A MANAGEMENT MODEL FOR A PHARMACEUTICAL CONTRACT RESEARCH ORGANIZATION

Submitted by

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It is good to have an end to journey towards, but it is the journey that matters in the end.

(Ursula K. le Guin)

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GLOSSARY OF ABBREVIATIONS AND DEFINITIONS

ABC/M	Activity-based Costing and Activity-based Management
Activity	An activity is undertaken as part of the steps to accomplish a task. It is a unique process, function, or task that processes inputs and produces outputs.
Activity cost information	Cost data linked to activities.
Activity capacity*	Expected capacity of an activity under normal operating conditions, with a specified set of resources, and over a long period.
Activity-based costing* (ABC)	Methodology that measures cost and performance of activities, resources and cost objects, assigns resources to activities and activities to cost objects based on their use, and recognizes causal relationships of cost drivers to activities.
Activity-based management* (ABM)	A discipline that focuses on the management of activities as route to improving value received by customer and profit achieved by providing this value. This discipline includes cost driver analysis, activity analysis, and performance measurement. ABM draws on ABC as its major source of information.
Activity model	An activity model is a tool to assist in understanding and defining the organization and can be presented as a hierarchical node tree.
Activity cost pool*	A group of all cost elements associated with an activity.
Activity driver*	Measure of frequency and intensity of demands placed on activities by cost objects. Used to assign costs to cost objects. It represents a line item on a service or customer's invoice or Financial Contract specifying activities e.g. protocol developed, statistical analysis or number of bioanalytical assays.
BC	Before Christ.
CRF	Case Report Form.
CRM	Client Relation Management
CRO	Contract Research Organization.
CBA	Cost Benefit Analysis.
CEA	Cost Effective Analysis.
CEO	Chief Executive Officer.
Control	Processes, information or material that constrain or govern how an activity will be conducted and regulate the transformation of inputs into outputs. It can assure quality and standardization.
Cost object*	Any customer, product, service, contract, project or other work unit for which a separate cost measurement is desired.
CV	Coefficient of Variance.
DoD	Department of Defence.

GLOSSARY OF ABBREVIATIONS AND DEFINITIONS

(continued)

FARMOVS	FARMOVS Research Centre for Clinical Pharmacology and Drug Development.
FDA	Food and Drug Association (of America).
GCP	Good Clinical Practice.
ICH	International Conference on Harmonization.
IND	Investigational New Drug.
Inputs	Resources, equipment, information, or materials to be transformed to produce the output of an activity.
NDA	New Drug Application.
Non-value-added Activity*	An activity that is judged to be or contain non-essential actions that do not contribute to customer value or the organization's needs. The attribute 'non-value-added' reflects a belief that the activity can be redesigned, reduced, or eliminated, without reducing the quantity, responsiveness, or quality of the output required by the customer or the organization.
Pareto analysis*	Identification and interpretation of significant factors using Pareto's rule that 20% of a set of independent variables is responsible for 80% of the result. Pareto analysis can be used to identify cost drivers or activity drivers responsible for the majority of the cost incurred by ranking them in order of value.
PMD	Project Management Division.
Project	A project is a group of activities performed for a customer/client/sponsor also referred to as a study.
Project/study	A project is similar to a study in the clinical contract research environment.
Process	Processes consist of several activities directed to common outcomes.
Productivity	The ratio between the profit generated and the head count (full time employees).
QA	Quality Assurance.
RFP	Request for Proposal.
Resource*	An economical element that is applied or used in the performance of activities. Salaries and materials, for example, are resources used in the performance of activities.
Resource driver*	A measure of the quantity of resources consumed by an activity. An example of a resource driver might be the percentage of total square meter of space occupied by an activity. This factor is used to allocate a portion of the cost of operating the facilities to the activity.

GLOSSARY OF ABBREVIATIONS AND DEFINITIONS

(continued)

Sustaining activity*	An activity that benefits the organization but not any specific cost object. These activities may take place at various organizational levels such as a company's division, or department. Examples of such activities are preparation of financial statements, operational management, and the support of divisional training programs.
Study	A project/clinical trial executed according to a research protocol.
Target cost*	Cost calculated as result of subtracting the desired profit margin from an estimated or a competitive-based price to arrive at, a desired production, engineering - or marketing cost. This may not be the initial production cost, but one that is expected to be achieved during the mature production stage.
Target costing*	A method used in the analysis of product and process design that involves estimating a target cost and designing the product to meet that cost.
Task	A task is an activity required to complete a project at hand.
Throughput*	The rate of production of a defined process over a stated period of time. Rates may be expressed in terms of units of products, batches produced, Rand turnover, or other meaningful measurements.
TIMS	Time Information Management System.
Value-added activity*	An activity that is judged to contribute to customer value or satisfy organizational need. The attribute 'value-added' reflects a belief that the activity cannot be eliminated without reducing the quality of output required by a customer or organization.
Waste*	Resources consumed by non-essential or inefficient activities.

*CAM-I Glossary (2001): Courtesy of Value Creation Group Inc.

CHAPTER 1

INTRODUCTORY CONCEPTS: REFLECTIONS ON CLINICAL RESEARCH AND DRUG DEVELOPMENT

The life which is not examined, is not worth living

Plato

1.1. INTRODUCTION: REFLECTIONS ON HISTORY

Clinical comparative trials have evolved throughout the previous centuries and modern technological and scientific development have steadily increased the pace of evolvement into the new millennium. The idea of a comparative trial is not a modern era concept as it was already known in the time of Elijah in the ninth century BC, however it took physicians 2500 years to learn from this biblical lesson. According to Reidenberg (1999), James Lind did his famous trial in 1774. He compared several different recommended treatments of the day for scurvy and disclosed that one worked, while all of the others were worthless. That was the first comparative trial documented and from there clinical research evolved and steadily became part of drug development. Today clinical evaluation of new drug entities or generic formulations is a global prerequisite to obtain marketing authorization. Governmental Regulatory Authorities require the submission of safety and efficacy data of drugs tested in humans as an integral part of the dossier submitted for marketing approval. Medicinal products are considered illicit unless approved by health authorities. The pharmaceutical company is therefore required to demonstrate quality, safety and efficacy in a long, tedious and heavily regulated process. Kaitin and Healy (2000) reported that the mean length of the clinical phase for an investigational new drug (IND) from filing an application to the new drug application (NDA) submission to the Food and Drug Administration

(FDA) of America, for the period 1996 – 1998, was 70.3 months (5.9 years), and the approval phase (NDA submission and approval) was 16.8 months (1.4 years).

The processes involved in proving safety, quality and efficacy are undertaken within time and budget constraints. Multiple projects running at the same time compete for limited resources to meet deadlines as the ultimate goal. The coordination of an individual project and the general management of the projects running simultaneously, are of strategic importance to guarantee speedy marketing authorization. Isaac Newton bemoaned the fact that he could calculate the motions of the heavenly bodies, but not the madness of people. Many managers today are in the same quandary as Newton was almost 300 years ago. They have to make decisions about complex systems with many interrelated yet unpredictable elements (Bonabeau, 2003). Getting new drug entities for competitive customers through clinical trials in the shortest possible time, needs an accurate model of the complex system's dynamics.

Throughput time and quality are two of the most important customer requirements Contract Research Organizations (CROs) must comply with to compete with rival companies. It follows from the aforementioned that to stay competitive a CRO needs a strategy, e.g. a management model, to manage this vital value-chain to meet customer expectations. Competitiveness is no longer solely about markets and niches, winners and losers, it is about people. There is no final solution, only one that is current. The key, therefore, is in recognizing that the strategy of management modelling should continually be enhanced by new ideas that optimize human resources. All knowledge, eventually, becomes obsolete, or freely available, and thus ceases to be the basis for a lasting competitive advantage. It is not the stock of a company's knowledge which provides a competitive advantage; it is the capacity to innovate, to develop new knowledge, that matters (Hodgson and Crainer, 1993).

Introducing new drugs to the market is becoming more difficult, not only because

of the strict requirements of regulatory authorities and the competitive environment of the industry, but because drug modulation is becoming more complex. Drugs mostly work on the induction or inhibition of endogenous enzymes and the exploration thereof, is largely exhausted. Biotechnology products hold the promise of exciting new treatments for many of the currently poorly treated diseases. The key question, however, is what benefit does a new drug bring, and at what cost (Walley, 2000). Biotechnology may bring new sources of molecules to the market, but this is still an evolving technology, as it may take many years before a return on investment can be expected from this source of research. The search for a new anti-AIDs drug led to sixteen leading companies bringing their research teams together in an R&D effort to bring a blockbuster drug to the market. This was not a humanitarian gesture, but commercial recognition that this is the best way of making money in this area (Hodgson and Crainer, 1993).

The complexity of bringing new drugs to the market puts even more pressure on CROs to be fast, different and cost-effective in the service they offer to the pharmaceutical industry. Therefore, over the past decade the competitive race, from drug discovery to marketing, has greatly intensified the operating environment for stakeholders and it will continue to do so in future (Getz and De Bruin, 2000). With increasing pressure to be first to market new drug entities, role-players along the value-chain need to re-examine every phase of drug development. This starts with exploring new approaches to drug discovery, continues by identifying therapeutic targets that optimize core competencies, and finishes by moving compounds more quickly into and through better-designed global clinical trials. Achieving this ambitious goal requires CROs to modify many traditional approaches to clinical research and the management thereof (Harwood and Neuer, 2002, Mercer, 2003).

The innovation of business processes is necessary, because the competitive pressure to move drugs efficiently through clinical testing to expedite registration

is a costly process, and a pharmaceutical company must invest about US$500[1] million (including US$200 million for dead-end leads) to develop just one new product. Marketing authorization has the objective of achieving high levels of peak sales at the largest possible profit margins. Delays to market can be costly because the opportunity cost of a one-day delay is estimated at $1.3 million in lost prescription sales for an average drug entering the market. The cost of a one-day delay may be as much as 10 times this average for a new blockbuster drug. Should the drug's return on investment be considered, and the product is to be launched within budget but six months late, this return will be 33% less than if it had been marketed within the planned time-frame (Zboralski and Harris, 2001).

1.2 CONTRACT RESEARCH ORGANIZATIONS AS PART OF THE VALUE-CHAIN IN CLINICAL RESEARCH

Newly developed drugs need marketing authorization by regulatory authorities before they may be sold in a country. CROs render services to the pharmaceutical industry to prove that new chemicals are safe and effective for use as medicinal products in humans. Services are provided from the development phase of a new drug to the marketing phase and thus CROs become partners with the pharmaceutical industry and part of the value-chain in the quest to put new drugs on the market. The pharmaceutical industry has a long product design and developing cycle and most of the costs occur and are designed in during the research and development stages (Kaplan and Norton, 1996). CROs form part of this unique set of processes for creating value and producing financial results once marketing authorization is obtained. To streamline processes and to lower costs the pharmaceutical industry outsources specific tasks in the drug development process to CROs. Services such as identifying investigator sites, monitoring data, processing statistical analysis and regulatory support are provided by CROs. The

[1] FARMOVS-PAREXEL's operating currency is USD although quotes are submitted in EUR and US Dollar or SA Rand for local subsidiaries.
The exchange rate on 05 May 2002 was:
USD = 10.47 ZAR; 1 EUR = 9.52 ZAR and 1 GBP = 15.39 ZAR.

outsourcing of these functions to CROs is expected to increase from nearly 30% of current R&D spending by pharmaceutical companies, to up to 50% in the near future. Research and drug development costs have increased steadily from the late 1970's. Pharmaceutical and biotechnology companies are expected to spend around US$43 billion on R&D (growing by 9% - 11% per annum) worldwide (CRO growth likely to decelerate, Script, 1999).

CROs offer innovative services to satisfy pharmaceutical sponsor demands for faster trials and globalization, providing volunteer populations worldwide. According to Martorelli (2002), in order to meet the competitive challenge to provide speedy services, CROs seem to take one of two tracks to gain a market share: they either strategically plan 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 given years, analysts predict that midsize contract research organizations will disappear, although niche players with special capabilities will probably survive. Martorelli (2002, p.1) has said that, *"somebody in the middle without a clearly differentiated service will be phased out"*. Therefore, the researcher is of the opinion that to stay in business, CROs will have to scrutinize management processes to cut waste and ensure customer satisfaction because the latter is linked to shareholder value. Mistakes made by a CRO 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 on CROs to help get drugs on the market. This implies that CROs need 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 through top sales. 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 products and bring them to a screeching halt. Therefore some CROs 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-off is made based on how much good will result versus how much harm. According to GOAL/QPC (2002), systematic innovation should be implemented as a springboard for breakthrough to remove the contradiction, rather than compromising by accepting the harm with the good. For example, to avoid risks involved with unused capacity when projects are cancelled, a number of projects are double booked with the possibility that if none is cancelled, capacity again is a constraint because of the lack thereof. 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 CRO customers. 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 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.

1.2.1 PAREXEL International: Global stakeholder in drug development

The extent of the service PAREXEL renders to the pharmaceutical industry and the competitiveness of the market will be discussed briefly. As the third largest contract research, medical marketing and consulting services organization worldwide, PAREXEL is unique in providing customized, integrated and expertise-based product development and product launch services. PAREXEL has a strong geographical representation in most European countries, America, England, Eastern Europe and South Africa, making the company an attractive partner for both international and local research projects (PAREXEL International and PAREXEL in the Nordic region, 2001).

PAREXEL seeks to help clients maximize the return on their significant investments in research and development, by reducing the time and cost of clinical development and the launching of new products. Outsourcing these types of services to PAREXEL, provides clients with a viable cost alternative to the fixed costs associated with internal drug development and advisory services. Focused on accelerating time-to-market, the company seeks to provide significant benefits to sponsors from this strategy, namely, a faster and less expensive

development and launch process that optimally supports the marketing strategy for the new product under development (PAREXEL Annual Report 2001).

PAREXEL faces intense competition and primarily competes against in-house departments of drug companies and other full service CROs. Some of these competitors have greater capital, technical and other resources than PAREXEL has. Although contract research organizations generally compete on high throughput, other factors are also of importance, namely (PAREXEL Annual Report, 2001, p. 15):

- previous experience;
- quality of services;
- the ability to organize and manage large-scale clinical trials on a global basis;
- the ability to manage large medical databases;
- the ability to provide statistical and regulatory services;
- financial strength and stability, and
- price.

PAREXEL International has 5 clinical pharmacology research units of which FARMOVS-PAREXEL, situated in South Africa, is one. Its geographical situation in the Southern Hemisphere may have advantages for recruitment for trials with seasonal constraints, but the distance from the main sponsors (Europe and the USA) is a negative factor to be taken into account when competing for clients. In addition, there is a growing tendency among drug companies to outsource to a smaller number of preferred CROs. With the global environment being so volatile, especially in upcoming Eastern Block Asian countries, e.g. Czechoslovakia, Romania, and Poland, the need for high throughput within budget and quality is emphasized. The Eastern Block Asian countries are entering

the contract research market with low competitive prices and with steadily increasing quality. A process of democratization in Central and Eastern European (CEE) countries has followed the collapse of the Soviet Union. The decline of the centrally directed command economies of Eastern Europe and the move towards a larger element of *laissez-faire* market-driven efficiency, has encouraged a dramatic influx of international clinical research into the region. According to Reljanovic (2001) regulatory audits, e.g. FDA audits, have confirmed a very high quality of clinical research in most CEE research projects, which makes them attractive partners, in terms of prices, for the rest of the world. India's largest pharmaceutical company, Ranbaxy Laboratories, says it could develop a new drug for just $120 – $180 million, compared with $500 – $880 million in the West, by employing a model built around superior risk management and cost-effectiveness (Script, 2003). CROs with substantial market shares have to take note of the competence acquisition and that India and the CEE may capture a significant share of the future revenues in an emerging opportunity arena. CROs which are presently market leaders, have to prepare themselves to compete for the future. According to Hamel and Prahalad, (1994, p. 125), "(a) strategic architecture doesn't last forever. Sooner or later *tomorrow* becomes *today*, and yesterday's foresight becomes today's conventional wisdom".

FARMOVS-PAREXEL, situated far from the European and American markets, has to correlate costs and performances, qualitatively, and quantitatively, with appropriate technology to be selected as a preferential service provider. To compensate for this negative aspect of being in the Southern Hemisphere, management has to evaluate its global competitiveness. Some clients historically loyal to FARMOVS-PAREXEL have contracted their research projects to CEE countries due to better prices. Therefore, FARMOVS-PAREXEL has to analyze the management of its core business processes in order to evaluate what possible measures should be taken to ensure that waste is removed from processes to improve its viability as a service provider of choice. A management approach

comprising a management model that can analyze the costs of operational processes in relation to the revenue generated, is a necessary requirement, and it should include aspects of best practices to be able to identify critical factors and problem areas for improvement to guarantee a competitive advantage over rival companies. Best practices can be defined as a methodology that identifies an activity as the benchmark by which a similar activity will be judged (CAM-I Glossary, 2001). To maintain a competitive advantage, management needs to be committed to best practices, focused on continual improvement of quality, beyond customer expectations, and at competitive prices.

FARMOVS-PAREXEL is a service providing company but also delivers a scientific report, a tangible product output. Because expensive equipment and programs are used in the operational divisions, the transfer of the overhead expenses to the product output is of importance. Due to ongoing technological developments, sophisticated equipment frequently needs to be replaced by state-of-the-art equipment to keep up with international technological developments in order to stay competitive. Allocating the overhead expenses to process activities and cost centres of the output, indirectly makes provision for the generation of the necessary revenue to replace equipment on a regular basis.

FARMOVS-PAREXEL is profit driven and project conflicts within time and budget may exist. The operational service providing divisions have to be coordinated and managed in such a way that the objectives of the clients are met in spite of in-house bottleneck constraints and resource restrictions. The relevant strategic operational business divisions provide the following services:

- Clinical Division: clinical execution,
- Project Management Division: coordination and management of projects,
- Information Technology Division: technological support,
- Bioanalytical Service Division: analytical determinations,

- Biometry Division: statistical analysis and data management,
- Financial Division: financial and support services,
- Quality Assurance Division[2]: quality control and monitoring support,
- Business Development Division: client relations.

1.2.2 Management of a CRO

Successful management of research projects in a CRO 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). 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):

- achieving the project objectives within time and cost parameters,
- doing so at the desired performance and quality level, while
- utilizing the assigned resources effectively and efficiently,
- delivering an acceptable project with a win-win philosophy, and finally
- meeting or exceeding the customer's expectations.

Today's CRO 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

[2] The name Quality Assurance (QA) changed to Quality Management in 2003.

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 funda mental concepts, techniques and approaches. Available for all to follow, the information and techniques can be used by every company manager. Thompson and Strickland (2003) 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 a CRO 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.

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 CRO. 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 CRO like FARMOVS-PAREXEL, 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 a CRO. It is essential for successful project management of a CRO to:

- trace costs;
- quantify time data generated on the main activities and processes undertaken by the operational divisions, and
- differentiate and allocate costs to the respective activities of each project.

Should an overrun of time seem to be evident, the project manager must know exactly what the cost to the company per day will be and which best practice remedial actions to initiate. At the same time, risk factors, e.g. unused capacity due to project cancellation, should be assessed and managed.

Despite the best efforts of the Food and Drug Administration (FDA) of the US, the pharmaceutical and CRO industries, the time associated with bringing drugs to the market continues to rise (Bruce, 1998). This is due not only to the complexity of developing new drug entities, but also to the ever-increasing *paper war* involved in the bureaucratic red tape of regulatory requirements and approvals to be obtained for clinical trial execution and the submission of a myriad of data and results, before marketing of a new product is possible. The USA and EU governmental regulation processes for drug registration are extensive and demanding. They require standardized processes and documentation on clinical research projects to demonstrate the bioavailability of drugs before they can be

approved for marketing. A CRO's business depends on sustainable understanding and complying with the comprehensive global and governmental regulatory processes. The guidelines regulating marketing authorization, of which the Food and Drug Association of America (FDA) and the International Committee for Harmonization (ICH) are the most general ones, are applicable to every CRO globally, executing clinical research projects to be presented as part of the dossier for the registration submission in Western countries. The conclusion to be drawn regarding an industry that is heavily regulated globally by legislation and guidelines, is that CROs competing for a market share should generally follow the same processes and encounter the same risk factors. The problem statements stipulated in this chapter could therefore well be extrapolated to other CROs. The guidelines regulate the larger picture of *how*, *when* and *where*, but the finer detail that determines the competitive edge and profitability, depends on effective management of the CRO within the constraints of this heavily regulated industry.

Costs continually have to be re-addressed so that wastage is kept to a minimum, in terms of both direct and indirect costs, while maintaining and even enhancing customer satisfaction. Excess costs feed on themselves, creating further excesses and inefficiencies (Johansson *et al.*, 1993). The bottom line is, that winning in the evolving pharmaceutical market of the 21st century, is about being *smarter, faster and different.* In the environment of the new millennium, the big and the slow will be consigned to the margins, where large-volume commodity markets offer *the only* opportunity to sell undifferentiated services, and at declining margins. 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 Phase 1 unit of a pharmaceutical CRO will be a valuable management tool for the manager of the 21st century. Implementation will quantify costs according to real-time, and evaluate the

pricing structure according to performance and operational processes for possible improvements. Using a model in which time can be directly linked to costs, can strategize efforts to get to the desired end results of meeting customer needs in a pragmatic way. Evaluating the cycle time and quality of projects, can give an indication of the performance of a division and its value-chain. The value-chain is a structured way of looking at a business's processes and costs that can be strategically insightful. It involves laying functions and processes out along a conceptual line coinciding with the addition of value during the procurement, production and delivery of the product or services offered. Strategic success is dependent on overall cost, not superiority at each stage of the value-chain. The cost of each strategic process in the value-chain should represent the best that can be attained in that process. Those costs then become an ideal or benchmark against which performance can be measured (Laser, 1999).

The aforementioned briefly describes the environmental demands evident in the pharmaceutical industry. Over and above the competitive environment, it is clear that the cycle time from discovery to market determines the profitability of a new drug. As stakeholders in the value-chain CROs need to manage time, costs and performance to guarantee commitment in realizing these vital objectives, because ultimately they determine sales at maximum profits. To streamline drug development, the clinical evaluation process is outsourced to CROs whose core business is to render clinical research services as part of the global value-chain of drug development. They form an integral part of the pharmaceutical drug development effort.

Many *best practices* are described in literature as management models, but a distinct management model for the management of CROs performing clinical evaluation of generic drugs in humans, still needs exploration and research. CROs 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 CRO, will be useful and the implementation of such a

management model will provide the necessary information for the evaluation of problem areas.

1.3 RATIONALE FOR RESEARCH IN THIS FIELD

CROs are not only service providers but are also profit driven and have to manage their value-chains within 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 should know which activities contribute to profitability and which incur unnecessary costs.

The fact that bringing a new product to market just *one day* earlier, can result in a 1 million US dollar (R1 047 000 000[3]) profit, emphasizes the considerable advantages to be gained by prioritizing activities. Streamlining internal systems and identifying non-value-adding activities to improve efficiency and throughput time to get drugs to market within the shortest time-frame, correlates directly with the profits (Smith, 2000). Streamlining of processes throughout the drug development value-chain needs to be done on a continual base because "If you always do what you always did – you'll always get what you always got" (Bryan *et al.*, 1998, p. xix). 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. Henry Ford is alleged to have said that businessmen go down with their businesses because they like the old way so well they cannot bring themselves to change. But it is not only about change, the future must be imagined, it must be built. 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

[3] Exchange rate used of R 10.47 per USD, 05 May 2002.

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 methodology of assessing the real time of activities and tracing it to cost, was traditionally used in the management of manufacturing companies. However, Wessels (1995) noted from an analysis of the costs of manufacturing companies and those of service-providing companies, that there is no difference in the basic cost structures of these companies. The cost element of a manufacturing company is also present in a service-providing company, that is to say regarding material, labour and other costs relevant to providing the service. However, as a rule these overhead costs are not directly relayed to the final product or output in a service-providing organization. These costs frequently make up the largest part of the total cost. This leads to a greater need for support services and sophisticated equipment in a service-providing company like a CRO, whose overhead expenses are extensive due to state-of-the-art equipment and resources with specialized expertise. 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 endeavour 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 market share with his new drug entity. A win-win relationship between the CRO 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 CRO 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.

1.3.1 Why a Management Model?

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, p. 532) 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 management model, 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.

1.4 PROBLEM STATEMENT

The following problem statement will describe some of the distinct problems relevant to a CRO and which have lead to the formulation of the objectives for this research.

This research was chosen to develop a distinct management model for a CRO, undertaking bioavailability projects, taking into consideration activity time traced to costs significant to CROs. Any strategy that is undertaken without the knowledge of the costs incurred and 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 CRO's value-chain, 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. The following aspects emphasize the rationale for developing a management model as primary objective to ensure service delivery at the best possible rate of return on investment (ROI) and value for the customer and the shareholders.

1.4.1 Price in Relation to Costs and Profitability

Pricing should be based on real-time cost data and a philosophy of adding value

for the customer and the company in relation to performance. Budgeting, forecasting of future revenue and pricing of new projects should be done on scientific evidence and not only by rule-of-thumb or by how much the customer is willing to pay. Actual costs derived from actual time data should be used to budget or quote, to evaluate project profitability and to determine the number of allocated/contracted new projects necessary to reach the predicted growth rate. Relating the cost estimate (quote) to the project time schedule in order to obtain information for planning decisions, the effect a particular cost estimate has on the projects schedule, and *vice versa*, may be considered.

To scrutinize the fees quoted for services and to determine whether divisional services are not over-priced or under-priced, real-time data can be used to determine if services delivered add value to both the customer and company. Projects should not be accepted on a basis of *first come first served*, but resources and expertise must be allocated to profitable projects. If the profitability of projects is not scrutinized, highly profitable contracts may be turned down due to limited capacity. Projects must be prioritized to allocate resources to profitable customers and projects rather than allocating resources to projects with low profit margins due to a *laissez-faire* management philosophy.

With the actual upper and lower limits of project costs known and with the annual marginal growth rate predetermined, the pricing structure can be formulated. The average number of projects that need to be contracted to realize the predicted economical growth rate can then be determined for the budgeting process with a win-win relationship between the customer and CRO. The number of contracted projects in relation to the number of requests to quote is also an indication of the acceptance, globally, of price, performance, and competitiveness.

For benchmarking purposes, a company can only look at its own costs and quality, because information about competitors will generally not be available. Prices derived from profits added to costs with a win-win philosophy also to add

value to the customer, should be a CRO management objective. In a highly competitive global market in which the use of the psychology of pricing keeps customers returning, the above-mentioned variables need scientific exploration and quantification.

Part of the research problem was to evaluate the fees quoted and the profitability of projects. According to Fox (1991) when submitting a bid for a research project there are two important concerns: what are your costs, and what are your competitor's costs? The only guide to a CRO competitor's costs is a company's own costs, but the cost objects that incurred the costs must be scrutinized to ensure that no waste is present, because the bid reflects the present value of future cash-flows. If a CRO quotes a narrow margin merely to be successful in a bid, it can be expected that its profits will also be low. FARMOVS-PAREXEL must evaluate actual costs in relation to its quoting system as well as the hit rate of quotes (the number of quotes accepted). The information gained from such evaluations is of importance in evaluating the company's short-term project profitability and long-term strategies to ensure that it is not losing its competitive edge. The activities driving time and costing factors during the execution of bioavailability projects/studies should also be identified. Process costs in relation to the quotes can be evaluated to ensure that the fees charged will cover the operational costs of the relevant divisions and that the desired profit margin will be achieved. The profits generated per head count and expressed as the productivity can be used to forecast revenue growth potential and optimal resource utilization.

1.4.2 Throughput Time and the Coefficient of Variance

The coefficient of variance (CV) calculated for process time is an indication of the time variation of the operational processes, i.e. the throughput time. Large variations in the execution of processes due to unforeseen events are a risk factor to be managed because of the cost and time implications they will have on the project. Especially if a price incentive as part of a performance-based

management model is implemented, process time should be predictable to ensure a win-win situation. Variation in process time, if quality is not at the desired level or *waste* is present in processes, will result in reworks leading to non-value adding time. Resource capacity that could have been allocated to value-adding activities will have to be allocated to repeat tasks. Therefore, *do it right the first time* should be established as corporate culture.

Cycle time is dependent on performance and quality. The coefficient of variance of operational services is an indication of process variation because of variation in throughput time, quality and process control. Pricing of services related to a quality and cycle time strategy should both seek answers to the question about where employees spent their time, because any activity, value adding or non-value adding, consumes time and resources, which drive costs. Management of these cost objects, e.g. customers, and continual improvement of the activity processes to acquire excellence with as little variance possible, are important. A quality output with as little variation in activity processes as possible needs to be developed, not only as a deliberate act, but as a corporate habit, a part of the culture.

Conforming to quality is inevitably part of customer satisfaction and maintaining a competitive advantage. To gain and retain a competitive advantage needs innovative and motivational leadership with a focus on continual improvement of performance. The endeavour to reach out continually to excellence and quality in project services is a never-ending process involving everybody and can only be achieved through people. Therefore, ongoing performance improvement to execute activities at a predicted quality level and timeline implies continual change which employees have to adapt to. Resistance to change is part of human nature. However, to achieve excellence change should not only be involuntary, intermittent deliberate acts but needs to become general practice in such a manner that the corporate environment of ongoing change and innovation becomes corporate culture. Quality manifested as part of the corporate culture will also

result in the retention of staff and therefore the retention of competence within the company.

1.4.3 The Number of Quotes, Price and Pareto's Law

The number of quotes issued in relation to the number eventually contracted to FARMOVS-PAREXEL is an indication of the historic trends of existing sales and the number of companies contributing to 80% of the contracts executed at FARMOVS-PAREXEL. The psychology of pricing to keep customers returning to FARMOVS-PAREXEL raises the question as to what the right price is for a specific customer.

If Pareto's Law is also applicable to CROs, it is of interest to know which customers contribute to 80% of the contracts executed at FARMOVS-PAREXEL. Those customers should be identified as well as those who do not contribute to the net revenue and are considered as a risk and burden to the company. Foreseeable benefits and anticipated risks associated with customers should be managed. Not every customer is profitable to the company. Therefore, should a general price be used in bids for all customers or should prices be based on performance, not only of the service providing CRO, but also of the customer?

Projects should not be accepted unconditionally, but should be evaluated for profitability according to a customer rating scale of valuable customers, potential new customers and risky customers. The number of quotes/bids submitted per client is evaluated to distinguish amongst the clients, i.e. those contributing to 80% of the revenue and those who are only a burden to the company. Clients not making a substantial financial contribution to the company's net revenue should be identified and categorized according to profitability.

The following sections will outline the objectives of the study and the methodology followed in this research project. the objectives are formulated from the perspective that an effective management model for a CRO should enhance

informed decision-making regarding what is of ultimate importance to its core business: throughput time, costs and optimal resource utilization, customer relations, imperatives for bottom-line profits, that which the shareholders are interested in.

1.5 STUDY OBJECTIVES

Considering the importance of the management objectives of time, performance and quality in relation to cost, a CRO has to manage these variables not only to meet customer expectations, but also to ensure that the profit margins for the organization are achieved. The aforementioned variables can only be managed if they are brought under control and they can only be controlled if they are known and quantified factors. To investigate the actual cost and time involved in generic drug evaluation processes, the development of a management model based on the methodology, which resolves around activities traced to cost, time and performance variables, was the objective of this research. Therefore, real-time costs of processes and activities undertaken were evaluated against best practices described in literature that will be pivotal in the management of a CRO.

Realizing the following objectives will contribute to the effective management of a CRO striving for excellence in products and service through the construction of a management model comprising the best management practices. Emphasis on the management of customer relationships, as well as time and costs as an objective in every activity undertaken, can enable an organization to manage its profitability. The following objectives are of importance in the management of a CRO if effectiveness and excellence are part of the mission and vision the organization strives for.

1.5.1 Primary Objective

The primary objective is to develop a management model with a customer focus for a Phase 1 unit of a pharmaceutical CRO. To formulate the model, process time and cost data were gathered and the Secondary Objectives were analyzed to

support the constructing of a generic management model for a pharmaceutical CRO.

1.5.2 Secondary Objectives

The following secondary objectives will support the primary objectives. Firstly, the input cost of projects was analyzed to make recommendations on the best competitive price structure for a CRO. Secondly, costs and throughput time were evaluated to identify cost drivers. If throughput time is predictable and variations in process time controlled, costs will be contained. Thirdly, the projects contracted in relation to the number of requests received were calculated to determine if the Pareto Law is followed and 80% of the company's business comes from 20% of its customers.

1.6 RESEARCH METHODOLOGY

The research methodology followed in this study was limited by the competitive and confidential nature of CRO activities. The research design and methodology were therefore in accordance with a case study perspective and the project data available at FARMOVS-PAREXEL were the only data analyzed. The project processes of 30 projects were analyzed with an activity focus. In the collection of actual time, cost centers, cost elements and cost drivers were identified and traced to costs incurred by operational activities. The technique to capture actual time in relation to cost is derived from a process analysis focus where time and cost variables are the centre of the methodology. In this research actual time of processes was calculated and traced to the cost and overhead expenses incurred by each process. The costing of real time was used as a complementary tool because the process analysis was considered as an appropriate tool for data collection. The research methodology will be described in more detail in Chapter Four. The following Study Synopsis (Section 1.7) gives an overview of the dissertation.

1.7 STUDY SYNOPSIS

Title of the study:	**A MANAGEMENT MODEL FOR A PHARMACEUTICAL CONTRACT RESEARCH ORGANIZATION**
Research investigator:	Yvonne Jacobs
Study centre:	FARMOVS-PAREXEL Clinical Research Organization Campus Avenue South, University of the Free State 9301 BLOEMFONTEIN, SOUTH AFRICA
Data collection period:	Data gathered from studies contracted from September 1999 to October 2000 and executed until June 2001.
Design of the study:	An explorative research project with the design classification of an empirical, textural and numeric exploratory and descriptive analysis regarding case studies executed at FARMOVS-PAREXEL.
Study objectives:	***Primary objective:*** • The primary objective is to develop a management model with a customer focus for a pharmaceutical CRO. ***Secondary objectives:*** • The input cost of projects was analyzed to make recommendations on the best competitive price structure for a CRO. • Costs and throughput time were evaluated to identify cost drivers. • The projects contracted in relation to the number of requests received were calculated to determine whether the Pareto Law is followed and 80% of the company's business comes from 20% of its customers.
Methodology:	Primary data sources were numerical and textural, obtained from activity, time and cost inputs of relevant projects. Secondary data was obtained from literature and the Worldwide Web. Validity and reliability assessment was done with an estimated ideal time calculated and compared to the actual time variables. Sample size n = 30 bioavailability projects. Statistical analysis was done with SAS Version 8.2, a statistical linear regression model and a productivity model.
Main criteria for project selection	**Project selection:** Research projects contracted to assess the bioavailability of two or more medicinal products. **Time period:** Projects with final scientific report submitted to sponsoring customer. **Project design**: Phase I studies, two- to four-way cross-over, multiple or single dose bioavailability studies. **Criteria for project inclusion into analysis:** Completed report at

time of analysis.

Results

Variables traditionally presumed to have an effect on time and cost factors were analyzed to determine which variables univariately associated with the dependent variables ($p<0.05$), have a statistically significant effect on time and cost. The variables proved to have a significant effect, i.e. if determination of a metabolite occurred, or if business was done with relatively large pharma companies, or if protocols were amended, they were entered into a multivariate analysis using a linear regression statistical model, with the end result that project mutation, i.e. protocol amendments, statistically significantly influenced cost and time factors.

The maximum productivity potential was determined by using a productivity gradient model, ($m = \Delta y/\Delta x$) calculated as the % profit divided by the head count. The maximum productivity potential was predicted using the gradient of the most profitable division (the Bioanalytical Division) as the output potential for every unit. This gradient is equal to the incremental % profit, divided by the head count per division. The above-mentioned gradient can be used to calculate the predicted head count (resource allocation) in order to achieve a projected output.

Conclusion

The results confirmed that project mutation, i.e. protocol amendments, had a statistically significant effect on the cost and time factors of a study. Conversely, concepts that seem to be realistic and relevant, e.g. that sample size, number of clinical phases and method development have a significant cost and time effect on study execution, were proved to be figments of the imagination. The results indicated that these variables have no statistically significant effect on study cost and throughput time. The pricing tool with which management calculates fees for services, needs to incorporate this information.

The 20/80 Principle of Pareto is also deployed in CRO business endeavours, consequently 80% of the results come from 20% of the effort.

The conclusion is drawn that a management model for a CRO revolves around a linear regression and productivity model, to assess the statistically significant effect of time on costs that, in the end, erode profitability.

1.8 CONCLUSION

We are caught in an inescapable network of mutuality, tied in a single garment of destiny. Whatever affects one directly, affects all indirectly.

Martin Luther King

With comparative trials evolved over centuries and with the continual development of science and technology, it may be argued that the mega-opportunities of the tomorrows will only be available to those companies who diligently positioned themselves in line with this development. To cash in on future innovations, CROs will have to develop niche services to satisfy industry's need for speed, differentiation, and affordability. To unlock potential markets in the highly competitive pharmaceutical industry, they will have to overcome hurdles of waste and reworks both of which have an impact on costs and the urgency of speed, which are pivotal in drug research and development. The perspective of this research is to identify activities, costs incurred, and the necessity of these critical factors in the endeavour to satisfy customer needs. The customers, carrying the checkbook, are inevitably the reason why a CRO is in business, and has a direct influence on the revenue generated, giving them a powerful point of leverage in any CRO. It is therefore necessary to review the customers as a cost object, their demands for services, corollary driving resource expenditure and the CRO's ability to control and recover these costs. The methodology based on tracking resource activities related to costs, is at the core of a variety of best practices with a customer focus.

Activity-based information systems are considered useful techniques to analyze activities and costs. The results obtained with these techniques provide information for financial decision-making and to pre-empt the re-engineering of processes. It follows that it will be useful to incorporate the methodology in a

management model for a CRO. The following two chapters will describe a few of the relevant management models considered as best practices pertinent to the construction of an effective management model for a CRO. Such a model should ensure that the data captured represent the dynamic process flow, the costs incurred in each endeavor and the impact of customer driven demands on resources.

CHAPTER 2

MANAGEMENT MODELS AND BEST PRACTICES

Financial performance is the result of operating performance and operating performance a derivate of human performance. The latter includes all the things that a company must do to win the competitive battle in its industry to attract, retain, and profitably serve customers. It varies greatly among industries, but generally includes activities such as customer acquisition, on-time delivery, developing new services and products, and running the company efficiently (Shapiro, 2002). These performance attributes comprise the objectives relevant to a CRO striving to keep shareholders happy. The challenge to create value for all interest groups through resolving a combination of dilemmas, i.e. to deliver greater variety, higher quality and more speedy throughput time at low costs, may be considered to be impossible. However, successful firms use strategic innovations to get ahead with a competitive advantage and stay ahead (Baden-Fuller and Stopford, 1993).

2.1 INTRODUCTION

According to Miske, (2000) the key to significantly lowering costs lies in understanding and controlling processes. The latter can only be controlled and understood if activity-based information is available through communication with the operating teams and customers; if root causes of problems are identified and prioritized, and re-engineering of processes together with action plans for improvement and change are implemented. The measurement of *as-is* process performance is necessary to set the baseline for change and for *to-be* processes that need to be implemented. With the input of benchmark opportunities and the evaluation of management models with a focus on activity-based information, a model can be constructed to established *best–of–class* performance to enhance

profitability.

2.2 MANAGEMENT MODELS

A management model is the organization's core logic for creating value. Therefore a successful management model will offer unique value, is hard to imitate or recreate, can easily be altered and is grounded in reality (Linder and Cantrell, 2001). Whereas business strategy is primarily about the overall positioning of a business within the business ecosystem, the term "management model" also includes key structural and operational characteristics of a business. In other words, when used properly, *management model* is a broader description of a business than just its strategy (Magretta, 2002).

A decision must just be taken when a management model is constructed as to whether the model will be used at a strategic level. This will significantly influence the extent of the activity analysis undertaken to formulate the model. If the model is only to be used by management as a high-level review tool, then the amount of analysis could be aggregated to a much more manageable level. Conversely, if strategic cost management is the key objective, then it may be necessary to go down to the level of individual tasks. It must be noted that the law of diminishing returns is highly applicable when comparing the objectives of the project with the effort, cost and accuracy of its outputs (Naidoo, 2002).

To construct a management model for a CRO, activity modelling is an essential component to establish the value-chain of the business. Because large systems and processes are difficult to understand and can be confusing, a model can provide a method for capturing, organizing and documenting the information about the business processes or systems in a visual way. (2002 d) describes a company's management model as comprising the internal business processes and the way the company engages the market. A model can be defined *as a representation of a complex reality* (Federal Aviation Administration, 2001). Modelling is the act of developing an accurate description of a system. Activity

modelling is the act of developing an accurate description of the activities performed by a system. When a process is modelled, the inter relationships of the specific activities the process consists of, at any level of detail, can easily be demonstrated. This allows critical analysis of each activity that comprises the process in the search for improvement opportunities. Because the facts about the activities are displayed in both graphical and narrative form, this analysis can be objective, rather than subjective. Problems with a process will be visible if they exist. In the most basic sense, a management model provides the mission to accomplish the vision: it is a method of doing business by which a company can sustain itself – that is, generate revenue (Sound Business Practices, 2003). The management model spells out how a company makes money by specifying where the profitable processes or activities are positioned in the value-chain. Some models are quite simple. A company produces a product or service and sells it to customers. If all goes well, the revenue from sales exceeds the cost of operations and the company realizes a profit. However, business processes are generally more complex, the modelling of businesses continues to evolve, and in many models, the concept of feedback is employed. In general, this refers to any process by which the service provider obtains information about whether and how the intended receiver has indeed preserved the received service. It is about developing performance for growth and change (Wadenhoe, 2003).

In business management, modelling it is not only of importance regarding how the customer has perceived the company's service, but also from management's point of view customers, products and transactions should be scrutinized in a methodical way. Managers should determine which customers, products and services do not fit their management model. By doing this, they will answer whether the company is managing profitability effectively and whether key managers' actions are aligned. Business process improvement is here to stay because CROs have to find ways to do more with less and provide a better service in the minimum amount of time. Speed, quality, process variability and cost are

the drivers of the need for process improvement and are thus important variables to build a management model on. CROs must become more focused on what these three variables as cost drivers mean to the company. Trade-offs between these variables at the expense of stakeholder satisfaction is possible, because companies can sacrifice product or service quality to gain speed by pushing employees to work harder and faster. However, rushing products to market with little testing could reduce customer satisfaction. Trade-offs at the expense of speed are also possible because speed can be eroded by the slowness of decision making in an inverted company; for example the ones used to increase stakeholder satisfaction, can reduce speed because of negotiations and frequent project mutations. Truly hyper-competitive organizations will find ways to eliminate the trade-offs. Trade-offs exist only if firms believe that they are necessities and stop looking for ways to do both alternatives. After all, it was once said that firms could not achieve low cost and high quality at the same time. Now this is not just a reality, but a necessity for survival in many industries (D'Aveni, 1994).

The generalization of organizational models is not possible because there is no universal model that can cater for individual company needs. According to Drucker, (in Herrero, 2000) there is no one best way to be organized. The general *rules-of-thumb* and *one size fits all* models are not the best ways to make critical strategic decisions. Micro modelling is a better option as it can give managers a more realistic picture of the options and help ensure that resources are appropriately allocated (Newsletter, 11 March 2003). Organizations are a result of ideas; people's interactions, goals, history, and geography and successful organizations do not correlate with any particular architecture. The business-operating model should fit the environment and culture of the people working there. For the best management model one should look around, benchmark well-run companies, and formulate a distinct model for a CRO from best-in-class models available.

A management model is the organization's core logic for creating value.

According to Linder and Cantrell, (2001) it is specifically:

- the set of value propositions an organization offers to its stakeholders, along with the operating processes to deliver on these;
- arranged as a coherent system, that both relies on and builds assets, capabilities and relationships, in order to create value.

Modelling has little or no value of its own. A model is a tool to assist professionals to understand their current environment. It is employed by professionals as a mechanism to improve business (CIM, 1993). According to Linder and Cantrell, (2001) successful management models share three characteristics:

Firstly they offer unique value – sometimes in the form of a new idea, a combination of product and service features that offers more value or lower prices for the same benefit.

Secondly, winning management models are hard to imitate. By establishing a key differentiator, such as customer attention or superb execution, these models build barriers to entry that protect their profit generating mechanisms.

Finally, successful management models are grounded in reality. They are based on accurate assumptions about customer behaviour. Their cost structures are linked to their revenue to indicate on a daily basis where in the value-chain they make their money. Many organizations lack a clear understanding of where they make money, why customers prefer their offerings, and how many customers actually scavenge company revenue generated by other customers.

A model is a representation of a complex reality and can be said to be the act of developing an accurate description of a system. Since organizations compete for customers and resources, a management model must highlight what is distinctive about the organization – how it wins customers, woos investors, and earns its

profits.

Lessons learnt from other industries can be applied to a management model for a CRO. A generic management model for a CRO should focus on project cycle time and process constraints resulting in delays in throughput time and project closure or non-profitable customers complicating the throughput time of other projects, which contribute to the risk of unused capacity, possible bottlenecks and non-value adding activities. Surveys of manufacturing executives in large successful companies in Europe, the USA and Japan, repeatedly rank three time-based characteristics among their top five competitive priorities to focus on, namely (Smith, 1995):

- dependable delivery;
- fast delivery, and
- rapid design changes.

CRO's, as part of the drug development chain, operate under these constraints and have to be committed to the above-mentioned parameters to expedite time to the market. Blockbuster new products have a short window period for top sales to gain economics of scale, before new developments start entering the market. Every activity undertaken in a CRO, such as partnering with the pharmaceutical industry should therefore be scrutinized for cycle time and bottlenecks to cut down on waste and to optimize the drug development process.

With the advent of competition on the horizon, CROs should realize the importance of understanding the customer and the total cost of providing research services to industry. These factors should be the focus when an effective management model for a CRO is constructed. According to Salisbury (1999) the key results to be obtained with the implementation of a management model are as follows:

- Identification of direct and indirect costs.
- Understanding of profitability by customer segment.
- Identification of activity costs by service territories.
- Ability to obtain per unit output costs.

In achieving long-term commitment to customer excellence and defraying the costs involved with meeting their demands, the CRO needs to have influence, needs to be profitable and needs strategic thinking and evaluation. The CRO should identify unprofitable customers and exploit ways to turn them into profitable customers. Market segments that are not optimally exploited need exploration because they may offer new business opportunities and the possibility of service diversification. Success in the market-place means profitability, but success is not permanent. Success and profitability can only be attained if profitable customers are obtained and retained.

The aim of this research is to compile a model with a focus on the above-mentioned, therefore to end this chapter the next sections will be used to discuss steps and techniques relevant to building a management model. An activity analysis and management modelling will help an organization to understand the first step in improving its business practices. The focus of this research analysis will be to document the current baseline, the *AS-IS*, and to project functional process improvements in the future as *TO-BE* processes.

2.2.1 Management Modeling and Pricing

Risk-benefit assessments of customers, projects, and unused capacity due to project cancellation, actual time and lag time of processes, are an integral part of business management and have a direct influence on profitability. FARMOVS-PAREXEL, as part of the global PAREXEL, has to meet the estimated revenue numbers and reach predefined marginal growth rates. Information gathered in a structured way on the activity time and costs of projects will enable management

to determine whether set targets will be met by monitoring forecasted and actual realization of revenue. Informative decisions can be made and the following can provide a knowledge base for financial decision-making:

- The methodology of pricing, based on actual performance, can be modelled as performance-based pricing with which actual costs can be covered in a profitable and win-win relationship between the CRO and the customer.
- An indication of the actual mean time of activities will ensure that the customer is not undercharged but that real costs to the company are covered. Data on cycle times provide the information for target-based pricing advantages, e.g. target-pricing.

Data on cycle times provide the information for performance-based pricing advantages to determine the shortest possible time-frame for a project, which can be used to calculate incentive objectives if the project is completed in a shorter time.

Rule-of-thumb pricing is usually based on what it is supposed the client will be willing to pay. However, the pharmaceutical market is a highly competitive and volatile market and for this reason pricing by *rule-of-thumb* cannot be considered as a best-practice method to employ. Strategic planners and those working on the 2004/2005 budget must be asking themselves whether business will carry on as before or if significant changes in the markets may be expected.

According to Brown (2001), GlaxoSmithKline purchasing managers must undertake to cut their costs over the next 3 years by 7% per year. If one of the largest pharmaceutical companies globally expects service providers to cut costs to retain their business, it could well be that the only CROs to do business with them will be those who can provide services without yearly price increases. The difference from historical trends may well be that price may no longer escalate with inflation.

The profitability picture that emerges from a management model with an activity analysis traced to real-time costs will help managers focus their attention and energy on improving processes that will have the biggest impact on the bottom line, i.e. the net revenue. This methodology will show how processes are linked to the generation of revenue and at the same time to the consumption of resources. By highlighting those relationships, an activity focused management technique can help managers understand precisely where to take actions that will drive profits (Cooper and Kaplan, 1991).

The demand for activities and related costs is always a result of the demand for different products or services, but is often generated because of individual client demands. It is therefore important for an organization like FARMOVS-PAREXEL not only to analyze the quality and cost-effectiveness of their service output (e.g. the analytical and final scientific report) but also to develop a focused customer strategy. As early as 1985, Porter (1985) predicted that from a strategic cost perspective, to have a strategic competitive advantage, a company should:

(i) Define its value-chain and assign costs and assets to activities.

(ii) Identify the cost drivers regulating each activity.

(iii) Examine possibilities of building a sustainable competitive advantage either through controlling cost drivers or by reconfiguring the value-chain.

This is still valid in the new millennium.

Pricing has a direct link to profits and is therefore the bottom line of business and a management model. It has a dual effect, on the one hand for the customer as the buyer and on the other hand the seller or service provider, e.g. a CRO. Pricing should not be rigid and formulated as *one price fits all,* but cost pertaining to special customer-demands should be taken into account. In contract research, some customers can be categorized as very demanding. CROs must know their customers and be careful not to be price takers but price makers. That means they

should be careful not simply to lower prices to capture market share or just to sign up a large customer, they should be careful not to let their ego get in the way of good business sense. A CRO should take heed to assign costs to resources and accordingly price its core services rendered in a structured model with a unique pricing psychology. According to Shapiro (2003), there are seven steps toward quoting a unique price that will be accepted by customers as justified:

Step 1: *Create customer value*. There are two parts to the creation of customer value. On the one hand, the CRO must provide a reason for the customer to do business with the organization. Focusing on the core customer values of convenience, availability, service functionality and relationship, creates a reason for the customer to sign a contract with a CRO. On the other hand, reasons for the customer not to do business, e.g. factors like low recruitment rates and quality, timelines not met and incorrect billing, should be eliminated.

Step 2: *Choose your customers*. The corollarfy to providing customer value is to choose customers where the value is recognized. Managers are beginning to understand that it is impossible to provide a meaningful reason to contract an outstanding service to all customers in all research situations. It is necessary to fit capabilities to the project or customers' needs and to match the research requirements to the CRO's capabilities. The CRO must focus its capabilities where they will mean the most to the project in question and to the customer. The real secret of being a price maker is to walk away from business if the CRO cannot provide superior value. Excellence in contract research business is to focus only on the market segments, defined by customer set or bid situation, to which the organization can bring superior value, as perceived by the customer. It is important to understand that both the perception of value and the reality are important. Some customers really have no interest in the special capabilities of the CRO. Such customers must be avoided. Management must also avoid prospective of customers who cannot perceive their superior value. Simply put, schizophrenia in business is fatal. A CRO must have an innate culture that

approximates a unique value, provided to a unique set of customers or contract situations.

A CRO is often asked to put in a bid to provide a service for which either the research service to be rendered or the customer can be defined as fitting the aforementioned scenario. The market segment that CROs operate in make this step valuable to incorporate into a management model if excellence in business operations and economic growth are company objectives.

Step 3: *Be different.* Many CRO managers may talk about uniqueness, but when the going gets tough, they attempt to imitate competitors. To be a price maker, *be different* is a prerequisite! The difference can be in the nature of the customer value created, the way it is created, or for whom it is created. The more different a CRO manages to be in its operations, the greater is the opportunity to set its own price. The window period for a differentiated product or service is unfortunately short and it will soon become a commodity defined as "undifferentiated" and expected by customers. A CRO like FARMOVS-PAREXEL, situated in the Southern part of Africa, needs to be sustainable in its innovation to be attractive as a service-provider of choice – compared to centralized European CROs with low labour costs.

Step 4: *Keep it simple*. The proverbial saying of, *don't shoot yourself in the foot,* is applicable if the CRO is mismanaging and complicating its own service line. Many companies offer many variations with minor differences that customers are encouraged to trade down to lower margin products or services, or just become so confused that they will not commit to signing a contact. It is difficult enough to compete with others in the industry, therefore one should be aware not to compete with oneself! The more simplistic service offerings have proven the easiest to manage, and in the long run, the most profitable to offer.

Step 5: *Determine customer value.* Develop a way of charging relative to customer value for each process transaction, based either on expedited timelines

met, the quality or the quantity of value provided. Often services can be priced not just by quantity, but also according to the performance or quality provided, the percentage of cost savings or a CRO may charge more for a project completed ahead of the deadline on the premise that time is money. There are many variations to performance-based pricing which may also include penalty clauses. The idea is that a CRO should base price on the value the customer receives and not so much on what he is prepared to pay.

Step 6: *Deliver on your promise.* If a CRO does not deliver on his promise, his customer will have a good reason to negotiate price. Happy customers whose expectations are met tend to dwell less on price, and generally to pay more quickly than dissatisfied ones. A CRO must rather under promise and over deliver than *vise versa*.

Step 7: *Be courageous***.** The final requirement is the simplest, but the most difficult. In large transactions, customers will emphasize price negotiation. During the process, it will be tempting to cut prices to retain the customer or to gain market share. But, if a company erodes the integrity of its price book, it becomes a price taker, not a price maker. For example, if a price is set and announced as not negotiable, one must not negotiate. Once management begin to negotiate, they cannot be a price setting company.

For a CRO to be different, to provide a service perceived by its customers as real value and to be particular in choosing its customers, requires courage and visionary leadership. However, one of the most useful mechanisms for guiding restructuring of the pricing structure is cost driver analysis. Cost drivers cause activities to be performed, and they may be positive (customer orders) or negative (customer complaints). By eliminating negative cost drivers, associated activity costs will also be reduced. During the data collection phase, each activity is identified as being either mission or non-mission related. Employees may be spending a disproportionate amount of time on activities that are not directly

related to the mission of their work group. Attempts to restructure the organization should be directed at shifting effort to mission-related activities. For example, the question as to whether the members of the marketing department are actually marketing or resolving financial problems, or preparing department reports, can determine whether the activity is mission related. Only the first activity contributes to their department's mission (Carlson and Young, 1993). Customer demands which result in negative cost drivers should be identified, e.g. customers who frequently experience drug formulation problems and are not able to provide the test drugs on time, with the result that the trial needs to be postponed. The CRO is then faced with the problem of unused capacity as a result of the rescheduling or cancellation of the trial. Such customers are cost drivers and should be managed, from the planning phase, with penalty clauses included in advance in the Financial Contract as remedial options.

Although costs are important and should be monitored and controlled, a CRO must ensure that cost reduction *per se* does not remain the overriding priority. Cost reduction just for the sake of lower expenses can impair performance and quality. Over and above the implementation of cost control and cost reduction systems, methods should be implemented to make the system work better operationally. Examples of these methods are reducing setup times of the bottleneck processes, reducing throughput times and postponing product mutation, e.g. in cases where customers keep on demanding changes to the design of a research project and delay project initiation or closure. Demands for project mutations result in processes being repeated. However to be cost-effective a CRO must aim to: *"Remove the trivial many, to focus on the vital few"* (Thacker, 2001, p. 3). Too many non-value adding activities complicate operational processes and should be reviewed for cost-effectiveness, so as to do it right the first time.

According to Palmer and Green (1999) performance should be measured and evaluated in four dimensions:

- Quality: The number of times it takes to "re-work" a task because of faults in the process.
- Productivity: The number of people needed to process a given output.
- Cost: The cost per task or unit of activity.
- Cycle times: The amount of time it takes to complete an activity.

The researcher regards the above-mentioned as the most important principles for a management model. The following sections will therefore briefly discuss models with a customer focus comprising dimensions of cost, quality, cycle times and productivity.

2.3 BEST PRACTICES AS INSTIGATION FOR A BUSINESS

Quality, cost and cycle times are of primary importance to a CRO because the behaviour of customers has changed the way in which competition is viewed. Companies are forced to do better because customers are not going to stay around if they do not. Meeting the objectives of marketing a new drug in the shortest possible period and of a predefined quality, sets the rules in the competitive battle to competing through speed, i.e. being able to satisfy changing customer needs quickly, accurately and quality-wise as the drug is moved through the clinical trial. The following dynamics will be briefly discussed as factors of importance for developing a management model for a CRO (Raman and Shapiro, 2000).

Large CROs have changed the competitive dynamics of the industry because of the kind of competitive advantage they have been able to gain through of the impact of their ability to get drugs efficiently through clinical trials. High recruitment rates, excellent quality, best business practices with corollary economics of scale, are the tools with which these CROs can change the nature of competition in the industry.

Customers are constantly becoming more demanding. Requirements for drug

development are becoming more complex and standards are becoming higher as technology develops. Technological development has made it possible to create many concepts in the never-ending quest for better, faster, and different drugs and medical devices. During the last decade, it has been all about competing through speed - being able to market pharmaceutical innovations successfully so as to grow profit margins for shareholders. The importance of speed contributes to the popularization of time and activity-based management models as best practices to employ.

2.4 ACTIVITY BASED MANAGEMENT PRACTICES

Activity-based management (ABM) is a management methodology with an activity focus whose major objective is to determine better ways of doing business. It is a management model aimed at improving processes with which to accomplish the objectives of the organization in a better, faster and cheaper way. To convert relevant customer information and the raw data of the activities and processes, to useful information to implement re-engineering of processes, requires a set of analysis tools that can be applied to the information. In recent years, the literature on management and leadership has grown steadily, and applications based on research findings may be more likely to succeed. The use of tested principles in business will also enable management to avoid reinventing the proverbial wheel. According to Cokins (2002) each operational process should be unified with synergy in an improvement program using best practices to get perfect results and to analyze processes for zero defects; to *get lean* and eliminate waste; to manage constraints for increase throughput and profitability; to implement ABM to get smarter and make better decisions.

The above-mentioned operating performance techniques to eliminate defects, waste and constraints are all derivatives of human performance. Human performance holistically involves many dynamics, but is primarily dependent on three: the personal capabilities of the individuals in the business; their individual motivation, and their ability to work together harmoniously (Shapiro, 2002).

Ultimately it is the emotional and intellectual energy of every employee that will win the competitive battle and consequently they should be judged not in terms of resources but rather in terms of resourcefulness (Hamel and Prahalad, 1994).

In today's hyper-competitive world, operating functions must be yoked together at every level - from the core central concepts of the strategy to the minute detail of each activity. The practice which links operating activities with a number of techniques, namely Benchmarking, Pareto analysis, Total Quality Management (TQM) Cost Benefit and Cost Effective Analysis and Six-sigma, to name but a few, are considered best practices and have developed into activity based management (ABM). Some of these practices will be discussed below as best practices with relevance to the construction of a management model for a CRO. The following best practices will be discussed:

2.4.1 Pareto Analysis

Pareto Analysis is a simple technique that helps to identify the most important problem to solve. It uses the Pareto principle - the idea that by doing 20% of work you can generate 80% of the advantage of doing the entire job. Vilfredo Pareto was an Italian economist who noted that approximately 80% of wealth was owned by only 20% of the population. This was true in almost all the societies he studied and was also found to be applicable as an analytical technique in other business and quality sectors (Mind Tools Book Store, 2003). A Pareto diagram is a special type of histogram that helps to identify and prioritize problem areas. The construction of a Pareto diagram may involve data collected from sources of not conforming to standards and reviewing of the analysis which indicates the frequency of occurrences of failure (Kerzner, 2003). The application of the technique is to list the problems to be solved or the options available; to group options where they are facets of the same larger problem; to apply an appropriate score (weight) to each group, and then to work on the group with the highest score. Pareto analysis not only shows one the most important problem to solve, it also gives a score showing how severe the problem is.

A Pareto analysis of activity costs is illuminating in that managers are often surprised to discover how few activities (at the top of the list) account for a large fraction of the total organizational cost. It is also surprising to note which activities show up at the top. Managers often have an intuition that an activity cost is too high, but intuition cannot justify significant investments in an activity. The relative positions of activity costs can provide information heretofore unavailable for justifying corrective investment. In a similar manner, a descending list of activity costs is produced for each cost of quality category, allowing managers to focus on the top offenders in each area. By focusing one's attention on the top of the sorted list, however, only gets half of the story. The activities at the bottom of the list are also candidates for attention. Important activities may not be receiving enough resources. A costly activity at the top may represent an internal failure cost resulting in reworks, while an ignored activity at the bottom represents a preventive item that, with small investment, could dramatically reduce the failure-related activity at the top of the list feeding the rework activities. That is the difference between value analysis and unconditional cost reduction. The latter implies that a management decision is just taken to cut costs by a fixed percentage. The reason for the cost could be non-value adding customer demands that could have been prevented, e.g. if a Pareto analysis was done to identify the non-value adding activities. Target costing or performance-based pricing systems can effectively be implemented if information of value-adding activities and performance is available (Carlson and Young, 1993).

The emphasis the CRO industry places on time-based competition, responsiveness and quality may rightfully raise the question as to whether customers still care about price. However, organizations can be assured that whether a business is following a low-cost or differentiated price strategy, customers will always be considering the price they pay for a product or service (Kaplan and Norton, 1996). In a CRO, amidst all the attention given to process time and quality measurements, one might lose sight of the cost dimension of processes. In the

CRO, as part of the drug development value-chain, the clinical trial costs are impacted on the bottom-line profitability of the new drug entity once it is marketed. Pareto's 80/20 rule can be applied to any business - also in respect of blockbuster drugs where the vital few (20%) will generate most (80%) of the revenue for the marketing company (Koch, 1995).

In general, the audit trail of detailed data is crucial for investigating the basis for activity costs because the clinical trial costs impact on the bottom-line profits of new drugs on the market. According to Carlson and Young (1993) if the old cliché *numbers speak louder than word* applies anywhere, it applies here. The numbers are arrived at through a logical estimation process (throughout the value-chain) to establish which part of the activities contribute to 80% of the revenue. According to Pareto's Law it will probably be from only 20%. The CRO's activity analysis to scrutinize the 20% value-adding activities and cutting of waste not only generates revenue for the CRO, but also for the customer, because the R&D costs affect the marketing price of the new drug entity. It is therefore good practice for a CRO to not only to list the activity resource consumption but to benchmark activities and processes with companies within the industry or with other industries to position its products and services in the market. A product can only be described by reference to a wide range of its characteristics, and shifts in market position require changes in customer perception of the product or service (Kay, 1993).

2.4.2 Benchmarking

Benchmarking can be defined as a continuous process of measuring performance gaps, establishing where best practices are and introducing changes capable of closing identified gaps. Benchmarking leads to action and eliminates complacency – it is a trigger for performance measurement. It is not measurement as such but a process of establishing degrees of competitiveness and inducing action to close any identified gaps. The process of benchmarking ensures that continual improvement is seen externally in terms of the competitive standards it

achieves (Zairi, 1996). From the definition, it follows that benchmarking determines the dynamics of competitiveness through the "standards" (or "criteria") management sets to help achieve organizational goals and specific departmental objectives, and it is also used to measure actual organizational and departmental performance. In these instances benchmarking is based on quantitative and financial data, enabling "measurable goals" and objective assessment of performance, set according to goals and objectives, to be decided upon (Belilos, 2000). Benchmarking is the search for industry's best practices that lead to superior performances for a specific company. However, while benchmark teams can expect to uncover best practices that may not have been considered prior to the benchmark program they will probably not find a company with exactly the same organizational layout, processes or goals to benchmark against. In setting out to benchmark a process the organization needs to scrutinize its own processes before benchmarking to any other company. Once the company's own processes are well understood the research can begin for a prospective partner, with the best-in–class processes for the benchmarking. According to Davis and Davis (1994) critical success factors, i.e. the limited number of areas in which results, if they are satisfactory, will ensure successful competitive performance for the organization, need to be defined. Critical success factors should be linked to the key business processes in the organization and should be quantifiable, measurable and indicators of process performance. They are selected as measures of business effectiveness (quality), efficiency (cycle time), or economy (cost). Critical success factors are used for the measuring of comparison in a benchmark study.

In an environment of increasing competition and greater pressure to reduce project cycle times, companies benchmark themselves against their rivals. In a dynamic and volatile environment like the pharmaceutical industry, where mergers frequently take place, one can ask if there is any value in benchmarking organizational processes. The answer is affirmative, as the examination of the approaches taken by other successful companies can provide structural examples

which can be adopted or adapted, based on the various situational factors of the company (e.g. strategically, geographically and culturally). Reviewing the company's key success factors and the resulting level of efficiency may provide evidence of the value of current processes.

Benchmarking activities to optimize corporate goals of a CRO are important in ensuring that the innovational best practices are incorporated in future activities *"…because what may be suitable for yesterday or today's circumstances is likely to be inappropriate tomorrow"* (Kermani and Findlay, 2000, p. 20). In the context of customer service the customer is to be assured of value for money and it will be necessary to have a clear understanding of the competitive market, of the product or of the service being sold at the price quoted, because there can be no sense of trial and error. Every mistake made is to the advantage of competitors and that is why benchmarking, according to Lynch (2000), is a way to improve sustainable competitive advantage. A comparison of one's practice with that of another organization is considered to display best practice in its field of operation. The aim of benchmarking is to identify areas of improvement in the use of organizational resources. However, benchmarking does not mean cloning, without due consideration of the success of other companies. What is best practice in one organization cannot readily be transferred to another without a thorough understanding of the learning curve and expertise that has gone into achieving the standard, and recognition of the impact of the process on the culture of the organization, in terms of both customer and employees (Cook, 1997).

Process attributes related to developing high-quality products and services should be the focus of all process improvement efforts. Therefore, identifying and quantifying performance gaps in quality-related areas are critical in a competitive environment. Failures in quality may be felt externally, which means that customers are not being satisfied (among other things), and/or may be felt internally, which invariably means that process costs are excessive. According to Davis and Davis (1994) there is substantial proof that *while quality costs - poor*

quality costs more.

The competitive advantage of an organization can be determined by benchmarking. If no explicit comparator is available, the relevant benchmark is the marginal firm in the industry. The weakest firm, which still finds it worthwhile to serve the market, provides the baseline against which the competitive advantage of all other firms can be set and the size of the competitive advantage can be measured. The difference in the value created by a highly successful firm with distinctive capabilities and the output achieved by the merely competent firm, is a measure of the net output of a highly successful organization. Benchmarking provides a direct link from competitive advantage to added value and is a useful tool for considering market positioning. Shifts in market positioning require changes in customer perception, as well as service and product attributes and a need to anticipate competitors' responses (Kay, 1993).

The companies against which process-performance metrics are compared may be within the same corporation, from the same industry, or from an unrelated industry. Unfavourable comparisons with other companies serve as an impetus to begin the search for better ways to conduct business activities. The search for the best way to perform business processes may yield improvement options that range from marginal changes to a radical departure from the existing processes. In this context, benchmarking is an integral part of business-process improvement initiatives that have generated significant savings for companies and appear to have broad support across all areas of business (Palmer and Green, 1999). A CRO does not only need to compare itself to others to improve, as the quality of processes and performances can also be evaluated in-house with a management model striving for zero defects.

2.4.3 Six-sigma

Sigma levels of performance are expressed in *defects per million opportunities*, which indicates how many errors would show up if an activity were repeated a

million times. Sigma levels are another way of communicating the same information. Re-evaluation of performance and cost effectiveness in clinical drug development is necessary to ensure competitiveness in global markets. Six-sigma can be incorporated in a management model to improve existing pharmaceutical processes, or to develop processes where none exists. Once a process is clearly understood, one can apply traditional process engineering approaches to continually improve the processes. Sigma (δ) is the statistical term used to denote the amount of variability in a process, product or service. Six-sigma is the statistical representation of zero variability (in reality, a variability of sixes represents 3.4 defects per million occurrences of opportunities for defect). Thus, the six-sigma methodology is a process improvement and design methodology, which can be applied to service organizations like CROs as well as to manufacturing industries to improve operational business processes, by removing sources of variability (Cost Technology Services, 2001). To estimate project timelines and ensure the quality of processes, CROs must be able to control variability and Six-sigma focuses on defect prevention, cycle time reduction, and cost savings. Unlike mindless cost-cutting programs, which reduce value and quality, Six-sigma identifies and eliminates costs, which provide no value to customers, that is, waste costs (Pyzdek, 1995). To ensure that activities undertaken are value adding, goal orientated and in accordance with the CRO's mission, Six-sigma methodology can ensure that the CRO focuses on value adding quality, with the aim of reducing what is of most importance to a CRO, *viz*. cycle time and costs, but within the constraint of high quality. Retrospective inspection of a product can never be a successful cost effective measure due to the reactive instigation of the process. Quality needs to control the process thereby rendering final inspection of the product completely redundant. Quality then becomes an invisible input (Price, 1990).

Much is written about the philosophy of Six-sigma and many definitions of quality, the main focus of Six-sigma, exist, but for a CRO the most appropriate

definition may be that quality is not only a *process* of continually improving the operating procedures but also one of delivering exactly what the customer wants. Among the elements of Six-sigma, Chaudron, (2002) qualifies the following with a distinct customer focus:

(i) Focus on quality and prevention of problems. Not only should employees inspect products or services while performing them to successfully prevent defects, quality control processes *per se* should be done before a product or service is supplied as well as during the service development phase, and then with the vital input of the customer.

(ii) Cooperation with the suppliers and customers. Another element of Six-sigma emphasizes cooperation with suppliers and service providers to the organization and a focus on customer satisfaction. Many organizations treat suppliers with indifference, often having many potential suppliers competing to give the cheapest price. Six-sigma emphasizes a different relationship, that of vendors being treated as business partners, working together to deliver a quality product. Thus, companies choosing to deliver a quality product have to collaborate with vendors and other service providers, e.g. the central laboratories, who should also implement the Six-sigma philosophy.

(iii) Continually improve and eliminate wasteful steps. Quality is a moving target. What is now a rare feature product soon becomes common and expected. To meet dynamic needs the organization itself must be dynamic. The social consequences of this would appear to be minor. However, in eliminating wasteful steps the elimination of whole work processes may be at stake. Employees may feel uncertain or self-interest may play a role and employees may resist the changes necessary to improve a process.

(iv) Encourage the proper climate, empower employees. For continual improvement to work, management must empower employees so that they are willing to innovate and act in an atmosphere of trust in a dynamic environment.

Employees can only improve the service to their customers in a climate empowering them to be proactive on their company's behalf – to alchemize their environments positively. The company climate, and in essence the corporate culture, must encourage creativity because creativity is fluid and adaptive. *"It welcomes change, initiates change, and survives change. It is evolutionary and revolutionary. It must be to survive"* (Bryan *et al.*, 1998, p. 151).

(v) Use the problem solving/problem prevention cycle. This cycle describes the steps that Six-sigma problem solving uses. The major elements are the gathering of information and actions to be taken, the use of brainstorming to generate possible ideas, and the evaluation of success. The cycle is also called the Deming Cycle and its components are *Do, Check and Act* (Price, 1990). Deming was a statistician who emphasized the importance of the consumer. He was the American originator of the quality revolution and the single greatest external influence on Japanese industry. He advocated that the consumer is the most important part of the production line and that reducing variation was the key to superior profitability (Koch, 1995).

(vi) *Use measurements to back decisions*. As mentioned above, the key to success is to deliver consistently according to the customer's need. To find out whether the company is successful and how well it is doing in serving its customers, this data can be graphed with Six-sigma for management and employees to use. As a knowledge base this data can be used to spot trends and to correct them before problems arise; to find out why defects occurred and to prevent them from happening again; and in product design to identify key characteristics that can affect the product or service development. Reducing quality costs by reducing errors, eliminating non-value-added activities and waste can maximize the profits of an organization.

Quality is meeting customer requirements, error free, at the lowest possible cost. A byproduct of quality improvement is an improvement in productivity. By

eliminating errors, non-value added activities and waste, resource capacity becomes available. Increased quality conformance reduces the production cycle time. It also decreases the use of machinery and equipment due to less rework. This results in a reduction in asset investment. Fewer resources are now required due to less rework and waste.

Why the emphasis on continual improvement? The answer for the pharmaceutical industry will be the same as that for the Motorola company, the originator of Six-sigma: *It is simply for survival!* The reason why Motorola came to the Six-sigma technique is that it was consistently being beaten in the competitive marketplace by foreign firms who were able to produce higher quality products at a lower cost. It would, however, be a mistake to think that Six-sigma is about quality in the traditional sense. Quality, defined traditionally as conformance to internal requirements, has little to do with Six-sigma. The latter is about helping the organization make more money and that is what business performance improvement is all about, because the cost of poor quality in performance results in 25% to 40% of a company's revenue being spent on sorting out problems. Companies using Six-sigma typically spend less than 5% of their revenues on problems or reworks (Cost Technology Services, 2001). Six-sigma is a technique through which potential problems can be detected before the product goes out to the customer. Proactive procedures have several benefits over remedial reactive actions implemented (Chaudron, 2002):

- Quality control and the need to inspect other people's work instead of motivating employees to continual improvement are non-value adding procedures. This inspection requires additional resources.
- If additional man-hours and costs are incurred to rectify the error, this adds to waste.
- If the customer finds the errors, this can cause dissatisfaction and loss of confidence and perhaps loss of the customer's loyalty and support.

The value of service quality benefits is rarely experienced in the short term, but has long term value because it is accumulative over time (Zeithaml, 2000). *Value*, is an ambiguous term, and the question as to whether value can really be measured may well arise. Furthermore, the question about whose value is at stake, may also be asked. Is shareholder wealth value or customer satisfaction value at stake (CPIM SAS, 2003)? Fortunately, Six-sigma and ABC/M in general serve as foundational methods to quantify the linkage between customers and the resources they consume, and measures what wealth creation is left over for shareholders. Investment in value-added activities that support products, services, customers, and market segments thereby increasing shareholder value, can be referred to as "value engineering the cost structure". This aspect is of importance for a CRO to understand how its competitive advantage is generated and corporate profitability is enhanced (Kennedy and Affleck-Graves, 2001). Profits may be lost when the sales and profit opportunity are permanently lost when a customer elects to switch to a competitor, or no longer contracts projects due to unmet expectations as a result of the CRO not meeting requirements agreed upon. Customer incurred costs, e.g. the costs incurred due to quality measures not being implemented or postponed; and lost profits due to cancellations, and the cost of a tarnished name due to negative publicity or as a result of services not satisfying customer expectations, have an impact on, and are reflected in the company's cash inflow (Cokins, 2003).

Another model to manage customer requirements at the expected level of quality and profitability is total quality management. Meeting customer requirements and expectations will incur costs and this aspect will be discussed in the following section.

2.4.4 Total Quality Management

Total Quality Management (TQM) is a systematic approach that links customer performance requirements for products and services to their specifications. TQM aims to produce to specifications company services and products with zero

defects. This creates a virtuous cycle of continual improvement that boosts production, customer satisfaction and profits. TQM is a never ending processes, which is undertaken for strategic reasons – to enable the business to prosper and grow in a highly competitive and fast changing global economy. ABC seeks to explain the reality of cost behaviour and to highlight costs that are excessive or add no value. TQM seeks to eliminate the enormous wastage caused by lack of quality. The focus of both processes is on the activities performed by the business. TQM lacks clearly defined measurement procedures, whilst ABC lacks a philosophy about how to improve the cost performance of a business seeking to change to or maintain a more competitive posture. ABC and TQM provide the vision and tools for success (Dilton and Glad, 1992).

TQM becomes more embedded into the culture of the company as more people strive for continual improvement in a collaborative environment, and as the need for management to play a more facilitative role across the organization is increasing. The need for ABM to be used as a tool for identifying suitable performance measurements, should also be increased so that successes can be underpinned and new horizons challenged (Marshall, 1995).

In general TQM can be used to:

- increase productivity,
- lower work costs,
- improve product reliability,
- decrease time-to market cycles,
- decrease customer service problems, and
- increase competitive advantage.

TQM methodology should be taken note of when formulating a CRO management model because of its focus to improving quality and performance. TQM methodology, with its focus on continual improvement and customer needs,

i.e. a management technique which is outcomes-based. CROs need to recognize that in order to survive and grow in today's challenging marketplace, true commitment in meeting customer needs through communication, planning and continual process improvement activities are a necessity for success.

TQM can be defined as a structured system for satisfying internal and external customers and suppliers by integrating the business environment, continual improvement and maintenance cycles, while changing organizational culture. One of the pivotal facts for implementing TQM is to be found in this definition. TQM is a strategy derived from internal and external customer and supplier needs determined through daily management. Identifying internal an external requirements allows continual improvement of quality, cost containment, and the delivery of output on time. TQM integrates all of these activities and information into a structured system (Clark, 2000). The **'Total'** of TQM implies quality that involves everyone and all activities in the company; **'Quality'** implies conformance to standards, meeting customer requirements, and **'Management'** implies that quality can and must be managed (Hansen, 2001).

According to Bain and Company (2002) TQM methodology requires managers to understand and assess customer requirements, to understand present and future customer needs and to design products and services that cost-effectively meet or exceed those needs. A customer focus is an important precondition for an effective management model for a CRO, and TQM involves improving quality from a customer's point of view. It requires managers to deliver quality by:

- identifying key problem areas in processes and improving them until they approach zero-defect levels;
- training employees to use the new processes;
- developing effective measurement tools of product and service quality;
- creating incentives for those employees linked to quality goals;

- promoting zero-defect philosophy across all activities;
- encouraging management to lead by example, and
- developing feedback mechanisms to ensure continual improvement.

From the above-mentioned it is clear that a company cannot improve quality, only people can. A focus on the development of people at each stage of the corporate ladder is therefore inevitable of importance. Management and functional staff need to participate in skill development programs aimed at behavioural and an attitudinal change and also need to internalize skills for strategic thinking to translate the organization's vision and goals into achievements. Programs designed to create an urge for quality in each employee are necessary over and above the need to implement change in organizational processes and company culture and climate. Human beings, globally, are capable of reaching supreme heights of excellence provided they are properly trained and motivated. Creating a cultural change to ensure commitment to improving the products and services of the company, as well as improving employee attitudes and enthusiasm, is essential. In the CRO industry, that means creating value to the benefit of clients and shareholders.

2.4.5 Cost Benefit Analysis

Cost-Benefit Analysis (CBA) estimates and totals up the equivalent money value of the benefits and costs of projects to establish whether they are worthwhile. In order to reach a conclusion as to the desirability of a project, all aspects of the project, positive and negative, must be expressed in terms of a common unit, i.e., there must be a "bottom line". The most convenient common unit is money. This means that all benefits and costs of a project should be measured in terms of their equivalent money value (Watkins, 2003). Therefore, all costs (inputs) and benefits (consequences) of alternatives are measured in monetary terms. The outcome may be expressed as ratio (benefit to cost) or in terms of net cost or benefit (benefit minus cost). When all the outcomes are converted to Rand

values, the benefit-to-cost ratios or the net costs or benefits can be directly compared so that the alternative with the greatest benefit can be chosen. For instance, by converting outcomes to Rand values, cost-benefit analysis would allow a CRO to compare the cost and benefits of a service (outcome = number of successes). Benefits can be timelines met, satisfied customers or improvement of quality (number of errors avoided). When the benefits of a service go beyond simple financial appraisal, cost benefit analysis may be used (Lynch, 2000).

One of the problems of CBA is that the computation of many components of benefits and costs is intuitively obvious but there are others for which intuition fails to suggest methods of measurement. Thus, a disadvantage of CBA is that it is difficult to convert some non-monetary units, such as errors avoided, into Rand amounts. Because of this, cost effective analysis is more commonly used (Jolicoeur *et al.*, 1992).

2.4.6 Cost-Effective Analysis

Cost-effective analysis differs from cost-benefit analysis in that outcomes are measured in non-monetary units, which must be identical for each alternative. The criteria for cost effectiveness are the ratio of the net increase of activity costs to the net effectiveness in terms of the outcome. The lower the value of this ratio, the higher the priority in terms of maximizing benefits derived from a given expenditure. The rationale for the division between the elements of the numerator (cost) and denomination (effectiveness) is straightforward. The former includes only resources drawn from the CRO budget; it describes the net change in the total number of Rands spent on an activity as a result of the process in question. The denominator (net effectiveness of the activity) includes the benefits conferred from the activity, measured in time saved or quality improved. The measured outcomes are then expressed in terms of the cost per unit of success or effect. Cost–effective analysis can be used to evaluate projects or services (Jolicoeur *et al.*, 1992).

After determining the scope of the project based on demand and having identified, quantified, and valued the costs and benefits of the project alternatives, the next step is to identify the most cost-effective alternative to achieve the objective of the project. A comparative analysis of the scale, technology, and timing of alternative project options or designs is often required. Such an analysis will take into account both market and non-market related costs in testing for productive efficiency. In cases in which alternatives can be defined that deliver the same benefits, it is possible to estimate the equalizing discount rate between each pair of mutually exclusive options for comparison. Alternatively, if the effect or outcome of a project can be quantified but not valued, the average incremental economic cost can be estimated, with the aim of establishing the project alternative with the lowest per unit cost.

Cost-effective analysis aims at identifying the least-cost option of a project for supplying the output to meet forecast demands. Least-cost analysis involves comparing the costs of the various mutually exclusive, technically feasible project options and selecting the one with the lowest costs. For example, it may be that the cheapest way of increasing the number of projects one project manager can handle can be achieved by means of more efficient time management of the existing project manager rather than by appointing additional project managers as extra resource capacity.

The alternative with the lowest present value of costs is the least-cost alternative. According to the Guidelines for the Economic Analysis of Projects, (2003) the above-mentioned average incremental economic cost for each alternative can be estimated, with the aim of identifying the alternative with the lowest unit costs. The average incremental economic cost is the present value of incremental investment and operation costs, with and without the project alternative, divided by the present value of incremental output, with and without the project alternative.

Programs and services can be standardized and conformed to management models with a customer focus. Every management model has the ultimate objective of containing production costs and meeting customer expectations, so as to retain the customer with a view to perpetuating future revenue growth. To manage and maintain customer relationships is therefore a necessary requirement of a management model for a CRO. Mismanagement of resources is a sure way to under perform, and in a highly competitive market it is crucial to play to win (Day, 2002).

2.4.7 Customer Relationship Management

Customers generate the revenues that keep the organizations in existence and deliver its profits; customers are therefore crucial in corporate strategy. In this context according to Lynch (2000), it is perhaps surprising that much greater emphasis has been given in some aspects of strategic development to competition rather than to the customer. Purchase decision for the customer is a competitive selection between the different services or products on the market. A CRO should not lose sight of the direct strategic importance of the customer, so it should try to influence his decisions when selecting a service-provider. Because of the pressure to consistently beat profitability goals, and its competitors, it inevitably means that the customers just have to be understood better and faster than any other company can and the knowledge is used to target them more effectively that anyone else can. Throughout history and as it is still evident today, customers expect to be treated personally, immediately and consistently. However, modernization with the proliferation of choices made possible by remote and online marketing techniques has made customers more independent and less loyal than ever. If their expectations are not met, they can switch to a competitor with the click of a button or even a toll-free call (SAS White Paper, 2001). It follows that the total value of keeping customers throughout the lifetime of a relationship by optimizing customer satisfaction, is not to be argued, but that it should be modelled and the risks associated with a given customer, including the likelihood

of defection to a competitor, calculated. The information can be used for segment analysis to identify the most valuable and profitable customer to help define appropriate target marketing programs.

As a rule, projects and customers are not always profitable and CROs can achieve their predicted budget figures but still lose out on potential profitability. In an era in which the requirement is for quality with the instigation to 'added value' over and above consumer needs, it is important first to uncover latent customer needs and then, in response, not only to meet those needs, but also to discover an added value that will surpass them. Some customers needs mutate consistently, resulting in a continual change of project scope and escalating costs to the company and low rates of return on the investment in such a particular customer. Byrnes (2002a) indicated that of the companies he researched, at least 30% of each company's business was unprofitable. Although a company can make a profit, it can lose out on the opportunity to grow profits. Process inefficiencies should not be seen as part of the system. Outputs should be made profitable both to the benefit of the company and the customer through management adjustments. Managers not only need to keep close to the customers, but should also be flexible and quick to respond to customer complaints and problems. They proactively need to gain a panoramic customer view, maximize the return on marketing campaigns, and improve customer acquisition and retention rates. Managers need to calculate the lifelong value of a customer. They multiply the early profit from a customer by the number a typical customer will repurchase from the company. When a profitable customer is lost, the remaining lifetime value of that customer is lost to the company. A company spends five times as much to find a new customer than they do to keep an existing customer. Customer service is one of the most important levers of profitability (Byrnes 2002b and Byrnes 2002d). It is a well-known fact that when an organization keeps its existing customers, the organization's bottom line is positively affected. According to (Byrnes 2002c) in most companies 20% – 30% of the business provides the profits, while 30% -

40% of customers, products, and transactions lose money. The key question is to identify which is which.

International Quality Standards (ISO 9001:2000), also now requires organizations to measure customer satisfaction (Excel Partnership, 2002). CROs could only benefit by following this queue and collecting data at all customer contact points and then turning that data into knowledge for understanding and anticipating customer behaviour and ultimate effect on company profits. While meeting customer needs they will be able to build more profitable customer relationships and gain a holistic view of each customer's lifetime value. The desired outcome of customer relationship management (CRM) is more customers that are profitable and that customer profitability and all attributable customer costs incurred throughout the organization can be measured (Barrett and McKenzie, 2001).

Any competent pharmaceutical executive will admit that good CRM systems are indispensable. However, if the question is put to the same pharma-executive as to how his company has embraced this concept globally, the answer is likely to be rather less forthright. According to a survey conducted by International Data Corporation, (Dawber, 2001) among the 300 large pharmaceutical companies in Europe and the US, only 12% were running CRM projects in their operational or production phases. However, it must be added that 28% were in the planning or implementation stages of CRM.

The direct strategic importance of the customer is evident as a focus in a management model and the following need to be explored (Lynch 2000):

- identification of the customer and the market;
- market segmentation and its strategic implications, and
- the role of customer service and quality.

Due to globalization the pharmaceutical industry faces not only logistical and technical barriers with customer relationships, but needs to overcome organizational and cultural hurdles as well. The perception should be followed that the customer comes first, the immediate competition second and the broader environment surrounding the organization last.

2.4.7.1 Analyzing the Customer and Market Segmentation

Because of its scope of work the CRO industry targets a specific group (segment) of customers in the pharmaceutical industry. These customers have specialized needs that should be met if a satisfactory result orientated service is to be provided and the customer's loyalty to be retained. To analyze customer and market segmentation therefore holds commercial advantages for the CRO. According to Dawber (2001) the advantages include:

- improved understanding of customer needs and benefits and the ability to identify which customers have the most positive commercial impact to build and maintain key customer relationships more efficiently;
- the best-practice commercial techniques appropriate for a special client;
- more strands of dedicated internal communication, and
- a single, corporate customized identity and approach, irrespective of the personnel involved.

Customer services can be tailored to individual requirements if the CRO knows exactly what to cater for.

2.4.7.2 The Role of Customer Service and Quality in CRM

Customers inevitably keep CROs in business and the latter provide a customer service to satisfy customer needs to such an extent, that loyal relationships between the relevant parties are built. Satisfaction *per se* will, however, not motivate customers to stay loyal to a CRO as the service-provider of choice.

According to Covey (1999, p. 241) *"Satisfied needs do not motivate"* – on the contrary, only unsatisfied needs motivate. Therefore, it is more than just satisfying customer needs. A holistic view of the role of customer service, delivered to a target population at an expected level of quality, justifies exploration. Serving a customer is a two-sided affair. On the one hand, it generates revenue for the company, but on the other hand it is also a cost driver that needs to be controlled.

Quality services are rendered at a cost. Service quality is not free *but it pays*, because meeting quality standards in service improves customer loyalty and, at the end of the value-chain, increases revenue and customer retention rate (Charchaflian and Berlin, 1999). Simple financial measures of profitability will not be enough to ensure the growth and survival of a business; they need to be linked to customer satisfaction and customer loyalty. Service quality, over and above the improvement of corporate reputation in the pharmaceutical industry, adds to the company's value-chain and reduces costs because of fewer errors and less recovery and reworks, which maximizes benefits and minimizes the burdens of customer dissatisfaction. According to Lynch (2000) there is substantial empirical evidence to support the fact that loyal customers are more profitable; they tend to account for the majority of the sales of most organizations and their loyalty means that they are less sensitive to price increases and may even attract new customers.

Williams (2003) confirms the aforementioned dynamics that to attract new customers costs organizations more than retaining loyal customers: the extra cost may be three to five times as much. Retaining existing customers can dramatically increase profits, however, approximately 10% of customers will leave an organization every year. If customers can be retained it is predicted that increasing customer retention by 5% will produce an 85% increase in profits. It is widely held that it is 5 to 10 times more profitable to nurture and expand an existing customer relationship than to have to create a new one to replace a lost

customer.

A customer–driven strategy with the aim of enhancing the importance of the customer's role can therefore be expected to increase a CROs profitability as well as customer satisfaction, and this leads to customer retention. However, the aforementioned is only possible if the CRO provides quality services in a timely manner. A CRO should focus on the following points as the foundation for a management model (Miller, 2002):

- customer satisfaction;
- preventing problems - do it right the first time;
- making decisions based on facts, not opinions;
- continual search for improvement;
- installing pride of workmanship at every level, and
- recognizing success.

With corporate focus directed at the customer and with a commitment to quality performance, it may be said that the CRO will provide a sustainable quality service to customers and shareholders. Quality can be defined not only as conformation to standards as, according to Miller (2002), to achieve quality you must produce a result that is perceived by your customers as meeting or exceeding their expectations and needs. Nevertheless, quality in business can be and should be viewed from a profitability perspective. Therefore, the classical scope of quality should be expanded beyond customer satisfaction also to encompass satisfaction of the investor and shareholder. Unless expectations from both sides of the transaction are met – referred to as a mutual valuation – then true quality has not been achieved. This new perspective acknowledges that investing additional capital intended to reduce defect rates and improve quality will not be sustained unless shareholders and investors feel assured of high quality financial returns to them (Cokins, 2002). Sustainability of quality implies that management

needs to structure each endeavour with the end in mind to meet customer and shareholder needs, beyond their expectations.

The following factors regarding to product or service output should indicate that a performance gap analysis should be done and that radical process re-engineering should be considered to improve quality (Davis and Davis, 1994):

- unacceptable products and services, e.g. returns, rejects, loss of customers;
- too much time spent on redoing work, e.g. phone calls, adverse comments, or publicity;
- excessive meeting time devoted to problem/issue resolution, and
- low morale or high personnel turnover.

Inevitably re-engineering and continual improvement are only possible through change. Process improvement should find targeted solutions so as to eliminate *root causes* of a business performance problem. According to Adams (2002), the emphasis should be on finding and targeting solutions to address the *vital few* factors that cause the problem. Customer requirements should be defined clearly so that measures can be used to measure and compare processes if customer expectations are met and so that customers get used to a sustainable high quality of service. Once customers have developed a low tolerance for defects, the company has acquired a unique marketing advantage over its competitors. On the other hand, every time the company has an unsatisfied customer, the competitors' market share increases.

Sustainable quality is to be achieved through continual change in the hi-tech environment the CRO industry operates in. Less than state-of–the-art equipment and processes will prove the saying that, *if you snooze you will loose,* to be true. Change and innovation have to be wilfully implemented because change happens either by planned action, or by reaction. Planned action for change is designed and implemented in an orderly and timely fashion in anticipation of future events.

Reactive change occurs haphazardly, and when one is in a hurry to manage a crisis. Planned change is thus preferable to reactive change.

Managers committed to successfully implementing customer relationship management to improve quality, must align behavioural and cultural commitment to customer quality. Ultimately, customers provide the revenue to generate the wealth of the company. Thus on the one hand the customer should be persuaded to choose the relevant companies' services rather than those of competitors'. On the other hand a culture change to move above and beyond commitment to meet customers' expectations should be part of the management model to ensure sustainable competitive branding and the reputation of the company. A precondition for behavioural and cultural change essential to align employees with the commitment of customer quality, should be implemented as part of the management model. Kanter (in Lynch 2000, p. 957) said on change, that *"The sad fact is that, almost universally, organizations change as little as they must, rather than as much as they should."*

Dynamic leadership is needed to motivate people to do more than what is expected of them, to transcend their expected performance. Only then can an idealised customer focus, to meet and exceed customer needs, be realized as an organizational objective. Customer needs are met with the ultimate goal of retaining and obtaining customers because economical growth is directly linked to the target market segment the CRO serves. To ensure continuity and growth of a CRO the company's business is dependent on consumers and the satisfaction of their needs. Profit, growth and stability all depend upon management's ability to orientate the organization to meet the needs of customers, because if a company does not attract and retain customers, it will not have a profitable business for long. However, delivering quality services to customers is both resource- and capital- intensive (Tanoury, 2003). CROs, due to the specialized services they offer, have to target that segment of the mass market with the specialized needs related to product design, development, marketing authorization, or comparative

trials. The greater the need satisfaction customers can derive from the CRO's services, the easier it would be for the CRO to achieve its own goals.

According to Strydom *et al.,* (2000) a management model for a CRO with a customer focus should:

(i) Compel management to focus more accurately on customer needs. A greater degree of customer satisfaction can be achieved if the services offered are developed around customer needs, demands, and preferences, e.g. special care should be taken at the protocol design stage to ensure that it is in accordance with customer's requirements.

(ii) New marketing opportunities and the development of separate market offerings and marketing strategies for market segments should be explored to grow the CRO business. These strategies incorporated into the management model can help guide the proper allocation of resources.

A customer focused management strategy recognizes that many of an organization's activities, and therefore costs, are related to servicing customers and are not product-driven. This approach enables companies to identify the true profitability of customers based on the specific resources used to service each customer group. Costs are allocated to the activity performed in the organization. Customer-related activities, e.g. possible reworks, rescheduling of project start dates due to customer induced project delays, are allocated to customer based cost drivers such as unused clinic capacity (as a result of the delay) or statistical analysis, analytical assessments or scientific reports. Product-related activities are allocated to the products/services provided and then allocated to customers based on the level of each product/service (Pickering, 1998).

Customers who make excessive demands on resources put unnecessary strain on the company's effort to provide quality high throughput services, at the lowest possible price. Time and resources allocated to non-value adding activities, e.g.

reworks or bids not be contracted, could have been allocated to more profitable customers who contribute to the company's revenue. The time and resources spent on non-value adding activities should be calculated and controlled.

Considering what the reality of profits and losses are, companies must take the time to define and measure their in-house work activities and directly associate them with the bigger and smaller consumers of their work. In addition to the products and base-services provided to customers, there are big users, small users, and those in between. However, since pricing is usually determined based on average-based standards, customer-driven imbalances are rarely reflected in the price. When the inequities are replaced with true measures of the cost-to-serve customers, the companies who have performed this analysis will realize that they make a lot of profit on the winners and then forfeit a fair amount on the losers. Both the profits and losses are probably large amounts and the company's revenue is based on the net difference (Cokins, 2001b).

In environments where customized products dictate the nature of the production process, e.g. when the output is a scientific research report, the activity drivers from both a product-profitability and a customer-profitability perspective are likely to be similar (Smith and Dikolli, 1995). Therefore, for a custom-made product either the customer or the product can be used as the cost object. Because of the latter, the costs incurred by the resources consumed by the customer demands can also be used to evaluate the profitability of customers.

2.4.8 Dynamic and Smart Pricing

Marketing objectives to identify potential customers and to nurture the relationships with current customers means that the market and customers must be categorized according to needs and available technology to render the service to the particular market segment. Pricing of services should be market and customer related because, as described in the aforementioned sections, costs are incurred by customer demands. Yet, prices cannot rise above that level to which competitors

can afford to reduce their prices and still sustain their enterprises, since customers will invariably collaborate with companies offering the lowest prices at the required quality (Schrader, 1993). Cost transparency is also a new reality, and companies will not be able to avoid it. That does not mean, however, that companies should automatically cut their prices. According to Sinha (2000), those managers who best understand the dynamics of cost transparency on the Net will be most prepared for the challenge. They can take several steps to mitigate the effects brought about by the Net's trove of information. For example, one strategy involves *price lining*, which is also called tiered pricing or versioning. Price lining is the well-known practice of offering different products or services at various price points to meet different customers' needs (Shapiro and Varian's, 1998).

Companies may also implement dynamic, or "smart", pricing - in which the prices they charge vary from one market to another, depending on market conditions, differences in the costs of serving individual buyers, and variations in the way consumers value the offering. Some companies are trying to do this with geographic segments by forcing shoppers to enter their zip codes before they can view prices. Companies that can implement this approach successfully can earn higher profits than those that have only one general price for a market segment they serve. Major airlines, auto dealers, and car rental companies have long practiced dynamic pricing. Lately, the strategy has been touted as a pricing panacea for e-commerce businesses, but managers need to be aware of its pitfalls and risks. Because the Internet allows customers to share information with one another easily, smart pricing is likely to create widespread perceptions of unfairness that may prove devastating to businesses in the end. Consumers will be unhappy if they believe they have paid more for a product than someone who was more persistent, more adept at bargaining, or just plain lucky. Companies should tread carefully when thinking about smart pricing. For most consumers, fixed prices are a security blanket that helps them feel they are being treated fairly

- or at least no worse than the next customer (Web pop-up, 2003).

The technique of pricing according to the customer segment of the market and price-led-costing has been applied by Toyota Motor Company since the 1960's. Their approach to ensure profitability, the target costing technique, is usually applied at the product design stage, and this approach links the cost of producing a product to target sale price and target profits. According to Reinstein and Bayou (1997), *Target Cost = Target Sale Price - Target Profit*, is one method of determining a product's target cost.

If either the customer or the product can be used as the cost object, the above-mentioned equation can be used to evaluate customers. The costs of activities undertaken to provide a customer with a specific product (e.g. scientific report or analytical analysis), should be equal to the price the customer will be prepared to pay for the product minus the profit that should be made. This technique could well be used by CROs because the advantage will be that the target costs incurred by customer demands will set the sales price of a service. Demands customers are not paying for should be scrutinized and not regarded as a priority.

2.5 CONCLUSION

The above-mentioned discussions imply that best practices methods available provide useful information for consideration when the *AS-IS* processes of a CRO are evaluated and a model for *TO-BE* processes is constructed. The value of a management model for a CRO is also not to be questioned because the value of modelling is evident, as for any other industry. To ensure that the corporate environment and everyday practices to attain excellence in business and customer satisfaction at the best possible profit margins are indeed in line with business objectives and not only lip service, it is necessary to measure activities in relation to their costs and profitability. Excellence is like a moving target only successfully aimed at through the operating performances of people. The dimension of human endeavour, speed and change are therefore unmistakably part

of the objective of excellence in business. A management model as the core logic to constructed value for a CRO is a means to an end to represent and outline the complex reality of all the dimensions at stake in the effort to reach the bottom line profits the shareholders expect.

Technical capability and production efficiency of a CRO, while necessary, are no longer the principal competitive determinants sufficient for success. What differentiates the successful from the unsuccessful CRO, is superior "world-class" systems of work processes that men and women throughout the organization understand, believe in and are a part of. These systems of clear work processes reduce bureaucracy and cycle times, increase responsiveness and innovation, and lower cost, thereby assuring customer service and organizational success. The pursuit of excellence, deep recognition that what you are doing is right, is the strongest human emotional motivator in any organization and is the basic driver in true organizational leadership. Striving for excellence in business is a constantly upward moving target, and continuous improvement is an in-line, integral component of everyone's job responsibilities – not a separate activity. This requires more than just *better-than-last-year* internal incremental improvement. The CRO market segment determines what is world-class performance. The relentless application of systematic processes that make it possible to manage quality, activities, and associated costs can make a CRO a leader in its industry. A CRO needs to escape the myopia of existing served markets with *AS-IS* competencies and build a futuristic *TO-BE* competence agenda. A review of best practices and innovations can help a CRO on the migration path to future revenue to be earned.

Sustainability of quality and staying on the competitive edge are intertwined with change. Organizations have to strive to attain the ever-increasing levels of efficiency, effectiveness and service quality improvement, because optimum results tomorrow cannot be guaranteed with the implementation of techniques designed yesterday. Without adapting new best business practice techniques

available, business processes will stagnate and sustainability of quality, effectiveness, and efficiency be hindered. The following chapter will describe an activity-based technique considered to have relevance in a time-based competitive environment.

CHAPTER 3

ACTIVITY-BASED MANAGEMENT MODELLING

Activity-based costing (ABC) per se*, is not a research objective, but because the technique has an activity and process focus, the elementary steps involved with ABC will be discussed as will the usefulness of time-data to evaluate performance and pricing, with the objective of finally formulating a management model with a customer focus as a conclusion of this thesis. The aim of this chapter is to give background information on a management model with a customer focus comprising activity and costs analysis. The researcher regards speed, quality, and cost of activities and processes, as the most important complementary techniques in a strategy to construct a management model for a CRO. The usefulness of an activity-based analysis and steps involved in activity-based costing as a process based management tool, with the ultimate goal of meeting customers' expectations, will be discussed.*

3.1 INTRODUCTION

This chapter discusses the basic elements of an organization through process and activity modelling and activity costing. Organizations comprise a fundamental part of society and organizations may be defined as a human grouping established to accomplish specific objectives. Organizations, e.g. a CRO, is expected to produce an output of products or services and, as members of that organization, employees who undertake to do the work are involved in the specialized work of divisions, coordination of activities, communication and the maintaining of relationships between people and customers. The first sections of this chapter will discuss the steps and techniques used to analyze functional processes by analyzing

the activities and tracing them to costs incurred. Activities are necessary to accomplish work and significant relationships arise from the people performing these activities and the customer whom the activities are performed for.

The methodology of the technique in which costs are assigned to the product or service that caused the activity transaction to occur, is well described in literature. The basic steps involved with this cost-management technique will be used to gather information on activities and processes to estimate the time of operational processes. The time aspect will be relayed to relevant costs incurred by the activities to establish performance profitability and best practices for operational processes. A company's performance can only result in sustainable profitability if customer expectations are met. Therefore, not only do the processes need to be scrutinized for possible waste but also the customer's profitability. With the relevant information regarding process time, cost, customer expectations, risks, and pricing, available, a management model can be formulated as a best practices model for a CRO.

A model constructed from a combination of relevant best management models has advantages. A single cost system or model cannot give managers all the information needed to promote operational efficiency to produce a quality service or product at the lowest possible cost. It is important to establish which activities employees spent their time on and whether the collective endeavour generated the expected revenue to the company. According to Kaplan (2001), cost systems must serve three functions – inventory valuation, operational control and product cost measurement. Before presenting the steps involved in operational activity and process analysis, background information to emphasize the purpose of operational process evaluation and recommendations for improvement, will be presented.

3.2 THE PURPOSE OF BUSINESS PROCESS MANAGEMENT

The contribution of CROs to the pharmaceutical industry has been invaluable, but

the challenge is to add real value to clinical drug development while maintaining stability, flexibility, and quality in their operations. Quality, timelines, and cost-effectiveness are necessary, but not sufficient to ensure continued success. The successful CRO must confront and deal with the central strategic challenge of diversifying its business. The onus is on CROs to differentiate themselves from their competitors. Some leading CROs have developed medical communication services and network facilities to allow access to *real-time information* on prescribing trends and other web-based information. Diversification cannot compensate for the negative impact of poor performance (Chiesa, 2000). Because of globalization with mega-mergers taking place in the CRO industry, businesses are not localized, and diversification of activities emphasizes the need for management to control performance within defined cost and quality constraints.

Global pharmaceutical companies have to promote the use of techniques, models and methodologies to dramatically improve the quality, availability, high-throughput, effectiveness and cost-effectiveness of business, to ensure a competitive advantage in the global industry. According to James (2000), the big pharmaceutical companies' financial expectations are not in harmony with the realities of business. This means that margins may fall and that the larger the company gets, the more difficult it will be to grow. Therefore, globalization through mega-mergers of companies will inevitably have to produce massive productivity gains, which will have to be made also in the marketing and R&D divisions which were previously not under pressure to help achieve the bottom-line figures.

The pharmaceutical industry's spending on R&D is consumer driven. To maintain year-on-year growth and economics of scale in a competitive market, it is critical for companies who want to compete on a world-class level to improve their profitability. By taking waste out of processes, reducing process variability, and facilitating better understanding of the markets, companies can improve profitability. Activity-based technology measures process and activity

performances, determines the cost of enterprise process outputs, and identifies opportunities to improve process efficiency and effectiveness (Terblanché and Opperman, 1996). The real key to applying advance technology tools successfully is to base their implementation on an information model that provides a direct link between business activities and their impact on financial performance (Capps and Hattery, 2000).

3.2.1 Business Process Management with Virtual-Reality and E-Commerce

Process management to control the variability of products, prices or services is not the only factor of importance to improve profitability and competitiveness, but one of the major issues facing pharmaceutical organizations is the fact that the environment is subject to rapid change. The Internet provides international access to information regarding positive or negative publicity about companies, and their products can relentlessly change the operating environment of a CRO and inevitably its market share (Holden, 1996). The explosion of information technology through the Internet's Worldwide Web sites has shifted power from suppliers and service providers to consumers, irreversibly (Cokins, 2002). Especially negative publicity regarding a product or a trial can immediately have a negative effect on company shares. Because of electronic-business being transparent and freely available globally, customers cannot only continually compare differences in services, products and performance, but also be exposed to negative publicity instantaneously. According to Willis (1999, p. 15), *"Publicity is the life blood of any product"*. The media often let the hype take over from the facts – ignoring the risk versus the benefit of any product or service.

Using electronic information systems, customers can seek the best cost-effective services at the desired quality. In an industry which will be dominated by the two hurdles, *affordability* and *fast throughput*, it will be difficult and probably impossible, to price a service differentially by market, as customers will source globally to seek the best prices and deals. The revolution in e-business will accelerate outsourcing, as the cost of sharing information digitally is low. This

will encourage companies to desegregate along their value-chains, keeping only those activities contributing to a competitive advantage. The new virtual value-chain for pharmaceuticals is likely to be both global and decentralized, built to contain cost, expertise, creativity, and customer relationship, quality, and time advantages. Companies will have to make substantial reductions in their operating costs and inventory, while becoming more responsive to customer needs (James, 2000).

3.2.2 Activity Control and Process Improvement

Activity based management methodology changes traditional business management practices to guide managers to emulate the best practices and establish process control to ensure consistently good performances. Activity based management supports the quest for continuous improvement by providing managers with new insights into activities and business processes (Covey, 2001). Cost management implies that the objective is not simply to count cost but to control it. Many costs are committed in the project design and planning phase before they are incurred. For cost management, Booth (1994, p. 10) wrote, *"Good vision requires a movie not a snapshot … (t)he dimension of time is required"*. A holistic view of the project cycle time traced to cost is necessary.

3.2.3 The Management of Drug Discovery

The performance of drug companies increasingly depends on their ability to discover innovative drugs (for which society is prepared to pay) and bring them to the marketplace rapidly. Drug research and development is so expensive that even the pharmaceutical giants can only mount significant efforts in a handful of disease areas. Once a lead compound enters the pre-clinical phase and the patent application is accepted, the clock starts ticking. The speed and accuracy of the execution of the processes have many commercial implications within the pharmaceutical sector. Drug companies that operate at the forefront of new drug development, are highly attuned to any aspect of the drug development process

which could reduce time to market and reduce the number of false leads. According to Houghton and Jarvis (2000) the literature is full of references to the fact that a day saved in development equates to over £1 000 000 (R1 539 000 000[4]) in revenues for a blockbuster drug. No large pharmaceutical company can afford the competitive disadvantage of having any aspect of its drug development pipeline slowed down by the use of procedures or equipment that are anything less than state-of-the-art.

Activity based management methodology, as an integrated part of a management model, will provide managers throughout the drug development value-chain with a management tool to estimate the costs of resources used to perform activities, the time it takes to produce the various outputs and the variances thereof. Activity analysis shows how activity usage varies with the demands made for these activities as well as resources used by the activities to produce the output. Management can then make informed decisions from drug discovery to the submission of the dossier for regulatory approval, to reduce unused capacity by either supporting a higher volume of business or reducing resource costs. According to Cooper and Kaplan (1991) different products, customers and distribution channels make tremendously different demands on a company's resources.

3.3 ACTIVITY-BASED BUSINESS MANAGEMENT

Drucker (1995) advocates a holistic view of business management involving the entire economic value-chain of the business. In his opinion, a shift in focus from cost-led pricing to price-led costing (target costing) will force companies into economic chain costing with a better return on investments. The company must know the cost of the entire value-chain and recognize which link in the chain needs to be undertaken more efficiently to improve performance of a given function and thus better profitability. Activity–based management (ABM)

[4] Exchange rate R15.39 to the GBP, 05 May 2002.

provides the tools and information to help management review the entire value-chain and the resource consumption each activity makes. ABM not only provides more accurate costing for activities and processes than traditional accounting methods, but it also allows for thorough operational analysis, constraint checking, and sensitivity analysis. Under an ABM approach, the cost of each activity is measured and assigned to those products or services requiring the activity, using appropriate assignment bases (drivers), thus providing an accurate holistic picture of the real cost of producing each product or service (Blankley, *et al.,* 2000).

ABM not only provides insight into the costs associated with company operations, but also the nature and efficiency of company operations. It can be used to identify whether an activity needs to be done and, if so, where it is done best. History, according to Drucker (1995), has shown repeatedly that a company, which enjoys a cost advantage (by identifying the costs of the entire value-chain and managing these costs), overtakes the established leaders in a market segment. Activity-based costing (ABC) is an information system that maintains and processes data on a company's activities and products. Information relevant in business management because it identifies the activities performed, traces cost to these activities, and then uses various cost drivers to trace the cost of activities to products. Cost drivers, such as the equipment, number of employees performing the work or the number of set-ups required per process, reflects the consumption of activities by the products or service (ARO, 2000). ABC systems differ from traditional cost accounting systems. By contrast, ABC systems focus on the activities performed to produce products or services. Costs are allocated, or "traced" to a product or service, because each unit of the output is assumed to consume resources, while conventional cost accounting systems focus on the number of units (production) of particular products (Cooper, 1999).

Human time is an economic resource that businesses buy or sell. Time is expensive. The cost of a product or service is largely the cost of people's time and a large portion of the corporate budget is allocated to purchasing human time

qualified as salaries, quantified in Rands. Reduced cycle time of processes reduces the cost of products and services because it reduces the amount of time (labour-hours) it takes to design, produce or provide a service. This in turn results in lower prices and an increase in profits and competitiveness. The net outcome of cycle time reduction is products and services that are better, cheaper and faster (Barrett, 1995).

Periodic re-evaluation of human and financial resources use efficiency in clinical drug development is essential to continued profitability (Gould *et al.*, 2000). To control and improve their operations, process owners use activity-based costing as a management tool, e.g. activity-based management (ABM). Because process analysis is the main activity of the management tool, management knows its business much better and can consequently evaluate value adding and non-value adding activities to ensure continued profitability. Gering and de Beer (1998a) wrote that some products or customers are profitable and are unwittingly used to subsidize others. The question as to which fraction of the customers is needed to achieve 80% of the profit can be asked. ABC is a powerful method of focusing top management on what is important. It is a method to prove which products and customers are profitable and which could be so. That will bring management accounting back into the strategic process with process evaluation of what do the employees do that contributes value to the company services or conversely what do the employees do that does not contribute value to the company's service (Carlson and Young, 1993).

There are various approaches for designing and implementing an activity and process analysis system. The most basic approach is to use ABC in conjunction with a company's current accounting system. The traditional accounting system is still used and the ABC structure is an add-on or shadow system to be used when specific information is needed for a decision. At the other end of the spectrum, ABC is used instead of the traditional accounting system. Every cost-related facet of the accounting system would be reported to the ABC structure. In order to

institute major organizational change, all employees must fully incorporate ABC into their work practices and use it as their primary source of business information. Costs, performance measurement systems, and all incentive systems have then to be tied to the ABC numbers. The advantage of using ABC as the sole accounting system is that it will be used consistently for daily decision-making and employees will not retreat to old practices. A traditional accounting system usually cannot report costs by processes because the purpose is to help the accounting department keep the books. The purpose of ABC is to help management do their job by making cost information available daily for decision-making. ABC is a method to measure the cost and performance, based on the activities the organization uses in producing the output, and it differs from traditional cost accounting techniques in that it accounts for all cost variables (QPR PowerPoint presentation, 2001). According to Brandt *et al.,* (1999) it was already noted in the early 1960's that because traditional cost accounting systems do not examine the cost of work activities, they could not accurately reveal the true cost of products. The real value of applying these advanced technology tools, e.g. ABC, successfully, is to base their implementation on an information model that provides a direct link between business activities and their impact on financial performance (Capps and Hattery, 2000). The model to obtain the necessary information on the business activities of a CRO should, however, not be constructed in such a way that it is too time-consuming to implement.

Cooper (1991) advises that there are risks involved in building complex ABC systems. Users can be overwhelmed by the detail provided by the system and the cost of implementing and maintaining a complex system can become excessive. For the purpose of this research, the concept of ABC will only be used to analyze activities to be able to track time according to operational processes and to allocate costs to the relevant processes. The basic sequence of building an ABC model will be discussed according to literature in the following sections, because the evaluation of process activities are considered of importance in defining the

time aspect of processes. Throughput time is one of the most important customer requirements in the drug evaluation processes. State-of-the-art equipment and quality processes alone are not what will determine a company's success, but meeting the timelines set as the development and testing objective will determine the competitive edge of a CRO. Thus, it follows that the construction of a management model for a CRO will be incomplete if the sequence of an ABC model is not researched and the usefulness evaluated.

3.4 SEQUENCE FOR BUILDING AN ABC MODEL

The name ABC implies, and as the technique portrays, that an activity concept is at the centre of this methodology. The ABC system maintains and processes data on activities, products, or services. These systems trace costs to products or services according to the activities performed to produce them. ABC systems are an important source of information on overhead activities and remove much of the distortion in product or service costs that is inherent to conventional unit-based systems (Turney, 1990). The resource and activity drivers (such as the number of personnel performing work or the number of set-ups required per production) reflect the consumption of resources used by the products or services. These costs should initially be available at the quoting and planning phase of a project, because the only opportunity for saving money in a project is during the planning phase - beyond that point money can only be spent (Miller, 2002). The estimated cost of the output should therefore be a known factor during the project design phase to ensure that costs are contained and profitability guaranteed.

ABC can also be defined as a method of measuring not only the cost but also the performance of the organization, based on the activities which the organization uses in producing its output. ABC accounts for all *fixed* and direct costs as variables, without allocating costs based upon a customer's unit volume (QPR, 2003). The following steps can be followed to formulate an ABC model (ECPI, 1998):

- gather the time data and calculate the costs;
- allocate the costs;
- determine the output costs and other performance measures;
- calculate unit cost of an output;
- determine the % of the operations undertaken, and
- forecast the financial baseline (unit cost x future output).

The models described in literature are basically similar as, for example the following, outlined by Roztocki (2001), illustrates:

- identify the activities;
- determine the cost;
- determine the cost drivers;
- gather activity data, and
- product cost calculation.

The traditional model for portraying the interrelationships between costs, activities, and products/services is the CAM-I Model or CAM-I Cross as illustrated by Raffish and Turney (1991). It was initially developed for manufacturing scenarios, but has grown over the past several years to include the service industry as an essential part of the functional process improvement and re-engineering effort to capture quantified cost and time data and translate them into decision information. According to the CAM-I Model (Raffish and Turney, 1991), activity-based costing is a structured methodology, as well as an information system, which maintains and processes data on an organization's activities and products and is illustrated in Figure 3.1.

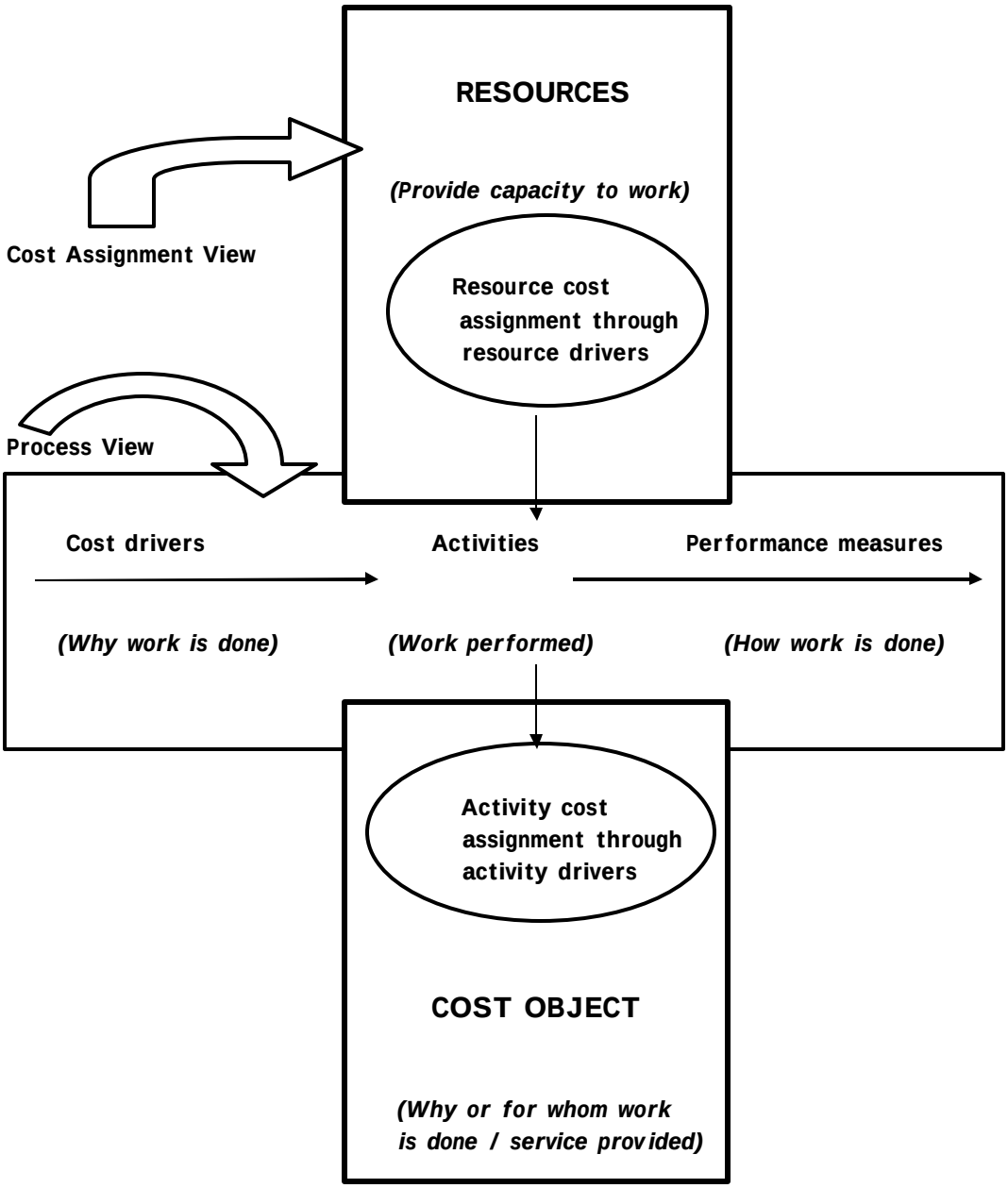

Figure 3.1 The activity-based costing structured methodology according to Raffish and Turney, (1991)

As illustrated, ABC can track the flow of activities in the organization by creating a causal link between the activity (resource consumption) and the cost object e.g. the customer. The resources (employees or equipment) provide the capacity to perform the work, therefore it may be said that the activities consume resources. Information gathered *via* activity analysis can provide a cross-functional, integrated view of the organization, including its activities and its business processes as customers make demands for relevant activities. These demands can be viewed as resource drivers and costs can be assigned through these resource drivers to the product-output, which can be a tangible product or a non-tangible one, e.g. a service provided. The entire process of *why the work is done*, a cost driver because of *the work performed via* activities undertaken, and the result *how the work is done*, the performance measure, outlines the process view with a demand-pull effect. Activity costs assigned through activity drivers as to why or for whom the work was done, e.g. the customer, is the cost object responsible for the demand-pull effect. The following categories define related information:

3.4.1. Activity

Total Cost of Activity: The total amount of direct and overhead costs associated with or allocated to a single activity, e.g. blood sample collection.

Cost driver: A measurable factor that represents the performance (amount of effort) and creates or affects the costs within a single defined activity, e.g. the number of inquiries, quotes, invoices or number of protocols and scientific reports.

Elapsed Time: The total amount of time (including the amount of time delay created while awaiting processing) consumed to complete the activity or an iteration of the cost driver, e.g. during the analytical method development, method validation and analytical determinations.

Cycle Time: The amount of time to complete one process, iteration of the cost driver without including delays during or between activities or wait time, e.g. during protocol development cycle time includes the in-house circulation and evaluation time of quality control.

3.4.2 Process

Total Cost of the Process: The total cost of all the activities in a process determined by the amount of the cost driver for each activity in relation to the output of the process in each operational division.

Cost of a Single Iteration: The total cost of a single incident or of the cost driver, e.g. protocol development, equals the total cost of a single iteration in the process flow.

3.4.3 Output

The Cost of the Output: The total cost of each of the activities, allocated by the applied activity drivers to the product output.

3.4.4 Identification of Opportunities for Re-engineering

Significant Cost Consumption: Activities identified which have an evidently larger consumption of inputs and mechanisms or of which the value of the output is less than the value of the inputs.

Significant Time Use: Activities identified, which have evidently larger time-frames of use or large non-value delay periods.

3.4.5 Evaluation of Alternatives for Re-engineering

Cost Comparison: Analysis of the allocated costs from the activity model to two or more alternative process methods.

Time Comparison: Analysis of the total time or cycle times of two or more alternative process methods.

ABC has a very definite procedural flow, a set of steps that define the performance process. It realigns the resources and managerial effort along the real functions of the organization rather than the structure of the organization elements. The first major step in the ABC process is analyzing the activities undertaken in the operational divisions.

3.5 ANALYSING MANAGEMENT ACTIVITIES

Activity analysis is at the core of ABC implementation and makes the technique of relevance for incorporation in a management model of a CRO. An activity is more detailed than a process, and management can evaluate the value added by undertaking it. Each activity is made up of a set of smaller tasks which make up the lowest unit that is costed in a typical model with an activity focus. Tasks are the detailed steps involved in performing an activity and their value is to understand what actions are involved in an activity. Incorporating tasks into ABC results in a large model but this does not yield significantly better information, according to Stratton (2001). ABC should not be too elaborate or excessively detailed. Pareto's 80/20 Law should be deployed in the design and construction of an ABC model and the amount of data and level of detail should meet the decision-maker's needs. The trade-offs between the relevance, significance, accuracy, and flexibility required to capture diversity of resource consumption at timely intervals, should be understood (Cokins, 2001a). Specifying and analyzing activities and processes, and identifying cost drivers from a value-added perspective, represent the major work that must be performed in the construction of an ABC model (Miller, 1996).

The breakdown of the process flow in the operational divisions of an organization like a CRO enables the identification of activities and tasks undertaken to produce the output. In a competitive market, internal benchmarking is an important step in performance and output evaluation to ensure timely remedial process improvement steps. Businesses want to know which of their products and services make or lose money so that they can stay competitive. There are numerous approaches to business process change, if deemed necessary. The most successful of these approaches are based on the premise that a process cannot be improved until it is brought under control. To bring a process under control firstly requires that it is articulated to a level of detail where it can be measured (CIM, 1993). The following diagrams demonstrate that activities are performed in a

structured hierarchical way as illustrated in Figure 3.2.

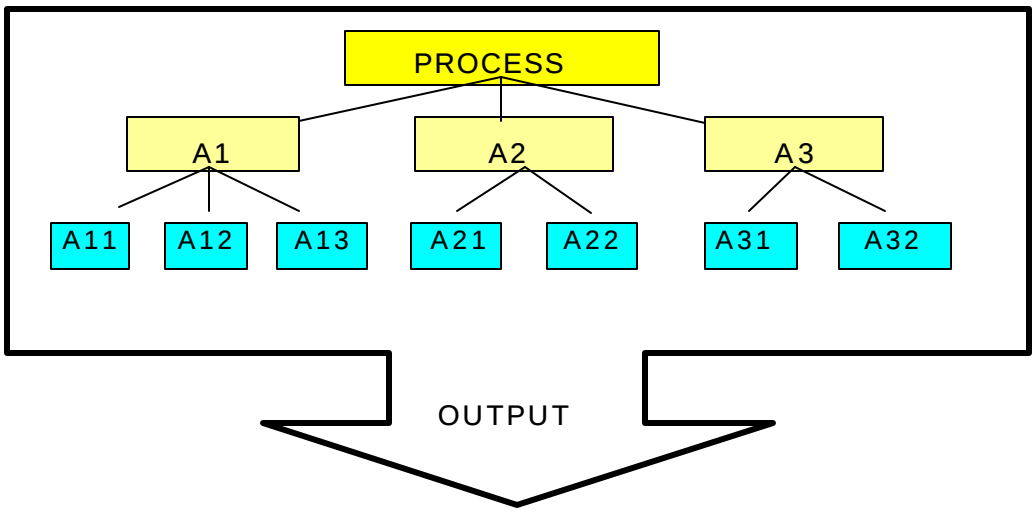

Figure 3. 2: Organogram of the Traditional Organization (CIM 1993)

According to Figure 3.2, processes undertaken by the business units in a CRO can be divided into tasks and activities. Activity 1 can be subdivided into Activities 11, 12 and 13. Identically, Activity 2 can be divided into Activities 21 and 22, and Activity 3 can be divided into Activities 31 and 32. In the same manner, all the processes can be broken down into smaller activities and in combination the process output (the product or service) is delivered.

On the one hand, activities belong to processes - you can add their costs up over time. On the other hand, products, service lines and customers also consume activities. There is usually a broad mixture of intermediate outputs of work, which the products, standard service lines and customers themselves are consuming. This type of costing is indeed ABC. If the objective is also business process management with a quality customer focus, then the attention shifts to understanding more about the activity costs. This not only includes activity cost drivers, and their individual levels of importance or performance, but also how the activities interrelate over time to make up the business process. For example, a

rocket and a railroad train are both moving forward, but not in the same direction, because one is moving vertically and the other horizontally (Cokins, 2001a). This analogy applies to ABC and the process view: it is not just about adding activity costs laterally per division, but it is related to a process across division and how the activities relate to each other in time, forming a sequence or network traversing across organizational boundaries. The demands (the pull effect) the cost object, e.g. the customer, put on the process, is illustrated below in Figure 3.3 (Cokins, 2001a). The illustration shows how the work activity costs are the starting point of the process's costs. After the costs are traced to the work activities, they are then either added over time to the products, service lines or customers, which are the final cost objects.

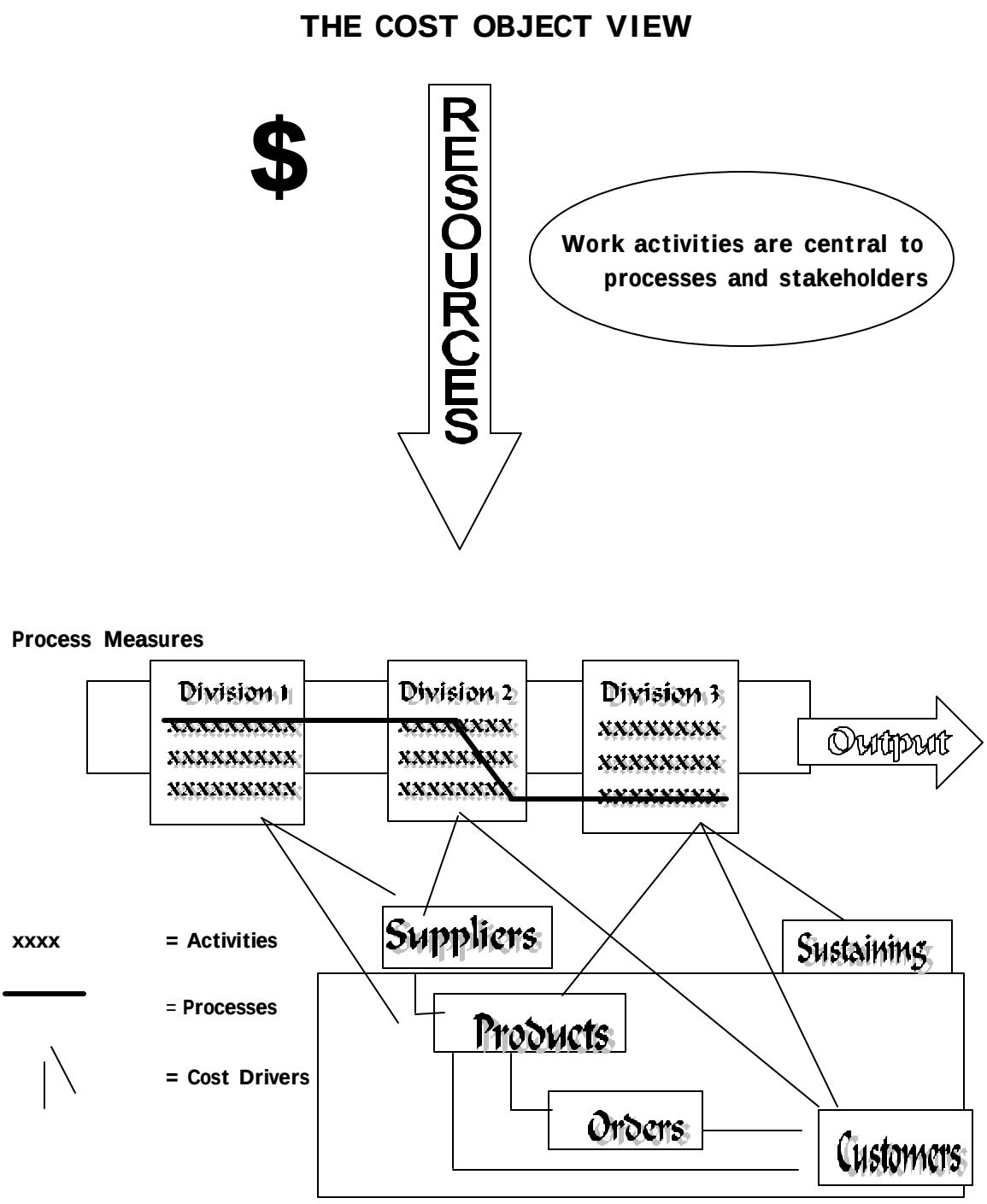

Figure 3.3: The Cost Object View according to Cokins (2001a).

3.6 GATHERING THE COSTS

CRO's individual activities may be tailor-made according to the services they provide and since individual needs differ, standardized outcomes are absent. For cost determination, this implies that a method is required which can be used irrespective of the presence of a standardized outcome. Only the ABC method meets this condition because the activity based cost method views production as a series of activities. The method assumes that it is possible to gather information on activities through expert opinions, interviews, observations, or registration forms. Since activities, rather than different types of input or output, are the main basis for cost determination, this method comes close to measuring the real cost of the product, including the real indirect (facilitating) cost (Paulus *et al*., 2002).

ABC is an accounting system that assigns costs to products based on the resources they consume (PricewaterhouseCoopers, 2000). Cooper (1991) has identified cost structure, competition, the existing costing system, and product diversity as factors conducive to the introduction of an activity-base costing model. In competitive industries, to allocate cost information accurately is essential for setting competitive outcome-based prices that still allow the company to earn a profit (Bamber and Hughes, 2001). The relevant direct and indirect expenses pertaining to selected activities, subdivided by function, should therefore be gathered within the organization at the lowest possible structural level. If overhead expenses are low, it is immaterial if the costs are gathered and allocated but if they are high, e.g. in a CRO, where expensive equipment and special expertise are needed, the cost implication will have an effect on the profitability.

According to ABC methodology it is not necessary to gather the costs on every task, but the costs assigned to activities and processes can be the best professional estimates available to support a comparative analysis within the context of the project (ABC Guidebook of the Department of Defense, 1995). ABC costs serve as a basis for comparison and fairly represent the best approximate cost that can be determined. The data is credible for comparative analys is though not totally suitable for absolute

measurement. Costs are abstract and intangible. They increase or decrease as workload changes affect their cost drivers. Since costs are not tangible, ABC operates as 'an imaging system' similar to radar, sonar or ultra-sound. Costs measure effects. Costs themselves are abstract but because costs measure effects, they illuminate root causes. ABC systems provide an enterprise-wide image of all the collective effects, plus the causal relationships relating to the cost effects. Costs give insights to root-causes, frequently through their inferences. One does not really manage costs; one can only understand the causes (reasons) of costs. Therefore, an organization does not manage costs, it manages the following (Cokins, 2001c):

- what causes those costs to occur (e.g. cost drivers), and
- the effectiveness and efficiency of the organization's people and equipment in responding to those causal triggers.

The percentage of cost allocated to an activity has a wide variance across products. The hierarchical activity list indicates how the total cost is divided among sub-activities. By itself, this observation is interesting, but of limited value. The obvious next question is "Why?" An activity analysis includes a record of how each person's time (and therefore salary) is allocated to the activities. A department's expense items, other than personnel, are also allocated to the activity. It is important to note that a department does not allocate its personnel costs as one single cost pool. Thus, when an activity's cost is out of line or when the cost is oddly split between product lines, the supporting data is easily available for explaining these anomalies.

The costs of resources in the organization "flow down" into the different activities. These costs are then allocated to the cost objects of the organization through the activities that generate them, as illustrated below in Figure 3.4.

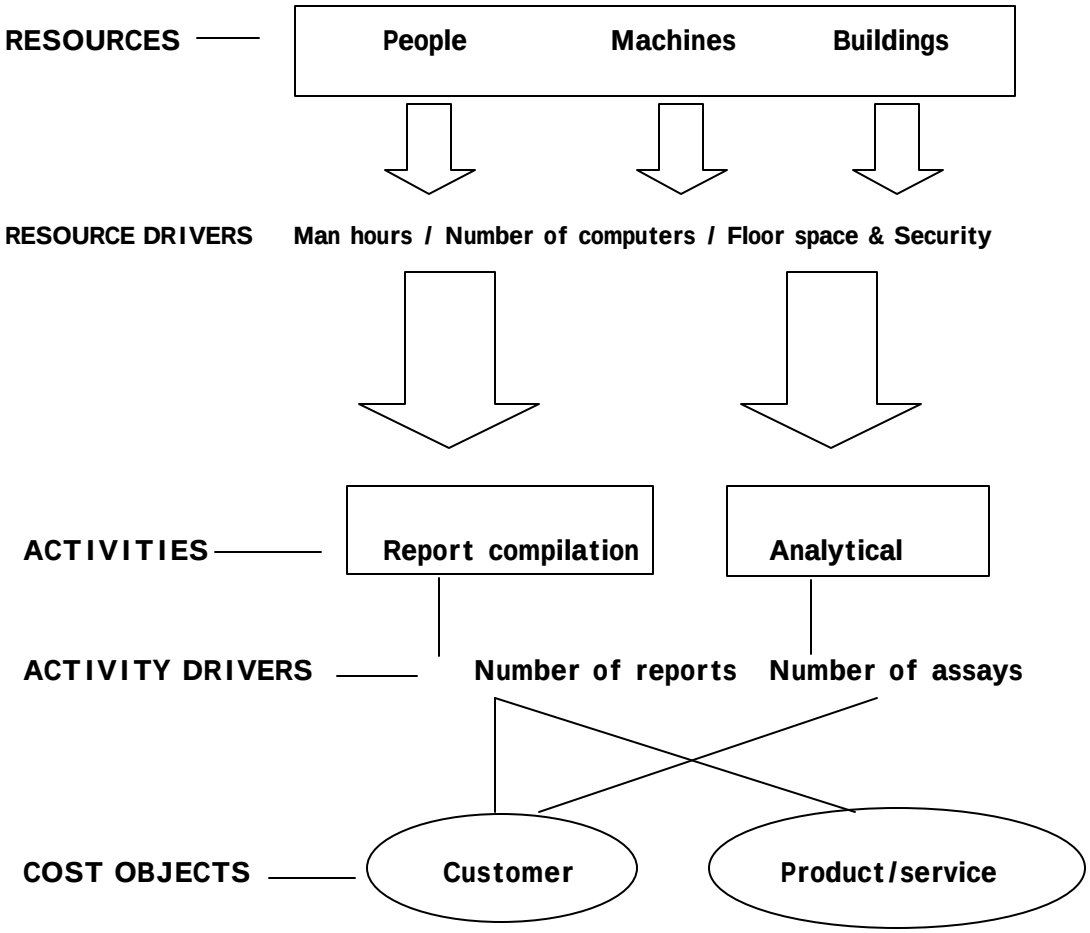

Figure 3.4 Cost objects according to QPR (2001)

The **first step** in gathering the costs of a project will be to identify the organizational resources to be allocated to the project. The resources includes everything necessary to get the job done, e.g. the manpower, equipment, rent, floor space, security and labour hours are identified and quantified according to the CRO's organogram.

In **Step 2** the cost of e.g. the man-hours, number of computers, furniture, floor space, cleaning services and security defined as the resource drivers, are distributed to the organizational structure per divisional process. The resource drivers are calculated pro-rata for each business unit's usage, to provide the service.

Step 3 involves the identification of categories of services provided by the organizational business units to provide the output of the CRO, e.g. the specialized activities undertaken by the strategic business units and what demands the activities put on the resource drivers.

Step 4 comprises selecting the appropriate level of representative costs. The number of protocols and special demands of customers correlate with the demands made on resources and are directly equal to the activity input, and generated costs.

Finally, the organizational costs of the input are redistributed to the operational elements. Thus, according to the activity input, dependent on the activity driver, generated costs can be calculated and distributed with the overhead costs as a total cost to the operational elements. The total costs incurred because of a clinical trial undertaken to produce a scientific report, can be calculated and allocated to the cost object, the client or service.

In the end, the customer, product or service is a cost object and dependent on how many reworks and non-value-adding activities were undertaken to satisfy customer demands, this cost object can lower the profit due to higher costs of

unnecessary repeated activities. The demand-pull–effect the cost object has on the costs has a final effect on the bottom-line profits of the organization.

3.7 TRACING COSTS TO ACTIVITIES

Tracing the costs to activities with ABC can be summarized as a two-step costing process based on the premise that activities consume resources, and products consume activities. ABC methodology consequently drives costs first to activities, and then from activities to products or customers. An activity's cost pool is a grouping, or aggregation, of all the individual costs associated with that activity. The different functional processes in a CRO use different amounts of the resources. The analyzing and tracing of costs of these resources to activities is combined to calculate the total costs incurred. The resulting cost for each activity will represent resource usage by that activity to convert inputs to outputs. Cost can be assigned to activities according to the function of the activity in the organization. By categorizing functions, it allows distribution rules to be applied and costs reassigned to areas where ultimately they will be allocated to the activity model. Functions can be categorized as unit-level activities, which are performed for each unit of product or service, e.g. the development of the protocol. Batch-level activities are performed for a group of products or services rather than for individual units. The analytical determination of samples, e.g. the method development, method validation, calibration, preparation of samples and the actual run of the samples, comprises a batch of activities undertaken to determine the concentration of the test drug in the samples. Then there are also product-, service- and customer-sustaining activities undertaken to support to individual products, services or customers. Facility-sustaining activities are general activities that support the organization as a whole but cannot be traced to the products or services, such as the CEO's activities. Because it is not possible to identify cost drivers for facility-sustaining costs, many ABC systems exclude these costs, or allocate them using a general allocation base (Bamber and Hughes, 2001). The three most important components of output costs are labour, direct

material and overheads (Faul *et al.*, 2000). Labour sustaining activities can be categorized as managerial and support sustaining activities, not contributing directly to the output and the operational activities with a direct contribution to the output (ABC Guidebook, 1995):

3.7.1 Operational Functions

The operational functions are those activities that contribute directly to the output. Determining the operating expenses is essential for the financial success of any business and especially important for CROs, which are under constant competitive pressure to expand services and to improve throughput time. They also need to develop new technology and methodologies constantly, all of which may require special state-of-the-art equipment and professional hands-on labour to produce the scientific reports containing the statistical analysis, analytical methods and determinations, as well as descriptions of the methods and processes followed. The operational, managerial and support activities are value adding (necessary) or non-value-adding (unnecessary) activities with direct or indirect costs. Direct cost means all costs associated with resources consumed in the production or delivery of a product or service for and to the customer. Indirect costs are associated with maintaining the business – for example, management and fiscal reporting, accounting, budgeting and auditing (McKenzie, 2001). Multiple categories of costs must be captured and identified in the activity model, with the aim of identifying and minimizing non-value adding costs. The objective is to obtain the best set of comparative and meaningful data available from existing data sources to determine how this will affect the organization's future chances for profit and to provide a basis for taking action to improve these chances (Bowler, 2001).

The cost of direct labour includes the labour costs of personnel directly involved in the product or service output. By contrast, indirect labour includes the wages of employees who are not directly involved in the product or service output, e.g. support personnel, cleaners, security and maintenance personnel. The distinction

between direct and indirect labour is an important one because direct labour tends to vary in direct proportion to a change in the volume of output. As a result, management is able to estimate the direct labour costs when planning the output production volume (Faul *et al.*, 2000). Personnel cost is the most significant variable expense of the organization. Alone it will account for 60% to 80% of the organization's total costs and can easily be traced to organizational functions according to the work people are assigned to do. Two data components of the labour force are to be estimated, namely the number of employees and cost of labour. Both of these factors will be important at different times in the ABC evaluation process (ABC Guidebook, 1995).

3.7.2 Managerial and Support Functions

Managerial functions serve as the leadership and co-ordination of the organization. Management personnel and their support staff do not contribute directly to the organization's output and must be distributed to the operational elements that do. If the support functions are divided for assignment to other elements, then the managerial costs are assigned as an integral part of the support cost total. Support functions contribute to services that benefit the entire operation but do not contribute directly to the output, and these functions are important to run internal operations smoothly. Costs for these internal requirements must be redistributed to the operational elements they support. Without the support of managerial functions, the operational output of the organizational core competencies will not be possible. As businesses have become more complex, the elements of cost/benefit have shifted and become mixed. Overhead costs are replacing the direct costs of labour and purchased material. These overhead costs increasingly comprise technology and the specialists who are needed to sustain the gains in productivity and manage the complexity of production.

ABC is particularly useful in companies with multiple products or services, because product or service complexity usually requires expensive overhead

support activities, which need careful cost management. Simplistic volume-based allocation methods used by conventional costing systems often produce distorted unit costs for products or services. Identification of the activities that cause costs to be incurred facilitates more precise costing of products and services, the reduction or elimination of non-value-added activities, and improved identification of the profitability of individual products and services (MacArthur, 1992).

3.7.2.1 Overhead Expenses

Traditional accounting never developed a meaningful approach towards allocating overheads. This may not be important if overheads represented a fraction of the total cost. However, with growing complexity, target marketing, and increasing competition, allocating overheads correctly is a prerequisite for maintaining a competitive advantage. On the balance sheet traditional accounting views the inventory, building, and equipment data as assets. Modern management sees these as an implicit interest cost whether the *asset* is debt, equity or written off through some accounting trick. This will not be seen in the account, but reflects the use of the company's assets. Nevertheless, if the cost of capital turns company profit into loss, the organization is losing value (Gering and de Beer, 1998b and 1998c).

According to Farnsworth *et al.*, (2001), the following overhead costs are relevant to laboratories and may well be applicable to CROs in general:

- quality control and quality assurance
- instrument leases/rentals, instrument maintenance contracts and the maintenance not covered by contracts;
- frequent upgrading of equipment, and
- personnel time off/instrument downtime.

Output overhead expenses are an encompassing concept and can include all costs with the exception of direct material and direct labour. That portion of the costs relating to the product or service overheads, but which cannot readily be identified as part of the direct costs of the finished product, is known as the production overheads and can include facilities, power, water consumption, maintenance and depreciation of equipment (Faul, *et al.*, 2000).

(i) Rental Equipment: Rental equipment is a variable expense that can be readily eliminated with organizational changes. These costs can also be allocated according to use. Major pieces of equipment used in support elements should probably be allocated as overhead expenses to each element served, based on the most representative evaluator of the service provided, e.g. rental for a photocopying machine should be allocated per division.

(ii) Facilities: Facilities are areas housing people and equipment performing the activities, and the maintenance and running costs of the facilities are usually captured in overhead expenses. Security and cleaning services will be allocated according to the floor space occupied by the operational division. Depreciation costs are allocated to organizational elements based on some use-factor determined by the accountant. Costs such as heat, light and power are allocated to projects and customers using a formula based on the facility's square footage occupied to produce the output (Titus, 1999). Land would not be included in any calculation since it does not depreciate (Stratton, 2001).

ABC, however, is a technique that measures the cost and performance of activities, resources, and cost objects, including overhead costs. Much of the overhead costs represent maintenance and control systems. Financial data collected on these logistics may be essential or redundant data. Theories and data drive organizational beliefs and misleading and incorrect numbers may perpetuate outworn beliefs and encourage the organization to make wrong decisions, or else reinforce resistance to the *right* decisions (Baden-Fuller and Stopford, 1992).

Because of the fact that many of the accounting systems tend to consolidate overhead costs or pay them centrally, there are often problems with defining and documenting separate amounts by type. Overhead expenses such as utilities, maintenance, security, etc., must be identified for applicability and relationship to the projects. The identification process should preferably be as detailed as possible since some costs may be used while others are excluded by a defined rationale. Truly fixed costs, which cannot be changed by minor organizational changes, may not have a significant role in the activity model.

The above-mentioned overhead expenses can be identified as direct or indirect expenses that can also be influenced by the consumption-driven demands of customers. A decision should be made on how to capture and identify these organizational costs. The direct costs of the support and managerial functions that have an apparent relationship to the organizational element should be determined according to the percentage of time devoted to the operational function.

3.8 ESTABLISHING THE OUTPUT MEASURES

To establish the output measures, work activities should first be mapped to understand all the dimensions of the business processes, how the organization behaves and works as a system. The focus then changes from a macro-view to the detailed level of the activity when the output is measured. Ideally, activity cost drivers should reflect a causal relationship between an activity and the cost object; measure how often the activity is performed, and reflect the level of effort required to complete an activity (Brand *et al.*, 1999). It can then be established how much of the cost of an activity is used for a unit of output and how much time, actual and elapsed, it takes for one unit of output. The activity output measures therefore serve as the ABC device to directly answer the *how many*, *how much* and *how fast* information needs of management. With the latter information available, a performance-based pricing system can easily be formulated to ensure that the customer pays according to services received. The relationship between customer demands and the costs incurred to meet the demands, can be determined,

because the cause and effect nature of the services and work performed can be identified. Establishing activity output measures enables management to conduct scenario analysis to evaluate service level alternatives (Cokins, 2001a).

A demand made by the cost object, e.g. the customer, generates activities which makes demands on resources with related costs. The more labour intensive the demands made by the cost object are on the resources *via* generated activities, the higher the total output costs will be. In a CRO, the organogram is generally not simplistic. Different operational strategic business units, with different output processes, synergistically provide services to produce the result, e.g. the scientific report. A bottleneck or delay in a unit will result in a downstream ripple effect and pressurize other units to reach timelines with accompanying costs. To compensate, for example, lost time, additional resources will have to be employed (either manpower or man-hours) to make up for lost time to ensure that set deadlines are met. The interdependency of activities performed in the process flow make additional demands on the resources if reworks are necessary and these costs need to be allocated to the product output and also to the final cost object, the customer.

Costs are allocated in a two-stage procedure: resources such as people, machines, materials and supplies are assigned to work activities, and each work activity is then reassigned to its product, standard service line or customer, based on its unique relationship with an activity cost driver. However, a multi-stage cost assignment as opposed to a simplistic two-stage assignment as to how much of the activity is consumed by a specific product or service line, is necessary. With an expanded cost assignment model, intermediate stages of activity-to-activity cost assignments and cost-object-to-cost-object assignments are possible. The expanded model destinations provide trace ability from beginning to end, from resource expenditures to each type of customer - *the origin of all costs*. This assignment network reveals that all costs originate *via* a demand-pull from customers, and the costs simply measure the effect. Not all activities can be

traced directly to products and service lines, but they can be traced to the work activities that consumed them (Cokins, 2001a).

The activity output of each division can be established by reviewing what the activity does and what it produces. After determination of what observable action of product the activity produces, the activity output of a particular activity can be established. Each activity may only have one primary output for measuring purposes. One primary output that can be measured easily should be used as the output measure for the activity. The operational divisions in a CRO have specialized outputs that can be analyzed, e.g. the planning phase of the project, clinical execution, the analytical determinations of the samples and the statistical analysis and report compilation. The final process to the product/service output occurs when the project manager compiles the results (output) of each division according to customer and regulatory requirements.

The output needs to be measured as the actual time and the total time required in executing the work from input to output. However, projects do not always run smoothly and delays are often inevitable. Then elapsed time should be taken into account. The time of the process from protocol development to the submission of the final report will represent the time from input to output and will include delays. The actual time is the time required to conduct the work of each of the activities from input to output without consideration of additional time for processing delays, postponements or normal backlogs. The elapsed time is the actual time, including any normal delays or routine pauses that occur within the regular activity processing. One factor that affects the total lapsed time and which would require a separate decision, is how to handle abnormal backlogs in the process flow that have occurred due to inefficiency, reduced resources, breakdown of equipment or unexpected work load. This backlog is an unnecessary delay in the workflow created by indecision or lack of control and response by management. If it arose due to the current procedures and policies, it must be addressed as an item for improvement.

The output measures determined must be the best representation of the data available, because if not accurate, a fair representation of the resources used and costs involved in the process will lead to bad management decisions. As the project manager is ultimately responsible for all customer/project requirements, the output measures must therefore not add to an already daunting list of tasks and activities. The technology and management processes must allow the project manager to effectively control the scope of a project and easily assess the impact of changes to requirements (Starbase Corporation, 2001). Requirements should be managed at the object level because requirements, resource capacitor and costs are linked, which makes *thinking outside the box* a prerequisite for CRO project managers.

The costs incurred by processes may have a detrimental effect on the rate of return on investment of the company, and therefore cost analysis should be viewed holistically. Feasibility studies to analyze requirements of customer demands are necessary if the capacities to handle customer demands are available. Thereafter a cost analysis of resources costs needs to be done to trace the activity costs to the product or service delivered, as required by the customer, to calculate the cost versus the rate of return on the capacity usage to guarantee predicted profitability. The following diagram illustrates the interdependency of inputs and outputs on profits. If the resource requirements are increased to handle activity requirements without analyzing the optimal resource capacity usage, resources costs will increase, resulting in lower profitability. The requirements in relation to the available capacity should be analyzed in a feasibility study to establish the final effect on the profitability as illustrated in Figure 3.5.

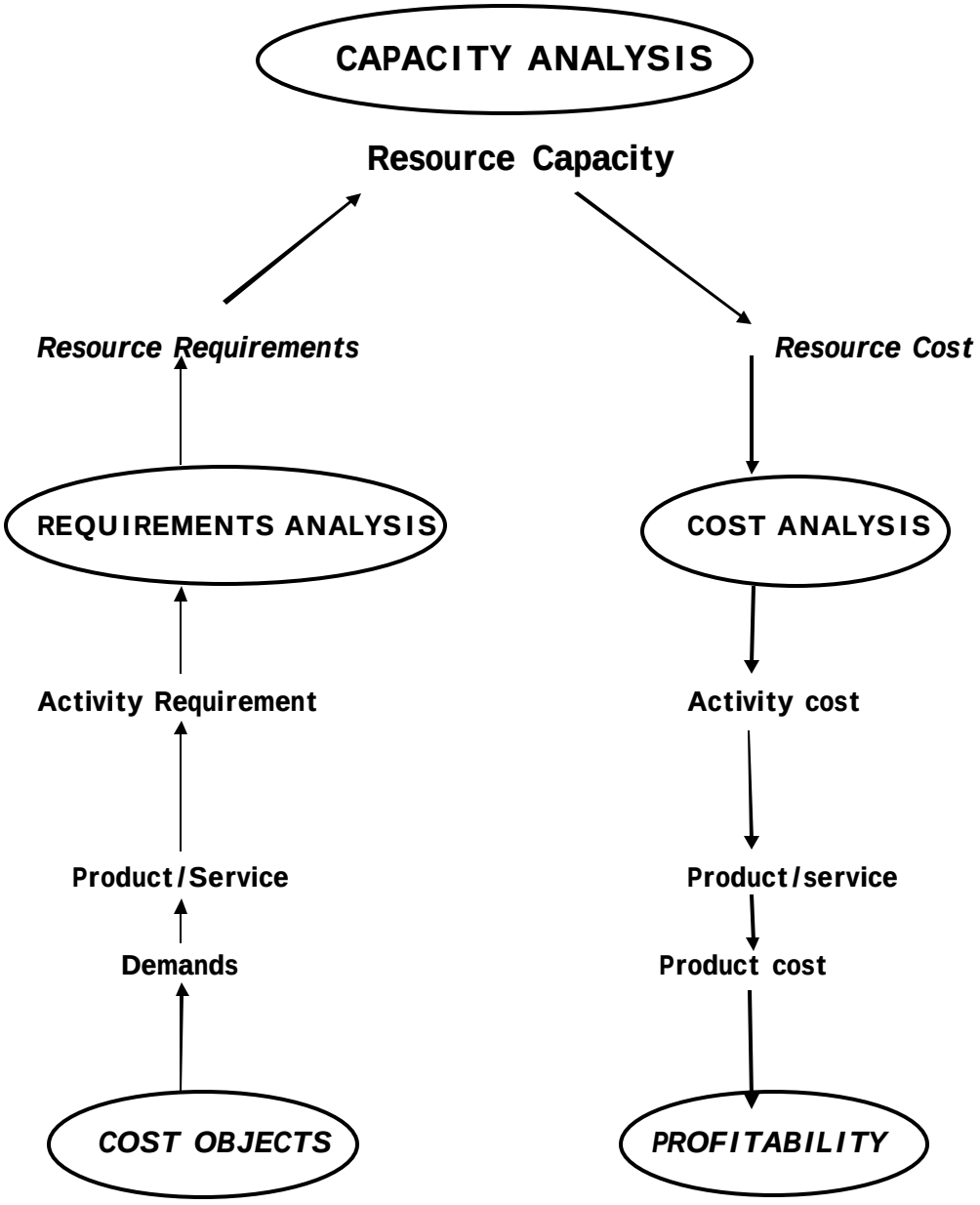

Figure 3.5 Capacity analysis according to Cokins (2003)

The determination of expenses and product cost can only be calculated after establishing what the activity requirements regarding the available resource

capacity usage will be and a requirement analysis has been performed. The resource cost can be calculated *via* a cost analysis of the activity cost, using the physical resource driver rates to calculate the product and service costs. These rates are regularly expressed in hours, full-time equivalents (FTEs), square meters, Rands or other relative units, and together with the resource costs they directly influence the profitability.

Cooper and Kaplan (1992, in Bamber and Hughes, 2001), discuss the importance of capacity in ABC. The latter can also be described as a resource usage model in which:

Activity Availability = Activity usage + Unused capacity.

The equation can be useful when a pricing structure for a CRO is considered because project cancellation often poses a risk to CROs, leaving them with unused capacity and loss of revenue. The risk of project cancellation and corollary loss of income can be spread over all the projects by charging an estimated fee for unused capacity.

3.9 ANALYSIS OF ACTIVITY AND PROCESS COSTS

The final step of an activity model will be to analyze the activity and process flow, in conjunction with cost and time measurements. This information will be reviewed and analyzed to determine the processes/activities identified for improvement. Activities and work processes are the objective of re-engineering or improvement and not the organizational elements. Merely reorganizing divisions will not achieve dramatic results. The major purpose of exploring an activity management model for a CRO is to allow the re-engineering effort to be applied to how the work is actually done and not to how divisions should accomplish the work.

Textbooks of management theory often classify organizations in a simple framework of structures and models. In reality, there are as many models as there

are companies. Each company has distinct strategies, cultures, resources and internal processes that dictate a unique organizational structure. Furthermore, dynamic changes in organizational goals and resources, as well as the business environment, mean that a static structure is not always appropriate (Kermani, *et al.*, 2000).

3.10 CONCLUSION

Action will remove the doubt that theory cannot solve

Tehyi Hsieh

The information outlined in this chapter endorses the fact that activity-based management incorporated in a dynamic management model is not to be negotiated, it is part of the activity-based competitiveness of the new millennium. The sum of all mechanisms employed within the activity to produce the output, within the constraints of available capacity, incurs costs with an effect on the bottom-line profits. The cost driver quantifies what is produced, e.g. a protocol or scientific report and the cycle time from input to output includes actual time (capacity usage) and elapsed time (unused capacity) which both have an effect on costs and profits. The process cycle is often driven by non-chargeable customer demands, with the result that non-value adding activities are undertaken. The sum of the total cost driver determined costs applied to the output as it passes through the activities, could highlight non-value adding costs. The non-value adding time traced to costs can be determined if the sum of the elapsed times of the activities in the process flow is compared to the real time of each activity logged without the delays. To ensure that the customer gets what he pays for, but also that he pays for what he demands and gets, especially if unnecessary demands are made, the profitability of the company has to be managed and not by merely left to chance. The possibility of managing the company's profitability is what makes an activity-based management methodology such a valuable technique to implement.

CHAPTER 4

RESEARCH METHODOLOGY

4.1 INTRODUCTION

The literature described in the aforementioned chapters emphasized the importance of time, quality and costs in business management and that there is a correlation between customer demands and these variables. The relationship between these variables is well described. However, a management model as it relates to activity-based management for a CRO is not generally explored. As described in Chapter One, CROs are part of the drug development value-chain to market new drug entities with an urgency for speed, at maximum profits. They operate in an environment where the characteristics of speed and quality in performance determine the competitive edge of the company. These characteristics, however, correlate with costs and price because both can only be attained at a cost to the company and that cost needs to be contained. The industry is also heavily regulated globally and performance needs not only to conform to these standards but excellence in quality and performance to add shareholder value, also needs to be embedded as company culture, as part of the company environment. Dearman and Shields (2001) observed that when volume-based cost information is used for products that are not homogeneous and volume-based, cost knowledge content without ABC or activity knowledge, adversely affects managers' cost-based judgment performance. Conversely, greater ABC, knowledge content and activity knowledge increase cost-base judgment performance. Thus, managers' cost-related judgment performance is linked to their cost-related knowledge. To align company performance to these objectives as part of the core business of the CRO, the need for an effective management

model that coordinates and combines available activity-based best practices as a generic model for CROs, is evident.

The decision as to what method to use in this research project was limited by the competitive and secretive of nature of the CRO industry. Therefore, the data needed for the analysis are not generally available and a case study was the only option for this research. Historical data available from scientific reports were used because of the lack of a custom developed electronic data-capturing program at FARMOVS-PAREXEL at the time of the empirical study. The other option, to collect real time data per hard copy, was experimentally tried as a pilot study in PMD, but without success. Because of the workload of the personnel, they were reluctant to keep a record of daily activities undertaken. Therefore, historical data were gathered from available scientific reports and source data. The methodology of activity-based management models is well described in literature. Information from these literature sources was used to evaluate best in class management models to construct a management model for a pharmaceutical CRO. The literature study also revealed the importance of a customer focus and the effect that non-value adding customer demands have on resources and consequently also on profitability.

4.2 RESEARCH DESIGN

Field research in management is generally associated with cross-sectional research, the systematic collection and analysis of data from multiple sites at a point and time; time-series research, collecting and analyzing longitudinal data studies from one or a small number of organizations; case studies, and in depth study of the experiences of a single organization at a single point in time. Field research is mostly descriptive and it helps to develop theories, to explain how the world is and how it maintains itself. Field research can also be used for testing theories. Such theories are generally about stability, equilibrium and optimality. The theories predict that people and organizations behave in certain ways (Kaplan, 1998).

The field researcher collects data that can test whether the actual behaviour of individuals and organizations is consistent with the hypotheses in the theory.

The field research method followed for this thesis was one of a case study. The data of a sample of contract research projects/studies from a single organization, FARMOVS-PAREXEL, over a period of 19 months was collected. The data were collected according to an activity-based methodology, analyzed with a statistical and productivity model, to construct a management model and to establish whether the actual behaviour of the CRO was consistent with theory and with the objectives formulated for this research.

The study can be defined as an explorative research project with the design classification of a case study with numeric exploratory analyzes of research projects executed at FARMOVS-PAREXEL.

4.2.1 Research Data

The data of the research project were divided into primary data and secondary data. The primary data consisted of historical activity and related costs incurred in respect of 30 bioavailability projects contracted to FARMOVS-PAREXEL. The selected projects were executed over a period of 21 months.

Secondary data were obtained from books, journal articles and information on the Worldwide Web (www), as well as from the University of the Free State's Library databases, and CD's were accessed *via* the Library Inter- and Intra-net. Real-time data were gathered from Final Scientific Research Reports.

4.3 SAMPLE SIZE ESTIMATION AND PROJECT SELECTION

During the year 2000, 66 bioavailability projects were contracted to FARMOVS *(FARMOVS-PAREXEL after October 2000)* of which 22 projects were either cancelled or not initiated at the time of the project selection and evaluation. The

remaining 44 projects were evaluated and a random judgment sampling of 25 completed projects with reports available, were selected. The main criteria for selection were the availability of a final scientific report. The sample size is equivalent to 57% of the projects contracted in 2000 considering the number of project cancellations during 2000. Over and above these projects, the last 5 projects contracted in 1999 and completed from the end of 1999 to 2000 were also added to the sample population to increase the total number of evaluable projects to 30. The sample size is equivalent to 50% of the average projects contracted per year if it is taken into account that approximately 60 projects (bioavailability and clinical studies) are completed per year. According to Viljoen and van der Merwe (2000), a sample size of 30 and more is considered a large sample size. In a large sample (e.g. 30 or more) taken from a population that does not have a normal distribution, it is considered that the distribution of the sample will be approximately normal.

4.4 DATA COLLECTION

To assess the activity time and costs of processes, relating to the assessment of the bioavailability of generic drugs was selected for standardization purposes. Project design, objectives, population for inclusion, and the fact that all the operational divisions are as a rule involved in the execution of these projects, largely standardize these projects which corollary contributed to their selection. Conversely, the objectives of Phase II and Phase III projects are generally to prove efficacy and tolerability in patients, and the protocol design, objectives and time-frames differ greatly. The time-frames for the patient studies (Phase II – III) projects are as a rule also much longer: they are usually multi-centered projects over and above the fact that all the business units are usually not involved in the execution of a study. Therefore, the cost associated with these aforementioned activities, and the output measures in relation to standardized activities executed during bioavailability research projects, will impose an improper distribution of output costs, which may change and distort the management model and

recommendations. The criteria were set to ensure a homogeneous sample of projects with the least accompanying variation in design, which may interfere with the scientific evaluation of the research results.

4.4.1 Criteria for Data Collection from the Selected Projects

Projects were evaluated with an activity focus to be able to trace the information to time and cost variables. To have process control in the multitude of different activities and different output measures it was essential to ensure the consistency and utility of the data. To ensure the consistency from activity to activity the following steps were used to collect data from the different projects:

(i) Representation – Activities of which the output of the activity represented all the effort employed and varied in direct relation to the increases and decreases of the activity performed, were selected. Costs incurred by the activity to convert inputs to outputs had to be traceable and a representation of the cost of the activity output had to be given.

(ii) Measurability - Activities undertaken to produce an outcome had to be measurable. The data had to be verifiable objective data, available and consistent. A prerequisite was that processes should produce one main, measurable outcome with a start and end date.

(iii) Homogeneity - The activities performed and outcomes produced were homogeneous between the selected projects to fit in with the total performance in the process flow for each business unit.

(iv) Detail - The inputs and outputs were sufficiently detailed to provide the relationship and cost distribution for the studies. However, they should not have been too detailed to make measuring and recording unnecessarily difficult. Therefore, activities were not evaluated at a micro level of tasks, but rather a macro view of processes per division was taken.

(v) Relativity - The cost associated with the activity and the output evaluated was in relationship to the rest of the operational activities of the divisions and of sufficient importance. If it contributed to just a very small portion of the total cost it was not included in the analysis.

(vi) Processes - Processes in each of the operational divisions with one primary output, were selected.

(vii) Cost drivers - The duration and total number of the selected processes, a measurable factor that represented the amount of effort, identified as cost drivers, were determined retrospectively from source data and study reports.

(viii) Costs - Costs and expenses incurred by the resources to perform the activity were traced to each cost driver. Cost per output unit, the total process cost divided by the total units of output, was calculated.

(ix) Time - Customized Excel spreadsheets were created for data entry of identified project activities with start and end times calculated. Costs were allocated to the cost drivers according to direct and indirect resources used. Real costs were compared with quoted fees in the financial contracts to estimate profitability. Actual time and elapsed time of each activity were calculated.

(x) Cycle time - The average life cycle of each study, as well as an estimation of the ideal time processes could have been performed in, were calculated.

(xi) Profitability - The ratio of the mean costs and the fees were used to establish to what extent divisional performances contribute to company revenue. The maximum potential profitability was calculated.

(xii) **Number of requests -** The requests received to bid for research projects and the number eventually contracted were collected over a period of 2 years to establish if the 80/20 rule of the Pareto law had been followed.

4.4.2 Accessibility of the Data

A bioavailability project was selected and evaluated for process time and related costs, if the final scientific report was available, to ensure that all the data were accessible. Time data for activities, cost drivers and related costs of Phase I, bioavailability projects conducted at FARMOVS-PAREXEL Research Organization, contracted from 17 September 1999 till 02 October 2000, were included in the cost and time analysis.

The final reports and source data used to obtain the data for this research project are available at FARMOVS-PAREXEL and will be archived for 15 years, unless the sponsoring company requests alternative arrangements. However, as a result of the confidentiality agreements between FARMOVS-PAREXEL and the sponsoring companies, the sensitivity of pharmaceutical research results, the data used in this analysis, will be identified by study numbers and the relevant reports classified as confidential will not be available to or accessible for review by an unauthorized person.

The accessibility of the data needed, the means of obtaining it as well as its treatment, interpretation and presentation, taking into consideration the confidentiality of the case studies, will be discussed below.

4.4.2.1 The Data Needed

Processes undertaken were identified to define relevant cost drivers in the execution of bioavailability projects. Time data pertaining to these processes were obtained from the final research reports and source data of the completed projects. The relevant costs and expenses were obtained from the Financial Division, FARMOVS-PAREXEL and traced to the cost drivers. The Financial Contacts (Appendix 9.2) of the selected projects were evaluated in relation to real-time costs to predict the profitability of the project.

4.4.2.2 The Location of the Data

Standardized activities are undertaken in the execution of bioavailability projects. Approximately one hundred and fifty (150) activities and tasks undertaken by the operational divisions were identified (Appendix 9.4). More could have been identified but this was deemed unnecessary for the scope of this research project. From these activities and tasks main processes with end dates were selected and the start and end dates were obtained from source data and research reports. The main activity pools and cost drivers identified as the relevant indicators of the outcome of the results were selected from the time and cost data sheets to be included in the process analysis. Activities broken down to low level tasks, e.g. literature search for protocol development, were deemed unnecessary for the purpose of this research.

4.4.2.3 The Means of Obtaining the Data

Retrospective primary data were obtained from hard copies of the financial contracts and reports archived, as well as from data available on the FARMOVS-PAREXEL intra-net or that stored on CD's, and source data available in the divisions. Informal discussions were undertaken with personnel of the strategic operational divisions as well as the Division of Finance. Formal questionnaires were not used to capture data.

4.5 DATA MANAGEMENT

Data capturing for this research was done manually from final reports and source data because of the lack of an electronic data capturing software program. The data were screened for irregularities such as unrealistic process start and end dates. Apparent inconsistencies were corrected.

4.5.1 Identification of the Activities

Activities were evaluated and value-adding activities pooled per division. Billable value-adding activities with real-time start and stop dates were selected

for the analysis. However, the quality assurance procedure as a non-billable activity was selected because auditing is a process to ensure conformation to international Good Clinical Practice (GCP) standards, and was considered as part of the company's outreach for excellence and zero defects.

4.5.2 Estimating the Costs of Each Activity

According to the definition of an activity-based technique, it identifies the cost pools, or activity centers, and assigns costs to products and services (cost drivers) based on the number of events or activities involved in the process of providing a product or service. It is about the resources, processes, and money required to produce a product or service. The elapsed time, the total time (including delays) as well as the cycle time (without including delays) resultant in the time consumed to complete one process of the cost driver, were calculated. Resources labour costs for the time consumed by the activities were calculated. A CRO is a service providing organization. Therefore, labour costs in relation to time were calculated for the activity pool in each operational division. The average labour costs were calculated per division by means of the average salaries of the unit, including management's salaries. The CEO's salary was not included in any of the calculations due to the fact that it is a fixed cost not contributing to a single division's output.

4.5.3 Identification of the Cost Drivers for the Activities

The value-chain in each of the operational divisions was evaluated. The output of each division, as well as value-adding processes undertaken to produce the output, were identified as cost drivers for the activities. The cost drivers for the activities per division are:

4.5.3.1 Project Management Division

The protocol development time from Version 1 to the Final Version of the protocol as well as the coordination of the project from Version 1 to the Final

Scientific Report completion, were identified as cost drivers. Although the project manager's time input is not only devoted to a single project, because more than one project is handled at a time, the coordination of the project is an activity undertaken throughout the life-cycle of the project from project initiation to close-out. Activities e.g., as amendments and deviations to protocols sample size were also evaluated for significance as cost drivers.

4.5.3.2 The Clinical Division

The times of the following activities were calculated separately:

- the period that the volunteers have to stay in-house in the clinic;
- preparation and filling in of the CRF;
- the screening of volunteers;
- handling of data and samples from screening to last blood sample, and
- for the Transit Laboratory: labelling, centrifuging, and storage of samples from first clinic day to last sample to Bioanalytical Division.

However, because the activities overlap and the times of some of the activities, e.g. the preparation of the CRF's were estimated, the decision was taken to pool the activities. The activity pool from screening to the last blood sample includes all the activities undertaken by the Clinical Division. There are also real-time start and end dates for this activity pool documented in the project scientific report.

4.5.3.3 Bioanalytical Division

Time data on the following processes were gathered and the significance as cost drivers evaluated:

- method development;

- method validation;
- assays of plasma samples, and
- analytical report compilation.

The lag time, *viz.* the time from the last sample receipt until report to PMD compared to the time of different procedures, was calculated, as was the cost due to lag time. The time data of the process from the time of the last sample received till the analytical report was forwarded to PMD was used for the calculation of the activity time and cost calculations. The reason for choosing this activity pool was that the sum of the time of the individual procedures (excluding lag time) was longer for some projects and shorter for some than the time which elapsed from last sample receipt to the Analytical Report completion, because activities were undertaken simultaneously. To standardize the activity pool to time data most realistic to a start and end date, the process from last sample receipt to report to PMD was selected for the calculation of the time and cost data, although the individual procedures were also calculated.

4.5.3.4 Biometry Division

The biometry division offers a 24-hour service for bioavailability clients at a special fee. The projects included in the random sample for evaluation were not contracted as such. The time of the statistical analysis included in this research project is therefore generally longer than 24 hours and includes actual time and delays. The time started with the date the concentrations were received from the Bioanalytical Division and continued until the data were transferred to the Project Management Division.

4.5.4 Allocation of Indirect Costs for the Activities

The indirect costs, e.g. the costs of quality control processes, were incorporated in the project management process and the cost included in the labour fee for the Project Management Division. Overhead costs were calculated, including rent, cleaning, security and support services, as well as depreciation of computers and

furniture. The cost for the cleaning and security services were calculated in accordance with the floor space each division occupies. The cost for support services were also calculated from the mean divisional salaries, estimating that 50% of their time is spent in support of the bioavailability projects.

4.5.5 Allocation ofthe Indirect Cost Rate to Each Activity

The indirect cost rate for the depreciation of furniture and computers, and the cost for quality assurance and support services (financial, cleaning and security), were calculated relative to time and divided between an estimated 60 projects in total. Support services are provided for bioavailability as well as patient studies; therefore, 50% of their time-input is allocated on a pro-rata base to the 30 projects evaluated in this research. The indirect costs were allocated for each activity pool (operational division) according to the head count and the floor space occupied per division per project.

4.5.6 Determination of the Cost Drivers to Estimate Resource Demands

The total cost of each cost driver was calculated according to the labour cost the activities consumed as well as the overhead costs allocated to the cost drivers. The labour cost was calculated using the average salary per division, including the manager's salary. From the actual quantity of the cost driver each cost object uses, the demands made by the cost objects on the resources were estimated. The profit per division was also estimated from the available actual cost of the cost object. The cost object makes demands on the resources in relation to the actual cost of the activities undertaken to produce the output. The ratio between the profit and the head count per division was calculated and presented as the productivity of a division.

4.5.7 Allocation of Activity Costs to Cost Objects

The cost object makes demands on the resources due to the activities undertaken by the resources to produce the output. By allocating the cost incurred by the

activities (undertaken by the resources) to the cost object, the total cost of the cost object can be estimated. With the real cost calculated to produce the required output, the profitability of the cost object can be determined.

4.5.8 Normalization of the Data

Data were normalized per:

- day (24 hours) or per hour if shorter than 24 hours;
- time (days or hours) were rounded up or down, and
- time and costs were calculated per unit output.

Individual salaries were not used in the calculation of labour costs, but the average salaries per relevant division were used in the analysis with management salaries included; however, the CRO's was excluded.

4.5.9 Cross Validation of the Data

The following steps were implemented to ensure cross validation of the data:

(i) Reproducibility: The sample size presents approximately 50% of the bioavailability projects conducted per year at FARMOVS-PAREXEL. Therefore the results obtained from this large sample of projects can be regarded as reproducible and having a normal distribution curve.

(ii) Precision: The cost data were calculated in relation to real time data, and not from estimated time data, except for the estimation of the Quality Assurance time. The precision of the data as a measure of the intrinsic ability of the research methodology to give consistent and distinct numerical results can therefore be assumed with confidence as being reliable and precise. However, models with estimated data are considered as acceptable in literature.

(iii) Specificity: The analysis of the data, descriptively and statistically, provided end results in line with the stated objectives of the research project.

(iv) Sensitivity: The calculation of the control cost (the cost associated with an

ideal time) can also be considered as a sensitivity analysis to simulate options for exceptions, such as time entry, to ensure that the same end result is reached in different situations. The results of the ideal-time cost analysis demonstrate the sensitivity of the method to a change in the numeric data of a primary variable, e.g. the time. Demonstrating sensitivity to a change in the numeric values of the primary objective is important to ensure the validity of the data.

4.5.9.1 Validity of the Data

Critical variance thresholds for time and costs were predefined according to the length and design of the project from start to end date. The data were screened for validity and unacceptable data outside predefined variance thresholds were checked visually and excluded if no satisfactory answer to the data query was found.

4.5.9.2 Reliability of the Data

The data consisted of measurable efforts. Discrete increments of work, with a definable time schedule with a start and end date for accomplishment and completion with tangible results and traceable costs, were collected. Levels of effort, e.g. work that does not lend itself to subdivision into discrete time scheduled increments of work, such as support services of the kitchen and project quality control, were not included in the analysis because time-frames could not be determined with start and end times or dates. There might be a difference between work capacity and work accomplished. By using both costs of work performed and work capacity, an integrated cost reporting system was developed that provides a basis for productivity analysis by measuring the profit of the output in relation to the head count per division. Although the cost for labour days used was an average cost for the division, and the sensitivity analysis was done by means of the ideal cost analysis, the average costs can be accepted as realistic and reliable.

4.6 THE CALCULATION OF OVERHEAD AND LABOUR COSTS

The allocation of the overhead costs for equipment was done in relation to the depreciation of the equipment in each division. All fixed assets were initially recorded at cost. Cost includes all costs directly attributable in bringing the assets to a working condition for their intended use. Depreciation was calculated on the straight-line method, to write off the cost of each asset to its residual value over its estimated useful life. The equipment of the division (business units evaluated in this research project) was expressed as a percentage of the total. The allocations were made to the following divisions (Table 4.1): Bioanalytical Division, 69%; Biometry 2%; Clinical Division 24%; Project Management 1%; QA 0.5%; Support Services 4%.

Table 4.1 Value of equipment used to calculate overhead costs per project per division

Division	***Value of equipment***	***Percentage of total***
Analytics	R 4 932 005	69%
Clinical Division	R 1 733 363	24%
Support Services	R 255 496	4%
Biome try	R 107 782	2%
Pharmacy	R 97 610	1%
Project Management Division	R 80 100	1%
IT*	R 58 600	0.8%
QA Division	R 36 939	0.5%
Business Development Group*	R 6 380	0.09
Regional Management*	R 1 572	0.02%
Total (100%)	**R 7 190 557**	

** Divisions were used only to calculate the total.*

The closing net carrying amounts for the period ended 30 June 2001 of the FARMOVS-PAREXEL Financial Statements were: Furniture and Fittings R 7 309 848; Computer Equipment R 1 243 372. The Cost Accumulated Depreciation: Furniture and Fittings R 3 118 160, and Computer Equipment R 564 358. For each operational division the depreciation was calculated according to the percentage of the total equipment. The results were converted to a single study by dividing the depreciation per division by 60 because it is the estimated capacity (bioavailability and clinical patient studies) that can be completed annually.

The depreciation of the computers was calculated in accordance with the head

count of each division, because one computer per employee is approximately allocated. Thereafter the depreciation was calculated per project because the cost of the deprecation must be allocated to every project undertaken. The rent (R 176 667 per month) and cleaning (R 30 000 per month) and security (R 13 174 per month) services were calculated according to the floor space usage of each division.

The Support Services Division dedicates 50% of its time to bioavailability studies. Therefore, 50% of the actual time of a project, from start to finish, was used to calculate the support services time and, accordingly, the cost per project, using the average salary for the Support Services Division. In all the calculations, the mean salary for the division was calculated by including the manager's salaries. The QA time spent on quality assurance of the bioavailability projects was calculated in accordance with an estimated 36 working hours per QA officer (an average of 5 working days) per project[5].

A project is allocated in general to a single employee because one primary responsible person is always dedicated to a project in each operational division. Clinical research is labour intensive and impossible without team effort, especially in the clinical division where a project nurse will be allocated to a project but, a team of project nurses will assist with the logistics of it. Conversely project managers are responsible for more than one project at a certain time and point. They work intermittently on a project and are responsible *inter alia* for the administrative management throughout the project's life cycle. The activity costs were calculated taking the resource input of one dedicated employee per study into consideration whether teamwork was employed or intermitted work was at stake.

[5] The information was obtained during an informal discussion (28 October 2001) with an auditor and financial officer.

4.7 DIVISIONAL PROCESS TIME, COSTS AND PROFITABILITY

The actual time data converted to labour costs for manpower input as well as the resource's usage of equipment and facilities (overhead costs) were calculated as the service cost for the 4 divisions. The costs of consumables were not included in the analysis. Labour costs (calculated in South African Rand per day) for a division, were calculated as the mean salary of the employees (managers included but CEOs excluded) in the division. The average salary per employee was used as the labour cost in the calculations.

The shortest possible time in which a process could have been completed was estimated as an idealistic time. For example, an ideal time was calculated with the assumption that only the analytical assays and report compilation were done, assuming that no method needed to be developed. Unnecessary lag time during the execution of operational functions was evaluated and the ideal time calculated with the lag time omitted.

The estimated profitability was expressed as the difference between the costs calculated according to the time consumed by resources, and the fee charged for a service. This evaluation is relevant when compiling a management model because fees charged, less costs incurred, will determine the operating cash-flow. PMD and the Biometry Division have negative profit figures. PMD's prolonged time can be attributed to the long cycle time and corollary cost input of a single employee to the life cycle of a study.

4.8 STATISTICAL ANALYSIS OF THE DATA

The data were entered on an Excel spreadsheet and exported to SAS (Version 8.2) for statistical analysis and calculation of maximum and minimum parameters as well as the medians/means, standard deviations, and coefficient of variance (CV). The statistical analysis was presented as a variety of tables and figures.

A management model was constructed from the data gathered and best business

practices evaluated. Time, expense and cost results are presented in table and figure formats for visual interpretation.

The unvariate association between numerical variable and the dependent variables cost and time were assessed using correlation coefficients. The univariate association between categorical variables and the dependent variable cost and time were assessed using Mann-Whitney and Kruskall-Wallis tests. All variables which were univariately associated with the dependent variables ($p<0.05$) were entered into a linear regression model.

4.9 LIMITATIONS OF THE CHOSEN PROCEDURE

The intelligent man finds almost everything ridiculous;

the sensible man hardly anything

(Goethe)

One needs a very open-minded attitude to a scientific investigation of business processes because there may in fact be no end point, but only a constant unfoldment (Brom, 2003). The following points, although debatable, can be noted as possible limitations of the chosen procedure to develop a management model by means of an evaluation of the workflow processes and corollary costs incurred by a pharmaceutical CRO.

Historical data of processes were used *viz.* activity pools (processes) with real-time start and end dates documented in source data or captured from scientific reports. Continual time logging on all levels of activities performed was not gathered. A macro-view of process evaluation was followed.

Questionnaires or extensive interviews with personnel were not used to gather information although discussions with individual employees, departmental heads, and personnel from the finance department were undertaken. Historical real-time

data were gathered from reports and source data.

The financial and research activities/processes in the CRO industry are considered as confidential intellectual property. Company information is not generally available for research purposes. Special permission was obtained from the board of directors of FARMOVS-PAREXEL to use the bioavailability projects as a case study. Therefore, only data gathered from research projects undertaken by FARMOVS-PAREXEL were used. Due to the confidentiality of contract research data, project information could not have been included in the results and information from other CRO's could not have been obtained to be included.

Limitations to an activity-based management model are also described in literature. Most activity-based models require substantial time to create, develop and to implement. Compiling data and educating people are slow processes. Changes in the organization's business processes inevitably result in changes being made to the model with more time being spent in updating and implementing the model to reflect those changes. Due to this, a point can be reached were the model is put aside because other relevant aspects of the business processes seem to have more direct effect on the bottom-line results than the activity-based model results have.

As a rule, people are not willing to undergo behavioural changes and a new initiative is not going to change the corporate culture in an organization. According to Leahy, (2001a, p. 4) "The success of an ABC model implementation has always been 20 percent getting the mechanics and methodology right, and 80 percent getting the people interested in using it." The development of an activity-based model may also be hampered by the theoretical drawback that it ignores resource constraints. In practice, most companies struggle to manage their constrained resources so they can increase production. The production processes are interdependent and the slowest process determines the performance of any production system. Therefore, managers should focus their attention on managing

resources to remove bottleneck processes with the goal of maximizing throughput (Yahya-Zadeh, 1998).

Part of the problem, according to Leahy (2001a), is that activity-based management was never designed to become an ongoing process. A company's general ledger information and its ABC/M information are ongoing processes resulting in two sets of cost data, which may be in conflict with each other. The question can rightfully be asked as to which set of data should be used for financial decision-making. The answer could lie in the latest activity-based costing development by which data are collected automatically and can be incorporated in a data warehouse, to be included in existing systems like the budget forecasting and project tracking software. Marshall (1995) is of the opinion that whilst activity-based management is not a perfect science it does offer a sense of financial pragmatism to the wider management process. In this respect, it is seen as a management tool and not as a solution in its own right, a factor that will lead to its gradual acceptance throughout the company.

A management model with an activity and cost focus can therefore be compared to a visitor who is responsible for bringing a double portion of joy - once on arrival and once on departure. After implementation, as the days and weeks pass, logging activities and tracing them to costs starts putting demands on the organization. As those demands grow, it becomes less welcome. It is clear after a while that it will be tough to have it around. For many companies, activity-based cost management has been like such visitor. When it is first introduced, everyone is excited about what this new tool will provide management with. However, usually, the solution targets a specific product, process or business unit in need of immediate improvement. Once that project is complete, some companies feel that the cost management tool has served its purpose and that keeping it around any longer would be pointless. If a company does try to use the new system more extensively, it can become burdensome to maintain, because the activity-based management database needs to be continually updated with new data. Sometimes

this information must be gathered manually from legacy transaction systems and the general ledger. Thus, companies attempting to use activity-based management for all their cost management needs often find themselves struggling over how to integrate their ABC/M software with the systems that hold their enterprise data. Because of these demands ABC places on company resources, FARMOVS-PAREXEL was not part of the time management system used by PAREXEL International.

A case study approach was followed for this research because economical and process time data is considered intellectual property and is not generally available on demand, which could be viewed as a limitation. However, such an approach will not limit the generalization of the results to other CROs. The operational research processes are globally harmonized and strictly regulated by national and international guidelines. Violation of any aspect of the regulations during the conductance of a research project will jeopardize the approval process of the dossier submitted to the relevant regulatory authorities for marketing approval. Because of this global standardization of the operating environment imposed by regulatory authorities, field research with data generated from a single CRO as a case study approach will be applicable to other CROs in the pharmaceutical industry.

The data obtained from 30 randomly chosen projects executed at FARMOVS-PAREXEL will be presented in the following chapter. The results will be presented to stress the significance of the set objectives for this study that a management model with a customer focus, based on activity management, is a necessity for a CRO. Corollary target costing is a useful technique because 20% of the effort generates 80% of the revenue. Customer demands, and for that matter customers themselves, should be categorized as profitable or unprofitable. The latter leads to the contribution that can be made by the evaluation of a variance analysis of process time. The effect of variation in process time that leads to non-chargeable costs, has a negative effect on the bottom-line profits

because reworks as a result of customer demands or bottle-necks, can lead to non-chargeable costs scavenging revenue. Boyd and Cox (2002) argue that, although an activity-based information system provides information for optimal decisions, note must be taken of production constraints.

The *better information in the hands of decision-makers* approach to reorienting business processes, is a simple and appealing line of reasoning, yet according to Mishra and Vaysman, (2001) a large number activity-based implementations and planned implementations fail to produce tangible benefits. Because of its greater accuracy, empowering of managers to make better operating decisions, it may allow them to make decisions to benefit themselves and not the shareholders.

Accurate and relevant cost information is critical to any organization that has to improve its competitive position. Activity-based management is a valuable concept that can be used to correct over-generalized cost systems. It is a means of creating a system that directs an organization's costs to products and services and ensures management of the drivers of the activities that caused the incurred costs. The basic distinction between traditional cost accounting and an activity-based model is that traditional cost-accounting techniques allocate costs to the output, based for example on direct labour hours required and number of days of equipment occupied. Therefore variance is inevitable according to volume of output units, cost of the output or the day's equipment occupied. Conversely, an activity-based model focuses on activities required to produce each output in the process or services and thus the consumption of the activities and resources (Report, Management Accountants, 1993). Activity-based information in isolation may be perceived as negative but, in synergy with other management tools can optimize resource utilization.

4.10 CONCLUSION

'Tis skill, not strength, that governs the ship

Thomas Fuller

The pharmaceutical environment, where the characteristics of speed and quality in performance determine the competitive edge, a robust model reporting the costs resources consume and thus giving visibility to contributions made to profit margins by type of customer, will fuel the competitive race between the leaders in this industry. It is about skill, competence, and resourcefulness. To make not only best use of resource allocation, but of resourcefulness in the application of resources. The methodology used to develop a model to capture time, the instigator of costs need not to be complicated. Any activity consumes resources and time and can be traced to costs and pooled together to calculate if the endeavour added value to the shareholder.

Chapter Four presents the methodology used to capture the time and cost variables consumed by the resources, ultimately to fulfill the primary and secondary objectives set for the thesis. The methodology used to develop a model to capture time, the instigator of costs need not to be complicated. Any activity consumes resources and time and can be traced to costs and pooled together to portray the customers contribution, a depiction of, if wining a bid is economically profitable or not.

The researcher identified field research as the preferential design to capture the necessary data to fulfill the primary objective set in Chapter One. The sample size estimation was based on the premise that the data collected on a random sample of 30 projects will have a normal distribution. To ensure a homogeneous sample population only bioavailability studies with final reports available were selected. The methodology determined for data collection, the criteria for evaluation was formulated to ensure that an activity focus was maintained and that

time information could be traced to cost variables with validity and reliability. The statistical testes to assess the univariate association between categorical variables and the dependent variables for cost and time were qualified.

The limitations of the chosen methodology are not considered to limit the usefulness of the final results to only FARMOVS-PAREXEL. The conclusion can be drawn that, because the CRO business is strictly regulated by international guidelines, their operational procedures are harmonized globally. The model so developed, with data generated from case studies, will also be applicable to other CROs.

The methodology outlined in this chapter will be used as fundamental basis for analyzing the data gathered from the selected case studies presented in Chapter Five, and for the construction of a generic management model for a pharmaceutical CRO in Chapter Six.

The methodology described to discern where re-engineering of processes should be considered, should be useful to any CRO due to the global regulated environment of the pharmaceutical industry. The conclusion can thus be drawn that, because the CRO business is strictly regulated by international guidelines, their operational procedures are harmonized globally. The model so developed with data generated from case studies, will also be applicable to other CROs. The popularity of data capturing of time, cost drivers and cost objects, according to literature and the fact that PAREXEL International uses a time a management program, emphasizes the importance of tracking time and resource usage as a result of customer demands. To implement such principles will need a structured strategy such as can be constructed by a management model, to provide steps to manage resource demands and ways of helping to institutionalize re-engineering of processes as part of the organization's culture (Martins, 2002). Institutionalization of change needs to be managed in a structured way and this implies the implementation of a management model.

CHAPTER 5

RESULTS AND DISCUSSION

Not everything that can be counted counts,

and not everything that counts can be counted.

Albert Einstein

5.1 INTRODUCTION

The operating environment of CROs and the capacity to move new compounds through clinical trials emphasize the need to outline the vision and mission of the CRO in a management model to effectively align every activity according to company objectives. A management model is an essential plan on how to maintain a competitive advantage and needs to be reformulated continually, because a company that stagnates on visions of the past will not survive the future. CROs will need an innovative vision to move the present into the future. The results presented will be used to formulate a management model applicable to future business.

The management model was constructed with accurate historical data by using as much real time data as was possible – balancing accuracy with effort, and not being too elaborate or excessively detailed. The Pareto's 20/80 Law of diminishing returns was also deployed in the design and construction of the management model and the amount of data and level of detail was chosen to meet the objectives of the researcher. The management model constructed to align

effort and efficacy of CRO processes was based on activity-based information because this methodology seeks to discover the causal factor, known as the cost driver, which determines the demand for the use of a particular overhead resource, known as an activity (Kennedy, 1996). The aim of this chapter is to describe the time and cost results obtained through the research of the objectives set in Chapter One and to make recommendations based on the findings, which will be presented as a management model in the final chapter. The study results will be depicted as summarized tables and figures with brief discussions.

5.2 DIVISIONAL PROCESS COSTS AND TIME

Customers are also known to generate additional reworks of processes owing to demands for changes to timelines, scope of work, protocol or report format mutations. The possibility of an ordinary straightforward project turning out to be a very costly project is always a risk. The overrun of one study does not only result in prolonged labour hours but, also inevitably has a spin-off on work capacity involving the rescheduling and delaying of other studies. The need for speed and constant demand on timelines, pressurize CRO resources. Clients and their demands, as cost centers, are also cost drivers with some clients more so than others. The demands of clients and prolonged process time should be viewed as cost objects, because functions that do not contribute financially to the bottom line, contribute to the cost input to finally outnumber the profit output (Brandt *et al.*, 1999).

The cost for PMD (R 66 452) tabulated in Table 5.1 is high, although only 1% of the equipment cost is allocated as overhead expenses. The cost is driven by process time related to labour costs[6]. PMD coordinates the study throughout the life cycle of the study therefore throughput time affects the average divisional

[6] The average labour cost for the Project Management Division is the lowest of the 4 divisions. Therefore it is not salaries that drive the cost.

cost. The clinical average cost is R51 793, although 24% of the equipment costs were allocated as overhead costs to the clinic.

The Bioanalytical Division has expensive equipment (69% of the total value) and therefore the largest part of the overhead expenses is allocated to this division. See Table 4.1.

Table 5.1 Divisional costs calculated according to actual activity time

n=30	PMD (ZAR)	BIOMETRY (ZAR)	BIOANALYTICS (ZAR)	CLINIC (ZAR)
Median	66 452	28 930	77 104	51 793
Min	49 273	24 589	6 447	42 901
Max	159 296	53 292	123 161	75 506

5.2.1 Actual and Ideal Process Times of Divisions

The ideal time for a study is estimated as 129 days, compared to the average actual time of 190 days. The average calculated from the aforementioned 2 cycles is 159 days, e.g. about 5 months, which experience shows is a generally realistic time-frame to aim for in the execution of a bio-study. The comparison is done to determine to what extent the actual time differs from an idealistic time and to indicate what a realistic time-frame to aim for in predictive planning will be. The average process times of the divisions are tabulated in Table 5.2.

Table 5.2 Average activity time of the actual, idealistic and estimated divisional process flow

Division	Actual Time (Days)	Ideal Time (Days)	Average of the sum of Ideal and Actual time (Days)
Project Management (study cycle time)	190	129	159
Biometry	16	4	10
Clinical	52	52	52
Bioanalytical	51	37	44

Because throughput time is an important selling point with marketing leverage, it needs to be incorporated as a critical factor into a management model.

5.3 DIVISIONAL COSTS IN RELATION TO FEES CHARGED FOR SERVICES

Biometry's throughput time is relatively short, but customer demands are often referred to Biometry for their input and, due to the short cycle time, one day (more or less) makes a substantial difference to the variables. To manage the individual line function process time and not just the general bottom-line budget figures, could represent a fortuitous turning point on the rate of return for company revenue and ultimately on the bottom-line figures. The average costs in relation to the fees, expressed as an estimated profitability for the divisions, are categorized per phase, because phase is perceived to be a cost driver.

5.3.1 The Costs and Fees Expressed as an Estimated Profit for PMD

The variability between the costs, fees charged and resultant differences calculated as a profit, is high, with large differences between 2-, 3- and 4-phase

studies as shown in Table 5.3.

Table 5.3 PMD cost in relation to the fee expressed as an estimated profit

2-Phase (n=20)		**Cost (ZAR)**	**Fee (ZAR)**	**Profit (ZAR)**
	Median	68 305	54 800	-12 500
	Min	49 273	26 130	-116 119
	Max	159 296	100 100	17 209
	CV%	*40*	*36*	-
3-Phase (n=6)	***Median***	61 027	80 487	15 886
	Min	58 951	39 195	-23 562
	Max	87 564	168 480	109 193
	CV%	17	*50*	-
4-Phase (n=4)	***Median***	70 877	66 430	-12 461
	Min	53 007	40950	-24 520
	Max	85 665	109 200	52 026
	CV%	25	41	-
Total (n=30)	***Median***	66 452	60 970	-11 503
	Min	49 273	26 130	-116 119
	Max	159 296	168 480	109 193
	CV%	37	43	-

The labour cost used in the analysis was allocated to a single project to standardize labour hour allocation throughout the research. PMD shows no profit and the variations in study costs, CV% of 37% (Table 5.3) is high if compared to the Clinical (15%, Table 5.4) and Bioanalytical (14%, Table 5.5) Divisions' variables, which are in line with each other. If the line of unity is considered as the line on which cost is predicted to be equal the fee, the data points are scattered to a great extent below the aforementioned line with no correlation (r = 0.04) between the costs and the fees, as depicted in Figure 5.1.

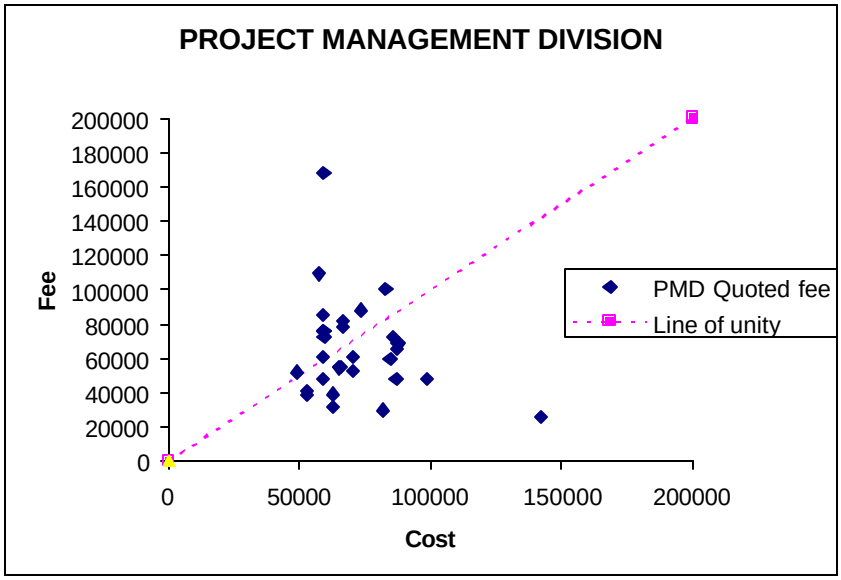

Figure 5.1 Project Management cost in relation to fees

Over and above *time* being a proxy for costs, *customer demands* are also a factor to consider as incurring costs. Especially the Project Management Division, which handles the project throughout its life cycle, has to provide a follow-up customer service for demands after study closure and unplanned prolonged cycle times have put inevitable additional demands on resources. PMD is dependent on the sponsor for prompt response and decisions. Two projects had unusually long cycle times of 425 and 422 days. The one project had a prolonged cycle time due to delays instigated by the sponsor's test product manufacturing problems, while the other long cycle time was due to problems with the analytical method which had to be developed for the metabolite instead of the mother substance, which was instantly metabolized, with the result that only the metabolite was detectable in plasma. Breakthrough research was done on the metabolic pathway of the drug, but the experiment scavenged company revenue in the process of discovery!

From a PMD perspective, project cycle time should be closely monitored because

it is evident that non-value adding time is a proxy for unbillable costs. Not only do extended cycle times drain company profits but also the customer service may be perceived as poor. It is mainly a project management function to control performance within time and budget constraints and thus it is of importance for inclusion in a management model.

5.3.2 Clinical Costs and Fees

In contrast with PMD the Clinical Division has a small variation in study cost (15%), with a larger CV% of 48% for the fees charged for clinical execution (Table 5.4). Although the clinical execution is dependent on the design of a study, e.g. the number of phases and the wash-out period of a study which might be regarded as a cost driver, the variation in cost between the studies is relatively low. Therefore the large variation in fees is unexpected, because if costs can be contained without large variations the fees are expected to be in line with the costs. Unpredicted profitability, because there is no correlation between costs and fees ($r = -0.03$), will make future forecasts of revenue problematic. If the aim with a management model is to ensure effective and efficient resource usage to the greatest possible advantage of the company, revenue should be predictable for services rendered, as should be forecasts of future revenue. The fees are calculated according to the number of phases and the number of subjects, but the results indicate that, according to the cost incurred, a predictable add-on profit is not generated.

Table 5.4 Clinical Division cost in relation to the fee expressed as an estimated profit

2-Phase (n=20)		**Cost (ZAR)**	**Fee (ZAR)**	**Profit (ZAR)**
	Median	52 617	156 765	102 532
	Min	42 901	61 230	8 669
	Max	75 506	252 850	188 726
	CV%	15	30	-
3-Phase (n=6)				
	Median	50 550	208 218	158 343
	Min	46 232	96 239	46 702
	Max	62 055	556 920	510 688
	CV%	1	66	-
4-Phase (n=4)	***Median***	50 823	168 253	107 010
	Min	44 779	101 556	56 777
	Max	72 801	271 856	219 894
	CV%	23	41	-
Total (n=30)	***Median***	51 793	167 468	116 028
	Min	42 901	61 230	8 669
	Max	75 506	556 920	510 688
	CV%	15	48	-

The variation in costs, fees and profitability of the Clinical Division (Table 5.4) and the Bioanalytical Division (Table 5.5) are in line with each other, with the CV's for the costs and fees being respectively 15%, 48%, and 14%, 44%. The fees quoted vary to a great extent between the studies, with the CV% much higher for the fees charged for the services than the cost input of the resources consumed in delivering the service.

The disparity between the costs generated to deliver the service and the fees charged for the service, shows that a price structure not based on actual cost but, on a rule of the thumb alone, is not an optimal costing model.

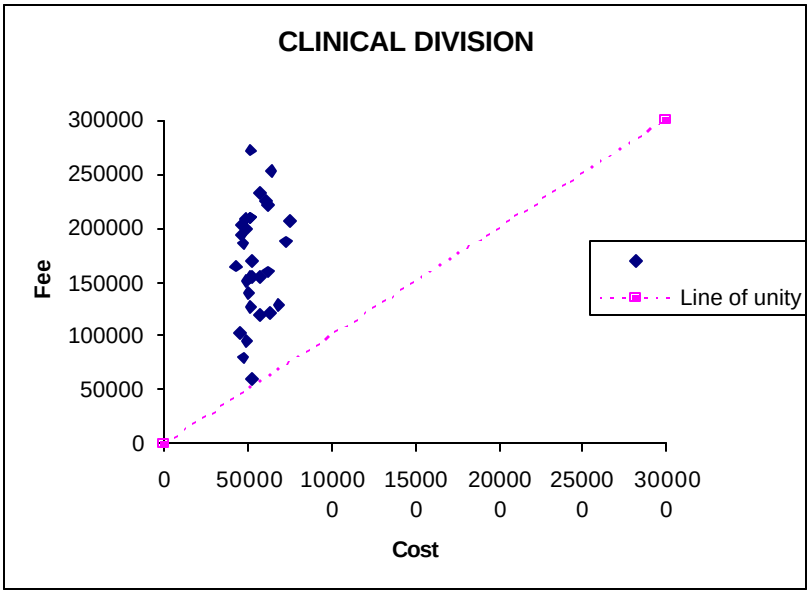

Figure 5.2 Clinical Division's cost in relation to fees

Figure 5.2 shows how low and well contained the clinical input costs are in relation to the fees with none of the studies below the line of unity were costs break even to fees charged for a service.

5.3.3 Costs and Fees Charged for Bioanalytical Services

Similar to the Clinical Division, the Bioanalytical Division's fees are not in relation to the costs incurred. However, the intra-study-cost does not vary much (14%) and is similar to the 15% variation of the Clinical Division's studies, as indicated in Table 5.5.

Table 5.5 Bioanalytical Division costs in relation to fees expressed as an estimated profit

2-Phase (n=20)		Cost (ZAR)	Fee (ZAR)	Profit (ZAR)
	Median	79 612	202 417	119 564
	Min	64 479	122 824	32 091
	Max	123 161	381 550	295 869
	CV%	16	38	-
3-Phase (n=6)	***Median***	76 985	326 307	246 773
	Min	65 166	137 150	54 545
	Max	84 706	499 486	423 204
	CV%	9	46	-
4-Phase (n=4)	***Median***	71 048	181 675	112 435
	Min	66 984	95 368	24 770
	Max	79 618	410 384	330 766
	CV%	7	64	-
Total (n=30)	***Median***	77 105	213 200	123 195
	Min	64 479	95 368	24 770
	Max	123 161	499 486	423 204
	CV%	14	44	-

Cash-flow generated, calculated from the difference between the study costs and fees (Table 5.5) varies greatly between studies (14%, 44%) with no cor relation evident between the fees and the costs. The data expressed in a scatter plot depicted in Figure 5.3 shows that there is no correlation (r = 0.01) between the fees and the costs. Similar to the Clinical Division the costs are contained with low variation. Although the Bioanalytical Division has the most expensive equipment the fees charged for analytical work done contribute to a profitable return on investment for the company.

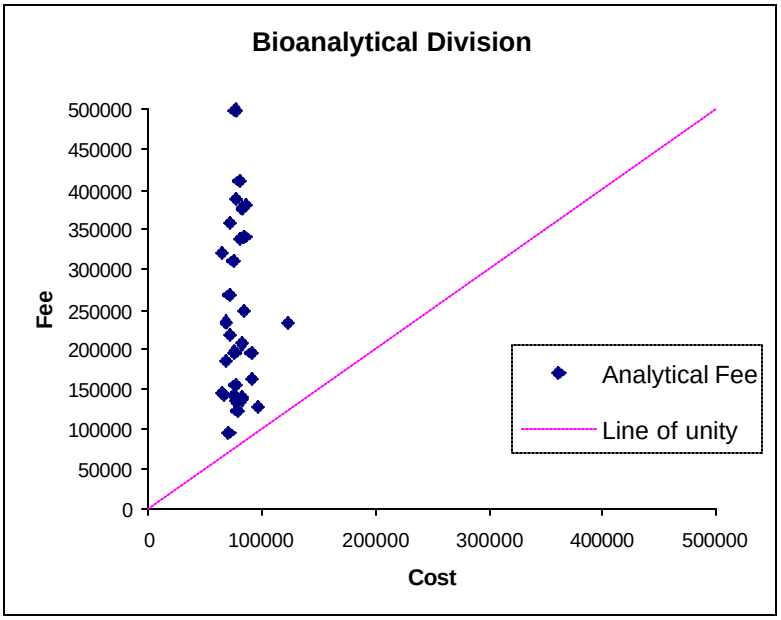

Figure 5.3 Bioanalytical Division's cost in relation to service fees

Evident from Figure 5.3 is that costs are contained above the line of unity with the cost of only one study slightly higher than the rest. The fees charged for the Bioanalytical Services vary over a range of approximately R 100 000 to R 500 000, but most important is that the costs are contained, because the CRO at study close-out, only banks the net difference.

The myriad ways of doing business always leave opportunities for improvement. Therefore, if the average time is considered that the different bioanalytical processes took, the actual mean time for method development and assay determinations are shorter than the time-frame for the administrative procedure of report compilation, as shown in Table 5.6.

Table 5.6 Bioanalytical Division's process time in days

n=30	Method development (Days)	Method re-instatement (Days)	Assays (Days)	Report compilation (Days)	Total process time (Days)
Median	19	1	13	21	66
Min	0	1	6	7	30
Max	62	143	45	82	181
CV%	86	298	54	57	40

The process time for report compilation, an administrative task, could be controlled and large variations in the performance eliminated. Method re-instatement has a large CV% of 298% compared to the analytical assay determinations, equipment-driven production delivered with more predictable time-frame and less variation. The statistical analysis and final report compilation by PMD are downstream activities dependent on the analytical results. Therefore, the Bioanalytical Division easily becomes a bottleneck if process time is prolonged and unpredictable. An operational process with the possibility of becoming a bottleneck in performance, where throughput time is always under pressure, needs to be regarded as a possible weakness and an action plan should be formulated for worse case scenarios.

5.3.4 Cost and Fees Charged for Biometry

Biometry's process flow is short but large variations in the process flow are noted. The fact that they offer a special 24-hour service on request indicates that a speedy service with predictable cycle time and low variation is possible. The cost in relation to the fees expressed as a profit result in negative figures, because cycle time and therefore input costs are not contained, as illustrated in Table 5.7.

Table 5.7 Biometry Division's cost in relation to the fee expressed as an estimated profitability per study phase

2-Phase (n=20)		**Cost (ZAR)**	**Fee (ZAR)**	**Profit (ZAR)**
	Median	28 770	31 200	-3 468
	Min	24 930	0	-28 261
	Max	51 063	120 000	87 977
	CV%	23	72	-
3-Phase (n=6)				
	Median	34 649	36 173	-3 936
	Min	26 450	17 550	-31 965
	Max	52 343	78 975	50 549
	CV%	*30*	*55*	-
4-Phase (n=4)	***Median***	28 411	46 930	11 091
	Min	24 589	19 890	12 472
	Max	53 292	70 720	40 058
	CV%	40	46	-
Total (n=30)	***Median***	28 930	32 760	-3 468
	Min	24 589	0	-31 965
	Max	53 292	120 000	87 977
	CV%	27	64	-

The higher cost in relation to the fees charged is evident from Figure 5.4. According to the scatter plot, a number of studies are below the line of unity, with one study, as an extreme case, generating zero revenue. The bioanalysis for the study was stopped as a result of drug formulation problems evident from the results on the first cohort of samples, with the result that no statistical analysis was done. Thus the fee of zero, with the corollary calculated profit indicated as a negative amount, is due to no fee being charged. The CV% (64%, Table 5.7) of the Biometry Division for the fee charged, is the largest. Because the division provides a 24-hour service on request and has the shortest cycle time for service, the large variation is somewhat unexpected.

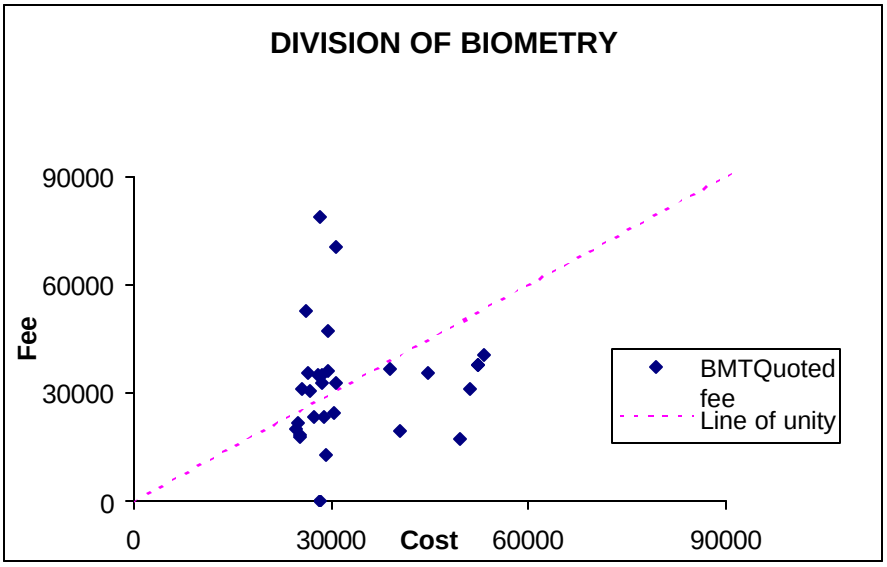

Figure 5.4 Biometry Division's cost in relation to service fees

The scatter plot (Figure 5.4) of the costs and fees shows the large variation of cost in relation to fee. The study cost is higher than the fee charged for the service and there is no correlation (r = 0.03) between the latter two variables.

5.3.5 Variation between Costs and Fees for the Divisions

The variation in the divisional cost for the different phases does not escalate according to the increase in the number of phases. The Bioanalytical Division has a decrease in cost variability for 2- to 4-phase studies; the conclusion can be made that the more phases a study has with repetitive work the lower the variability is in the processes. The large cost variation for Biometry is related to the time range: The statistical analysis took from 0 to 81 days with an average of 16 days. Variation in time may be presumed to be a result of the design of a trial, i.e. whether it is a 2-, 3- or 4-phase study but, as illustrated in Table 5.7, no trend is evident in the CV% between the phases.

The large differences in profitability for the divisions, especially for Biometry and PMD Divisions (Tables 5.7 and 5.3), need to be explored. The fees for services are calculated per subject and number of study phases, because the CV percentages for the Bioanalytical and Clinical Divisions are in line with each other (14% and 15% respectively), but the divisions with administrative and statistical analysis services have a larger variance in their cost input. The first mentioned (Clinical and Bioanalytical) division's difference between the fees and costs is proportionally better in adding value to company revenue than those of the Biometry and Project Management divisions, which could indicate that the cost drivers have not been identified. To link the pricing structure to subjects enrolled (sample size) does not seem to be the ultimate cost effective pricing model because these variables have traditionally been presumed to be cost drivers but have never been tested for significance with a statistical model. The pricing for PMD and Biometry should have an entry level price of at least a target cost plus profit, and the average target cost is (Tables 5.3, 5.4, 5.5 & 5.7) at least R 66 000 (CV% 37) for PMD; R 52 000 (CV% 15%) for Clinical; R77 000 (CV% 14%) for Bioanalytical, and R 29 000 (CV% 27%) for Biometry. Alternatively, especially for price sensitive customers, target price costing should be calculated and a service provided which has been tailored according to a target cost added to the desired profit.

5.3.5.1 Variation between Subject Remuneration and Fees for the Divisions

It is interesting to note that the amount paid out to subjects for their participation in the studies as remuneration, is equal to the fees charged for the statistical analysis (a core function and pivotal to clinic al research) and the administrative coordination of PMD as illustrated below, with PMD getting 11 %, subject remuneration 8% and Biometry 9%, of the fees. Figure 5.5 also shows the Bioanalytical and Clinical fees in relation to subject remuneration.

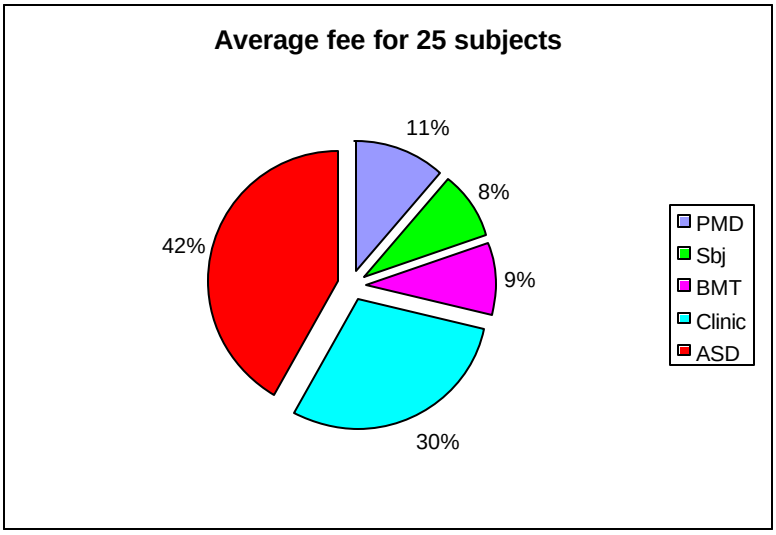

Figure 5.5 The average fee per division for a Bioavailability study with n=25 subjects

The estimated profit calculated, taking only the input cost in relation to the fee charged into account, indicated that only two of the divisions (Bioanalytical and Clinical) generate substantial revenue for the company. From the results, it is evident that the pricing system should be reconsidered because a CRO must critically evaluate which of its services make or lose money to stay competitive, and should improve business processes to enhance profitability. The main constraint for clinical research in South Africa, over and above the global problem of study cancellations, is the tediously and drawn-out regulatory authority approval process, which erodes profits drastically due to a lack of urgency which causes delays in study initiation for South Africa. Because of the competitive leverage throughput time has, South Africa cannot compete with countries with shorter regulatory approval cycle times, if the latter is pivotal for decision making in contract allocation. This constraint emphasizes the need that those division's which are not obliged to obtain national regulatory approval for a service, e.g.

statistical analysis, site management and bioanalytical, have, to generate revenue by delivering these services to compensate for losses from the clinical division.

Success in pharmaceuticals dictates sound decisions based on accurate knowledge of complex variables. The activity *accountant* should be used as a critical factor of a management model during all stages of functional process evaluation to identify possible revenue earning improvements. Revenue growth may be realized by raising prices on products, services and customers, where revenues are not covering costs. However, such situations are easier to detect if activity-based analysis traces costs, profit and assets employed down to individual products, services, and customers. For some large customers, especially in the cases of specialized, niche products or particularly demanding customers, prices can be increased, or equivalently, large discounts eliminated, without losing market share, to cover the costs on currently unprofitable products and customers. However, profitability by product, service and customer, provides signals regarding the opportunity for repricing, or emphasizes the success and failure of past pricing strategies. For homogenous products and services, a simple price index, such as net revenue per output or price per unit, will reveal the trends in pricing strategy for the company and industry (Kaplan and Norton, 1996). The consequential evaluation of the divisional output-cost will require agility, adaptability, determination and vision, along with the incentive and commitment to innovate and change processes where deemed necessary to speedup throughput time and lower input costs to an ideal cost.

5.3.6 Ideal Divisional Costs

The costs were calculated for processes synchronized for the best-predicted throughput time, e.g. the bioanalytical time was calculated as the best possible time for assay determination and report compilation; the clinical real activity time was taken as the idealistic time, and the biometry time was estimated with the project management time calculated according to the divisional processes and report compilation. The ideal total project cost expressed in ZAR (Table 5.8),

calculated from the ideal activity time as tabulated in Table 5.2.

Table 5.8 Project cost calculated according to the ideal activity time of the divisions.

n=30	PMD	Biometry	Analytics	Clinic	Total
Median	56 204	27 875	72 709	51 793	207 810
Min	46 897	24 589	63 451	42 901	182 742
Max	76 050	41 025	88 415	75 506	258 986
CV%	14	14	9	15	10

The ideal estimated best possible times for the divisions have similar variation in throughput time if bottlenecks (see section 2.2) in processes are eliminated. The conclusion can be made that the large CV% (Tables 5.3 & 5.7) can be lowered if lag time is eliminated in every process undertaken. The Bioanalytical Division's ideal time, based on the best possible time for the assays and report compilation, has the lowest CV% as an indication of the low variation the division could ideally have if methods can be developed in advance and method validation can be done within a day. With the corporate mission to *'follow the molecule'* where future drug development is anticipated, methods could be developed in advance to be offered to industry as competitive leverage, e.g. to shorten throughput time. Project cycle time can be saved if development is done in advance and will result in a cost saving from point of origin to point of consumption, in order to meet customer requirements. A management model should be more that a mere cost-reducing functional model. Business logistics should be aligned to core competencies and be a source of competitive advantage because of the impact on

customer service. In a highly competitive marketplace where products, price and quality are easily imitated, e.g. as in the upcoming markets of India, Brazil, Poland and Russia which are offering quality at very low prices, superior customer service can be the key element that ranks one firm above another. Thus the logistics function of activities plays a vital role in the successes or failures of a company (Lin *et al.*, 2001). The ideal throughput time needs to be reproducible in bio-studies to ensure that a service can be rendered at an ideal target cost CV% of 10% (Table 5.8). It is a futuristic ideal to pursue because excellence in customer service means, without variation, getting the right product to the right customer at the right place, in the right condition and at the right time, at the lowest possible cost.

The average project life cycle from protocol development to the final report which has been submitted to the customer, differs from an estimated ideal time (190 days *vs.* 129 days) and indicates that activities should ideally be undertaken within narrower timelines and with throughput time speeded up. The lag time (delays) arises when queries are received or the sponsor experiences drug-manufacturing problems. The variation in cycle time is exceptionally high due to 2 projects, which ran over 422 and 425 days respectively compared to the shortest cycle time of 108 days. Although problems are unforeseen, this emphasizes the importance of predictive planning, using scenario planning to proactively manage risks and avoiding extended cycle times. Idealistic timelines for processes need to be set as best- and worst-case scenarios during the planning phase. As part of risk planning, each division needs to prepare an operational plan of action if it seems evident that the ideal timelines will be overrun, and scenarios of risk management options should be in place for implementation. The argument used in air navigation should be followed, i.e. that *you plan your flight and then you fly your plan*. The management model should be the flight plan, outlining the predictive planning and risk management steps. Risk management and predictive planning for worst-case scenarios not only protect the interest of the CRO but also that of

the customer. Therefore, Performance-based Pricing, e.g. the inclusion of liquidating indemnity clauses in the financial contract if the CRO is unable to meet the agreed milestones, is receiving attention in literature (see Sections 2.4.1) and industry as part of predictive planning.

5.3.7 Profit per Head Count Expressed as Productivity

The median profit generated by each division was expressed, as productivity per division, using a model, *viz.* productivity = profit %/head count ($m = \Delta y/\Delta x$) to calculate the divisional contributions. The productivity of the line function divisions is presented in Figures 5.6, 5.7 and 5.8 using the % profit (Tables 5.3, 5.4, 5.5 and 5.7) divided by the head count per division. It is evident that the incremental profit of the Clinical and Bioanalytical Division's effort is decreased by the loss of the Biometry and Project Management Divisions as illustrated in Figure 5.6.

The results indicated that if the productivity managed by the Bioanalytical Division can be imitated by the other three divisions, the maximum production potential will increase by 92% as illustrated in Figure 5.7.

Alternatively, the current profitability can be maintained with fewer employees. This means that the head count for the divisions can decrease to: Clinical from 41 to 21, Bioanalytical from 30 to 16, Biometry from 11 to 6, PMD from 23 to 12 and Support Services and business sustaining staff from 32 to 17, as illustrated in Figure 5.8.

5.4 NUMBER OF CONTRACTS ALLOCATED IN RELATION TO THE NUMBER OF BIDS SUBMITTED

The number of quotes/bids submitted to customers and the number accepted by the clients and contracted over a period of 2 years were analyzed. The Pareto rule of 20/80 was applied to the analysis of the Requests for Proposals (RFPs). The relationship between the number of requests for RFPs and the actual number contracted was evaluated. All costs are mainly regarded as service or product driven but, many costs are customer driven. Over a 2-year period (1999 – 2000), 632 RFPs were received of which 99 were contracted. Sixteen percent (16%) of the customers contracted studies, in line with the 20/80 Pareto Principle.

Forty-two percent (42%) of the companies contracting the aforementioned business are considered relative big pharma companies. The latter is useful information, because if big pharma is fuelling the cash-flow to keep stakeholders happy, then the 22 companies (requesting 163 RFPs), of which none were contracted, only scavenged revenue. Considering the resources consumed by the activity to compile a proposal and quote, this process needs critical evaluation if such a large percentage is non-value adding, because it contributes to overhead costs. According to Lin *et al.,* (2001) research indicates that overhead costs represent around 37% and 66% of the total costs of manufacturing and service companies respectively. The number of RFPs should be seen as overhead costs to the company but with future possibilities. However the rate of return on these activities should be monitored as part of the supply chain process to provide an efficient, effective flow of services in order to provide a reliable customer service. Customers with RFPs not contracting any of their requests, should be targeted strategically with a management model to change them from cost burdens into profitable customers or should be pruned like dead wood from a tree because of their negative contribution to the growth of the company.

The highest number of requests for proposals came from German customers,

thereafter from South African pharmaceutical subsidiary companies, with the third largest customer support coming from Switzerland. The latter contracted the largest number of its requests and Germany the largest percentage in relation to the total number of RFPs received. Table 5.9 summarizes in descending order, the number of proposals requested as well as the num ber contracted per country. It is evident (Table 5.9) that the American market is still an underutilized marketing opportunity. Customers from France contract only 5% of the requests for proposals and the cost to serve such customers should be calculated and managed. If the tenets of the Pareto Law are followed and 80% of the revenue is generated from approximately 20% of the customers, to be competitive a company must know its sources of profit and understand its cost structure. For outright unprofitable customers, the CRO must explore the possible options of raising prices, or surcharging them for the extra work. The causes of the extra work done for the customers must be reduced; the delivery systems must be streamlined so that it costs less to serve them, or their behaviour should be altered so that these customers place less demands on the CRO. Table 5.9 displays the number of RFPs per country and also the number of RFPs expressed as a percentage of the total requests.

Table 5.9 RFPs received and allocated over the 24-month period of 1999 - 2000

Country	n=RFPs	Country	n=RFPs contracted per country	Country	% RFPs contracted per country
Germany	194	**Germany**	40	**Germany**	21%
SA	116	**SA**	25	**SA**	22%
France	102	**France**	5	**France**	5%
UK	74	**UK**	6	**UK**	8%
Switzerland	36	**Switzerland**	11	**Switzerland**	31%
Denmark	25	**Denmark**	2	**Denmark**	8%
Iceland	23	**Iceland**	1	**Iceland**	4%
Canada	17	**Canada**	3	**Canada**	18%
India	14	**India**	3	**India**	21%
USA	10	**USA**	2	**USA**	20%
Cyprus	7	**Cyprus**	0	**Cyprus**	0%
Netherlands	6	**Netherlands**	1	**Netherlands**	17%
Ireland	2	**Ireland**	0	**Ireland**	0%
Sweden	2	**Sweden**	0	**Sweden**	0%
Japan	1	**Japan**	0	**Japan**	0%
Spain	1	**Spain**	0	**Spain**	0%

Table 5.9 shows the possible markets to be targeted to generate future revenue, e.g. Japan and the USA. The proverbial argument not to *put all one's eggs in one basket* is also true for CROs. Unfortunate events, e.g. critical or major audit findings becoming known *via* informal communication as well as *via* the media,

can have a negative effect on collaborations and future customers may be influenced not to do business, causing a negative effect on cash-flow. The clientele bases should be broadened and the few large customers that generate 80% of the revenue should be balanced with marketing strategies to turn the unprofitable customers into profitable ones.

5.5 CONSTRAINTS CROs NEED TO COPE WITH

Some customers have a reputation of cancelling or postponing studies, which are a constraint, CROs have to cope with. Clinical trial cancellations mean unused clinic bed capacity which is not easily filled if a study is cancelled on short notice, and the cancellations have a spin-off effect on the rest of the divisions which is reflected in the cash-flow. This constraint (unused capacity) is difficult to control in a Phase I Unit. During 2000 a large number of studies (23 of the 66, 35%) were cancelled or postponed and 11 of the studies contracted in 2000 were only executed and/or completed with the relevant revenue generated in 2001 (Appendix 9.3).

CROs are partakers in risk sharing with the pharmaceutical industry's value chain. Sponsor demands due to R&D problems or unfavorable results affects the CRO negatively because of prolonged cycle times or cancellations as a result of problems encountered with development work. If clinical development time is cut, costs will be cut for both the CRO and the pharmaceutical company. That is why study cycle time, from recruitment of subjects to the final report, should be a win-win opportunity for both the CRO and sponsor. Hoang *et al.*, (2003) are of the opinion that a cost factor to enhance study cycle time should be calculated and allocated as overhead expenses. Recruiting levers like branding and volunteer support services are necessary to expedite study/trial cycle time, e.g. by keeping subjects motivated and committed to complete the study. The screening of subjects also generates costs because approximately two healthy volunteers are screened to include 1 subject in a bioavailability study and two subjects can be expected to withdraw from a study, as indicated in Table 5.10.

Table 5.10 Subjects screened, enrolled and completed per protocol

Study[7]	Planned for completion	Enrolled and randomized	Drop-outs	Discon-tinuers	Completed	Screened	No screened to include 1
1	44	45	1	0	44	60	1.4
2	40	41	1	0	40	53	1.3
3	12	12	0	0	12	14	1.2
4	18	22	2	0	20	34	1.9
5	24	28	1	1	26	42	1.8
6	26	30	4	0	26	41	1. 6
7	26	28	1	1	26	45	1.7
8	26	32	1	3	28	47	1.8
9	20	24	1	0	23	33	1.7
10	24	26	0	0	26	38	1.6
11	18	23	2	2	19	31	1.7
12	18	23	1	2	20	35	1.9
13	18	22	0	0	22	27	1.5
14	6	9	0	1	8	11	1.8
15	30	32	2	0	30	38	1.3
16	34	36	1	0	35	51	1.5
17	48	54	1	2	51	74	1.5
18	12	16	1	2	13	23	1.9
19	24	26	1	0	25	35	1.5
20	34	36	0	0	36	41	1.2
21	24	26	0	1	25	45	1.9
22	40	44	4	0	40	58	1.5
23	24	24	1	0	23	28	1.2
24	24	25	0	1	24	30	1.3
25	12	14	1	0	13	31	2.6
26	18	22	2	2	18	31	1.7
27	20	22	1	1	20	33	1.7
28	24	26	1	0	25	28	1.2
29	14	14	0	0	14	21	1.5
30	9	12	0	0	12	20	2.2
Mean	**24**	**27**	**1**	**1**	**25**	**37**	**2**

5.6 FACTORS IMPACTING ON COST AND TIME

Traditional beliefs and concepts of what is perceived as cost drivers, e.g. sample size, method development and number of study phases, were tested for relevance. Costs versus fees were examined to determine if a correlation exists between these variables because costs have an impact on the business-operating margin. Revenue should also be predictable with a measure of certainty because budget

[7] Study numbers used in the analysis were coded from 1 to 30 with no correlation with the actual study nos.

targets and company growth rates need to be forecasted. Therefore, a business model has to categorize cost drivers with statistical significance.

5.6.1 The Impact of the Number of Phases per Study on Cost and Time

The number of phases (profile periods) a study has may be perceived to influence the resource input due to the increase in clinic days, time and resource consumption with a consequential cost implication. However, the cross-over design of a bioavailability study, and consequently the number of phases of the trial (2-, 3- or 4 phases), has no statistically significant effect on the cost or time factors as the results tabulated in Table 5.11 show.

Table 5.11 Cost and time for different number of phases per study

Phases	**2**	**3**	**4**
n	20	6	4
Min (Time)	108	133	120
Max (Time)	425	219	214
Median (Time)	162.5	142.5	171
Min (Cost)	199 114	237 441.5	230 666
Max (Cost)	381 485	207 950	192 973
Median (Cost)	226 844.5	252 713	268 746
p-value for difference between phases for time = 0.5588*			
p-value for difference between phases for cost = 0.6504*			

** Not statistically significant*

5.6.2 The Impact of the Sample Size of a Study on Cost and Time

The protocol sample size (number of subjects included), the number of cross-over phases and the profile period of the clinical phase are inevitable constraints on the cycle time of a study and need advance planning to ensure that resource utilization is optimal. The sample sizes of the studies evaluated differ from nine volunteers to 54 volunteers with a median of 25 subjects per study. The number of subjects enrolled in a study to a great extent determines the resource input for the clinic, because of the number of CRFs to be completed for the Bioanalytical Division for assay determination and statistical analysis. Although a myriad of entries and data are captured, the process flow involves repetitive input that is streamlined, and the learning curve from experience also plays a role. The results presented in Table 5.12 show that the number of subjects enrolled in a study, whether the sample size is < 25 or = 25, do not have a significant statistical effect on the time or cost factors of a study. Although there is a perception that sample size is a cost driver, the statistical model proves this to be a misconception.

Table 5.12 Cost and time for studies with < 25 subjects and = 25 subjects enrolled

	Studies with < 25 subjects enrolled	**Studies with = 25 subjects enrolled**
n	14	16
Median (Time)	185.5	155.5
Min (Time)	120	108
Max (Time)	378	425
Median (Cost)	242 067.5	218 671.5
Min (Cost)	192 973	199 114
Max (Cost)	326 681	381 485
p-value of difference between studies with < 25 *vs.* = 25 for time = 0.3492*		
p-value of difference between studies with < 25 *vs.* = 25 for cost = 0.3390*		

** Not statistically significant*

5.6.3 The Impact of the Number of Subjects Screened for a Study on Cost and Time

As tabulated in Table 5.10, an average of two subjects need to be screened to include one in a study and an average sample size of 25 subjects is usually included in bio-studies. The results in Table 5.13, however, show that there is no correlation between the number of subjects planned for enrolment, the number enrolled, the number screened and the cost or time.

Table 5.13 The impact of number of subjects planned for enrolment, enrolled and screened for enrolment on cost and time

n= 30 studies	**Subjects planned for enrolment**	**Subjects enrolled**	**Subjects screened**
Correlation (r) with actual time *(p-value for significant correlation)*	0.01 (0.9652*)	0.03 (0.8952*)	0.08 (0.6572*)
Correlation (r) with total cost *(p-value for significant correlation)*	-0.01 (0.9408*)	-0.02 (0.9003*)	0.07 (0.7073*)

** Not statistically significant*

5.6.4 The Impact of Size of Pharma Companies on Cost and Time

Business relationships with relatively big pharma companies seem to be profitable, probably because they are better geared for R&D, product development processes are under control to a greater extent and unnecessary delays are eliminated. The CROs may also inadvertently take greater care to meet the timelines of a large customer. The results tabulated in Table 5.14 indicate that the difference in time and cost factors for services rendered to either relatively large or small pharma companies is statistically significant.

Table 5.14 Cost and time of relatively big and small companies

	Relatively small pharma companies	**Relatively big pharma companies**
n	16	14
Median (Time)	207.5	145.5
Min (Time)	119	108
Max (Time)	425	251
Median (Cost)	256 121	214 651
Min (Cost)	192 973	206 792
Max (Cost)	381 485	279 414
p-value of difference between companies of different size for time = 0.0275*		
p-value of difference between companies of different size for cost = 0.0159*		

** Statistically significant*

5.6.5 The Impact of Protocol Amendments on Cost and Time

Project mutation after the planning phase is described in literature (Section 2.2.1) as costly and should be avoided. Unfortunately it is an opportunistic objective not always avoidable. Management should take note, however, of the negative cost implication of project mutation, e.g. which an amendment has on the cost and time factors of a study after the implementation phase as illustrated in Table 5.15.

Table 5.15 The impact of amendments on cost and time

	Studies with 0 amendments	**Studies with 1 amendment**	**Studies with 2 amendments**
n	19	9	2
Median (Time)	154	211	401.5
Min (Time)	108	137	378
Max (Time)	251	422	425
Median (Cost)	216 607	252 713	354 083
Min (Cost)	192 973	213 343	326 681
Max (Cost)	279 414	354 143	381 485
p-value for the difference time factor for protocols amended or not amended = 0.0122*			
p-value for the difference cost factor for protocols amended or not amended = 0.0159*			

* *Statistically significant*

Because of the fact that project mutation has a negative effect on the project costs, the financial contract should make provision to charge an additional fee for protocol amendments. Studies with 2 amendments took 137% longer than studies with one amendment, and 260% longer than studies with no amendments. Therefore, a fee should be quoted upfront if any change of work scope is deemed necessary due to changed sponsor requirements.

5.6.6 The Impact of Method Development on Cost and Time

The average time for method development is 33 days and for method validation 16 days. If methods for the determination are available, method re-instatement is done. The average time for method re-instatement is 17 days, compared to the 33 days if method development has to be done prior to the analytical determination

of a drug. There is, however, no statistically significant difference to the cost if method development is done or not done (p-value = 0.4144).

Similarly there is no statistically significant difference to the time if method development is done of not (p-value = 0.2670), as illustrated in Table 5.16.

Table 5.16 Cost and time of analytical method development and method re-instatement

	Studies with no method development (method re-instatement)	**Studies with method development**
n	13	17
Median (Time)	154	169
Min (Time)	108	120
Max (Time)	425	422
Median (Cost)	224 626	247 908
Min (Cost)	199 114	192 973
Max (Cost)	381 485	354 143
p-value for difference in time between studies with method development or without method development = 0.2670*		
p-value of difference in cost between studies with protocol amendments or without amendments = 0.4144*		

** Not statistically significant*

From Table 5.16 it is interesting to note that there is no relevant difference in time and cost if method development and validation needs to be done or if a method only needs to be re-instated (median 169 days and 154 days). Therefore the assumption can be made that the method re-instatement process should be re-engineered to cut back on timelines and equipment idle time.

5.6.7 The Impact of Metabolite Determination on Cost and Time

Although method development does not make a statistical difference to the cost and time of a study, the determination process of a metabolite has a statistically significant effect on both the time and cost factors of a study, as demonstrated in Table 5.17.

Table 5.17 Cost and time factors of studies with or without metabolites

	Studies without metabolite determination	**Studies with metabolite determination**
n	20	10
Median (Time)	151	215.5
Min (Time)	108	136
Max (Time)	422	425
Median (Cost)	222 681	268 705.5
Min (Cost)	192 973	211 014
Max (Cost)	354 143	381 485
p-value of the time factor for the difference if a metabolite has been determined or not determined = 0.0262*		
p-value of the cost factor for the difference if a metabolite has been determined or not determined = 0.0278*		

** Statistically significant*

5.6.8 The Impact of the Number of Deviations per Study on Cost and Time

How many amendments to the protocol had to be written due to customer demands or improper planning, or the number of analytes to be determined, can drive costs. The number of deviations from the protocol brings about additional and unnecessary administrative work and can also reflect negatively on quality due to the violation of compulsory protocol adherence. The median for deviations from the protocol is 5 per study, as recorded in Table 5.18.

Table 5.18 Deviations and amendments per study

Study[8]	Deviations	Amendments	Study	Deviations	Amendments	Study	Deviations	Amendments
1	5	2	**11**	11	1	**21**	6	1
2	6	1	**12**	8	0	**22**	6	0
3	2	2	**13**	6	0	**23**	1	0
4	5	1	**14**	1	0	**24**	3	0
5	13	0	**15**	7	1	**25**	1	1
6	12	1	**16**	0	0	**26**	10	0
7	7	0	**17**	12	0	**27**	3	0
8	5	1	**18**	6	0	**28**	2	0
9	5	0	**19**	7	0	**29**	3	1
10	1	0	**20**	2	0	**30**	4	0

Table 5.19 Correlation with actual time and cost for the number of deviations per protocol

n=30 Projects	Median	Minimum	Maximum	Correlation (r) (*p*-value)
Time	157	108	425	0.25 (*p*-value 0.1776)
Cost	228 019	192 973	381 485	0.29 (*p*-values 0.1168)

Table 5.19 indicates there is no correlation between the variables time (r=0.25), cost (r=0.29) and the number of deviations documented. Therefore the number of deviations per protocol may presumably reflect the quality or the feasibility and how executable the protocol is, but have no impact on the time or cost factors.

A competitive company must ultimately translate its strategies into actions, and management should scrutinize project processes and predetermine timelines and

[8] Studies number chronologically with no reference to the actual study numbers.

remedial risk management operations before the initiation of a project. From the studies evaluated it is evident that certain processes have a statistically significant effect on the time and cost factors of a study where other processes traditionally perceived to drive costs have no statistical significant effect on cost or time. The results prove that concepts and traditions need to be tested with a statistical model and the results incorporated in a management model as an action plan through which activities are effectively aligned with the company's vision and mission.

5.7 LINEAR REGRESSION AS A STATISTICAL MODEL

The variables significantly impacting on time and cost with the univariate analysis (studies with metabolite determination, amendments and those done for relative large pharma companies) were entered into a multivariate analysis and the following parameter estimates determined for the variable time (Table 5.20).

Table 5.20 Model with the parameter estimates for the va riable time

Variable	DF	Parameter estimates	Standard error	t-value	Pr > | t |
Intercept	1	161.9790	20.8867	7.76	<.0001
Metabolite	1	33.7971	25.5591	1.32	0.1976
Amendment	***1***	***70.5773***	***21.7902***	***3.24***	***0.0033****
Large pharma company	1	-30.5605	25.6213	-1.19	0.2437

** Statistically significant*

The results obtained with the multivariate analysis indicated that amendment(s) was the only variable with a statistical significant effect on the time factor of a study. Similar results were found for the cost of the study, as tabulated in Table 5.21.

Table 5.21 Model with the parameter estimates for the variable cost

Variable	DF	Parameter estimates	Standard error	t-value	Pr > | t |
Intercept	1	231121	11194	20.65	<.0001
Metabolite	1	22193	13698	1.62	0.1173
Amendment	***1***	***35522***	***11679***	***3.04***	***0.0053****
Large pharma company	1	-21473	13732	-1.56	0.1300

** Statistically significant*

5.8 CONCLUSION

There is nothing as useless as doing efficiently
that which should not be done at all

Pieter F. Drucker

The CRO sector was created to assume part of the drug development risk and to save time and money in R&D for the pharmaceutical industry. Positioned as such, it can be expected that the sector should benefit from near-, intermediate-, and long-term pharmaceutical research and development spending and compound development trends. Because clinical trials represent the largest single portion of research spending, most CRO's, like FARMOVS-PAREXEL, focus on the clinical evaluation of new drug entities in humans as their core business. To maintain market growth in a competitive environment with large role players like Quintiles, Covance and PPD, FARMOVS-PAREXEL will have to be careful to price contracts appropriately and to deliver on time as promised. According to

Capek and Kyle (2001), a volume increase is expected to be the main driver of growth in the CRO industry. To be able to handle the spiral of increased volumes *do it right the first time* will have to be not only CROs *talk* but also their *walk*.

Opportunities in the pharmaceutical industry are available to each and every CRO in the world, trying to gain or maintain a competitive advantage. To compete for these opportunities companies will have to face industry-prevalent challenges by harnessing their knowledge to make better and quicker decisions. That is why outsourcing to CROs started, because the pharmaceutical industry is prepared to spend money to save time. In business you can spend time to save money, or you can spend money to save time. The latter is in line with the culture of the new millennium, *viz. the big will not eat the small but, the fast that will eat the slow.* Large mergers are allegedly not going to continue to take place but the smaller cost-effective companies will be the providers of choice in future. Therefore, to ensure that a value-added service is provided to pharma companies, a linear regression model can be used to identify the cost drivers to be included in a management model. An ideal management model will focus on cost-effectiveness and speed to move beyond simple cost reduction, to create value for the end user, the customer and company shareholder.

Processes with a significant effect on time and cost variables, like project mutations, should be taken note of. Project costs can only be saved during the planning stage of a project, and the significant effect protocol amendments have on the time and cost factors of a study emphasize the need to ensure that a study is executable before initiation. After project initiation, changes deemed necessary will contribute to money being spent and loss of revenue if *AS-IS* scenarios have to be changed to *TO-BE* practices. Most CRO contracts extend over months and a contract that is mis-priced with no correlation between the cost and the fee, can create a long-running drag on earnings as was shown in the research analysis. For this reason a management model should outline strategy, based on statistical evaluation and not on concepts and traditions. Real time activity costs need to be

the basis for a management model and if volume and not price increases will drive growth in the future, the managing of cost drivers, and the optimization of performance to utilize time effectively should be management's strategic philosophy. Inevitably, as *time is money*, a management model formulated with best practices will have to align stakeholders to the changes foreseen for the new millennium, i.e. that the fast will overtake the slow. Speed will be the variable pivot to managing the ever-increasing volumes CROs will have to handle, if the competitive edge is to be maintained.

Managers need to discern how to innovate and meet the need for speed by knowing what factors drive cost and time. Therefore, the results documented in this Chapter will add value to the knowledge-base of managers enhancing informed decision-making, i.e. that the following factors have no impact on cost and time:

- number of phases of a study;
- sample size of a study;
- subjects planned for enrolment, subjects enrolled or subjects screened, or
- analytical method development.

However, the univariate analysis proved a statistically significant difference for cost and time if:

- services are rendered to relatively large of small companies;
- protocols are amended, and
- metabolite determination has to be done.

The multivariate analysis showed that only protocol amendments impact cost and time statistically significantly.

Furthermore:

- A ratio of profit in relation to the head count per division indicated that productivity per head count should improve to increase the production output or conversely the head count can be decreased.

- The Pareto Principle is followed in the handling of the RFPs because, only 20% of the effort contributes to 80% of the results, as predicted by the Pareto Law.

CHAPTER 6

CONCLUSION AND RECOMMENDATIONS

Humans are good at discerning subtle patterns that are really there, but equally so at imagining them, when they are altogether absent.

Carl Sagan

6.1 INTRODUCTION

To reflect on how business in the pharmaceutical industry and *per se* clinical trials evolved into the new millennium with CROs increasingly becoming an integral part of the pharmaceutical industry's value chain, as they enter into alliances with pharma companies, one needs to discern the potential of the partnership. The testing of drugs in humans is outsourced to CROs and as the interface is put in place between pharma and CROs, it inevitably becomes the means to put demands on CROs to increase throughput efficiency. The latter relates to the competence of a company and the measure with which it can use lessons learned from the past and evolve the present into the future.

The activity-based technique implemented to calculate the time and cost factors of the operational processes were evaluated for significance with a statistical and productivity model, to discern what variables are to be included in a management model. The statistical linear regression model used in this research also demonstrated the importance of testing variables, traditionally presumed to drive costs. The statistical model is pivotal for inclusion in a management model because the analysis proved that some variables drive costs while, on the contrary, others had no statistically significant effect on time or cost factors, although they

might be perceived as costs drivers. The productivity model discerns what the estimated percentage of profiting per head count is, to distinguish which services make or lose money. Thus, incorporating a statistical linear regression model as well as a productivity model in a management model for a CRO, is advisable to guarantee that informed decisions are taken on facts and not on traditional concepts.

6.2 THE MODELS AND TECHNIQUES USED TO CONSTRUCT A MANAGEMENT MODEL FOR A CRO

The primary objective of the research was to develop a management model with a customer focus for a pharmaceutical CRO's Phase 1 Unit executing bioavailability studies. Variables traditionally presumed to have an effect on time and cost were entered into an analysis to determine which variables univariately associated with the dependent variables ($p<0.05$), have a statistically significant effect on time and cost. The variables with a significant effect, were entered into a multivariate analysis using a linear regression statistical model, with the end result that project mutation, i.e. protocol amendments, statistically significant influence cost and time.

To realize the primary objective described in Chapter One, the information obtained were used as background information in the construction of the management model. Firstly, the input cost of projects was analyzed to make recommendations on the best competitive price structure for the CRO. Secondly, costs and throughput time were evaluated to identify cost drivers. The identification of cost drivers is important, because if throughput time is predictable and variations in process time controlled, costs will be contained because time instigates costs. Thirdly, the applicability of the 20/80 rule of Pareto on projects contracted in relation to the number of requests (RFPs) was researched. The calculation confirmed that the Pareto Principle is applicable to CROs business and that only 20% of the effort provides 80% of the results.

The multivariate analysis with the statistical linear regression model, proved that protocols that need to be amended have a statistically significant effect on time and cost and that these costs need to be defrayed, although this was never done in the past. The productivity model calculating the % of profit per head count is an indication of the measure in which a service adds value to the shareholders and therefore it is useful for inclusion in a management model. The aim of any business is to get the perfect product from point A to Z in the shortest time possible because business efforts should preferably be billable within a 30-day banking cycle. That is the bottom line the shareholder is interested in and obviously the ultimate aim of all business operations is to keep the shareholder happy. Thus, a CRO must know which of its services are making money, which activities drive costs and which erode profits. Resource allocation should be made promptly to services that generate the profits. Resource consumption by divisions eroding profits need to be identified as the *trouble babies* and should be re-engineered. The results emphasize that cost drivers and production capacity and profitability per head count are not taken note of and emphasize the need for pricing structures based on informative calculations, tested for significance with a statistical model. There should inevitably be balancing levels between performance input and resultant output from a time and cost management perspective.

6.3 RECOMMENDATIONS AND A MANAGEMENT MODEL FOR INFORMATIVE DECISION MAKING

The results obtained with the activity-based management technique, the linear regression model and the productivity model are presented as best practices for inclusion in a management model for a CRO. A statistical model is postulated to determine, with univariate and multivariate analyzes, which variables statistically significantly drive time and costs. The variables identified as significant cost drivers may not have been perceived as cost drivers and divisional head counts have never been regulated by productivity calculated in accordance with

divisional profitability. The information obtained from the relevant costing technique and models, will therefore be postulated as recommendations and thereafter as a management model.

Recommendation 1: Because of information obtained from the research results and informative writings, the methodology of *target costing* is postulated as a recommendation for a costing method for a CRO. Instead of fixed prices and a strategy of *one size fits all,* services should be based on performance and customer needs. The equation to determine the cost of a bioavailability study should start with the price the customer is willing to pay minus the target profit. Therefore the competitive price is the starting point and services need to be adapted to what can be delivered at the calculated target cost (target price – profit = target services cost). This methodology is applicable especially for price sensitive customers, e.g. if a bid needs to be competitive with Eastern European countries or India. A competitive price with which market share can be increased can be estimated, and the service adapted according to the activity cost and profit. With variables such as CV%, time and cost factors known, resource allocation can be made to ensure that the activities involved in the service will not over run the target cost.

Recommendation 2: A CV% was calculated for the mean process cycle-time per operational division because variation in time is a proximal cause of variation in cost to the company. Therefore large variations in process time influence profitability if a fixed fee is charged for specific processes regardless of the real time-cost factor. Employees must also be partakers in the process to add value for customers and shareholders alike. Idealistic timelines should be defined during the planning phase as *as-if* scenarios of a study. Should employees meet these timelines an incentive must be offered as a cash-bonus, because value is then added to all stakeholders. If only the *as-is* traditional/realistic timelines were met, baseline salaries must be earned because no additional value was added to customers or shareholders. Performance-base pricing can add value to all stakeholders.

According to the estimated profit, calculated as the difference between the fee charged and the output cost, the Clinical and Bioanalytical Divisions retrieve their costs and thereafter generate a profit. The other two divisions, Biometry and PMD, erode profits. The cost to the company each resource makes on the budget should be compared and aligned according to capacity, capabilities and performances. Variation in throughput time needs to be monitored because an over run on time has a detrimental effect on the cost to the company, an invisible factor eroding the profits. The profitability of the Bioanalytical Division needs to be imitated by the other divisions and the total revenue generated could double (a 92% profit increase), or if current results only need to be reached, the number of full-time employees can be decreased.

The service rendered by the Biometry Division, the statistical analysis of bioavailability studies, is not profitable to the company, and re-engineering of the service is obviously necessary. A core team of employees needs to be dedicated to the analysis of bioavailability at a minimum wage, but with the incentive of a cash bonus if 24-hour timelines are met. With fixed timelines to be achieved, variation in service time (CV%) and corollary cost to the company will be lowered and value will be added to all stakeholders. Diversification to services other than bioavailability studies e.g. statistical analysis of clinical (Phase I to IV) studies, should be promoted because these customers are not generally price sensitive. Higher fees for these studies are easily negotiated and consequently the profitability of the Biometry Division will be increased. The activities of the Division should be targeted to add value to company revenue because it is not subjected to regulatory authority approval constraints as is the Clinical Division. Therefore Biometry should not spend time on unprofitable activities such as bioavailability studies, but rather do more profitable clinical Phase I to III work.

Recommendation 3: Volume is predicted to drive profits in the new millennium, but volume also drives cost. Therefore, before a strategic decision is taken to go for volume to generate the required bottom-line profits, a CRO needs to calculate

the costs to be incurred. Volume has an effect on price and on costs - it can drive both. Pricing strategies need to calculate a service fee taking both into consideration. The profit per head count needs to be calculated and those services not contributing to bottom-line profit, need to be identified as *trouble babies* and have to be discontinued or re-engineered. Resources must be reallocated to activities making money and those services not making money should be discontinued. If the Biometry and Project Management Divisions are not generating profits they are eroding profits. The Project Management Division needs to follow suit and re-engineer processes to improve productivity/performance. Although it can be argued that a project manager can handle more than one study simultaneously, which will have an effect on the figures, benchmarking with other PAREXEL units, e.g. the Berlin and Northwick Park Units which operate with a few (approximately 3) project managers, needs to be done. Therefore volume of work done is not necessarily going to grow profits, but working promptly and effectively taking note of cost drivers, and with profit forecasts calculated per head count, will cause profit margins to grow.

Recommendation 4: The low (16%) hit rate of RFPs contracted needs to be investigated. The service to compile RFPs is non-billable and generates labour and overhead costs. The 20/80 Principle is employed because 80% of the RFPs represent effort with no gain which is nothing more than a system leakage, eroding profits. Instead of going for volume by increasing the number of RFPs, and driving more costs, customer expectations, diversification of service offers and deals to meet individual customer needs, should be explored. Customer behaviour patterns, demands and the special needs of price sensitive customers have to be researched to find ways of meeting these needs and to turn the potential 80% clientele bases into profitable customers.

6.3.1 Management Model for a Pharmaceutical CRO

The management model constructed for a pharmaceutical CRO provides valuable

insight into relationships between operations and resource usage. The model comprises a statistical and productivity model using activity-based cost and time information with which maximum performance potential can be predicted. The model comprises the following steps:

1. Gathering time and cost data of line function processes with activity-based management methodology, following the 20/80 principle regarding effort and results obtained, i.e. time and cost data collection need not be too complicated or detailed.

2. Analyzing the time and cost data statistically with SAS or Excel and tabulating median costs, time and estimated profitability (difference between the service fee and costs).

3. Determining which variables are statistically significant with a univariate analysis, using a statistical linear regression model. The analysis confirms that process-related time and cost factors are statistically significantly better when business is done with large pharma companies. However, metabolite determination and project mutations, e.g. amendments to protocols, drive time and cost factors significantly.

4. Determining with a multivariate analysis which of the statistically significant variables (identified in the univariate analysis) are statistically significant. The results from this analysis indicate that amendments drive time and cost factors significantly and that the pricing schedule should provide an option to defray these costs.

5. The maximum productivity potential can be determined by using a productivity gradient model, ($m = \Delta y/\Delta x$) calculated as the % profit divided by the head count. The maximum productivity potential can be predicted using the gradient of the most profitable division as the output potential for every unit. This gradient is equal to the incremental % profit, divided by the head count per

division.

6. The above-mentioned gradient can be used to calculate the head count (resource allocation) in order to achieve a projected output. As illustrated in Figure 5.7, the divisional head count, with the productivity adjusted to the Bioanalytical Division's productivity, can result in the incremental total profit increasing by 92%.

7. If the profitability does not need to be increased but, only the profitability calculated in Chapter Five needs to be realized (Tables 5.3, 5.4, 5.5 and 5.7), i.e. the status quo needs to be maintained, the head count can be decreased, as illustrated in Figure 5.8, if the productivity is adjusted to the Bioanalytical Division's (the most productive unit's) productivity. The model is used to predict the minimum number of resources (head count) necessary to realize a predicted output (Figure 5.8).

8. The 20/80 Principle of Pareto is deployed in CRO business endeavours. It discerns which effort proximate the results and indicates unrealized capacity and profits should be optimized (Table 5.9 and Section 6.2).

6.4 EXPECTED IMPACT OF RESULTS

The results obtained with the activity-based methodology and evaluated with a linear regression model and a productivity model can be used to construct a management model as an informative tool with which critical decisions can be taken. A management model needs to outline the actions and plans to put strategy into practice and to assist management to align company processes and strategy with the company's vision and mission statements.

Processes for re-engineering can be identified because measures of "as-is" process performance set the base line for change initiatives with a focus on commercial benefits of "to-be" best in class performances. Divisions in alliance with each other must be cumulatively profitable, to realize future success in synergy. Thus

the Biometry Division can make a profitable contribution to revenue growth and activities need to be re-evaluated. Methods and motives to grow future business opportunities needs to be explored in every domain of free market economics.

The results identified project mutation, e.g. protocol amendments, as a cost driver but, it will also drive time and cost factors for the sponsoring company because delays in the regulatory process can be expected if trial protocol changes are deemed necessary. According to the new European Union (EU) Directive on Clinical Trials[9], it is suggested that each amendment to a protocol may be subjected to a 35-day hold period. Therefore amendments not only drive cost and time factors for a CRO during the study execution phase, but the sponsor's approval process of the dossier by the Regulatory Authorities, according to the EU Directive, Article 10(a), will also be delayed. This gloomy scenario of unnecessary delays and costs generated can be changed, if the results of this research and the contents of the new EU Directive are taken note of and amendments to protocols limited to avoid negative effects. These research results and the new EU Directive underline the impact of amendments as a cost and time driver.

The results that the Bioanalytical Division is the most profitable are not in accordance with general perceptions. The overhead expenses of the division are the largest because of the expensive equipment used in the laboratory. However, although 69% of the value and depreciation of the equipment are allocated to the division, it generates the largest percentage of profit for the company. Using the division's production output as a baseline for capacity optimization for all the divisions, a maximum production output can be predicted as an output increase of 92% or resource requirements, e.g. the head count can be decreased from 137 to

[9] Detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities, notification of substantial amendments and declaration of the end of the trial, April 2003, section 4.2.6 cited in Zuckerman and Klingmann, 2004.

72 if the current output needs to be maintained. However, the Bioanalytical Division can improve identified potential bottlenecks, e.g. report compilation and validation processes, to further optimize their performance and productivity output (Table 5.6).

6.5 CONTRIBUTIONS OF THIS STUDY

The results emphasize that activity-based information provides process-related cost data that can be analyzed with a statistical model and a productivity model to support the construction of a management model with a customer focus for a pharmaceutical CRO. The conclusions drawn from these research results can be summarized as the following contributions:

Activity-based management delivers financial intelligence as a critical factor to construct a management model. The activity-based data analyzed with a statistical model identify possible revenue improvements to be made by identifying variables that drive time and costs significantly. A linear regression model is the most appropriate statistical model with which to analyze variables and to determine which variables need to be included in the management model.

Cost in relation to fee and profitability have large CVs for Biometry and PMD and they do not have the same profitability profiles as do the Clinical and Bioanalytical Divisions. Results obtained with the activity-based analysis should be used to ensure that cycle time is in relation to the budget and that all the divisions are profitable and contributing to revenue growth. The productivity model shows how the Biometry and Project Management Divisions erode profits and that services and the head count (executing bioavailability studies) need to be reconsidered.

Activity time factors need to be evaluated to identify bottlenecks, e.g. in B iometry (Table 5.7), where costs in relation to the fees have large CVs, and in the Bioanalytical Division, where the individual processes have large CVs (Table

5.6), processes can be re-engineered to improve throughput efficacy. PMD needs to log the throughput time of individual studies to ensure optimal time-frames for bioavailability studies. The ideal time and cost factors proved to have low CVs (between 9% and 15%), which need to be imitated in actual cycle times (Table 5.8).

The CVs of the variables costs and fees vary considerably between studies and need to be controlled with predictable timelines determined during the planning phase. Throughput time has competitive marketing leverage and can be used in branding. However, the large variation in throughput time has an effect on the cost to the company and inevitably on profits (Tables 5.3, 5.4, 5.5 and 5.7).

Negative profitability figures for PMD and Biometry prove that these divisions as a rule do not make a positive contribution to company revenue growth. A pricing schedule based on a target fee that equals a target cost + profitability needs to be implemented taking significant cost drivers, e.g. if amendments were written, into account.

Predictive planning and risk management for worst and best case scenarios need to be done for every study, taking note of factors driving time and cost, e.g. amendments and the constraints of study cancellation. A large number of studies (35%) were cancelled in 2000. The overhead cost of unused capacity needs to be calculated and offered as a discount for customers recruited to contract development work with lenient timelines and study initiation within a 4-6 month time-frame. Unused capacity can then be offered at a discount to add value to both parties, as a win-win deal.

The low RFP hit rate of 16% of the requests contracted, emphasizes the need for a marketing strategy to target the unprofitable customers and change their behaviour. Customer profiles and profitability need to be researched inclusive of their needs, expectations and behaviour patterns to formulate a strategy for customer relationship management to increase customer profitability as an add-on

to the input cost in the value-chain.

The 20/80 Rule is applicable to CRO activities. Note needs to be taken that 80% of the results come from 20% of the effort and the 20/80 rule needs to be applied to every endeavour, to identify which activities contribute to bottom-line revenue growth. Effort should be balanced against results obtained.

Business segmentation shows that Germany provides frequent business opportunities, but untapped markets specifically with large pharma companies, e.g. the USA and India, need to be targeted to grow future revenue. Business with large pharma has a statistically significant effect on cost and time variables therefore alliances with large pharma companies need to be targeted strategically as future business opportunities.

Categorizing cost drivers with statistical significance is crucial because perceptions of what drives cost and time do not necessarily have an effect and *vice versa*. To know beforehand which cost drivers have bottom-line effects on revenue when quotes are compiled and discounts negotiated, is a necessity, especially when collaboration with small compa nies is at stake or there are customers who frequently request protocol mutations, or when metabolite determination is included in the analysis.

The productivity/performance analysis indicated that an estimated revenue growth of 92% is possible if the divisions can become more competitive and profitable and the profitability performance of the Bioanalytical Division can be imitated.

The results emphasize the importance of effort needing to be balanced against results and that a number of aspects play a role and need to be considered if informed decisions are to be taken concerning the execution of a study. Regarding cost drivers, e.g. when metabolite determination, business relationships with small pharma companies and amendments to protocols are at stake, management's judgment has to be aligned to keep the company focused on its

vision and mission. CROs determined to win the competitive battle and maintain their leadership positioning in future, will have to put customer focused strategies into practice.

A management model for a CRO revolves around financial measures, process measures and alliance measures within the constraints of cost, time and performance. Within these constraints the present must be improved for future gain to keep all stakeholders, i.e. shareholders, customers and employees, happy. Firstly, the CRO's portfolio of what it does, e.g. the diversified services it provides to meet customer needs, or whether it goes for volume to meet bottom-line profits or niche services, incurs different levels of costs, and if no service is rendered, idle capacity also incurs costs, thereby eroding company profits. Management must know what generates its cost-drivers. Secondly, the environment in which activities occur is of importance because CROs need to think globally and act locally. The environment and the competition regarding services rendered change all the time, and consequently so do the demands of customers for services, throughput efficiency and price. Lastly, the process risk concerning how services are perceived by customers is of importance for CROs. Customer relationships and performance during every endeavour to meet customer needs, are constraints CROs must manage, to guarantee on-going corporate profits and economic growth. Loyal customers are an important and integral part of the present and future success of CROs. Throughput efficiency is dependent on the CRO's management ability to unlock maximum value from negotiations and collaboration with customers. Success will depend on resource capacity optimization and profitability.

6.6 RECOMMENDATIONS FOR FUTURE WORK

The low hit rate of RFPs should be a target for investigation and the reason for the low number of studies contracted considered as an action plan to improve customer relationship management. The volume of RFPs handled is extensive and if it is volume and speed that will generate the cash for further growth, the

cost of the volume and timeline constraints as a result of the volume, should be calculated. Non-value adding volume is a loss of revenue. The number of requests for quotes indicates that FARMOVS-PARXEL is considered as a reputable CRO and that the company has the competitive advantage of branding. The importance of branding can, however, be extended further and services priced according to customer needs and demands. When times are good, pricing sins can easily be forgiven. However, when the economy sours, a misguided pricing strategy can shrink profitability, warp customer relationships, and destroy a brand (Wreden, 2002). Pricing strategies should cater for the whole spectrum of customers, from upper big pharma companies who want to fly *business-class* with state of the art high-tech services, to the smaller bio-tech or generic company whose personal needs will be met by an *economy-class* package. Companies must have a choice of services to choose from and should be kept loyal to the brand by offers fitting their needs. Ways to improve branding and to keep customers loyal to the brand should be explored because it is more costly to replace a customer than to keep one.

The studies contracted in relation to the number of RFPs received and compiled, confirmed the 20/80 rule of the Pareto. Therefore, 80% of potential customers are *not* contributing to the bottom-line profits. These companies should be targeted and the following questions addressed, e.g. whether business with a specific client should focus on:

- volume or margin;
- ways to improve profitability by altering the design of a study, the logistics or the services provided to the customer;
- contract amount and if additional customer service demands justify the budget or rebates/discounts offered;
- how the customer can be influenced to alter his behaviour to do business differently and become more profitable;

- if the customer is price sensitive, how a win-win performance-based deal can be negotiated;
- whether the services offered fit the needs of the customer and whether all the services add value to the customer's needs or are unnecessarily sophisticated, activity intensive services rendered which the customer is not prepared to pay for, and
- performance in relation to price, i.e. whether the customer gets what he pays for.

6.7 AVAILABLE APPROACHES RELEVANT TO THIS RESEARCH

Available approaches to this project are any economical analysis technique producing comparable results correlating the cost of input to that of output. According to Thornton *et al.*, (1992), the correct course of action depends on the probabilities and the values placed on the possible outcomes. Multiple approaches are available to any project with benefits as well as risks, an inevitable part of any chosen approach. A management model constructed according to a single methodology may not be as effective for a CRO as a model constructed from a combination of best-in-class models, because the model must not only fit the core business of the company but also the company environment. The fact is that speed, quality and price are the most important variables in the competitive environment a CRO operates in. It follows that the researcher focused on activity and process-based models in the collection of the data for the construction of a management model for a CRO.

Conversely the question can be asked: if an activity focus is so important and was the chosen methodological approach for this project, why have Japanese companies, following the KAIZEN philosophy, been able to prosper and grow using traditional costing methods (Patel and Russell, 1994). The reason can be that cost reduction is built into the Japanese approach to management while accounting procedures are used to reinforce management strategies, linking

accounting practices and cooperate goals, and not merely for measuring what is happening. Many Japanese companies continue to use direct labour hours, justified by management as creating the desired strong pro-automation incentive throughout the organization. Therefore, the significance of cost is not lost, because Japanese management focuses on the design and pre-production stages where the majority of a product's cost is determined, based on the maximum price expected to be borne by the market, and the product acceptable quality is designed within the cost. The emphasis on cost should be enhanced by a management philosophy that *cost is everybody's business!* The key to competitive success lies in continual improvement involving *everybody!* However, a change from what was accepted a few years ago when the Japanese popularized the concept of *kaizen*, encouraging everyone to strive for small continual improvements in their work output, was when it became clear that incremental improvements could be self-defeating. According to Hodgetts (1998), it discourages innovation and rethinking of the big picture. A holistic view of the value-chain and output to add customer value is emphasized lately as the *name of the game.*

A major strength of the Japanese approach is probably the recognition of human creativity and respect for workers as a prerequisite for the ultimate use of the available human resource necessary for achieving the cost objectives. The practice of cost aware management could only be beneficial, if incorporated into CRO operations. The above-mentioned philosophy postulates that creative people can adapt to change and innovation and it is an idealistic vision for a CRO. This philosophy can be combined with activity-based management strategies, which can be described as tracking the moving target of time and performance electronically. It entails the electronic capturing of real time data of all the activities undertaken by employees. There is then no need to use historical data of activities undertaken at the end of a research project. A number of software programs available on the market have the ability to track and log time spent by employees against activities, operational specific activities, as well as support

activities. Performance can continually be compared to the budgeted figures, customers can get what they pay for and shareholders can be assured, of not losing their investment. The programs can prompt employees to log their activities into a database.

The electronic data-capturing program can link internal costs to the activities through the allocation of time. An intranet-based tool can be used as a support tool to improve financial decision-making in terms of the project cost and shareholder investment. FARMOVS-PAREXEL should be requested to implement the TIMS (Time Information Management System) program used by PAREXEL International, due to the importance and value this technique is to management's decision-making.

The advantages of the system will be that the real time resource consumption of each project can be monitored in accordance with the financial contract. As soon as the resources allocated to the project need to be increased, the sponsor's approval for the additional costs can be obtained in advance to ensure that the costs will be chargeable to the sponsoring company. The program also tracks personnel performance to inform management on what activities the personnel spent their time. Waste, non-value adding activities and reworks will be identified, and productivity data will be more accurately available.

If the software program is implemented at FARMOVS-PAREXEL the program will log a time data trail on all divisional activities per project, not only of the bio-projects, so data on every project will be available for analysis and managerial decision-making. The process could work as follows: Data on the company's transaction system will be stored in a data warehouse, where it is organized, cleansed and processed for input into an analysis program. The activity-based information extracted from this information will be available to management, enabling them to stay current with the business and make the following options available to them:

- understanding and acting on cost drivers;
- making information available through retrospective performance review as a learning curve, to support resource allocation decisions for future projects;
- creating data to facilitate pricing decisions;
- encouraging lateral and vertical coordination and communication across projects and functions, and
- enhancing information for contract negotiations regarding activity time and customer demands on resources.

The limitation of the program is the time spent by employees to log activities. Some may even resent the exercise because of the burden in terms of effort in logging every activity according to the time spent on it. Meetings have to be logged retrospectively or in advance. However, because of the benefits to be gained by the system, PAREXEL may take a decision that TIMS must be implemented at FARMOVS-PARXEL as a tool to monitor individual activity input. Time tracking is considered as one of the key elements for effective financial management of projects. Time, a proxy for costs, should be managed and everybody should be involved, even the customers.

With a corporate vision of a continual outreach to excellence, activities running behind schedule in one division have a spin-off to other divisions, hampering the meeting of timelines/deadlines set for a study. However, it takes more than just plugging numbers from the data warehouse into the model. The CRO needs to know the purposes the activity-based information is going to serve. For example, it may might seek overall improvement in operational efficiency, to reduce costs within a specific department or to support resource allocation. The CRO needs to design the model to provide efficiently the types of analyzes their core business requires.

A management model should include the basic activities associated with the core

competencies of the CRO. The company's management systems should be compatible with one another. For example, the accounting system should not produce data that conflicts with the time-tracking system. To have figures in the activity-based model that can be relied on, care should be taken that there are no contradictions and that the systems are comparing apples to apples before analyzing the data generated (Leahy, 2001b). Changes will invariably need to be made to both the activity data-collection process and the data extracted from the general ledger to ensure compatibility with the specialized software to suit the special needs of the company (Dikolli, 1996). The traditional general ledger view simply describes: "What was spent." With the growing complexity of organizations, this does not always give the whole picture. With an activity-based view of the same information, a fair charge-back system that reflects the true consumption of costs by end-users and service recipients can be mapped (Book review, 2002). Therefore, the best model should incorporate time tracking of external and internal expenditure on projects, budgeting to support projects and accountability for expenditures, as key elements for effective financial management of projects. There is continual development in the field of activity, cost, time and performance management tools to make the implementation not only time and cost effective but also a dynamic process. Performance and productivity management is the driving force of successful organizations. It ensures that individuals and teams work together to achieve a sustainable competitive advantage. Business process re-engineering has as a foundation, in its strategic intent, a focus on the customer. That is, all core business processes begin and end with satisfying the customer. Re-engineering is about reorienting the business processes from the perspective of the customer; of thinking in processes and not in functions, and of ensuring that all activities are adding value (Weiss and Hartle, 1997).

6.8 CONCLUSION

There is the risk you cannot afford to take [and]

there is the risk you cannot afford not to take

Peter Drucker

The final two Chapters of the research combine the initial chapters' documentation of the tenets of activity-based costing and the methodology followed in this research to present the results in a descriptive textural context as well as statistically. The primary objective set out in Chapter One to construct a management model for a CRO, was fulfilled and all variables, which were univariately associated with the dependent variables ($p<0.05$), were entered into a linear regression model to determine with a multivariate analysis which variables have a statistically significant effect on the time and cost. For the purpose of this thesis, the aim of constructing a management model with which the company intends to profit from its broad array of processes and activities, was achieved. The definition that a theory is a set of statements that makes explanatory or causal claims about reality, was explored to assess the best set of statements with which a model can be constructed for a CRO. Therefore, as informative writing in literature confirms, good theories and models provide causal accounts of the world; allow the researcher to make predictive claims under certain conditions; bring conceptual coherence to a domain of science; simplify the reader's understanding of business in the pharmaceutical, and contract research industry. The theory was confirmed that companies should know their cost drivers, as well as which of their services make or lose money, emphasizing that pricing schedules should preferably be structured not only by rule of thumb but, be based on target costs.

The results indicated that project mutation, i.e. protocol amendments, had a statistically significant effect on the cost and time factors of a study. Conversely concepts that seem to be realistic and relevant, e.g. that sample size, number of clinical phases and method development have a significant cost and time effect on study execution, were proved to be figments of the imagination. The results indicated that these variables have no statistically significant effect on study cost and throughput time. The pricing tool with which management calculate fees for services needs to incorporate this information.

Any business service is available at a price. According to Cowell (1991) *"For a fee, there are now companies that will balance your budget, baby sit your philodendron, wake you up in the morning, drive you to work, or find you a new home, job car, wife, clairvoyant, cat feeder, gypsy violinist. Or perhaps you want to rent a garden tractor? A few cattle? Some original paintings? Or maybe some swingers to decorate your next cocktail party? If it is business services you need, other companies will plan your conventions and sales meetings, design your products, or supply temporary secretaries or even executives" (Business Week 30 Oct, 1971, p. 50).*

Throughout decades, services have been available for every possible need if the customer is prepared to pay the price. Globally customer needs may have been the same over a period of time, as illustrated by the Business Week citation published three decades ago, management models and strategies of service providers evolve continually over time. Sooner or later *tomorrow* becomes *today*, and yesterday's foresight becomes today's conventional wisdom. CROs compete for market share *via* the price and effective throughput of the services they offer. A management model is therefore an informative tool to dictate how, where and what services should be rendered to generate the cash that fuels the journey to meet the visions and mission of the company, to assess the effect of time on costs that, in the end, erode profitability. It is a tool to keep management's judgment based on sound information gathered from cost centers explored and evaluated -

because *what is unsought will go undetected* (Sophocles)[10]. Assessing the time and cost factors of activities with a linear regression model, predictive claims under standardized conditions can bring conceptual coherence to a domain of business, and simplify our understanding of the risks we cannot afford to take, and the risk we cannot afford not to take.

A model to calculate the productivity of divisions provides the financial intelligence of the profits associated with certain services. Process-related costs driven by resource requirements have bottom-line impacts on profits. The head count from an operational perspective should mirror the profitability, and care needs to be taken that the relationship between operations and resource usage adds value to all stakeholders. The objectives of this research were successfully realized because not only was the management model formulated but, the results presented added value to the knowledge base of CRO operations. It is evident that concepts, theories and traditions used in CRO business operations need to be tested with a model because what may be perceived to be profitable may in fact be a system leakage of profits. It can be argued CROs are *good … at discerning subtle patterns that are really there, but equally so at imagining them, when they are altogether absent.*

[10] Sophocles cited in Cameron, J. (1995)

7. ABSTRACT

There are countless ways of management and doing business, which also means that there is unlimited room for improvement. Anything we do can almost always be done a little better.

Konosuke Matsushita. Founder of Matsushita Electrical Company

Competitive success for a Contract Research Organization (CRO) entails unlimited process improvement to sustain excellence.

Chapter One describes the generic business environment CROs operated in which customers dictate the pace of competition through asking for higher standards of quality, speedy delivery, reliability, and lower prices, as markets are becoming increasingly saturated. Opportunities for market growth and maintaining market share, are testing experiences for all CROs. This imposes the tenets of theories and models on CROs so as to understand the critical factors that have a statistically significant effect on their bottom-line figures. CROs need to take note of causal factors driving time and costs, even at the height of their success. Therefore, Chapters Two and Three present informative writings on the tenets of best-practices and activity-based management, because best-in-class principles must be reviewed to contemplate which risks to take; which new ideas to implement; which critical factors will drive success, and which will challenge the myths distinctive to the contract research environment.

Informative writings, documented as background information, were used to evaluate the results presented in Chapter Five. During the construction of a model for a CRO in the final Chapter, an attempt is made to explain phenomena experienced in everyday life and to discern aspects necessary to sustain competitive success in contract research. For the purpose of this

research a model is defined as a set of statements that make explanatory or causal claims about reality, statements that aim to represent everyday phenomena as accurately as possible, and simplify our understanding of the CRO business environment. This research is aimed at developing a management model to explain the particular phenomena applicable to a pharmaceutical CRO and can be classified as an empirical study, analyzing existing primary and numerical data, gathered from a case study.

Although management models are well described in literature, this research adds value to an aspect still to be researched, i.e. a management model comprising the most applicable best-practices for a pharmaceutical CRO. Because throughput time is of utmost importance in clinical drug research programs and because time consequently generates costs, an activity-based methodology is considered the best-in-class information tool to gather the necessary data for the calculation of time and cost factors for a CRO.

The results presented in Chapter Five, analyzed with a statistical linear regression model using univariate and multivariate analyses to discern which variables have a statistically relevant effect on time and cost factors, were used to formulate the management model in Chapter Six. The productivity model presented shows that if the productivity of the operational divisions imitates the output of the most productive division, the profit can almost be doubled, or conversely, the same profit can be maintained but, with a reduction in the number of full time employees.

This holds win-win benefits for the company and the customer, especially if cost can be used as leverage in a competitive market. Pricing is a complex instrument because of the two-sided conflict and competitive nature of the buyer-seller relationship where the one's gains are the other's loss. The researcher evaluated time, costs and pricing to make pricing a win-win element through which improved throughput efficacy can provide greater customer value and higher profits to the shareholder.

Secrecy agreements are signed between CROs and sponsoring companies and therefore project information is the intellectual property of the sponsoring company. This limiting factor inevitably made a case study approach for this research project a necessity. Research

information should preferably have been included from different CROs worldwide, and a case study approach may be regarded as not meeting minimal design requirements for comparison. However, a single, well-designed case study can provide a major challenge to informative writings and theory. It can provide new insight into traditional concepts and figments of the imagination, and identify statistically significant cost drivers to sustain the knowledge base to make recommendations on the optimization of resource utilization. As CROs enter foreign markets, global harmonization of clinical trial standards serve to provide uniformity in processes in trial execution. Guidelines reach beyond the sponsoring country to regulate quality and ensure uniformity of trials globally. Thus, the results obtained from FARMOVS-PAREXEL case studies can be extrapolated to other CROs and the model formulated, as a result of global uniformity enforced by regulations universally applicable to CROs.

The project was important because in the quest for developing new drugs, CROs compete *inter alia* as providers of choice on timelines and price. The interpretation of the results emphasized that factors traditionally perceived as cost drivers, may not have statistically significant effect on time or cost factors. The synergy between techniques applied from the theoretical fields of accounting and project management, i.e. to quantify and optimize resource utilization, provided the information to formulate a unique management model for a CRO. The lack of outcome based research results, from a management perspective, on resource consumption during the execution of bioavailability studies, emphasizes the importance of this research project.

The research results indisputably prove that concepts and traditions need to be tested with a statistical linear regression and productivity model as the core logic of a management model for a CRO. The results conclusively indicate that a management model with a customer focus for a pharmaceutical CRO is a necessity to align financial performance measures, which are pivotal in the alliance with the customer and shareholder.

Keywords:

- Contract Research Organization;
- Management model;
- Activity-based management;
- Activity-based costing methodology;
- Customer Relationship management;
- Clinical research environment;
- Bioavailability studies;
- Project management;
- Productivity model;
- Cost drivers.

7. ABSTRAK

Daar bestaan ontelbare wyses van bestuur en besigheid doen, wat ook beteken dat daar onbeperkte ruimte vir verbetering is. Enige iets wat ons doen kan feitlik altyd 'n bietjie beter gedoen word.

Konosuke Matsushita, stigter van Matsushita Electrical Company

Mededingende sukses vir 'n kontraknavorsingsorganisasie (KNO) noodsaak onbeperkte prosesverbetering om voortreflikheid vol te hou.

Hoofstuk Een beskryf die generiese besigheidsomgewing waarbinne KNOs bedryf word en waar kliënte die pas van mededinging dikteer in hul vraag na hoër standaarde van gehalte, vinnige aflewering, betroubaarheid en laer pryse soos wat markte toenemend versadig word. Geleenthede vir markgroei en die behoud van markaandeel, is aangeleenthede wat alle KNOs toets. Dit skryf die leerstellings van teorieë en modelle aan KNOs voor, ten einde die kritieke faktore wat 'n statisties beduidende effek op hul winssyfers het, te verstaan. KNOs moet kennis neem van oorsaaklike faktore wat tyd en koste aandryf, selfs ook op die kruin van hul sukses. Om hierdie rede bevat Hoofstukke Twee en Drie leersame beskrywings van die leerstellings van bestepraktyke en aktiwiteitsgebaseerde bestuur, omdat beste-in-klas-beginsels in oorweging geneem moet word ten einde van hulp te wees by besluitneming oor watter risiko's geneem moet word; watter nuwe idees geïmplementeer moet word; watter kritieke faktore sukses sal meebring en watter faktore die mites, kenmerkend aan die kontraknavorsingsomgewing, sal uitdaag.

Informatiewe werke, aangeteken as agtergrondsinligting, is gebruik om die resultate wat in

Hoofstuk Vyf aangebied word, te evalueer. Met die uitleg van ’n model vir ’n KNO in die finale hoofstuk, word gepoog om verskynsels wat in die alledaagse lewe ondervind word, te verduidelik en om aspekte te onderskei wat nodig is om kompeterende sukses in kontraknavorsing vol te hou. Vir die doel van hierdie navorsing is ’n model omskryf as ’n stel verklarings wat verduidelikende of oorsaaklike aansprake omtrent die realiteit maak, stellings wat ten doel het om alledaagse verskynsels so akkuraat as moontlik weer te gee en ons begrip van die KNO-besigheidsomgewing te vereenvoudig. Hierdie navorsing is daarop gemik om ’n bestuursmodel te ontwikkel om die spesifieke verskynsels wat van toepassing is op ’n farmaseutiese KNO te verduidelik. Dit kan geklassifiseer word as ’n empiriese studie wat bestaande primêre en numeriese data, versamel uit ’n gevallestudie, analiseer.

Alhoewel bestuursmodelle goed beskryf word in die literatuur, voeg hierdie navorsing waarde toe tot ’n aspek wat nog verder nagevors moet word, naamlik ’n bestuursmodel wat die mees toepaslike bestepraktyke vir ’n farmaseutiese KNO vervat. Aangesien omsettyd van die uiterste belang is by farmaseutiese navorsing en deurdat tyd gevolglik koste meebring, word ’n aktiwiteitsgebaseerde metodologie as die beste beskikbare metode beskou om die noodsaaklike data vir die berekening van tyd- en kostefaktore vir ’n KNO te versamel.

Die resultate verkry in Hoofstuk Vyf word met ’n statisties lineêre regressiewe model geanaliseer, deur gebruik te maak van ’n enkelveranderlike en ’n meerveranderlike analise om veranderlikes te onderskei, wat ’n statisties beduidende effek op tyd- en kostefaktore het. Die produktiwiteitsmodel wat in Hoofstuk Vyf aangebied word, toon dat indien die produktiwiteit van die bedryfsafdelings die uitset van die mees produktiewe afdeling navolg, die wins feitlik verdubbel kan word, of omgekeerd kan dieselfde wins gehandhaaf word, maar met ’n vermindering in die aantal voltydse werknemers.

Dit hou wenvoordele vir beide die maatskappy en die kliënt in, veral indien koste gebruik kan word as hefboom in ’n kompeterende mark. Prysbepaling is ’n komplekse instrument vanweë die tweesydige konflik en kompeterende aard van die koper-verkoper-verhouding waar die een se wins die ander se verlies is. Die navorser het tyd, koste en prys geëvalueer om prysbepaling ’n wen-wen-element te maak waardeur die verbeterde omsetdoeltreffendheid

groter waardetoevoeging vir die kliënt en groter winste aan die aandeelhouer kan verskaf.

Vertroulikheidsooreenkomste word tussen KNOs en opdraggewers onderteken en daarom is projekinligting die intellektuele eiendom van die borgmaatskappy. Hierdie beperkende faktor maak noodwendig 'n gevallestudiebenadering vir hierdie navorsingsprojek 'n noodsaaklikheid. Die ideaal sou wees om navorsingsinligting van verskillende KNOs wêreldwyd in te sluit en 'n gevallestudiebenadering kan daarom beskou word om derhalwe nie aan die minimum ontwerpvereistes vir vergelyking te voldoen nie. 'n Enkele goed ontwerpte gevallestudie kan egter 'n groot uitdaging aan informatiewe werke en teorieë bied. Dit kan nuwe insig in tradisionele konsepte en versinsels van die verbeelding verskaf en statisties beduidende kostedrywers identifiseer om die kennisbasis te steun, ten einde aanbevelings te maak oor die optimisering van hulpbronbenutting. Namate KNOs buitelandse markte betree, dien globale harmoniëring van kliniese navorsingstandaarde, om eenvormigheid in prosesse tydens die uitvoering van die navorsing te verskaf. Riglyne strek verder as die land wat borg om sodoende gehalte te reguleer en eenvormigheid van navorsing globaal te verseker. Die resultate wat dus vanaf FARMOVS-PAREXEL-gevallestudies verkry is kan geëkstrapoleer word na ander KNO's asook die model wat geformuleer is vanweë globale eenvormigheid wat afgedwing word deur regulasies wat universeel op KNOs van toepassing is.

Die projek was belangrik omdat KNOs, in die soeke na die ontwikkeling van nuwe geneesmiddels onder andere meeding as verskaffers van keuse wat betref tydlyne en prys. Die interpretasie van die resultate het beklemtoon dat faktore wat tradisioneel as kostedrywers beskou is, dalk nie 'n statisties beduidende effek op tyd- of kostefaktore mag hê nie. Die sinergie tussen tegnieke toegepas uit die teoretiese velde van rekeningkunde en projekbestuur, dit wil sê om hulpbronbenutting te kwantifiseer en te optimiseer, het die inligting verskaf vir die formulering van 'n unieke bestuursmodel vir 'n KNO. Uit 'n bestuursperspektief gesien, beklemtoon die gebrek aan uitkomsgebaseerde navorsingsresultate oor hulpbronverbruik gedurende die uitvoer van 'n biobeskikbaarheidstudie, die belangrikheid van hierdie navorsingsprojek.

Die navorsingsresultate bewys onteenseglik dat konsepte en tradisies getoets moet word met ’n statisties lineêre regressie- en produktiwiteitsmodel as die kernlogika van ’n bestuursmodel vir ’n KNO. Die resultate toon gevolglik aan dat ’n bestuursmodel met ’n kliëntefokus ’n noodsaaklikheid vir ’n farmaseutiese KNO is om finansiële prestasiemaatstawwe, die sleutelaspek in die verbintenis met die kliënt en die aandeelhouer, te belyn.

Kernwoorde:

- Kontraknavorsingsorganisasie;
- Bestuursmodel;
- Aktiwiteitsgebaseerde bestuur;
- Aktiwiteitsgebaseerde kosteberekeningsmetodologie;
- Kliënteverhoudingsbestuur;
- Kliniese navorsingsomgewing;
- Biobeskikbaarheidstudie;
- Projekbestuur;
- Produktiwiteitsmodel;
- Kostedrywers.

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9. APPENDIXES

9.1 STATISTICAL ANALYSIS

Note: Studies presented are numbered chronologically.

Appendix 9.1.1

Divisional Costs Calculate According to Actual Activity Time

Study	PMD (ZAR)	Biometry (ZAR)	Analytics (ZAR)	Clinic (ZAR)	Total (ZAR)
Study 1	159296.00	42275.00	123161.00	56753.00	381485.00
Study 2	158162.00	44717.00	90317.00	60947.00	354143.00
Study 3	142249.00	40534.00	91337.00	52561.00	326681.00
Study 4	86848.00	30618.00	82913.00	68286.00	268665.00
Study 5	73170.00	38893.00	77687.00	62055.00	251805.00
Study 6	87043.00	29470.00	85681.00	75506.00	277700.00
Study 7	58999.00	27506.00	71837.00	52672.00	211014.00
Study 8	70157.00	28820.00	64479.00	57280.00	220736.00
Study 9	57174.00	26159.00	71497.00	51962.00	206792.00
Study 10	58951.00	26450.00	74362.00	48187.00	207950.00
Study 11	87564.00	30404.00	82605.00	52140.00	252713.00
Study 12	65444.00	27970.00	70921.00	51624.00	215959.00
Study 13	70259.00	28625.00	83587.00	48951.00	231422.00
Study 14	53007.00	24589.00	70598.00	44779.00	192973.00
Study 15	59442.00	25638.00	80991.00	47272.00	213343.00
Study 16	66452.00	28720.00	76053.00	45382.00	216607.00
Study 17	59287.00	28426.00	76282.00	46232.00	210227.00
Study 18	85665.00	30662.00	79618.00	72801.00	268746.00
Study 19	65172.00	32023.00	76522.00	50909.00	224626.00
Study 20	66452.00	26706.00	68332.00	46122.00	207612.00
Study 21	59296.00	52343.00	84706.00	51563.00	247908.00
Study 22	82891.00	29516.00	82389.00	64124.00	258920.00
Study 23	81712.00	28261.00	96389.00	51340.00	257702.00
Study 26	98599.00	51063.00	68690.00	61062.00	279414.00
Study 27	58853.00	25346.00	81986.00	62878.00	229063.00
Study 24	53051.00	24930.00	78232.00	42901.00	199114.00
Study 28	49273.00	25092.00	75578.00	57181.00	207124.00
Study 25	62460.00	29041.00	76319.00	46949.00	214769.00
Study 29	84580.00	53292.00	66984.00	49684.00	254540.00
Study 30	62757.00	49515.00	65166.00	49537.00	226975.00
Total	2324265.00	987604.00	2375219.00	1629640.00	7316728.00
ArithMean	77475.50	32920.13	79173.97	54321.33	243890.93
ArithSD	28658.99	9007.57	11384.14	8360.68	45214.96
Median	66452.00	28930.50	77104.50	51793.00	228019.00
Min	49273.00	24589.00	64479.00	42901.00	192973.00
Max	159296.00	53292.00	123161.00	75506.00	381485.00
n	30	30	30	30	30

Appendix 9.1.2

Clinical Division's Cost in Relation to the Fee Expressed as an Estimated Profit

		Clinical Division		
Study	Phase	Cost	Quote	Profitability
Study 1	2 x	56753.00	232213.00	175460.00
Study 2		60947.00	225134.00	164187.00
Study 3		52561.00	61230.00	8669.00
Study 4		68286.00	128245.00	59959.00
Study 6		75506.00	207025.00	131519.00
Study 7		52672.00	154635.00	101963.00
Study 8		57280.00	154635.00	97355.00
Study 12		51624.00	127060.00	75436.00
Study 13		48951.00	199920.00	150969.00
Study 15		47272.00	185354.00	138082.00
Study 16		45382.00	203580.00	158198.00
Study 19		50909.00	140700.00	89791.00
Study 20		46122.00	193440.00	147318.00
Study 22		64124.00	252850.00	188726.00
Study 23		51340.00	154440.00	103100.00
Study 26		61062.00	158895.00	97833.00
Study 27		62878.00	120640.00	57762.00
Study 24		42901.00	164424.00	121523.00
Study 28		57181.00	119765.00	62584.00
Study 25		46949.00	79040.00	32091.00
Total		1100700.00	3263225.00	2162525.00
ArithMean		55035.00	163161.25	108126.25
ArithSD		8457.89	49945.72	49187.92
CV%		15.37	30.61	45.49
GeomMean		54446.48	154717.34	91591.95
GeomSD		1.16	1.42	2.04
Median		52616.50	156765.00	102531.50
Min		42 901.00	61230.00	8669.00
Max		75506.00	252850.00	188726.00
n		20	20	20
Study 5	3 x	62055.00	222095.00	160040.00
Study 10		48187.00	207331.00	159144.00
Study 11		52140.00	170511.00	118371.00
Study 17		46232.00	556920.00	510688.00
Study 21		51563.00	209105.00	157542.00
Study 30		49537.00	96239.00	46702.00
Total		309714.00	1462201.00	1152487.00
ArithMean		51619.00	243700.17	192081.17
ArithSD		5555.50	160121.48	162100.62
CV%		0.76	65.70	84.39
GeomMean		51386.38	210900.35	149862.14
GeomSD		1.11	1.76	2.15
Median		50550.00	208218.00	158343.00
Min		46232.00	96239.00	46702.00
Max		62055.00	556920.00	510688.00
n		6	6	6
Study 9	4 x	51962.00	271856.00	219894.00
Study 14		44779.00	101556.00	56777.00
Study 18		72801.00	186485.00	113684.00
Study 29		49684.00	150020.00	100336.00
Total		219226.00	709917.00	490691.00
ArithMean		54806.50	177479.25	122672.75
ArithSD		12365.06	71894.42	69219.34
CV%		22.56	40.51	56.43
GeomMean		53861.51	166709.13	109240.95

GeomSD	1.23	1.51	1.74
Median	50823.00	168252.50	107010.00
Min	44779.00	101556.00	56777.00
Max	72801.00	271856.00	219894.00
n	4	4	4

Total calculated for n = 30 studies

Total	1629640.00	5435343.00	3805703.00
ArithMean	54321.33	181178.10	126856.77
ArithSD	8360.68	87316.05	87953.47
CV%	15.39	48.19	69.33
Median	51793.00	167467.50	116027.50
Min	42901.00	61230.00	8669.00
Max	75506.00	556920.00	510688.00
n	30	30	30

Appendix 9.1.3

Bioanalytical Division's Cost in Relation to the Fee Expressed as an Estimated Profit

		Bioanalytical Division		
Study	Phase	Cost	Quote	Profitability
Study 1	2 x	123161.00	232960.00	109799.00
Study 2		90317.00	196040.00	105723.00
Study 3		91337.00	163644.00	72307.00
Study 4		82913.00	377507.00	294594.00
Study 6		85681.00	381550.00	295869.00
Study 7		71837.00	358514.00	286677.00
Study 8		64479.00	320684.00	256205.00
Study 12		70921.00	269176.00	198255.00
Study 13		83587.00	248776.00	165189.00
Study 15		80991.00	339326.00	258335.00
Study 16		76053.00	197353.00	121300.00
Study 19		76522.00	135080.00	58558.00
Study 20		68332.00	186160.00	117828.00
Study 22		82389.00	207480.00	125091.00
Study 23		96389.00	128480.00	32091.00
Study 26		68690.00	234700.00	166010.00
Study 27		81986.00	141440.00	59454.00
Study 24		78232.00	122824.00	44592.00
Study 28		75578.00	142420.00	66842.00
Study 25		76319.00	156767.00	80448.00
Total		1625714.00	4540881.00	2915167.00
ArithMean		81285.70	227044.05	145758.35
ArithSD		12805.36	87024.21	89370.84
CV%		15.75	38.33	61.31
GeomMean		80445.01	212074.65	119647.63
GeomSD		1.15	1.46	1.95
Median		79611.50	202416.50	119564.00
Min		64479.00	122824.00	32091.00
Max		123161.00	381550.00	295869.00
n		20	20	20
Study 5	3 x	77687.00	389376.00	311689.00
Study 10		74362.00	311467.00	237105.00
Study 11		82605.00	137150.00	54545.00
Study 17		76282.00	499486.00	423204.00
Study 21		84706.00	341146.00	256440.00
Study 30		65166.00	146848.00	81682.00
Total		460808.00	1825473.00	1364665.00
ArithMean		76801.33	304245.50	227444.17
ArithSD		6907.27	141049.45	139638.05
CV%		8.99	46.36	61.39
GeomMean		76532.14	273244.51	181487.41
GeomSD		1.10	1.70	2.25
Median		76984.50	326306.50	246772.50
Min		65166.00	137150.00	54545.00
Max		84706.00	499486.00	423204.00
n		6	6	6
Study 9	4 x	71497.00	218920.00	147423.00
Study 14		70598.00	95368.00	24770.00
Study 18		79618.00	410384.00	330766.00
Study 29		66984.00	144430.00	77446.00
Total		288697.00	869102.00	580405.00
ArithMean		72174.25	217275.50	145101.25
ArithSD		5332.02	138397.38	133583.47
CV%		7.39	63.70	92.06
GeomMean		72030.37	187557.31	98345.11
GeomSD		1.08	1.86	2.99
Median		71047.50	181675.00	112434.50

Min	66984.00	95368.00	24770.00
Max	79618.00	410384.00	330766.00
n	4	4	4

Total calculated for n = 30 studies

Total	2375219.00	7235456.00	4860237.00
ArithMean	79173.97	241181.87	162007.90
ArithSD	11384.14	106831.00	107462.76
CV%	14.38	44.29	66.33
Median	77104.50	213200.00	123195.50
Min	64479.00	95368.00	24770.00
Max	123161.00	499486.00	423204.00
n	30	30	30

Appendix 9.1.4

Bioanalytical Division's Process Time

Study	Method Development (days)	Method validation/ re-instatement (days)	Assays (days)	Report compilation (days)	BAD total (days)
Study 1	56.00	1.00	13.00	41.00	111.00
Study 2	1.00	1.00	25.00	24.00	51.00
Study 3	10.00	143.00	6.00	22.00	181.00
Study 4	25.00	6.00	13.00	17.00	61.00
Study 5	5.00	4.00	33.00	15.00	57.00
Study 6	14.00	9.00	13.00	37.00	73.00
Study 7	46.00	1.00	17.00	17.00	81.00
Study 8	3.00	1.00	10.00	16.00	30.00
Study 9	12.00	1.00	22.00	17.00	52.00
Study 10	18.00	1.00	22.00	25.00	66.00
Study 11	2.00	2.00	13.00	40.00	57.00
Study 12	30.00	7.00	13.00	36.00	86.00
Study 13	1.00	7.00	7.00	25.00	40.00
Study 14	0.00	1.00	8.00	24.00	33.00
Study 15	43.00	1.00	24.00	28.00	96.00
Study 16	19.00	1.00	27.00	20.00	67.00
Study 17	0.00	5.00	45.00	15.00	65.00
Study 18	20.00	1.00	24.00	12.00	57.00
Study 19	20.00	19.00	11.00	31.00	81.00
Study 20	31.00	1.00	17.00	7.00	56.00
Study 21	17.00	16.00	12.00	22.00	67.00
Study 22	2.00	1.00	23.00	33.00	59.00
Study 23	0.00	1.00	7.00	82.00	90.00
Study 24	25.00	1.00	17.00	27.00	70.00
Study 25	26.00	18.00	8.00	13.00	65.00
Study 26	14.00	5.00	15.00	20.00	54.00
Study 27	62.00	2.00	9.00	20.00	93.00
Study 28	31.00	1.00	33.00	10.00	75.00
Study 29	20.00	2.00	12.00	19.00	53.00
Study 30	42.00	1.00	11.00	15.00	69.00
Total	595.00	261.00	510.00	730.00	2096.00
ArithMea	19.83	8.70	17.00	24.33	69.87
ArithSD	17.13	25.88	9.18	13.97	27.69
CV%	86.37	297.51	54.02	57.42	39.63
GeomMean		2.55	14.94	21.59	65.71
GeomSD		3.58	1.67	1.62	1.42
Median	18.50	1.00	13.00	21.00	65.50
Min	0.00	1.00	6.00	7.00	30.00
Max	62.00	143.00	45.00	82.00	181.00
n	30	30	30	30	30

Appendix 9.1.5

Biometry Division's Cost in Relation to the Fee Expressed as an Estimated Profit

		Biometry		
Study	Phase	Cost	Fee	Profitability
Study 1	2 x	42275.00	37180.00	-5095.00
Study 2		44717.00	35490.00	-9227.00
Study 3		40534.00	19656.00	-20878.00
Study 4		30618.00	32760.00	2142.00
Study 6		29470.00	47320.00	17850.00
Study 7		27506.00	23660.00	-3846.00
Study 8		28820.00	23660.00	-5160.00
Study 12		27970.00	35200.00	7230.00
Study 13		28625.00	35200.00	6575.00
Study 15		25638.00	31200.00	5562.00
Study 16		28720.00	32760.00	4040.00
Study 19		32023.00	120000.00	87977.00
Study 20		26706.00	30420.00	3714.00
Study 22		29516.00	36400.00	6884.00
Study 23		28261.00	0.00	-28261.00
Study 26		51063.00	31200.00	-19863.00
Study 27		25346.00	18590.00	-6756.00
Study 24		24930.00	21840.00	-3090.00
Study 28		25092.00	17940.00	-7152.00
Study 25		29041.00	12740.00	-16301.00
Total		626871.00	643216.00	16345.00
ArithMean		31343.55	32160.80	817.25
ArithSD		7295.65	23202.93	23404.28
CV%		23.28	72.15	2863.78
GeomMean		30668.89		
GeomSD		1.23		
Median		28770.00	31200.00	-3468.00
Min		24930.00	0.00	-28261.00
Max		51063.00	120000.00	87977.00
n		20	20	20
Study 5	3 x	38893.00	36855.00	-2038.00
Study 10		26450.00	35490.00	9040.00
Study 11		30404.00	24570.00	-5834.00
Study 17		28426.00	78975.00	50549.00
Study 21		52343.00	38025.00	-14318.00
Study 30		49515.00	17550.00	-31965.00
Total		1825473.00	364665.00	226031.00
ArithMean		37671.83	38577.50	905.67
ArithSD		11146.58	21368.80	27917.58
CV%		29.59	55.39	3082.54
GeomMean		36343.20	34525.55	
GeomSD		1.34	1.66	
Median		34648.50	36172.50	-3936.00
Min		26450.00	17550.00	-31965.00
Max		52343.00	78975.00	50549.00
n		6	6	6
Study 9	4 x	26159.00	53040.00	26881.00
Study 14		24589.00	19890.00	-4699.00
Study 18		30662.00	70720.00	40058.00
Study 29		53292.00	40820.00	-12472.00
Total		134702.00	184470.00	49768.00
ArithMean		33675.50	46117.50	12442.00
ArithSD		13328.55	21363.12	25070.90
CV%		39.58	46.32	201.50
GeomMean		32018.88	41774.70	
GeomSD		1.42	1.72	

Median	28410.50	46930.00	11091.00
Min	24589.00	19890.00	-12472.00
Max	53292.00	70720.00	40058.00
n	4	4	4

Total calculated for n = 30 studies

Total	87604.00	1059151.00	71547.00
ArithMean	32920.13	35305.03	2384.90
ArithSD	9007.57	22446.13	23966.15
CV% %	27.36	63.58	1004.91
Median	28930.50	32760.00	-3468.00
Min	24589.00	0.00	-31965.00
Max	53292.00	120000.00	87977.00
n	30	30	30

Appendix 9.1.6

Project Cost Calculated According to the Actual Activity Time of the Divisions.

	Divisions				
Study	PMD (ZAR)	Biometry (ZAR)	Analytics (ZAR)	Clinic (ZAR)	Total (ZAR)
Study 1	68679.00	40932.00	88415.00	56753.00	254779.00
Study 2	68436.00	41025.00	86027.00	60947.00	256435.00
Study 3	59356.00	38520.00	76752.00	52561.00	227189.00
Study 4	66942.00	30618.00	71331.00	68286.00	237177.00
Study 5	65148.00	29159.00	75971.00	62055.00	232333.00
Study 6	76050.00	29470.00	77960.00	75506.00	258986.00
Study 7	54246.00	27170.00	67547.00	52672.00	201635.00
Study 8	58866.00	28820.00	67052.00	57280.00	212018.00
Study 9	53906.00	26159.00	69352.00	51962.00	201379.00
Study 10	54197.00	26450.00	73933.00	48187.00	202767.00
Study 11	75977 .00	30404.00	80031.00	52140.00	238552.00
Study 12	58017.00	27635.00	74782.00	51624.00	212058.00
Study 13	64614.00	28290.00	69002.00	48951.00	210857.00
Study 14	47065.00	24589.00	66309.00	44779.00	182742.00
Study 15	54392.00	25974.00	74128.00	47272.00	201766.00
Study 16	55459.00	27713.00	75195.00	45382.00	203749.00
Study 17	54830.00	27755.00	78856.00	46232.00	207673.00
Study 18	72593.00	30326.00	72755.00	72801.00	248475.00
Study 19	55070.00	27995.00	72662.00	50909.00	206636.00
Study 20	48923.00	26706.00	64900.00	46122.00	186651.00
Study 21	54245.00	27170.00	67547.00	51563.00	200525.00
Study 22	69818.00	29516.00	81531.00	64124.00	244989.00
Study 23	69234.00	28932.00	83520.00	51340.00	233026.00
Study 26	59678.00	32603.00	72980.00	61062.00	226323.00
Study 27	54100.00	25346.00	65257.00	62878.00	207581.00
Study 24	51862.00	24930.00	70939.00	42901.00	190632.00
Study 28	46897.00	25092.00	70430.00	57181.00	199600.00
Study 25	51467.00	27363.00	63451.00	46949.00	189230.00
Study 29	56949.00	30468.00	70845.00	49684.00	207946.00
Study 30	54438.00	27363.00	65595.00	49537.00	196933.00
Total	1781454.00	874493.00	2195055.00	1629640.00	6480642.00
ArithMean	59381.80	29149.77	73168.50	6406.46	216021.40
ArithSD	8316.57	4198.70	6406.46	8360.68	22069.79
CV%	14.01	14.40	8.76	15.39	10.22
GeomMean	58838.27	28895.07	72904.81	53742.76	214962.74
Median	56204.00	27875.00	72708.50	51793.00	207809.50
Min	46897.00	24589.00	63451.00	42901.00	182742.00
Max	76050.00	41025.00	88415.00	75506.00	258986.00
n	30	30	30	30	30

Appendix 9.1.7

Projects/Studies Cycle Time with and without Lag Time, Subjects Completed per Study and Profile Time

for Phases	Study	Actual production time of output	Actual and elapsed time of output	Completed per protocol (n=)	Time constraint: Days clinical completion
2 x	Study 1	266	425	44	26
	Study 2	137	422	40	38
	Study 3	460	378	12	23
	Study 4	229	217	20	86
	Study 6	252	217	26	105
	Study 7	207	136	26	54
	Study 8	162	168	28	62
	Study 12	190	155	20	49
	Study 13	135	169	22	40
	Study 15	178	137	30	39
	Study 16	129	157	35	31
	Study 19	184	154	25	47
	Study 20	125	157	36	33
	Study 22	165	204	40	75
	Study 23	163	202	23	42
	Study 26	214	251	18	62
	Study 27	194	136	20	82
	Study 24	123	119	24	30
	Study 28	162	108	25	70
	Study 25	133	147	13	38
3 x	Study 5	265	177	26	74
	Study 10	176	136	26	42
	Study 11	149	219	19	42
	Study 17	129	135	51	35
	Study 21	218	137	25	51
	Study 30	211	148	12	45
4 x	Study 9	138	131	23	53
	Study 14	100	120	8	36
	Study 18	232	214	13	99
	Study 29	211	211	14	37
	Total	5637.00	5687.00	744.00	1546.00
	ArithMean	187.90	189.57	24.80	51.53
	ArithSD	68.20	82.78	10.10	21.39
	CV%	36.29	43.67	40.73	41.51
	GeomMean	178.63	176.90	22.82	47.77
	GeomSD	1.36	1.43	1.53	1.48
	Median	177.00	157.00	24.50	43.50
	Min	100.00	108.00	8.00	23.00
	Max	460.00	425.00	51.00	105.00
	n	30	30	30	30

9.2 EXAMPLE OF FINANCIAL PROTOCOL AND CONTRACT

9.3 UNUSED CAPACITY CONSTRAINT: CANCELLATION / POSTPONEMENT OF STUDIES

Appendix 9.3

Studies for the year 2000 numbered chronologically and including the dates of the statistical analysis

Study of 2000		Data receipt date	Statistical report date	Study of 2000		Data receipt date	Statistical report date
1/200		26/10/00	03/11/00	34/2000	not done		
2/2000	not done			35/2000	not done		
3/2000		04/09/00	20/09/00	36/2000		11/07/00	19/07/00
420004		04/08/00	16/08/00	37/2000		13/12/00	19/12/00
5/2000		07/06/00	12/06/00	38/2000		29/09/00	17/10/00
6/2000	not done			39/2000	not done		
7/2000	not done			40/2000		19/12/00	19/12/00
8/2000		13/10/00	17/10/00	41/2000		02/05/01	08/05/01
9/2000		12/12/00	13/12/00	42/2000		02/05/01	09/05/01
10/2000		12/06/00	15/06/00	43/2000		03/05/01	08/05/01
11/2000		25/04/00	02/05/00	44/2000		06/05/01	07/06/01
12/2000		26/04/00	02/05/00	45/2000	not done		
13/2000		15/05/00	07/06/00	46/2000	not done		
14/2000		06/10/00	10/10/00	47/2000		07/11/00	09/11/00
15/2000		01/03/00	02/03/00	48/2000		20/11/00	21/11/00
16/2000	not done			49/2000		24/11/00	13/02/01
17/2000		17/11/00	21/11/00	50/2000	not done		
18/2000		18/12/00	19/12/00	51/2000		30/01/01	01/02/01
19/2000		02/11/00	06/11/00	52/2000	prelim results		Assays stopped
20/2000		07/07/00	13/07/00	53/2000	not done		
21/2000		18/07/00	24/07/00	54/2000	not done		
22/2000	not done			55/2000	not done		
23/2000	not done			56/2000		07/11/00	09/11/00
24/2000		20/03/01	10/05/01	57/2000		13/06/01	25/06/01
25/2000	not done			58/2000		08/12/00	19/12/00
26/2000	not done			59/2000	not done		
27/2000		02/08/00	10/08/00	60/2000	not done		
28/2000	not done			61/2000	not done		
29/2000	not done			62/2000		06/04/01	23/04/01
30/2000	not done			63/2000		04/05/01	10/05/01
31/2000		17/07/00	19/07/00	64/2000		12/06/01	20/06/01
32/2000		17/08/00	18/08/00	65/2000		24/04/01	08/05/01
33/2000		29/09/00	06/10/00	66/2000		22/01/01	22/05/01

9.4 LIST OF ACTIVITIES

Activities and tasks performed by CRO employees

ACTIVITIES PERFORMED AT PROJECT MANAGEMENT (PMD)

PMD Initiating process - request from sponsor

Acknowledgement of receipt of request to quote

PM register study as preliminary number on the intra-net

Allocation of temporary number/file prepared

Literature search

Specialists input requested

Protocol outline compiled

Cost estimate compiled

Specialists signatories obtained

Protocol outline & cost estimate to sponsor

Liaison with sponsor

Study allocated

Timelines / clinic dates booked

Dates altered/finalized

Follow-up on quote by PMD

Correspondence/liaison

Meetings

PMD planning process

Allocation of number/Network registration

Draft protocol compilation/CRF/ Informed Consent Document (ICD)

Randomization schedule requested from Biometry

Circulation of draft protocol

Protocol finalized/comments evaluated/incorporated

Final protocol for relevant protocol signatories

Distribution of final protocol in-house

First invoice requested

Payment requested for ETOVS submission

Regulatory submission documentation

Regulatory approval of protocol to sponsor

Regulatory approval of protocol to monitor

Signatory page forwarded to Sponsor/Regulatory board/Ethics Committee/Monitor

Amendment compilation/circulation in-house

Amendment regulatory submission

Amendment signatories

Amendment regulatory approval distribution

Distribution of amendment

Amendment signatory page to Sponsor Regulatory board/Ethics Committee/Monitor

Medication and pure drug substance shipment inquiry/request

Quality Control (QC) - PMD/Clinical Research Associate (CRA) file

Status reports to sponsors

Meetings

PMD close-out phase

Actual sampling times entered into data base (double data entry)

CRF's summarized for the report

Biometry file compiled for statistical analysis

Project report compiled

Analytical report/biometry data received and included in report

Preliminary results to sponsor

Circulation of report

Comments evaluated: incorporated/rejected

Report and Case Report Forms (CRF's) to sponsor

Project documentation submitted to Quality Assurance (QA)

Invoice requested for final payment

QA review documentation for archiving

Archiving of documentation

QA feedback meetings

Quality control Process

QC Protocol

QC Pre-study study file

QC Post-study study file

QC Report

QA Protocol

QA Pre-study study file

QA Post-study Study file

QA Analytical data

QA Report

Monitoring feed back meetings

Medication file preparation

Checking of medication

Printing of labels

Dispensing and randomization, transfer to clinic

Pre study QC process

Medication file QAed

Post study reconciliation/drug accountability

File QCed - post study

Medication file QAed

Meetings

ACTIVITIES PERFORMED DURING CLINICAL EXECUTION

Input in preliminary protocol

Protocol evaluation

Study initiation meeting

Study dates booked/altered

Recruitment of subjects

Duplication of CRF's

Source data preparation

Motivation of subjects/reminders - telephonically

Screening documentation/CRF's prepared

Screening process

Laboratory safety results evaluated

Transit Laboratory

Protocol requirements evaluation

Print labels

Transit laboratory preparation of blood/plasma tubes

Check samples received

Centrifuge blood samples

Document discrepancies

Transfer plasma to labeled plasma tubes

QC plasma samples before transferred to Bioanalytical Division

Controlling process:

QC - clinic/CRF's/Nurses file

QA of pre-study documentation (CRF's & nurses file)

Monitoring report corrections made

Blood samples to the transit laboratory and process QCed

QC witness dosing and check blood & plasma tubes

Information on number of subjects dosed - PMD inform sponsor

Additional subjects to be included PMD liaison with sponsor

Monitoring feedback meetings

Clinical close-out phase

CRF's completion/corrections

Transit laboratory transferal of plasma

QC process of completed CRF's

Actual sampling times QCed

Safety laboratory results evaluated/repeated

Clinical post study on CRF's & nurses file

Safety laboratory results computer entered

Actual sampling times QCed

Safety data entered into data base

Feedback meetings

Quality control process

QC Protocol

QC Pre-study study file

QC Post-study study file

QC Report

QA Protocol

QA Pre-study study file

QA Post-study Study file

QA Analytical data

QA Report

Monitoring feed back meetings

Review final report

ACTIVITIES PERFORMED DURING THE ANALYTICAL EXECUTION

Literature search and method development

Analytical method development

Analytical development validation

Analytical preparation of plasma

Ordering of analytical chemical substances

Analytical division document receipt of plasma samples

Temperature regulation/documentation

Sample inventories documented

Analysis of possible outliners for re-analysis

Assays of plasma samples

QC of analytical data

QC Evaluation of analytical data

Results forwarded to PMD/Biometry and QA

QA of analytical report

Review final report

ACTIVITIES PREFORMED DURING THE STATISTICAL ANALYSIS

Statistical estimation of sample size for protocol

Input in protocol outline and cost estimate

Prioritizing of projects/deadlines

Input into protocol objectives and statistical analysis

Development of CRF's

Double data entry of CRF's

Data management

Data queried resolution

Preliminary results to sponsor

Forward finalized data to PMD

Timelines assessment/planning of projects

Statistical analysis of the data

Statistical analysis of safety/concomitant medication/Adverse Events (AEs)

Data screens development/validation of programs

Data management

Closure of data base

Statistical report compilation

QC statistical data

Review final report

ACTIVITIES PERFORMED DURING THE IMPORT/EXPORT PROCESS

Tracing of parcel at customs/airport

Retrieval of parcel from customs

Packing/shipping of study related material