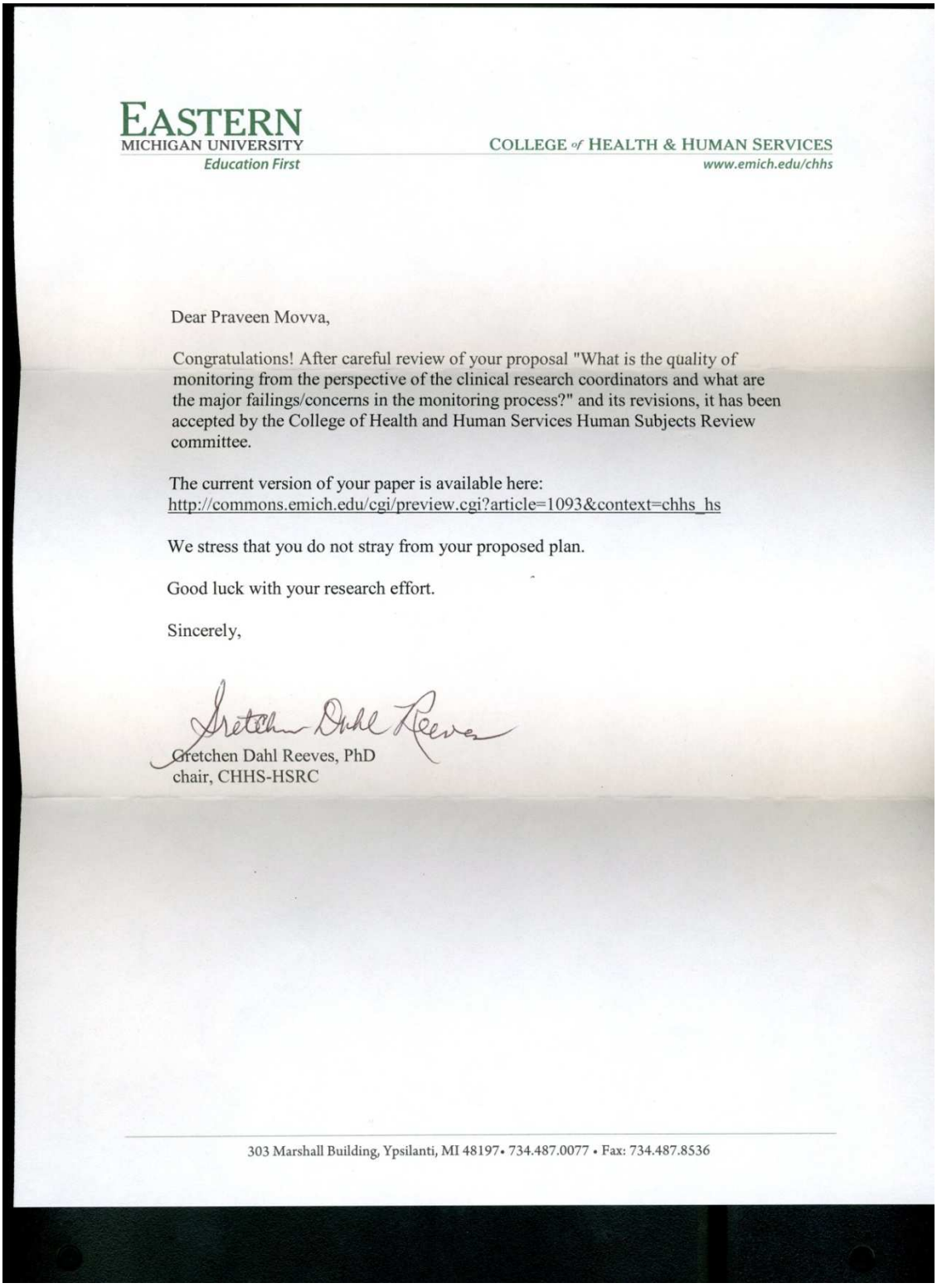
Survey Responses Expressed by the Clinical Research Coordinators about the Quality of Monitoring in Clinical Trials Today as Compared to Five to Ten Years Ago

Quality of monitoring has increased.
Monitors are better prepared now.
Quality of monitoring is very good.
There is minimal improvement.
All the monitors, I have dealt with are exceptional.
More thorough, very particular about following GCP and keeping clean data.
To me, the quality of monitoring in clinical trials has dramatically increased due to the electronic technology improvement as compared to 5-10 years ago.
I mostly worked on NIH sponsored trials in basic science and there is no monitoring. I did work on one clinical trial for a drug company sponsor and the monitors are proficient.
Study monitors can be inconsistent, especially when monitors change during the study. Compared to earlier, the consistency as well as overall quality has improved.
The monitors I have worked with are very helpful in variety of ways. In particular, one monitor was very useful in determining what exactly the CRF's were asking and educated me about some parameters and measures. Other monitor focuses on regulatory aspects and data review for accuracy, it is a great help in going to the sponsor to clarify any questions we have.
It's getting slightly better; the best monitor's are the ones who have worked as a coordinator before. Most likely, they know where to look and what common things

should be corrected?
Each monitor is different and most of them are well trained, knowledgeable and eager to help.
No significant change in monitoring.
Quality of monitoring is same and study monitoring depends on the complexity of the study that we are doing at the time of the monitoring visit.
I think there are many new monitors who are not being trained or mentored as well as may have been the case 5-10 years ago.
The quality of monitoring is not as good as 5-10 years ago. From my experiences, the monitors today are overwhelmed with too many sites or too many studies.
I feel the quality of monitoring five years ago was much better than today. Today monitors are overwhelmed with workloads and they don't really have the knowledge, some of them don't have experience.
I have seen a dramatic decrease in the experience and competence of monitors visiting my site during the past five years. In general, there are good monitors (certain CRO's).
Every monitor does things differently; they all want us to do things differently and don't understand our IRB procedures as well as operating procedures.
Varies by monitor. Monitors does not look at the data in the same way FDA does i.e., monitors focus on verifying data and do not look for inconsistencies.
I feel the quality of monitoring has gone down because monitors are over worked. Monitoring quality has gone down because of the amount of sites and patients the monitors are responsible for.

Many companies are using in – house monitors, instead of a monitoring company and many in-house monitors are not versed with the correct monitoring procedures.
Monitors change frequently during the course of the study and data requirements change from monitor to monitor. Some monitors have been the way too demanding of time or schedule and they don't even understand that the coordinators have multiple studies or commitments. Either the sponsor needs to invest in training or increase number of monitors to avoid the huge turnover in industry studies.
I found that monitors can be super helpful as well as experienced, at the same they make the things difficult. Really the quality of monitoring depends on the CRO. I found that every monitor is a bit different in their requests and style. Some are very easy to work with, while others are extremely difficult. It's hard to answer their questions and make blanket statements. 60 to 70% of the monitors I have worked with are not helpful in cleaning up our regulatory and subject binders.
The quality has gone down and monitors are responsible for too many protocols. The communication between CRO, sponsor and site is not good. On an average, we are seeing new monitors every six months.

Appendix A: College of Health and Human Services Human Subjects Review Committee Approval Letter



EASTERN
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Dear Praveen Movva,

Congratulations! After careful review of your proposal "What is the quality of monitoring from the perspective of the clinical research coordinators and what are the major failings/concerns in the monitoring process?" and its revisions, it has been accepted by the College of Health and Human Services Human Subjects Review committee.

The current version of your paper is available here:
http://commons.emich.edu/cgi/preview.cgi?article=1093&context=chhs_hs

We stress that you do not stray from your proposed plan.

Good luck with your research effort.

Sincerely,

Gretchen Dahl Reeves

Gretchen Dahl Reeves, PhD
chair, CHHS-HSRC

303 Marshall Building, Ypsilanti, MI 48197• 734.487.0077 • Fax: 734.487.8536

Appendix B: Survey Completion Request or Online Survey Consent Form or Email Survey

Survey Title:

"Perceptions of Clinical Research Coordinators about Quality of Monitoring"

Dear Clinical Research Coordinator:

As a part of my master's thesis, I am requesting your participation in a survey.

You are being invited to complete this survey about quality of monitoring and major concerns/failings in the monitoring process from the perspective of clinical research coordinators. You were selected as a possible participant in my search for clinical research coordinators in Google and finally, I found your email contact in the website of the institution or company or clinical trial center that you are working. I strongly advise you do not use employer issued device (laptop, smart phones etc.) to respond to this survey. This research project is done by Praveen Krishna Movva from Eastern Michigan University.

Your participation is voluntary and you may choose not to participate. If you decide to participate in this research survey, you may withdraw at anytime. Your participation and responses will be kept anonymous. There are no direct benefits associated with your participation, but your input is valued. There is no known risk involved in your participation.

As a researcher I respect your rights to privacy and I hold in the utmost respect your responses to this survey and I will keep the survey results confidential. I am not

collecting any kind of personal identifiable information and personal health information during the course of this survey.

The data will be collected via the online survey (Google Docs) and the results of the survey will be held by me. I will hold the data on a password protected personal laptop; there is no access to anyone. I will be protecting the laptop from theft and the word document containing email list for survey is both encrypted and password protected. The folder on my laptop (password protected) containing the results of the survey will be deleted upon the submission of the dissertation and the password protected document containing email list for survey will be deleted upon the completion of survey.

I will be sending the survey to potential participants by using Google docs and the survey tool or document or form containing emails will be deleted forever upon the analysis of results. Privacy Policy of Google http://www.google.com/intl/en/policies/privacy/

I have taken all reasonable measures to protect your identity and responses. However, email and the internet are not 100% secure, so it is also suggested that you clear the browser history to protect your privacy after completing the survey.

The procedure for survey involves answering six demographics questions and fifteen questions about monitoring practices. The survey takes about 15 to 20 minutes to complete.

Click on the following link to access the survey:

https://docs.google.com/spreadsheet/viewform?formkey=dHY4bkNzdGowbTRIVFJ0TmJTX3NkZUE6MQ

By clicking on the link above, you are indicating that:

- You have read above information.
- You voluntarily agree to participate.
- You are a clinical research coordinator.

I hope you will respond. This survey will be available for approximately two weeks to allow your participation.

If you have any questions about the study, please contact Dr. Stephen A. Sonstein, Professor and Director of Clinical Research Administration, Eastern Michigan University, ssonstein@emich.edu.

Thank you in advance for your participation!

"This research protocol and informed consent document has been reviewed and approved by the Eastern Michigan University Human Subjects Review Committee for use from November 7 2012 to November 6 2013 (date). If you have questions about the approval process, please contact Dr. Gretchen Dahl Reeves (734-487-3236, Chair, College of Health and Human Services Human Subjects Review Committee, greeves@emich.edu).

Appendix C: Survey

Survey Title:

"Perceptions of Clinical Research Coordinators about Quality of Monitoring"

Survey Questions include six demographic questions and 15 questions related to monitoring practices.

Demographic Questions:

1. What is the highest degree (or) level of education you have completed?
    - High School Graduate
    - Associate degree
    - Bachelor's degree
    - Post-baccalaureate certificate
    - Master's degree
    - Doctorate degree
    - Other(Please Specify)
2. Which of the following best describes your educational background?
    - Nursing degree
    - Life Science degree (e.g. Pharmacy, Biochemistry, Biology)
    - Health Science degree (e.g. Clinical Laboratory Science, Physical Therapy)
    - Clinical Research degree
    - Other (Please Specify)
3. Which of the following best describes your current work setting?

- Private Practice site
- Academic site (University or Teaching Hospitals)
- Community Hospital (Not Academically affiliated)
- Site management organization (organizing a group of sites centrally to do studies)
- Contract research organization (company or organization contracted by a pharmaceutical, medical device or biotechnology company to conduct clinical trials)
- Other (please specify)

4. Which of the following describes your current working pattern? (Select all that apply)
    - Medical device clinical trials
    - Pharmaceutical clinical trials
    - Investigator - initiated clinical trials
    - Government (or) Foundation – sponsored clinical trials
    - Other (please specify)
5. About how long have you been working as a clinical research coordinator?

- ≤ 2 years
- > 2 to 5 years
- > 5 to 10 years
- > 10 years

6. How many clinical trials have you participated in where you have interacted with a monitor?

A “monitor” is a professional who evaluates and analyzes clinical data and coordinates activities to ensure compliance with protocol and overall clinical objectives. Synonyms of monitor are clinical research monitor, clinical trials monitor, clinical research associate etc.

- 1 to 5
- 6 to 10
- 11 to 20
- > 20

Monitoring Practices Questions:

1. In general, how satisfied are you with the skill and competency of the monitors with whom you have interacted?

- Very satisfied
- Satisfied
- Not sure
- Dissatisfied
- Very dissatisfied

2. In general, how satisfied are you with the monitor’s level of understanding of the protocol and its requirements?

- Very satisfied
- Satisfied
- Not sure

- Dissatisfied
- Very dissatisfied

3. In general, how satisfied are you with the review of the informed consent process conducted by the monitors with whom you have interacted?

- Very satisfied
- Satisfied
- Not sure
- Dissatisfied
- Very dissatisfied

4. In general, how satisfied are you with the review for protocol deviations conducted by the monitors with whom you have interacted?

- Very satisfied
- Satisfied
- Not sure
- Dissatisfied
- Very dissatisfied

5. In general, how satisfied are you with the review for accuracy and completeness of CRF entries and source documents against each other conducted by the monitors with whom you have interacted?

- Very satisfied
- Satisfied

- Not sure
- Dissatisfied
- Very dissatisfied

6. In general, how satisfied are you with the review for reporting of adverse events conducted by the monitors with whom you have interacted?

- Very satisfied
- Satisfied
- Not sure
- Dissatisfied
- Very dissatisfied

7. In general, how satisfied are you with the review for accuracy of drug accountability records conducted by the monitors with whom you have interacted?

- Very satisfied
- Satisfied
- Not sure
- Dissatisfied
- Very dissatisfied

8. In general, how likely are the monitors with whom you have interacted to fail to review FDA and IRB approvals prior to study initiation?

- Very Likely
- Likely

- Not sure
- Unlikely
- Very Unlikely

9. In general, how likely are the monitors with whom you have interacted to provide adequate technical support to the site staff about the study?

- Very Likely
- Likely
- Not sure
- Unlikely
- Very Unlikely

10. In general, how likely are the monitors with whom you have interacted to help the site staff in resolving the generated queries?

- Very Likely
- Likely
- Not sure
- Unlikely
- Very Unlikely

11. In general, how likely are the monitors with whom you have interacted to provide site monitoring reports in a short time frame after completing a monitoring visit?

- Very Likely
- Likely

- Not sure
- Unlikely
- Very Unlikely

12. In general, how likely is it that there is an increase in work load following the completion of a monitoring visit?

- Very Likely
- Likely
- Not sure
- Unlikely
- Very Unlikely

13. In general, in a clinical study, how much do you believe the quality of the data at your site reflects upon the monitors with whom you have interacted?

- Very much
- Moderately
- Not sure
- Minimally
- Does not reflect

14. Has your site been audited or inspected in the past three years? If so, has the monitor been helpful in preparation for the audit or inspection?

- Very much
- Moderately

- Not sure
- Minimally
- Not at all

15. In general, what is your opinion about the quality of monitoring in clinical trials today as compared to 5-10 years ago?