

An Effective Management Approach for a First-Time Study Lead

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ABSTRACT

Becoming a first-time study lead from a programming study team member is a significant step that comes with various challenges. Perseverance plays a substantial role in their development process, which helps to overcome these challenges. Programming of tables, listings, graphs, and datasets is mostly a logical and technical task, whereas leading the study involves additional management tasks. The successful accomplishment of any project is determined by the technical and management approach used by the study lead. Lead can adopt different management approaches, which include technical and leadership skills, effective communication, team motivation, stakeholder relationship, proper planning, and risk management. These factors allow study leads to create a committed and robust team that is dedicated to achieving the best result.

This paper illustrates certain key features of an effective management approach that can be implemented to ensure effective and robust study management. It may be relevant and helpful to those hoping to be a study lead or those who recently took study lead responsibilities for the first-time.

INTRODUCTION

Study management can be described as the process of understanding, planning, organizing, and managing responsibilities using the available resources to accomplish a specific objective within the timeline with the highest quality. Study lead should know how to identify and avoid challenges, or at least minimize their impacts, monitor the progress of the study as well as the team members. The study lead's experience, background, and personality help to reduce stress, but there are scenarios where a more planned strategy will be needed. Based on the challenges and responsibilities, the study lead needs to adopt various technical and project management approaches to achieve the targeted timeline and objectives. In this paper, we will focus on several crucial tasks in detail that all lead programmers need to follow for effective study management.

TECHNICAL MANAGEMENT

STUDY SPECIFIC DOCUMENT REVIEW

Several documents contain information about the study, such as design, types of assessment, data collection, and its analyzing method. There are three documents, protocol, case report form, and statistical analysis plan, that all study-lead need to review and understand to get a good hold on the study. It also helps to clarify any doubts before starting any programming activities. In the following section, we will discuss each of the three documents in brief:

1. Study Protocol

The study protocol is a document to describe the objective, design, methodology, statistical considerations, and sponsor details of the clinical trial. It also defines the safety of the subjects enrolled and the integrity of the data collected in a clinical trial. Since it is a critical document for the study, it includes more detailed information than it's required for a programmer. It is always better to read the entire document but focus more on the sections critical from a programming perspective. Following are some examples of the section to review in the document:

- Protocol Summary
- Schedule of Activities
- Introduction
- Objectives and Endpoints

- Study Design & Study Population
- Study Assessment and Procedures
- Appendix Information

2. Case Report Form (CRF)

The case report form (CRF) designed for a study is used to collect the clinical trial data for each subject in a clinical trial. The collected data will be transferred into a dataset and available for the programmers to start with the programming. The investigator selects answers from the drop-down list or writes for all the relevant questions available in the CRF. Annotating the CRF (acrf.pdf) with the SDTM domain is very helpful in understanding the following items:

- Variable Mapped from CRF to the SDTM Domain
- Data Formats
- Codelist
- Expected Values in SDTM Variables
- Type of Data Collected
- Method of Data Collection

3. Statistical Analysis Plan (SAP)

Statistical Analysis Plan (SAP) document outlines the statistical strategy and procedures for the study in detail. It also describes all the analysis outputs, which will be included in the clinical study report (CSR). Changes to exploratory or other non-confirmatory analysis made after the protocol have been finalized is documented in a supplemental SAP (sSAP). The additional planned analysis (i.e., those specific to the analysis of PK data or PROs) will be documented in an sSAP or separate analysis plan. The SAP is a handy document for the programmers to prepare all the deliverables. Some of the example section in the SAP are described below:

- SAP Summary
- Responsibilities for Analysis and Blinding
- Definition of Analysis Endpoints and Populations
- Statistical Methods
- Interim Analysis Timeline (Safety & Efficacy)
- Sample Size and Calculations for Safety and Efficacy Analysis

GOOD UNDERSTANDING OF STUDY DATA

Understanding and reviewing the study data is a very critical part of the programming. As defined by the CDISC, “SDTM provides a standard for organizing and formatting data to streamline processes in the collection, management, analysis, and reporting.” Being a study-lead, you will be the first person to approach in case of any queries related to data by your team. Without the understanding of the data, it is not possible to answer questions raised by the group, which eventually leads to compromised quality work or impact on timelines. In either case, it is not a good sign for the study-lead and put all your efforts at risk. It also a responsibility of a study-lead to report identified data issues to Data Management (DM) so that they can be fixed in the next load of the data.

1. Review of SDTM Data

Study-lead and statistician will review SDTM data, which will be used for analysis and reporting. The first step in the data review is to identify the SDTM, MedDRA, and WHO drug dictionary version and cross-check against the study data standardization plan (SDSP). It is also essential to check if

available data follows the CDISC standard or company-specific (sponsor-defined) standards. Report any findings or discrepancies to the project manager or study coordinator as it is critical from the compliance point of view.

Reviewing the mapping specifications provides a good understanding of how raw datasets and aCRF relates to SDTM domains. It also helps to ensure that all the raw datasets and forms are mapped to the SDTM data. It consists of all details on variables which are helpful in the ADaM programming. Running the Pinnacle 21 tool to validate the SDTM data against the CDISC standard provides a comprehensive report on the possible compliance issues.

2. Perform Edit Check

After receiving or creating SDTM data, the next step is to perform an edit check on the available data to identify any potential data issues. The tool and platform used to perform edit-check are different from organization to organization. Still, the most critical part is to identify such issues and report them to the data management for their review. Following are some example of the edit-check list, which is crucial for any study in any therapeutic areas:

- End Date > Start Date
- Age Group is not consistence with the protocol or SAP (e.g., reported age is 6 years, but the protocol or SAP specifies the age group between 18-65 years)
- Death reported for a subject, but the death date is missing
- The adverse event occurred, but AE start date or AE term is missing
- The correlation between Adverse Events and Concomitant Medication dataset
- Required variables should not be missing
- Possible wrong units, i.e., 170 m in height, 101 C in temperature, etc.

WRITING DATASET SPECIFICATION

To produce TFLs (tables, figures, and listings) for a data monitoring committee (DMC), clinical study report (CSR), or publication, it is required to have analysis datasets. The industry standard for creating such datasets is CDISC ADaM (Analysis Data Model). Dataset specifications provide details on format, codelist, derivation, and required variables to generate tables, figures, and listings (TFLs). However, the mock-up shell plays a crucial role in preparing the dataset specifications as it helps to identify the necessary datasets and variables in each of the datasets. The following section will describe in brief each of the two parts required in writing the dataset specification:

1. Review Mock-Up Shell

The mock-up shell is a document that describes the number of TLFs needed for the analysis. It is a dummy template that resembles the original outputs to help programmers to identify the programming requirements. The mock-up shell document contains company standards and study-specific templates. It also includes some programming notes that may not be provided in the protocol or SAP. Reviewing the mock-up shell helps study-lead to identify the following items:

- The number of ADaM datasets required in the analysis
- Identify the parameters, variables, coded terms, and sorting order requirements in the ADaM datasets
- The number of outputs based on the company standard macro
- For non-standards outputs, it helps to identify the number of programs that can be borrowed from other study and the number of programs that needs to start from scratch
- It identifies the requirements of title, subtitle, and footnote for each of the outputs
- It helps to identify the programming resources and delivery timelines

2. Writing ADaM Dataset Specification

After reviewing the required documents, and having a good understanding of the SDTM data, writing a dataset specification is another important task in the programming process. Most of the organization have a standard specification template for the ADaM datasets. However, the study lead needs to pay attention to some critical variables derivation since it may differ from study to study. In general, writing the specification for safety datasets is the responsibility of the programming team, and efficacy datasets are the responsibilities of study statisticians. However, Demographic and Baseline related datasets specification should be a joint effort of both programmer and statistician. Few key points need to be considered while developing the specifications:

- Follow the CDISC ADaM Implementation Guide (ADaM IG)
- Maintain the traceability between SDTM and ADaM dataset by naming the dataset based on the SDTM domain (e.g., ADAE for Adverse Events, ADCM for Concomitant Medications)
- Define the derivation based on the information provided in protocol and SAP
- Schedule a meeting with a study statistician to discuss the derivation for critical variables, and document it upon mutual agreement
- Review the mock-up shell to verify all datasets and variables required for TFLs are included, and nothing missed out
- Request study statistician to provide guidance in a complex statistical model to the programming team

PREPARING SUBMISSION PACKAGE

The preparation of the data package comes into play after Interim Analysis (IA) or CSR when preparing for the submission to the FDA, PMDA, or country-specific agencies. In general, a submission package will be created once and can be reused for submission to all countries in the world with little or no modification. There is a guide prepared by the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) at the FDA. It provides FDA Guidance on Providing Regulatory Submission in Electronic Format. The submission package contains two types of packages, Dataset package and Office of Scientific Investigation (OSI) package. It is a responsibility of the study-lead to review the submission package in detail before delivering it for management review. The contents requirements in both packages are discussed below:

1. Tabulation & Analysis Submission Package

It is important to understand the technical specifications for the submission of the dataset package to the FDA. The dataset package is divided into two parts: Tabulation data package and Analysis data package. The required content under each of the data package is explained below:

Tabulation Data Submission Package Checklist

- SDTM datasets as SAS® transport (XPT) files
- Data definition file in define.xml (and define.pdf) format
- Stylesheet
- Annotated CRF
- Study Data Reviewer's Guide (cSDRG)

Analysis Data Submission Package Checklist

- Analysis datasets as SAS transport (XPT) files
- Data definition file in define.xml (and define.pdf) format

- Stylesheet
- An Analysis Data Reviewer's Guide (ADRG)
- An Analysis Results Metadata (ARM)
- SAS programs used to create all analysis datasets and TFLs associated with primary efficacy analysis in a text (.txt) format.

2. OSI Submission Package

The FDA Office of Scientific Investigations (OSI) has the responsibility of verifying the integrity of data submitted to the Center for Drug Evaluation and Research (CDER). As a study-lead, it is useful to follow the guidelines and technical requirements published by the FDA. To assist with this process, OSI has outlined the following three-part information request:

Part I : Tabular Listings of Site Information

Part II : Line Listing by Site

Part III : Site-level Dataset

Once all of the above parts is completed, Submission package required the following items:

- Site-level dataset in transport (XPT) files
- Data definition file in define.pdf format
- Combined tabular and line listings file in PDF format
- BIMO Reviewer's Guide if applicable

PROJECT MANAGEMENT

PLANNING AND RISK MANAGEMENT

Planning is the process of establishing the schedule, activity, and required resources for a study that should be achieved within a specific time. Planning should also identify the potential risks that could arise during the conduct of the study, and a study lead needs to come up with a risk management plan. Risk management is a practice of finding, examining, and responding to risks that could affect the progress of the study activities. It should be a part of the planning, and the study lead should have a contingency plan that deals with these unexpected risks. Planning and risk management are crucial in predicting the timeline of the study, and in most cases, it guarantees success. It also helps the team members to focus on their roles and responsibilities, which would improve the efficiency of teamwork.

1. Scope and Timeline Projection

Setting the timeline for a study requires a breakdown of the activities. The analysis of activities helps in fulfilling the deliverables set within a specified duration. Starting a project without knowing the exact amount of work that needs to be done is very dangerous in meeting timelines. There is a strategy known as rolling-wave planning, which helps in scheduling the scope that you are sure enough of knowing how to plan it.

An activity list is another tool that is very useful during scope projections and timeline setup. It shows a list of activities that have been completed, ongoing, and the next activity with their corresponding timelines.

There is another MS office tool known as MS Project, which is very helpful in listing the activity in chronological order with its expected start and end date. It also helps us to determine the target completion date of all the events in the plan. If there are any changes in the plan or updates required in the timeline, its built-in functionality adjusts the timeframe of the following activities automatically, which reduces the manual efforts of new timeline calculations.

2. Planning Resources

An effective plan for a study does not include listing activities to be delivered only. Study planning involves resources planning to have a clear understanding of the quantitative and qualitative support needed and at what stage of the planning. The very first stage of resource planning is creating a study scope and timeline, where dependencies and deliverables are clearly defined. As a study lead, it is crucial to plan the timeline based on available resources only.

Without appropriate resource planning, it is difficult to control the study deliverables and timelines. Resource planning requires some inputs, such as pre-requisite, techniques, and tools. Pre-requisite is a structure of study scope that is deliverable oriented. It shows the study with manageable sections; hence it is easier for the managers to figure out the type of resources needed and plan them accordingly. The Excel spreadsheet is a commonly used tool for resource planning.

3. Work Prioritization

Work prioritization is the sole cornerstone of productivity and once taken care of, time management is never a problem. At most workplaces, work prioritization is the major challenge. Due to the workloads and complexity, every scope feels more important than the other. Creating a master tasks list where all activities are recorded is one of the excellent strategies of prioritization. Once the tasks list is prepared, it is further broken down in terms of urgency and the resources it needed to be accomplished. The breakdown can be categorized in terms of low priority, medium priority, and high priority.

It is crucial to set up regular meetings with the study statisticians and clinical team to figure out the priority schedule. Its real priority can further rank the three categories mentioned above. At the end of every week, write down the essential things which need to complete next week. This approach helps in managing all tasks comfortably by retaining its priority.

4. Accepting and Managing Risk

It is essential to accept that there is a likelihood of risks occurring for any project. Many projects face some challenges either in terms of resources or failure to deliver within a time frame. Upon identifying the potential risks, a study lead can change their initial plans, which could help to avoid these risks. It is an excellent practice to have some buffer days between tasks in the initial planning to cover this type of unexpected risks.

Mitigation of risks entails limiting risks impact, which is essential in carrying out any study or project. In this case, the study lead could limit the risk so that it does not occur or ensures it is fixed without affecting the study timelines or quality. One of the mitigation strategies the study lead could adopt is training the team members about the study's planning and deadlines, probable risk, identifying and handling them.

COMMUNICATION

Communication is an essential skill for a first-time study lead. Some projects fail due to a lack of effective communication, while others have ineffective consultations. Communication is the exchange of ideas, knowledge, skills, and experience. For any project to be successful, the study lead needs to ensure consistency and effective communication with the study team, management team, and stakeholders. As a result, team members learn more about the study and understand its scope, requirements, progress, and timelines. In today's global workplace environment, the study lead should consider the diversity of the team, location, language, culture, and existing barriers when choosing the mode of communication. It helps to determine the most convenient method of communication.

1. Active Listening Skills

It is crucial not to interrupt or try to answer the question before you know what your stakeholders or team members are asking. Giving feedback or answering such questions is critical to convince or increase trust with stakeholders or team members, and active listening skills play a crucial role in it. Moreover, team members likely to be more open, share their ideas and views, which creates

more options for ideas and solutions to the challenges in the process of study management. It helps to get the best out of each team member or stakeholder.

There are six key active listening skills that everyone should have to become a good listener.

- Pay Attention
- Withhold Judgement
- Reflect
- Clarify
- Summarize
- Share

2. Regular Follow-Up

Follow-up regularly serves several purposes, especially confirmation of previously issued instructions or guidelines and their execution. The primary function of monitoring the study is to control the functions and effects of the project. Besides, it enables the study-lead to maintain flexibility in the decision-making process through feedback received from the team members or stakeholders. It also helps to evaluate the understanding of the stakeholders towards study requirements, and its scope.

The study lead should do a regular follow-up to identify the work progress, detect the problems, and manage it before the database lock to avoid risks post database lock. It also assures stakeholders of an effective, systematic, and professional management of the study. A study that supervised systematically is likely to be delivered on time with the highest quality and compliance. Lack of regular and persistent follow-ups may lead to delays and low productivity.

3. Team Meeting and Discussion

Working as a team is not easy, mainly when some of the team members work remotely or associated with different departments. Therefore, it is very crucial to have a team meeting for the members to have a general view of the progress. A well-organized meeting has a significant influence on the team members. The information shared during the team meeting strengthens the interpersonal bonds, improves productivity, improves communication, boosts the team's self-confidence, and satisfaction of the team members. Meetings and discussion help to address critical issues hindering the completion of a task.

Meeting and discussion create a platform that allows team members to share their opinions regarding a particular issue. Sharing information opens new doors for productivity, research, and co-operation. It also creates a learning platform presenting an opportunity for the team members to learn from challenges, progress, and insights shared during the team. MS Excel or MS OneNote is a potent tool to document all the meetings with its agenda items, discussion, task list, timelines, study progression, and resolution. Lead can share the workbook with all the team members so that they can review it time-to-time to get up-to-date information. It also helps team members to enter any issue or concerns in the issue log, which needs to be discussed in the next meeting.

LEADERSHIP SKILLS

Leadership skills portray a positive image that other team members can emulate and create a productive team. Whether you are a study lead or manager, all good leaders required some excellent skills to help positively involve stakeholders or team members. Effective leaders can maintain a strong relationship with colleagues, be a good team player, handle and delegate responsibilities, and ability to solve problems. These skills would enable the study-lead to create a conducive and productive environment where all the team members are inspired to improve their skills. Whether you are looking to move up on a career ladder or looking for a promotion, leadership skills are the most valuable asset to have. Following are some of the critical points which need to be considered as a study-lead:

1. Stakeholder Relationship

Effective and robust management can be achieved through strong work relationships with the stakeholders and team members. Study management involves various processes and standards, and unless there are people in the team, it cannot be successful. Teams are built with people from a different community, and every team member of a study team has unique skills, knowledge, and expertise. Creating sustainable and flexible working relations helps to establish a productive working environment. As a first-time study lead, it is crucial to building a strong and faithful relationship with the study team, stakeholders, and management team.

In order to build a strong team, study lead needs to understand the characteristics, strengths, and weaknesses of each of the team members. It will help lead to identify the best talent for each task in the list and assign the work accordingly. It is a significant factor in study management to achieve a timeline with excellent quality.

2. Scalable Approach

Effective leadership required to tackle the present problems and foresee future ones while ensuring continuous work growth of the study. It is a vital role that shapes the team for the betterment of the project. An essential aspect of effective leadership is the ability to delegate tasks to team members and learn to have the authority required to get things done on time. It not only ensures the more amount of work can be done but also helps to build team member's confidence. The study lead must be an effective communicator, along with excellent time management skills.

A leader must influence people. To do that, they need to exhibit attributes like transparency, integrity, and high ethical standards. It helps to create model behavior for the people working in the team. In today's scenario, leaders should think about long-term goals and make decisions accordingly. There is no specific approach for effective leadership, but there are several characteristics, as discussed above, which can be incorporated by the leaders that differentiate them from the others and lead to success. To become an effective leader requires a lot of learning, periodic assessment, and the ability to adapt according to the current situation.

3. Negotiation

In the negotiation process, two or more people discuss an issue to reach a mutual agreement. It can be within a team, organization, or with external stakeholders. Good negotiation contributes significantly to the success of a project. Negotiations are vital as it helps to build a strong relationship that can result in a satisfactory outcome for all the stakeholders involved. Before starting a negotiation, the lead should be clear about the interest and goals of the stakeholders involved in the discussion and have extensive knowledge of the subject. The aim must be to achieve a positive outcome for all sides. Most importantly, negotiation must be started with an open mind.

During the process of negotiation, the viewpoints of everyone must be taken into consideration. They must take place in such a way that it enables all the stakeholders involved to explore the possible options together. Inter-personal skills are essential for a successful negotiation. The study lead needs to evaluate the request received from the statisticians and the clinical team and work on the timeline. We need to discuss the scope and timeline with the programming team and come up with the conclusion if it is feasible. If the given deadline is not reasonable, the study lead needs to provide a new timeline with justification to the clinicians and statisticians.

APPRECIATION AND TEAM MOTIVATION

A first-time study lead should focus on motivating team members to boost their productivity and loyalty. Team motivation will unlock all the potentials and would be an excellent idea to get the best from the team. Firstly, motivated team workers are characterized by increased productivity that enables a study-lead to accomplish targeted goals. Motivated team members are also satisfied with their roles meaning they focus on meeting the timeline with all their efforts. Appreciation and motivation also lead to the personal

development of each member, enabling them to give their best over the years. The study-lead can motivate and appreciate the team members in various ways:

1. Encouraging Teamwork and Rewards

Encouraging teamwork would increase the productivity of each team member since it promotes the spirit of encouragement among the team members. Co-operation can be improved through team building activities that help members to bond and transform them to be more open in airing their opinion during meetings, which are essential for the team. It would also be perfect for each member to realize their role and importance in ensuring the project succeeds.

Rewarding team members who do outstanding work is one of the factors that motivate team members. It challenges the other members to work harder and increase their productivity in healthy competition. Rewarding team members should be fair to avoid creating an unhealthy work environment where some members feel mistreated. The study-lead can encourage and reward team members in multiple ways:

- Writing a specific thank you e-mail and cc e-mail to the management team.
- Provide updates in a team meeting for a significant contribution of a team member to the unique technical difficulties.
- Send a proposal to a manager to issue an inspiration award to certain team members.

These encouragements and rewards promote an atmosphere of co-operation and create a bond among the study team, which helps the team to work effectively and efficiently.

2. Providing Developing Opportunities

A study-lead should also trust team members to whom they motivate. It would entail giving them opportunities to learn as well as improve their skills. The initiative is essential since it contributes to their growth. These opportunities develop specific team members based on their strengths and weaknesses. By giving a development opportunity to the member, it will increase their loyalty and commitment toward the project.

3. Feedback

Team members commit themselves to make a study succeeds, and achieving these goals, motivates them to work even harder. The lead needs to share both positive and negative feedback of the members. Members identify their strengths and weaknesses and work on it to achieve great results. It is one of the factors that enable them to improve on their future projects creating a better platform to improve the overall performance of the team. Normally, the manager collects feedback from stakeholders on a yearly basis, and share these comments with each team member. Study lead can collect feedback on a more frequent basis and informal way. This feedback helps the entire team on better handling certain situations and opening the door for better management.

CONCLUSION

There are various challenges that first time study-lead are prone and tend to destabilize their performances. These could affect the overall timeline and quality of the study, which means they should look out to adopt strategic management approaches to achieve the targeted goals and objectives. The study lead should ensure they can cooperate with each of the team members by making it easy to overcome these challenges. Technical management is the key as it required a thorough knowledge of the study, programming, submission requirements, and data standards. They also should have strong leadership skills that will enable them to lead, inspire, and motivate team members towards a common goal. Planning is crucial in ensuring they plan and handle the various tasks that could undermine the success of the project. Managing risks increases the chances of a successful project since it gives the study lead an opportunity to handle these risks in advance. Lastly, open communication is crucial in creating a bond between team members and the study lead. The effective management approaches would generate confidence and trust between the members as well as the first-time study lead that is vital in the success of a project.

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