Chapter 1

1. Introduction

The pharmaceutical industry has a lengthy product design and development cycle and most of the costs occur during the research and development stages (Kaplan and Norton, 1996). Clinical Research Operations and Decisions form part of this unique set of processes for creating value and producing financial benefits once marketing authorization is obtained. To streamline processes and to lower costs the pharmaceutical industry outsources specific tasks in the drug development process to clinical researchers. Services such as identifying investigator sites, monitoring data, processing statistical analysis and regulatory support are provided by study managers. According to Martorelli (2002), in order to meet the competitive challenge to provide speedy services, Clinical Research Organizations (CROs)/Pharmaceutical Industry seem to take one of two tracks to gain a market share: they either strategically plans to become mega-CROs, or they become niche players by being different in meeting industry needs. Industry observers believe that midsize CROs will disappear mostly through mergers and acquisition activities by larger CROs and by non-CROs with a strategic interest in entering the business.

Within few years, analysts predict that midsize contract research organizations will disappear, although niche players with special capabilities will probably survive. Martorelli (2002) has said that, “somebody in the middle without a clearly differentiated service will be phased out”. Therefore, the opinion that to stay in business, CROs/Pharmaceutical Industry will have to scrutinize management processes to cut waste and ensure customer satisfaction because the latter is linked to shareholder value. Mistakes made by them result in dissatisfied customers, and this inevitably increases the competitive advantage of its competitors.

The volatile competitive environment, within which the pharmaceutical industry operates, steadily increases the pressure to help get drugs on the market. This implies that industry needs to utilize resources efficiently to put drugs through clinical trials in order to assist the sponsoring company in gaining and retaining a competitive marketing advantage. CROs are increasingly being relied upon to augment internal resources during peak demands in drug developing activities. In large multinational pharmaceutical companies, there are often more projects to pursue than can be coped with by the internal resources available, and CROs provide a “virtual” and immediate availability of resources.
In addition, the use of these organizations allows a pharmaceutical company to access expertise that may not exist internally, assign appropriate resources to project tasks, and obtain quality strategic input into the drug development plan. A key component in the rush to market new compounds is improved trial designs. Poor study/project design with unrealistic inclusion and exclusion criteria, can sabotage the most promising product vs. products and bring them to a screeching halt.

Therefore, some CROs/pharmaceutical companies diversify their offerings, e.g. study design and niche services leading to reduced trial time and that initiative, could become the hot ticket to reach a larger segment of the market. A trade of is made based on amount of risk vs benefits. The trade-off between the constraints of the cost and time factors and the contradiction that for economical and market growth the company incurs additional expenses needs to be tested by for minimum return on investment (ROI). Although the customers have always been a key element in business, since they hold the checkbooks, the implication of their demands on the bottom-line profits should nevertheless always be considered (Cokins, 2002).

Reduced time from discovery to market is the most prominent homogeneous need of pharmaceutical industry. Answers to the relevant pharmaceutical industry’s question, as to how they can speed up clinical and regulatory steps to deal with the surge in drug discovery, must be found by CROs. Jones (2001) is of the opinion that the tools currently exist within the corporate managerial processes to respond to this challenge as do the methods for streamlining clinical testing of the drugs.

To meet that need in a competitive way, CROs/pharmaceutical industry will have to offer niche services that are not only faster and affordable but also different. To survive the competitive battle, more CROs will diversify in an effort to differentiate themselves from other contract research organizations.

Identifying the needs of the target customer population has important implications that have to be taken into account when formulating a management model comprising niche services that are different, affordable and of high quality. The strategy to exploit opportunities to offer innovative niche products and services, must take into account time and cost management programs developed and accepted over time as best practices. In the 21st century, lessons learned from the past should be built on because low defects, timely delivery and minimal cost – will always remain key elements of business.
Chapter 1: Introduction

Successful management of research projects in a CRO/Pharmaceutical Industry can unfortunately mean different things to different people. If timelines, cost, and performance levels are not defined in advance, any outcome may be regarded as acceptable. People often misunderstand the concept because they have ongoing projects within their company and they consider project management as "the art of creating the illusion that any outcome is the result of a series of predetermined, deliberate acts when, in fact, it was dumb luck." (Kerzner, 2003, p. 3)⁵. Project managers need to be outcome-orientated and achieve predefined target results within the time constraints set by the project scope. Management of the business units entails that project constraints should be managed bearing the following in mind (Kerzner, 2003)⁵:

1. Achieving the project objectives within time and cost parameters,
2. Doing so at the desired performance and quality level, while
3. Utilizing the assigned resources effectively and efficiently,
4. Delivering an acceptable project with a win-win philosophy, and finally
5. Meeting or exceeding the customer’s expectations.

Today’s clinical research study managers not only have to consider the short-term objectives of the projects in the pipeline, but should also think strategically about their company’s position globally and about future business. They have to consider the impact of changing environmental demands on the company. The project manager has to be result-orientated and must monitor the external situation of the pharmaceutical industry closely enough to know when benchmarking results indicate the necessity for strategy changes to be instituted.

Competitors in the pharmaceutical and CRO markets are acquainted with the same fundamental concepts, techniques and approaches. Available for all to follow, the information and techniques can be used by every company manager. Thompson and Strickland (2003)⁶ are of the opinion that the difference in the level of success between competitors lies in the relative thoroughness and self-discipline with which managers develop and execute their strategies for present and future projects.

Visionary leadership is needed to evaluate quality, performance, and price because it is of utmost importance in a competitive market. In an industry with a low throughput time, and excellent quality, the revenue generated will not have to cover the additional time a competitor with a longer throughput and additional reworks will have to cover. The lower the throughput time and number of reworks and related costs, the higher the profitability in relation to a competitor with a longer throughput.
Chapter 1: Introduction

Managing time and performance within budget constraints emphasizes the trade-off between these critical factors, which are vital for successful innovation, and management through the instigation of best practices. When emphasizing a system approach, it should be recognized that even the smallest change in a process could easily affect all downstream activities of an organization. Muir's Law states that if “we try to pick out anything by itself; we find it hitched to everything else in the universe” (Pearce and Robinson, 1997, p. 839).

Trade-offs are always based on the constraints of the project (Kerzner, 2003). This is especially true of activities undertaken in a clinical research study. A delay in one service providing division pressurizes all downstream activities in the other divisions to cut back on timelines to ensure that the final date for project completion will be met.

Effective project management is therefore a prerequisite in a clinical trial where excellence is part of its mission statement, and project completion within predefined timelines can be met without the necessity of crisis management and trade-offs between cost and performance inevitably having to be made. Qualitative data is inadequate to demonstrate the potential of meaningful improvements, particularly in an environment in which revenue and work hours are major determinants of performance and efficiency. The quantitative characteristics of process analysis in relation to time can make the technique a key component to analyze and evaluate processes undertaken by an industry.

It is essential for successful project management of an industry to:

1. Quantify time data generated on the main activities and processes undertaken by the operational divisions, and
2. Differentiate and allocate tasks to the respective activities of each project.

The real opportunities lie in pioneering new approaches to business management, technology, competitors and customers (James, 2000). There are creative strategic options for management to instigate smarter, faster, and creatively different innovative services to customers. Developing a management model for a clinical research will be a valuable management tool for the manager of the 21st century.

Implementation will quantify activities according to real-time, and evaluate the timeline structure according to performance and operational processes for possible improvements. Using a model in which time can be directly linked to activities, can strategize efforts to get to the desired end results of meeting customer needs in a pragmatic way.
Many best practices are described in literature as management models, but a distinct management model for the management of clinical research performing clinical evaluation of drugs in humans, still needs exploration and research. Clinical trials are operating in a strictly regulated environment that can be described as competitive, dynamic and volatile. A combination of best practices as a management tool for a Clinical trial will be useful and the implementation of such a management model will provide the necessary information for the evaluation of problem areas.

1.1 Rationale for research in this field

Clinical research studies are not only for service providing but are also profit driven and have to manage their research time, cost and at the desired performance level of excellence. Cost containing is thus important because the higher a company's cost is above that of close rivals, the more competitively vulnerable it becomes. Therefore, the primary activities and related support activities that create value for stakeholders, i.e. the company’s value-chain, should be identified and evaluated (SAS Performance Management, 2003). Mission orientated, value – adding processes should be defined as the essential activities required in accomplishing a task.

A management model constructed with a focus on essential value adding activities is pivotal to staying competitive and making ever increasing profits (Gourdie, 2001). One of the basic principles for doing business is satisfying the customer and continually improving the business processes. Satisfying customers is important because they are paying for the product or service and want to get their money’s worth. A company that seeks to satisfy customers by providing them with value for what they buy and the quality they expect, will get more repeated business, referral business and reduced complaints and service expenses, e.g. from reworks (Kurtus, 2001). Process management methodology focuses on individual activities within a company. Looking at how different processes interact also requires looking at the downstream impact of what one is doing (Leahy, 1999).

A holistic view to evaluate how well the company performs for its shareholders is essential. CROs, as part of the pharmaceutical value-chain, have to take an objective, holistic view of their business to eliminate non-value-adding tasks and bottle -necks causing unnecessary delays which incur unchangeable costs. The 20% activities that contribute to 80% of the revenue, according to the Pareto Principal, are the chargeable value –adding activities (Koch, 1995). A CRO/Pharmaceutical Industry should know which activities contribute to profitability and which incur unnecessary costs.
Chapter 1: Introduction

Research in this field of expertise is therefore relevant because the challenges of tomorrow have to be met not with the best practices of today, but with new innovative strategies formulated with a futuristic vision of tomorrow. Senior management must have a point of view on what values and behaviours should be encouraged, and what kind of people should feel comfortable working in the company: a view on which new benefits of functionalities will be offered customers over the next decade; what new core competencies will be needed to create those benefits, and how the customer interface will need to change to allow customers to access those benefits most effectively (Hamel and Prahalad, 1994).

The challenges of marketing services in an international business environment, as the world shifts towards an integrated global economy, enforce the need for managers to evaluate and benchmark their services. From a managerial perspective, it is necessary to observe, under standardized controlled conditions, activities and business processes, and to calculate costs of activities to identify areas for improvement. Without the right people, tools and processes a CRO cannot be a leader in the market and stay among the top companies. Research into the activities undertaken and finding out how to increase performance in less time and within limited budgets, can provide the answer to the quest for continual improvement and sustainable competitiveness. Accounting and budgeting data are the most tangible of decision factors considered by decision makers (Woodridge et al., 2001).

The cost effectiveness of projects will not be assessable if all costs are not traced to project activities. The guiding principles for achieving the competitive edge include participative management, which means accountability, responsibility, and authority in the hands of individuals accomplishing the tasks.

These principles are implemented through the cross functional application of an integrated management model for continual improvement and customer acquisition (Jackson and Frigon, 1996). Sustainable competitive advantages in business are only possible if customer acquisition and retention are company objectives. Therefore, an integrated management model that merges the interests of customers as buyers and the company as the seller can be a powerful tool to gain a panoramic customer view; to align and efficiently, deploy resources with marketing opportunities and to measure quality with the final objective of sustainability of a competitive advantage.

This endeavor is grounded in a performance based pricing technique, because in this marketing element, the relationship of buyer-seller is made clear. Emphasis is placed not only on cost to the company and the price, but also on the customer, with an interest in gaining a
Chapter 1: Introduction

market share with his new drug entity. A win-win relationship between the Company and the customer ensures that customers only receive and pay for what they value and that non-value-added service and product components are removed. Customer satisfaction is linked to throughput time and cost, which will be incomplete without the aspects of quality. If companies go with the flow and manage projects without the visionary leadership of tracking actual time with the ultimate goal of staying within predefined timelines, performance and quality, costs cannot be contained nor customer satisfaction guaranteed.

To gain and retain a competitive advantage a pharmaceutical industry must control the time, performance, and quality factors as prerequisites for controlling the cost factor of operations in the endeavour to meet or exceed customer expectations. Any endeavour should start with the end in mind, and meeting the customer’s expectation, is the ultimate goal of any business operation because customers are only retained if their needs are met. Meeting these needs are idealistic but not without problems.

1.2 Why a rational approach?

Managing an organization from a value chain perspective is not easy. Products and services must be managed in such a way that customers are willing to give up resources for them. Approaches to giving customers what they wanted, that may have worked in the past, are likely no longer to be efficient or effective. Today’s dynamic competitive environment facing global organizations, demands new state of the art solutions.

That is why understanding how and why value is determined by the marketplace, has led some organizations to experiment with a new management model – as defined by Robbins and Coulter (2003)17 as: “a strategic design for how a company intends to profit from its broad array of strategies, processes, and activities”. For the purpose of this thesis, the focus will be on the latter part of the definition for a rational approach, i.e. on processes and activities. Business strategy, although pivotal to the management of a business, will not form part of the research and data capturing processes.

1.3 Problem statement

The following problem statement will describe some of the distinct problems relevant to a clinical research and which have lead to the formulation of the objectives for this research. This research was chosen to develop a distinct management approach for a clinical research, undertaking cancer research project as an example, taking into consideration particular activity and time significant to clinical research management.
Chapter 1: Introduction

Any strategy that is undertaken without the knowledge of the resources used is not necessarily geared to deliver the best possible value. “It is not cash that fuels the journey to the future, but the emotional and intellectual energy of every employee” (Hamel and Prahalad, 1994, p. 139). Therefore, it is imperative to evaluate the environment and to understand the capacity and management thereof, resource planning and budgeting, so as to make sure that the emotional and intellectual energy of human resources is applied to the right operational areas.

1.4 Purpose and objective of this study

The main goal for any organization is to generate profits and revenue for the stakeholders. The task of determining how to run a lean and trim operation for any organization is complicated by issues such as manufacturing and operational lead times, replenishment cycles, unexpected surges in demand of a product, review frequency and the failure of establishing realistic target service levels by all involved in the operations.

The need to constantly generate profits for any organization forces management within the organization to evaluate and understand the internal and external factors that have the potential to create the most variance. Management of organizations is a complex process. In turn, organizations constantly seek methods and use tools that will help them understand their operations and optimize their operating processes for higher profits.

These studies by identifying the salient features of Critical Paths Analysis, Meta Analysis and Interim hopes to offer the reader insight into the potential problem areas and methodologies or options that can be used to understand and evaluate the problem. In addition, these studies also evaluate the similarities and differences in the concepts of the different rational approaches in clinical trial decision making process.

This thesis aims to study the following topics

1) To better understand sponsors strategies in the design and execution of clinical trials.
2) To identify factors that may delay, hinder, or lead to unsuccessfully completed trials, and
3) To develop an operational approach of clinical trial decision-making.

It is important to recognize however, that any reader realize that the topic and discussing of this topic is generic and individual organizations might require understanding the internal factors and culture in any organization wanting to implement and use this study. Evaluating the process is however, the first step in any improvement and change process in
Chapter 1: Introduction

an organization. Scheduling, supply chain management and logistic planning in an organization is an important factor in successful achievement of any project.

Rational approaches are undertaken for a number of reasons. This study will identify some of these project variables that involve critical path analysis, meta analysis and interim analysis. It would be impossible to find a realistic definition of project management that did not have, “situation that needs attention,” “plan of action” and/or “implementation of the plan” in the wording of its text.

Most often, projects are generally over budget; they take longer than the projected time; or they simply have the wrong people selected for the tasks. Projects generally have a team assigned to them. Team effort and interaction is integral to the success of the project. The morale, skill and motivation of the team members in the project-team play an important role in the success of the project.

There are many organizational variables such as the structure and systems that affect the decision-making styles. And as a consequence, so is the project management styles implemented by the project leader. Management styles have gone through faster evolutions in the past three decades than they have in the past three centuries. Information and technology available to modern day managers is much better and reliable than in the past. Overload of information however, can be prohibitive. There is the fear that the individual inspecting the records might not be able to filter through the noise in the data, which might preclude arriving at the correct conclusion. Planning and monitoring of the project are more complicated in today’s world of increasing outsourced operations.

No two projects are ever alike. This is true even if the starting variables for each are the same. Many of the internal and external environmental variables, economy of the region, the worker skill levels, cost of manufacturing and doing business and social changes affect project completion. In project management methodology, failure to manage (and control) any one variable can result in the overall failure in completing of the project. Such projects, even when complete, result in decreased profits and lowered market acceptance. With markets becoming more global and organizations operating in more than one continent, the environment has become further complicated. Coordinating efforts and synchronizing tasks has become more critical in this environment. Virtual teams for projects are becoming more common; and the risks associated with these types of project teams are much higher.
Chapter 1: Introduction

1.5 Importance of this study

The mission and the goals defined in the organization are often the guiding factors in any strategy planning. Understanding the core competencies of the organization and supporting factors needed to achieve the objectives should be the bases of any knowledge management endeavor of the organization. Many external factors such as the competition in the industry for the same product or services and business strategies such as customer relationship management, supply chain management and logistics and planning all depend on the understanding of the critical path and critical chain that the project goes through from the start to the finish of the project. In the current marketplace, customers are becoming more aware of the choices available to them. Competition is more on a global scale than on a regional scale for any organization.

Lead times are shorter. Product maturity period is also shorter. Obsolescence of products takes place within a shorter duration of time. Profitable periods are shrinking constantly. Most organizations are realizing that too many poor product launches can cost the company its reputation and consequently its profit margin. By recognizing potential problems that can occur, decision-makers in project management situations can plan and prepare the person accordingly for the situation. Competition is very intense in modern day organizations. Companies are increasingly striving to differentiate their products and services in the market in order to gain higher profits and market-shares.

It is beyond the scope of any one study to completely investigate and study the impact of every variable that has created conditions that can disrupt a project from timely completion or launch. With this in mind, this study aims to identify the relationship between a few variables in clinical trial management, design and analysis. Finally answer some of the questions that typically arise, associated with these tool applications for projects.

1.6 Scope of the study

This thesis only investigates rational approaches or methodologies in a much generalized format. This is without stressing the importance of these factors on any specific industry. For example, the project management needs of the large, complex and randomized trials can differ significantly from the small, simple and non randomized trial. While both industries often use project teams for implementation of the task and completion of the project, the approaches to using these methodologies might not always run parallel in vision of execution. Such approaches will differ considerably even within the same industry based on the internal culture and the mission objectives of the organization in the industry.
Chapter 1: Introduction

Organizations today are also increasingly using virtual project management teams. They are procuring expertise and materials from all corners of the world. Therefore, these processes are even more complicated than in the past. These environments also create their own problems and bottleneck that have to be also considered when studying and process or situation. The need to increase profits and revenues has forced many establishments to try to optimize their resources. Every organization is created to serve and develop specific functions, procedures, and responsibilities. If these goals are achieved properly, the long-term stability of the organization is accomplished; and, in many cases, guaranteed. Increasing efficiency and productivity have always been key factors in implementing any change.

1.7 Motivation of the study

In some ways, explication of researcher motivation at the end of a research programme is more difficult than it appears. The motives prevailing at the end of the programme, driving the effort to a conclusion, are likely to be somewhat different from the ones which originally launched the project — or, at least, related in obscure ways. Originally, of course (as is often the case), my topic was a subject of general interest in need of pharmaceutical company and developing a rational approach.

The initial motivation to study the procedures for accelerated approval arose out of a personal experience: waiting for Fast Track approval of what was thought to be a highly promising oncology drug (one of the new molecularly targeted therapies), making unsuccessful attempts to gain pre-market access to the drug, and ultimately seeing the drug application bungled by the sponsor and rejected by the regulatory authority, meanwhile watching different concepts on uplifting the operational level of pharmaceutical industry. That experience created in me a strong desire to understand what went wrong with this Fast Track drug application, which then led to questions about what happens when new regulatory categories are created.

The central idea of whole research is application of rational approaches and congruent project management & analytical concepts to facilitate success of large clinical trial. Why such application is possible because clinical trial consists of well defined activities often of known duration, clinical trials are very expensive these days – a planned and well understood schedule and resource management will definitely build the quality of the trial study design, effect size and appropriate methodology is very important and clinical trial success based on go or no go principle i.e. trial futility or a perfect decision.
Overall Research Contents 3 different domains:-

1. Critical Path Analysis: - to avoid complexity in schedules, enhancement of project control and handling project constraints for optimized decision.

2. Meta Analysis: - to establish the presence of an effect, determine the magnitude of an effect, resolve differences in a literature and determine important moderators of an effect in the study design and decision.

3. Interim Analysis: - affects decision-making process from the vested interests, and potential conflicts of interest that may influence investigators or sponsors in their decisions about trial methods and potential termination by the approach.

   Rational approaches explained, what is learned during the course of a study or development program into how it is completed, without compromising validity or integrity. The goal of these approaches are making better and more timely decisions to allocate all study resources more efficiently, reduce timelines, and better achieve informational goals compared to traditional study and program approaches.

1.8 Ethics of the study

The research centre was a Pharmaceutical Company based at Ahmedabad. Centre has well developed Department of Pharmacology Research and the said centre of excellence was recognized and certified by the Nirma University, Ahmedabad. The centre has a set of procedures to review proposed research for ethical accountability. The centre has developed a standard level approach beginning with a checklist for self audit to be used for proposed research for which no ethical risks have yet been identified. Higher levels of assessment may be required if ethical risks are revealed in the self audit. In the proposal for this research I completed an assessment procedure and taken required defined coursework and obtained the review and signature of my supervisor. In the subsequent carrying out of the programme, I have made no changes to my purposes or approach that would in any way modify the original goal of the research.

In this research programme, the documentary sources used are publicly available and not ethically sensitive. Given that I am not seeking sensitive, personal, or proprietary information, I have not requested, nor have I encountered, ethically sensitive data. Likewise in study detail I have used simulated data for the purpose of analysis and interpretation of results.
Chapter 1: Introduction

I have not collected personally sensitive information about my workplace. In each formal steps, whether in person or over the telephone, I have asked permission to record, offered the option in publications and presentations, offered the ability to review resulting interview transcripts for accuracy, given the option of reading and responding to papers prior to publication.

Given the relatively uncontroversial nature of my research, there was no justifiable reason to conceal my purpose for these rational approaches to be used in the clinical study, although I believe it was important to position myself in absolute neutrality, is of course impracticable.

1.9 Limitations of the study

This study is conducted using both primary and secondary research method. While primary research can identify the trends and issues in any one organization or pharmaceutical sector, it does not provide a complete and comprehensive overview of every industry. The data that was evaluated for this study was obtained from simulated data of a pharmaceutical company, books, magazine articles, journal articles and other peer reviewed periodicals and the Internet.

This study reflects the common trends observed in the literature reviewed. The literature is largely based on the personal opinions and viewpoints of individuals who have worked extensively in this field. It constitutes an important aspect of the printed and published opinion. Adequate collaborative information was sought and reviewed to present as complete a picture of this topic as possible without concentrating extensively on any one topic or area of concerns. Sufficient collaborative information was verified for any given point of view prior to introducing the concept in this thesis.

There is an advantage to conducting secondary research as compared to primary research. Secondary research methods are cheaper. The time factor is not as critical as in primary research. There are however, some limitations to using secondary data. Primary data collection on the other hand can reveal facts and features of any one industry in the manufacturing field more clearly and comprehensively. Primary research is expensive and also dependent on the quality of the information gathered. The integrity and the quality of the data can become questionably if the population from which the data has been collected is not adequately diversified and independent.

The term “project” can be applied to a wide variety of organizations and an even wider variety of situations. This study will focus on project undertaken by the pharmaceutical
organization. There is no perfect project plan. Every plan has to be tweaked and modified at periodic intervals as the project process progresses. This study does not attempt to define a project plan to reduce risks and improve decision-making.

References:


