THE MICROECONOMICS OF PRICE POLICIES IN THE PHARMACEUTICAL INDUSTRY

For the Degree of Master of Commerce by Dissertation

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TABLE OF CONTENTS

Chapter 1	Introduction	3
Chapter 2	The Microeconomics of Price Policy in the Pharmaceutical Industry	10
Chapter 3	Efficiency in Pharmaceutical Pricing? An Examination of Ramsey Pricing and the TRIPS Agreement	35
Chapter 4	A History of Pharmaceutical Price Regulation	55
Chapter 5	Regulatory vs. Environmental Constraints on Pharmaceutical Pricing	72
Chapter 6	A Pharmacoeconomic Study	89
Chapter 7	Regulation or Competition for Pharmaceutical Price Control	104
Chapter 8	Conclusions and Recommendations	116
References		121
Appendices		129
Appendix 1	Wealth Effects and the Value Maximising Principle	
Appendix 2	Detail of Retail Prices (Historical) for Statins	
Appendix 3	The Economics of Parallel Trade in Pharmaceutical Products	
Appendix 4	Presentation to PhRMA	
Appendix 5	Competition Commission Finds GSK and BI in Contravention of the Competition Act	

CHAPTER 1

Introduction

1.1 Introduction

Healthcare, it can be argued, is a commodity that has a social constitution. The reason may be because healthcare is seen to have its foundation in socio-economic principles but has evolved through scientific study and business application into a profitable business. The delivery of healthcare in South Africa and in many parts of the world has come under immense scrutiny from policy-makers, high-volume purchasers, patient-consumers and the healthcare community. Arguments criticizing the high cost of healthcare delivery range from levelling the blame on one component (pharmaceuticals, medical fees, inadequate medical scheme cover to name a few examples) to a condemnation of the entire healthcare delivery system. The healthcare cost deliberation has also shifted to the centre stage in many public-policy debates and certainly caught the imagination of the public and journalists alike. It is an emotional debate. A review of related literature of the past fifty years (such as the Sainsbury Report (1967), the Kefauver Hearings (1963) and the Snyman Report (1962)), reveals that healthcare and the cost of healthcare delivery are some of the most frequently debated areas amongst the citizens and policy makers of both the developed and developing world.

Pharmaceutical prices, more often than not, have been cast as the primary reason that the delivery cost of healthcare is so high. The methods used by pharmaceutical companies to promote their products – elaborate conventions, colourful brochures and generous amounts of free samples (certainly in previous years) to physicians may have contributed to this perception. Furthermore, the fact that the absolute cost of manufacturing a single capsule or tablet (including drugs that are no longer under patent) is a small fraction of the actual selling price also tends to raise the public ire.

A greater understanding of pricing structures is necessary to appreciate this sector. The writer's own experience in the area of healthcare that involves insurance for medical risks (medical schemes - the private healthcare funding system) suggests that it is crucial that pharmaceutical pricing structures be understood against this backdrop. Therefore the main reasons for undertaking this study are:

i. to appreciate the pricing structures of pharmaceuticals to inform policy debates;

ii. the current empirical evidence[1] in the South African market has indicated that pharmaceuticals are unfairly priced and has prompted the Department of Health to introduce price regulations[2]. One goal of the research is to ascertain whether this is accurate; and

iii. to obtain a broader knowledge base of the issue of pharmaceutical pricing practices in the South African healthcare market.

It was with this approach that the area of pharmaceutical pricing and the topic was decided upon.

1.2 Research Topic

This writer's study has its foundation in institutional economics, primarily focussing on the role of medical schemes in the South African context. Thereafter an exploration of transaction costs was undertaken. The understanding of transaction costs involves the broader understanding of the market exchange mechanism. In particular and for example, it was issues that had been expanded upon by the economist Ronald Coase in his paper 'The Nature of the Firm' (1938) that eventually led to establishing the foundations of transaction costs – that issue was the centralised system of governance in the Soviet Union. Simply stated Coase, on his first journey to the United States (in the 1930's), interviewed the heads of the major corporate enterprises. He wondered whether the many specialised businesses in the United States were more efficient than the large centralised structures in the former Soviet Union. The basic question that Coase ruminated upon was why the companies in the United States didn't grow larger than they already were. It would appear to be perfectly logical if a company can vertically integrate its operations, then it would be more efficient because it would not have to trade on the market for upstream and downstream resources. This quandary is partially addressed by the transaction cost approach since the transaction cost of using a hierarchy eventually exceeds the transaction cost of using a market. It can be shown that the larger the firm grows above a certain threshold level, the larger the burden of transaction costs tends to be. The hierarchical structure would eventually become so cumbersome as to generate diminishing marginal returns to profits.

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[1] The Treatment Action Campaign's and other AIDS treatment advocates declared a victory for activists, people with HIV/AIDS and poor people everywhere as pharmaceutical companies unconditionally withdrew from the lawsuit against the South African government's Medicines and Related Substances Act, Act 90 of 1997. This occurred when the 38 pharmaceutical companies who originally sued the Minister of Health and the government, dropped their case on April 19th, 2001.

[2] Act 90 was changed to introduce price controls and exit prices on the selling price and the dispensing fee for medicines. Changes to the Act 90 of 1997 and its subsequent incorporation into Act 101 of 1965, resulted in the Amended Act 101 of 2004.

The writer has an understanding of the issues that impact the insurance industry such as moral hazard. The ideas explored by Milgrom and Roberts (1992) include bounded rationality, motivation and signalling together with the theory of the 'economic man'[3] (Simon, 1957, p.165) and deepened the appreciation of the aspects that make up economic thought. The simple analysis of classical economics forms the basis of a maturing of thought and the development of new concepts and ideas.

The African National Congress's (ANC) *White Paper for the Transformation of the Health System in South Africa* (Notice 667 of 1997 in the South African Government Gazette No. 17910) commonly referred to as the 'White Paper', also appealed to the writer's subject on how healthcare issues facing the country could be addressed. The White Paper is a broad-based policy document that has immersed healthcare policy direction on its current path. The writer contends that although this policy resonates with noble intentions, it does tend to ignore some important basic economic tenets. The primary argument is that it has not reflected thoroughly on the funding of and the operational hurdles associated with the implementation of its proposals. An example would be the proposal for a National Health Insurance Plan, the implementation of which is unlikely if it cannot be supported by the tax base. A second example would be the provision of drugs to treat local common diseases – the fiscal burden of providing drugs, particularly in a climate where some multi-national drug companies are balking at reducing prices for essential drugs, citing that their patent rights would be compromised[4]. The writer wishes to focus more closely on the issues of patent rights in terms property rights.

Ronald Coase's later article "*The Problem of Social Cost*" (1960) broached the issue of property rights in a manner that included the concept of welfare gains. It was this exploration by Coase that nurtured the idea of trying to investigate how pricing structures in the healthcare sector could be made more efficient so as to increase welfare gains in the long-run. Furthermore

[3] In his groundbreaking works, Herbert Simon developed the concepts of the 'economic man' and the 'social man' with static and dynamic characteristics respectively. Furthermore the latter group are adaptive and the former are maximising. These concepts formed part of his foundation for later theories.

[4] Drugs are protected by patents. The argument is that the drug company invests heavily in research and development (R&D)in order to produce more effective drugs and if they cannot recoup their sunk investment, there would be no initiative to undertake such R&D

Anderlini and Felli (2001) looked at the robustness of the Coasian solution in light of *ex ante*[5] costs. Their ideas play an important role in highlighting what changes would be feasible.

1.3 Research Problem and Hypothesis

1.3.1 Goals and Objectives of the Study

The objective of the study is to inform the reader about the significant relationships that occur in the healthcare sector and in particular, show how these relationships impact onto the pricing structure of pharmaceuticals. Healthcare is a complex area that tends to bring out strong emotive arguments regarding policy decisions. Furthermore, South Africa is in the throes of healthcare reform as outlined in the *White Paper* and the nature of the relationships between the various stakeholders, including patients, is changing.

The goal of the study here is to understand whether a Coasian solution could exist in the current healthcare paradigm. A Coasian solution is the realisation of the Coase Theorem which addresses the issue of inefficiencies. The Coase Theorem guarantees that when property rights (for example, patent protection) are allocated through a negotiation where the agents involved in this negotiation are fully informed and rational then the outcome of this negotiation would be efficient because the agents involved would ensure that there are no unexploited gains from trade. Coase expounded on property rights and in the pharmaceutical industry, property rights can be defined to include patent rights.

1.3.2 The Research Problem

The main hypothesis is whether or not a Coasian solution can exist in the current healthcare paradigm, given that there is a substantial change in the healthcare arena and more changes are expected in the future. A number of questions relating to this hypothesis can be raised and include:

i. how efficient is the nature of the relationships between the stakeholders in the healthcare industry?;
ii. what aspects of the industry can change in order to create greater levels of efficiency? How can these changes be made?;
iii. what lessons can be learned from healthcare systems that are regarded as more efficient? How can alternate healthcare systems inform the issues at hand?;
iv. are there any efficient pricing structures that can be utilised?; and

[5] *Ex ante* costs are costs that are incurred prior to a negotiation and are directed toward maximising the future outcome of the negotiation. *Ex post* costs are costs that occur after the negotiation in order secure that the intended result does happen.

v. ultimately, could an efficient relationship can exist between the supply and usage (demand) for medicines?

1.4 Research Design and Methodology

The next four chapters will provide the theoretical background leading up to the empirical chapter, Chapter 6, which was planned as a pharmacoeconomic study, taking data from drug trials and then conducting a cost-effectiveness study. Early attempts to obtain data from pharmaceutical companies proved fruitless, notwithstanding several months of trying and several promises of data from various quarters. The situation was alleviated to a degree with the use of international clinical trial data. Clinical trial data can be applied to different population groups for many diseases because sample groups from different countries would reflect similar results. The use of this data is prudent because treatment protocols are targeted at patients who already suffer from the disease being addressed. The writer then decided it would be prudent to survey a number of pharmacoeconomic studies that had already been conducted and analyse the results in terms of what could be used in the South African setting. Once a study was identified, the costs were recalculated to reflect local prices and a cost-effectiveness study was undertaken.

The simple pharmacoeconomic analysis of Chapter 6 is then used to challenge the notion that current prescribing practice is efficient for one particular drug. A basic scientific and mathematical technique of proving the correctness of a theorem states that if the one can show the exception to the rule, then the rule is not foolproof. Similarly, the same logic can be used in an economic manner in order to ascertain whether an efficient relationship can exist between the supply and usage (demand) for medicines. The null hypothesis asserts that in a negotiation where property rights are assigned, an efficient solution can be reached if the agents involved in the negotiation are rational and fully informed. An efficient solution will ultimately lead to higher welfare gains in a process of redistribution of wealth through growth.

1.5 Outline of Dissertation

Chapter 1 has outlined the flow of the chapters that will be followed in the study. The flow of the study developed from a theoretical basis to empirical analysis.

Chapter 2 introduces the basic concepts of transaction costs and the Coasian solution to economic problems. It explores a number of microeconomic concepts including the economics of

institutions, hold-up costs, motivation and moral hazard. Furthermore it looks at issues pertaining to the firm in terms of the Coase theorem and transaction costs.

Chapter 3 looks at the advantages of using Ramsey price structures in the current healthcare paradigm. Furthermore the recommendations from the World Trade Organisation's (WTO) trade related aspects of intellectual property rights (TRIPS) agreement regarding patent rights are also illustrated for use in dealing with the patent and licensing aspects of pharmaceutical manufacture. This chapter also sets the basis of the discussion in Chapter 5.

Chapter 4 concentrates on the history of pharmaceutical price investigations, particularly those that had an indirect yet profound effect on the pricing of drugs. Notably, the Kefauver-Harris Amendments in the USA (1963), the Sainsbury Report in the UK (1967), the Snyman (1962) and Steenkamp (1978) Reports in South Africa. The study also considers experiences from Australia and Canada since these countries have produced far reaching and exhaustive research that overlaps with the scope of this study. The Ontario Provincial Government in Canada for instance has been using pharmacoeconomic analyses as part of its decision making process from the early 1990's and is widely regarded as a world leader in this area. The experiences from these countries could hold invaluable lessons for South Africa.

Chapter 5 explores specifically the constraints that drug manufacturers face in the pricing of their products in South Africa, and in particular from a regulatory and competitive framework. Issues such as competition laws, reference pricing and free market pricing are investigated.

Chapter 6 investigates the cost-effectiveness of a particular therapeutic class of drug called statins. Statins are a class of drug that is primarily used to treat problems associated with high cholesterol. This exercise is specific to South Africa. The significance is that high cholesterol leads to coronary problems which are recognised as the world's leading lifestyle disease. The two top selling drugs in the world, Lipitor and Zocor, are both classified as statins (*Med Ad News*, May 2005).

Chapter 7 makes broad observations regarding regulations, competition and price with the objective of comparing competition and regulation in setting prices and the specific recommendations thereof. It also cites studies that have demonstrated the impact of regulation on the pharmaceutical industry.

Chapter 8 draws conclusions from the study and makes recommendations on the above-mentioned hypothesis. It draws attention to the fact that the least costly option in the short-run may not be the best direction for the long-run and relies on the results of the empirical study done in chapter 6. Furthermore, it uses the experiences from other countries to identify efficiency goals in the current healthcare system (with particular reference to pharmaceuticals). In order to achieve greater efficient in the healthcare system it recommends greater use of Ramsey pricing structures and limiting the use of uniform pricing in South Africa.

CHAPTER 2

The Microeconomics of Price Policy in the Pharmaceutical Industry

2.1 Introduction

Any assessment of price policy requires an examination of microeconomic principles, especially those governing price and costs, and in particular, transaction costs. In Chapter 2, the writer seeks to discuss the microeconomics of price policy by examining three major areas of academic interest, namely: issues surrounding the firm; transaction costs and the Coase theorem; and issues associated with motivation and bounded rationality. The first two areas of interest identified relate to microeconomic theory.

2.2 Transaction Cost Economics and a Coasian World

Transaction costs can be defined as the spectrum of institutional costs, including, *inter alia,* information costs, the cost of drawing up and policing contracts, analysing, implementing, specifying property rights and negotiation costs. Williamson (1979, p. 239), who has written extensively on the topic, defines three dimensions of a transaction: uncertainty, transaction-specific investment, and frequency of exchange. It was Coase's argument in 1960 that economic efficiency[6] can be attained as long as property rights are *fully allocated and that any transaction-cost inhibiting trade* is not too high (emphasis added). Key to understanding Coase's analysis is the definition of *ex ante* costs, or expected costs before the transaction takes place. The work of Anderlini and Felli (2004) explore this aspect of transaction costs. More importantly, they go further by exploring second-order transactions which are contingent on the first-order transaction and the degree which *ex ante* transaction costs in the second-order transaction may lead to failures of the Coase Theorem. In particular, they look at the 'hold-up problem' or the post-contractual opportunism that appears when participants involved in a Coasian negotiation are accountable for the *ex ante* costs necessary for the negotiation to take place. An exploration of the ideas of Williamson (1979, 1998) and Coase (1937, 1960) including the reservation raised by Anderlini and Felli (2004) is the basis of the first section of Chapter 2.

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[6] There are a number of ways to define **economic efficiency**. For the purpose of Coase's argument, the writer is referring to **Pareto efficiency** which is a situation where, in the allocation of available resources, no further **Pareto improvements** can be made. A situation is considered efficient if no person can be made better off without another person being made worse off. **Pareto improvement** is a situation where a change that makes at least one individual better off, without making any other individual worse off (a win-same situation).

The field of transaction cost economics has a broad spectrum. Williamson identifies transaction cost economics as a '*product of two recent and complementary fields of economic research*' (1998) and goes on to explain that the first is *new institutional economics* and the second one is what Moe (1984; 1990) called the *new economics of organisation* (emphasis added). Both research areas focus on expanding the theory of the firm as a production function contrary to the firm being regarded as a governance structure. In turn, new institutional economics comprises two components: the first deals with the so-called 'rules of the game', which primarily relates to an analysis of the institutional environment. The second deals with the various institutions of governance as addressed by Williamson (1998). The origins of both streams of thought can be found in the work of Coase: in *The Nature of the Firm* (Coase, 1937) and notably in *The Problem of Social Cost* (1960).

One of the more important contributions of transaction cost economic theory is that it has attempted to examine the inner workings and structures of a firm, something that tended to be glossed over by the prior and even classical economic assumptions of a firm. Williamson expounds on Coase's idea that vertical integration within a firm is limited because of the inhibiting effects of transaction costs. Williamson, in developing his ideas, observes a market economist's view that firms are profit maximizing and cost minimization entities which is, by implication, an equilibrium theory. Furthermore, the theory assumes bounded rationality on the part of the stakeholders. He extends Coase's analyses to infer that there are both transaction and production costs, as is expounded upon in Figure 2.1 where Williamson creates a system of governance or infrastructure for commerce. Transactions costs would then be the costs incurred, or rather the penalty for deviation from this system of governance. In the broader economy, this system of governance represents an efficient market characterised by perfect competition and information that is available to all stakeholders. If firms want to minimize their total costs, which made up of both production and transaction costs, then they need to take cognisance of the situations that might result in lower transaction costs in the market or the hierarchy.

Williamson makes certain assumptions regarding his theory, and that is the existence of bounded rationality[7] and opportunistic behaviour[8] associated with the stakeholders. These

[7] Bounded Rationality as defined by Milgrom and Roberts (1992) is the limitations on human mental abilities that prevent people from seeing all possible contingencies and calculating their optimal behaviour. Bounded rationality may also include limitations on human language that prevent perfect communication of those things that are known.

[8] Opportunistic behaviour is self interest behaviour unconstrained by morality.

assumptions remain constant in the analyses in order to keep the system of governance constant in the advent of changing variables.

2.3 The Value of Transaction Costs

One consideration is that if the system of markets and prices is efficient, then why are there firms? What is their contribution to the economy? What is the mechanism that determines where transactions are concluded? What is the cost of carrying out a transaction? Ronald Coase (1937) first raised these issues in *The Nature of the Firm.* Transaction costs form part of the costs associated with running a market system. The divergent nature of firms and their products require solutions, which instigate transaction costs; Co-ordination and motivation costs are amongst the most obvious types. Coase raised the issues that centred on transaction costs, both hierarchical and market-based, which lead to inefficient solutions.

Co-ordination costs are the costs of creating the space for the buyer and seller to conclude their transactions (Milgrom & Roberts, 1992, p. 29). An example of this is the Johannesburg Securities Exchange (JSE) and specifically the costs involved in setting up the infrastructure required to facilitate commerce. Other examples are the costs associated with advertising, research, communication, and losses resulting from unrealised transactions.

According to Milgrom and Roberts (1992, p. 30), there are five types of transaction attributes that are central to the market analysis;

i. asset specificity;
ii. the frequency and duration of a transaction may foster low cost routines (where an infrequent transaction may require more time and effort and be more costly);
iii. the uncertainty and complexity of the transaction that is contingent on the nature of the contract;
iv. the difficulty of performance measurement of the transaction, particularly when the outcome is intangible (such as the services of a lawyer in a legal case); and
v. connectedness to other transactions refers to the interdependency of transactions. An example is software development where transactions of firms reflect design connectedness. Designs need to be co-ordinated in order to reduce relative costs and compatibility is paramount.

Transaction cost analysis, like most methodologies, has its limitations. Its basic principle is that economic activity is focused on value maximising trades which potentially could be diluted because of transaction costs. Therefore minimising transaction costs is crucial for ensuring commercial success. There are two main issues: Firstly, total costs do not only comprise transaction costs and production costs but include a number of other costs that are contingent on the organisation and the technology. The conceptual split of production and transaction costs is easily addressed in theory, but proves extremely difficult in practice.

Secondly, Coase postulated that all wealth-maximising trades occur if transaction costs are not too high and if property rights are well defined, hence efficient organisations would tend to minimise transaction costs. There are different efficient solutions to the resource allocation problem and efficiency alone may not be a strong enough criterion to be the only basis of analyses. Firms often try to maximise their total value through a series of transactions. Moreover, in practice, the aspects of efficiency may differ between the view held by the firm's shareholders and that of the firm's managers.

A third aspect, though not proposed by Coase, but still significant is the issue of *ex ante* behaviour and reputation. The Coase and Williamson arguments do not consider these salient aspects of business conduct which include business reputation and trust. Transactions are regarded as first–order transactions without any deepening of the relationship occurring between the transacting parties. Williamson (1998) does point out that opportunism does occur some of the time. However, this cannot be predicted upfront. In order to encourage commerce, firms rely on their reputations. Reputation, trustworthiness and profile are business assets that a firm tends to build upon as part of its ongoing business activity.

Influenced by Coase's thinking, Williamson (1998) expounded upon the idea of different levels of social analysis that is available for assessing new institutional economics, as illustrated in **Figure 2.1**. He describes the advent of economic activity which he refers to as 'economising'.

Referring to figure 2.1, the activity of first-order economizing takes place at level 2, where the institutional environment must be accurately assessed for the viable functioning of the economy (Williamson, 1998, p. 25). Level 2 is furthermore the *outcome* of politics, and lays down the parameters in which economic activity takes place. The economics of property rights are raised as a key consideration at this level. Furuboten and Richter (1991; cited in Williamson, 1998) say that

modern institutional economics attempts to focus on the institution of property rights, or systems of norms that govern the acquisition and transfer of property rights. The right of ownership is another discussion that is widely raised at this level and particularly concerns the right to use, appropriate or change the form of an asset. Contemporary examples of property rights being debated in mainstream policy making include a diverse range of issues such as environmental concerns, intellectual property rights, copyright protection, pollution impacts, patent rights, hunting rights and reproductive rights. The questions raised by these concerns are significant; Who has the right to the exclusivity of the environment? Who has a greater right to life – the mother or the foetus? Whose right is damaged through pollution – the consumer or the resident next to the factory?

Level 3 looks at those areas where governance institutions are active. Second-order economizing characterises the third level, where governance structures are established. Operations at level 3 take the conceptual rules from level 2, and apply them in practice. Level 4 however focuses on marginal analyses, is not primarily involved with transaction cost economics, and thus falls outside the main discussion presented here.

A number of questions have been posed that deal with the discrete structural analysis of governance at level 3. These are designed to answer the crucial question:

What is transaction cost economics? - *The study of the 'additional costs' (over and above the purchase price) associated with conducting a transaction, whether those costs consist of time, money or inconvenience*.

According to the Wikipedia online dictionary (http://en.wikipedia.org/wiki/Transaction_cost), transaction costs also have specific terms associated with them; for instance, search and information costs are the costs associated with finding the goods to purchase, bargaining costs are costs associated with settling on a mutually agreed upon price for the good and policing and enforcement costs are costs associated with ensuring that the parties involved keep to their side of the bargain. Key areas of study include: the distinction between institutional environments and institutions of governance; adaptations of the central problem of economic organisation; comparative economic organisation; the issue of private ordering; and, finally, the behavioural attributes of human players (Williamson, 1998, p. 29).

Some theorists, such as Milgrom and Roberts (1992, p. 20), consider the problem of economic organisation by analysing the importance of organisational constructs through expounding the main tenets of an organisation. The structure of the organisation is analysed from

Figure 2.1

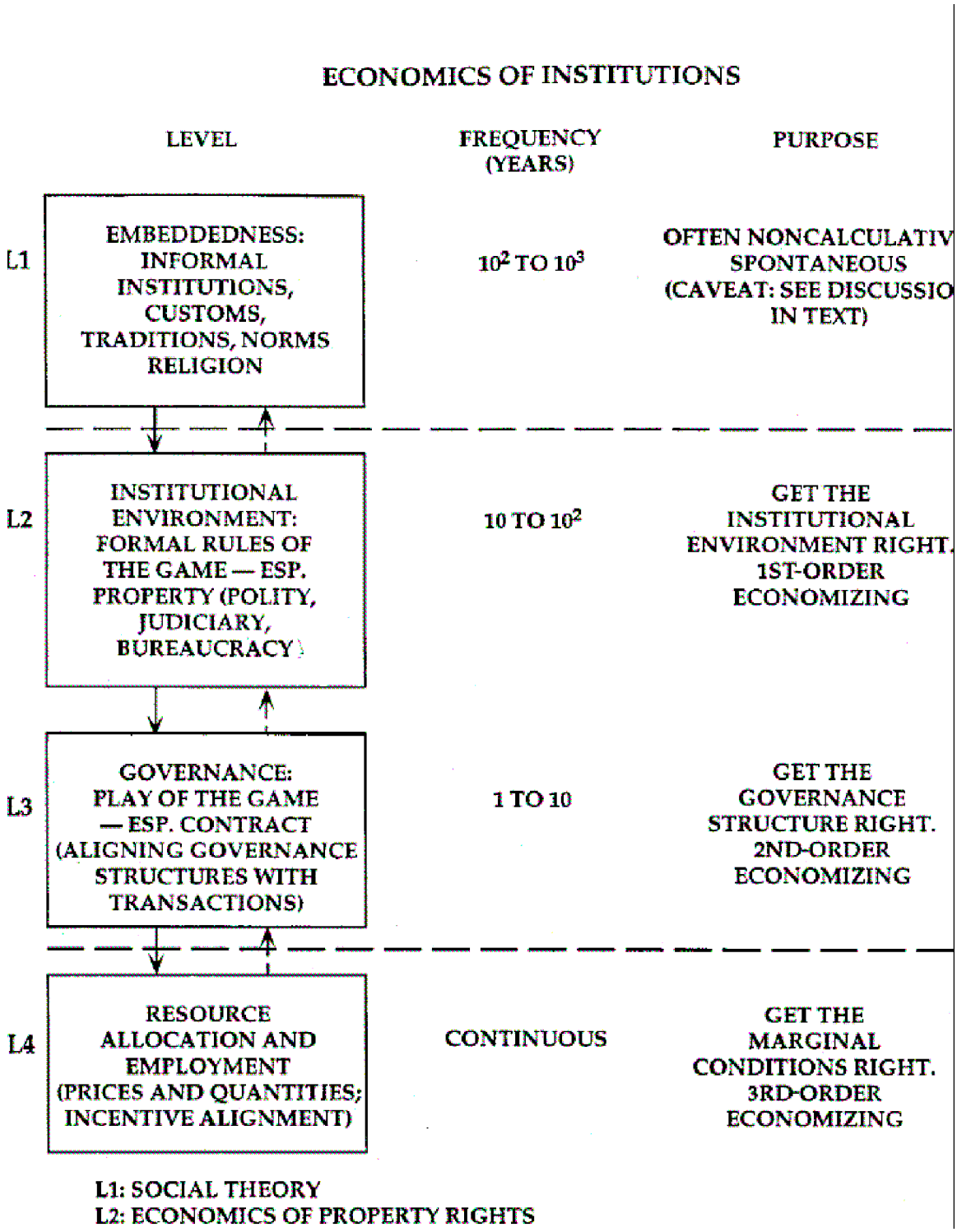

Figure 2.1: Level 1 is where the traditional norms and customs reside and this has the longevity of time. Level 2 is the institutional environment - the structure here lays down the 'rules of the game' that defines the parameters of economic activity. Level 3 is where the institutions of governance reside – a legal system that supports the system of contracts and governance models. Level 4 deals with marginal analyses – price, output, incentive alignments etc. Transaction cost economics resides in levels 2 and 3.
Source: Williamson 1998, p.26

various perspectives, *inter alia*, the value maximising position, efficiency, organisational objectives, transaction costs, and wealth effects. A snapshot of the major organisational structures of the past century embodies the significance of the organisation (Milgrom and Roberts, 1992, p. 20).

2.1.1 What are the phenomena of interest?

The question of why there are so many kinds of organisations has been frequently asked by academic researchers (e.g. Hannan & Freeman, 1977) but it simply echoes the broader question asked by Coase as to why firms exist when there is already a marketplace. Williamson develops Coase's question by postulating that the broader query goes beyond the 'market and firm dichotomy' to include *inter alia* hybrid contracting, regulation, non-profit public bureaux and so forth. He especially invites the study of the variations that exist *within* these categories (emphasis added), such as hierarchical variants within firms (Williamson, 1998, p.30). The inter-play between firms in a vertical relationship occurs with parties that are somewhat aligned in terms of parity. Where there are disparities between the contracting parties, however, then the transaction becomes the primary focus. The characteristic of the transaction, rather than the differences between the associated parties, is the core of the analysis.

2.2 The description of human agents and motivation

The question of motivation is a central economic problem in both management and organisation; it is also one that has been well researched. Milgrom and Roberts (1992, p. 137) argue that although contracts allow participants some flexibility in their future dealings with each other, they also allow participants to behave opportunistically, e.g. a 'hold-up' problem or imperfect commitment. Real contracts, as they point out, are certainly not complete. As a result, participants can end up with malaligned motivations, which can then allow for self-interest and exploitative behaviour to develop. The motivation problem then becomes one which works toward overcoming opportunistic behaviour. The research proposed here will furthermore explore Milgrom and Roberts' treatment of bounded rationality, which describes the limitations under which participants work and sign contracts.

Motivation costs consist of two parts: informational incompleteness (including informational asymmetry, which was briefly visited earlier in this section) and imperfect commitment (Milgrom & Roberts, 1992, p.29). Information incompleteness is the situation where one or more of the parties involved in a transaction does not have the relevant information

regarding the product (usually the purchaser). The lack of information and resulting lack of transparency yields a set of circumstances that is not mutually advantageous to all of the parties involved. The classic example illustrating this type of transaction is the used car that may be a lemon[9]. The salesperson may have knowledge regarding the vehicle's history or reliability but does not reveal this bit of information. The piece of information might be important to the sale in the sense that if this information was revealed, then it may influence the buyer's decision to purchase the vehicle. A 'street-smart' salesperson would recognise any indecision on the part of the buyer and respond by not revealing the piece of information indicating that the car is indeed a 'lemon'. In order to allay the fears of the buyer and protect their reputations, many dealerships offer comprehensive maintenance plan. In this instance, the maintenance plan represents additional and unnecessary (inefficient) arrangements to protect against opportunistic behaviour (the salesperson not revealing any of the vehicle's faults) may be made in order to conclude the transaction. These are costs over and above the cost of the product – and are the costs of doing business, i.e., transaction costs.

Imperfect commitment, on the other hand, deals with parties who, after having made certain commitments, would like to forsake their earlier commitment. Consider a supply chain situation where a manufacturer makes a specific product for a supplier of raw materials at a previously agreed-upon price. The supplier provides the raw materials for the product. Moreover, the manufacturer arranges with a supplier to commit to investing in machinery specifically designed for the manufacture's product. The supplier (after having invested in this machinery) is at the mercy of the manufacturer, who may subsequently try and influence the previously agreed-upon pricing structures. This can be done in a number of ways, including forcing the supplier to reduce the selling price of the raw materials, claiming increased costs of production or by decreasing the rate of output, is an example of the 'hold-up' problem.

Motivation is a central problem in economic management and organisation. The dilemma of motivation arises because individuals have different perspectives on a particular set of circumstances: for instance individuals have their own private interests, which may not be aligned with those of other individuals, in a specific setting. The manner in which efficiency is lost in the economy through bounded rational behaviour is examined in this section, as are inefficiencies of private information. A further area of discussion is *moral hazard*, which can be a form of post-

[9] A 'lemon' usually refers to a bad product masquerading as a good one. Typically, the salesperson knows the full extent of the problem but won't reveal this information because it might jeopardise the sale.

contractual opportunism. The 'hold-up' problem is a subset of moral hazard. Herbert Simon (1957) argued that one of the fundamental assumptions in economic theory – that of the 'economic man' characterised by one who tends to minimise cost and maximise profit (or benefits) – is naïve. He conceptualised the word "satisficing"[10] (Simon, 1957, p. 204, Bannock *et al*, 1998, p. 369) to describe the continual adjusting of behaviour to reflect the influence of new experiences and information in the market. Such behaviour attempts to reach a minimum threshold without endeavouring to obtain the highest possible outcome. Simon's assertion implies any decision undertaken by behaviour in the marketplace is bounded with rationality, uncertainty and lack of awareness – this is satisficing. In the theory of the firm, satisficing implies that the firm treat profit as a constraint rather than a profit maximising goal. Moreover, once the critical level of profit has been attained then the firm's priorities are rearranged to focus on other goals.

To continue along this vein of thought and if we assumed that people behave in their own self-interests and there are situations where these are not necessarily aligned with the goals of their organisations or the goals of the economy. Under these circumstances some behaviour may be considered socially profligate. The problem is that the future is unforeseeable, which limits one's ability to describe all the possible contingencies that *could* impact on desired outcomes. Incentives can be significantly influenced and aligned by contracts that are written in order to align incentives with those of the organisation and ultimately with that of society. Society comprises individuals and organisations which make it viable for contracts to be re-written in order to address incentives that appear to be a problem.

It has been ventured that a complete (comprehensive) contract comprises three parts. First, it allows for relevant contingencies to be built in. Second, the parties to the contract must be willing and able to devise an efficient course of action in the event of these contingencies occurring. Third, participants must abide by the terms of the contract once agreed (Milgrom & Roberts, 1992, p. 127).

An additional aspect is the concept of *bounded rationality* which was explored initially by Simon (1957, p. 199), and extensively expounded upon by Williamson (1998, p. 30). Bounded rationality describes the behaviour of humans who are deliberately rational, but in a limited manner.

[10] Wikipedia (the online dictionary) states that the word 'satisfice' was coined by Herbert Simon in 1957. Simon says that people are only 'rational enough', and relax their rationality when it is no longer required. This is called bounded rationality.

The bounded rationality problem, when applied to contracts, means that not all contingencies are accounted for in the contract and could be affected by, for example, limited foresight, unexpected costs, corrective actions, or even vague language (Milgrom and Roberts, 1992, p. 130). Typically, vertical integration arrangements constitute such examples. Some terms or sections of these contracts, referred to as *relational contracts* (such as bilateral or unified contracts as in the case of franchise arrangements) are deliberately unspecified and cannot be made binding by a court of law. These contracts allow the participants some flexibility in their future dealings with each other, but more significantly, it allows them to behave opportunistically since they have *imperfect commitment*, hence the post-contractual opportunism such as the hold-up problem. Milgrom and Roberts point out that real contracts are certainly not complete contracts (1992, p.128).

Incomplete contracts can result in agents having misaligned interests, fostering inconsistent and perverse self-interest and opportunistic behaviour. The motivation problem aims to tackle this kind of behaviour. People do renege on their promises, for instance, through fear of losing money by not trusting a trading partner's motives. The fact of the matter is that contracts cannot realistically describe every contingency, something that gives rise to contractual incompleteness. Williamson succinctly addresses the issue of opportunism by saying:

> "If candid reference to opportunism alerts us to the avoidable dangers, which the more benign reference to frailties of motive would not, then there are real hazards in the more benevolent construction. Attenuating the *ex post* hazards of opportunism through the *ex ante* choice of governance is central to the transaction cost economics exercise." (Williamson, 1998, p. 31),

Reneging on a contract occurs more frequently when large specific investments are required by the contract. A specific investment is used to create an asset. The *specificity* of an asset is the percentage of investment value lost when the asset is re-deployed to its next best use (Milgrom & Roberts, 1992, p.135). The need for this action arises when one of the trading partners reneges on their contractual undertaking in an attempt to extract more value than the originally agreed-upon terms. The remaining trading partners are forced to re-deploy assets to the next best option. As alluded to earlier, this situation results in a *hold-up problem* – reflecting the nature of post-contractual opportunism.

In some instances, a potential trading partner that is concerned with building a reputation for the longer-term, a reputation that is more visible and has more to lose with a damaged reputation. Such a trading partner may take preventative measures to alleviate the incidence of

post-contractual opportunism. For this reason, it is often advisable to deal with large reputable firms, especially where the parties involved are risk-averse.

Informational asymmetries (or private information) at the time of the contract being sealed are another contributor to inefficiency in contracting. Information asymmetries become apparent when agents try to misrepresent details or hide particulars of themselves in order to get a better deal (Milgrom and Roberts, 1992, p.144). The insurance industry often encounters this type of dilemma; insureds often do not reveal the true extent of the risk that they are likely to pose when selecting a certain level of cover. Furthermore, the insured may choose a particular benefit specifically because it covers the problem or risk that he or she wants to insure against. The behaviour described is termed 'adverse selection' or the selection of a benefit solely based on what can be extracted from the risk pool without revealing the nature of the affliction upfront.

The used car dealer scenario can be used as an example. The dealer may have information that would lower the *expected* price of the vehicle, whereas the potential buyer might be genuinely concerned about the lack of warranties, or even simply feign disinterest, even though he or she wants to purchase the vehicle. The value-maximising outcome would be for both parties to gain from the trade or transaction. If each side named a price that represented their true expectation, then trade would immediately occur if there were gains to be made from either side. However, even if the value maximising outcome is for the buyer to purchase the vehicle, the deal may fail because the parties withhold their respective bits of information. The existence of private information usually means that certain value-maximising plans may not be realised. In the insurance environment, particularly in the medical schemes environment, the concealing of certain information by the purchaser in order to qualify for higher-level benefits is regarded as common practice. For example, if a scheme offers a particular benefit in an option, then the option tends to attract people who are subject to the condition covered by the benefit.

Bargaining can give rise to another cost: that is, obtaining an 'information advantage' which is considered to be a loss to society. The costs of providing incentives for bargaining are high and increase substantially with a larger number of participants. *Free riders*, or participants who stand to gain from the process and do not want to pay, are a substantial drain on the efficiency of the process. Adverse selection, the condition arising from pre-contractual informational asymmetries, is a widely documented phenomenon in insurance circles. A well-known example is that of medical insurance taken out by couples or single women who are planning to have children

in the foreseeable future. The medical and accommodation costs associated with the pregnancy will be covered by the insurance plan when the baby is born. Plans to start a family are considered privileged information and deliberately not disclosed (in some cases) when medical insurance cover is sought.

Furthermore, medical insurance plans that cover specific conditions are susceptible to adverse selection, since they tend to attract people suffering from those ailments. Adverse selection also poses a problem of medical schemes being able to measure risk or 'risk-rate'. Current regulation obviates the impact that observable characteristics such as age and sex can have on the ability of the scheme to risk rate by making these characteristics insubstantial. Several non-price related methods have been developed in order to try and alleviate the effects of adverse selection. Medical schemes tend to limit benefits, insurance companies insist on co-payment or 'excess' for short-term payments, and lengthy questionnaires also double-up as a limited pre-screening technique. Adverse selection also impacts the cost of supplying a product in addition to the potential revenues that could be brought into being by the supplier (Milgrom & Roberts, 1992, p. 149). Stiglitz and Weiss (1981) developed an adverse selection model to specifically address credit rationing and non-market means of credit allocation that proved to be highly effective.

Moral hazard - another term coined by the insurance industry - refers to the post-contractual tendency of the insureds to change their behaviour in a way so as to increase the probability of larger claims against the insurance company (Milgrom and Roberts, 1992, p.167). The fact that people take out insurance can be viewed with some trepidation, since they could be acting in a manner that is beneficial to themselves. Those who take out insurance for some specific event may have an incentive to become careless and even cavalier regarding the limitation of behaviour that could result in a loss.

In the larger economy, however, the term 'moral hazard' has come to describe contractually-bound behaviour that is inefficient (Milgrom and Roberts, 1992, p.179). This behaviour typically arises from the differing interests of contracting parties in a principal-agent relationship with the agent acting on behalf on the principal. The problem arises when the agent has differing views or goals to that of the principal. In particular, the situation is exacerbated when the principal cannot determine the performance or actions of the agent. The relationship between a medical scheme broker and a medical scheme illustrates the principal-agent behaviour. The agent is driven by the commission earned from selling the highest number of contracts in the long term,

irrespective of the 'risk-level' of the potential members that is being signed up. The medical scheme is primarily looking for the lowest-risk members or members that would be low claimants, namely the young and healthy. Why does this conflict exist? The scheme cannot control the risk contingent on the type of member that the broker signs up - in any market segmentation, the misaligned incentives basically exist because of the inability of schemes to refuse cover – which is a legislative requirement. This in turn is brought about by the schemes' limited ability to be selective primarily because regulation does not address an inherent principal-agent problem[11] but creates an artificial problem brought about the legal inability to refuse cover.

2.3 *Ex ante* Transaction Costs and the Robustness of the Coase Theorem

Anderlini and Felli (2004, 1998) reflect on a Coasian solution as a negotiation about payment of costs regarding any future negotiations. This, in turn, gives rise to a new set of *ex ante* costs and a new hold-up problem. Their paper considers the extent to which the presence of *ex ante* transaction costs may impact a Coasian solution leading to the failure of the strong version of the Coasian Theorem.

Anderlini and Felli assert that in its strongest form, the Coase Theorem can be interpreted as guaranteeing an efficient outcome is the result when potential mutual gains outweigh the bargaining costs, regardless of the manner in which property rights are assigned (2004, p.1). This position appears to be problematic when the empirical facts are considered. Markets and economies are replete with situations where a Pareto improving negotiation may be possible, but are foregone because of the impending costs of bargaining (Anderlini and Felli, 2004, p.1)[12]. Essentially, they take issue with the strong version of the Coase Theorem and attempt to show that the potential gains from trade are outweighed by the impact of transaction costs.

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[11] Wikipedia defines the principal-agent problem as the problem that treats the difficulties that arise under conditions of incomplete and asymmetric information when a principal hires an agent. Various mechanisms may be used to try to align the interests of the agent with those of the principal, such as piece rates/commissions, profit sharing, efficiency wages, the agent posting a bond, or fear of firing. The principal-agent problem is found in most employer/employee relationships, for example, when stockholders hire top executives of corporations.

[12] The Anderlini and Felli paper "Transaction Costs and the Robustness of the Coase Theorem" was a theoretical working paper Series 406 sponsored by Suntory and Toyota International Centres for Economics and Related Disciplines (STICERD). The paper first appeared in 1999 and this writer initially used the 2001 version and later the 2004 version. The latter version of the Anderlini and Felli paper is due for publication in the forthcoming Economic Journal (2006) published by the Royal Economic Society. A fuller treatment of the paper's proposals and mathematical substantiation are addressed in Appendix 3.

The issue of when transaction costs are paid, before or after the negotiation[13] is key in determining whether the negotiation will take place or not. In creating their model to demonstrate this assertion, Anderlini and Felli (2004, p.3) put forward that "...the primary effect of *ex ante* transaction costs is that they may generate a constrained inefficient outcome". The most basic version of their model asserts that agents may not end up exploiting any of the gains from trade and any potentially beneficial negotiation may not even occur. Moreover, when the choice of *ex ante* costs is exhaustive, the escalation of *ex ante* costs corresponds to the level of detail of the negotiation. This allows the parties to achieve a greater surplus from the negotiation because the parties have investigated more thoroughly the potential gains from trade. However, the Anderlini and Felli model asserts that agents may negotiate a less detailed contract because of the high initial *ex ante* costs, thereby foregoing potential gains from trade. Exploration of this theme is important for understanding the negotiation process in South Africa, particularly when the concern is about the granting of compulsory licences for much needed drugs. This line of thinking can be used to try and understand why the Department of Health rejected offers from some of the large multi-national drugs companies who were trying to assist with cheaper and even free drugs for HIV/AIDS treatment. Those companies included Glaxo Wellcome, Bristol-Myers Squibb, Pfizer and Boehringer Ingelheim (Reekie, p. 171).

Consider a Coasian negotiation where the two agents enter a negotiation that might yield a surplus of a random size. The surplus generated by the negotiation is exogenously given because the extensive form of the negotiation is itself exogenous, for example, such as a negotiation involving compulsory licences or parallel trade. This surplus is shared by the agents.

The assumptions associated with this negotiation highlighted in the Anderlini and Felli model are agreeable to that of a normal Coasian negotiation. Firstly, the agents must pay a given *ex ante* cost before the negotiation takes place. Secondly, if the distribution of *ex ante* costs is such that if either one or both of the agents are not able to potentially recoup their *ex ante* investment, then the negotiation will not take place. This may be possible even if the total potential surplus exceeds the total *ex ante* costs and it is socially efficient for the agents to negotiate the division of the surplus and pay the *ex ante* costs. Anderlini and Felli (1998) highlight situations where this might occur. Furthermore, thepossibility that agents will not negotiate a socially efficient contract

[13] It might be prudent at this point to highlight the fact that there are two sets of *ex ante* costs involved in Anderlini and Felli proposal. There is a set of *ex ante* and *ex post* costs for the first tranch of the transaction. The second and subsequent tranches also have *ex post* and *ex ante* costs associated with them. It may be possible that these costs outweigh the gains from trade.

has been described by Anderlini and Felli as a 'source of inefficiency' and in contract theory, it is known as the 'hold-up problem' (2004, p.3).

Of relevance to the South African situation is that multinational drug companies may not feel secure in their negotiation of prices for the supply of drugs to the national Department of Health and the private sector in the current healthcare paradigm. They may not be able to recoup their *ex ante* investments such as research and development.

Referring back to the to the agents negotiation, before the *ex ante* costs are paid, they negotiate a transfer of funds that would compensate the agent but does not recoup his *ex ante* loss, and this is contingent on the agent paying the initial *ex ante* costs. The problem arises when the payment of the *ex ante* costs is contingent on the compensating transfer.

The model then investigates a second tier negotiation which involves a whole new set of positive *ex ante* costs. Additionally, the second tier *ex ante* costs must be paid for the second tier negotiation to occur, and before the first order costs are paid and the first order negotiation takes place[14]. It is possible that the second tier *ex ante* costs do not get paid. It is a recursive relationship in that *ex ante* costs associated with first tier negotiation will, in turn, not get paid as well. The model then goes to show that the actual surplus will not materialize. This outcome is significant in that it survives the restrictions of a negotiation that is conducted in a Coasian spirit, that is, the outcome of the negotiation at each stage should yield an efficient outcome. Since the overall outcome is not efficient then by implication, it is not Coasian.

Why is it significant whether a negotiation is Coasian or not?

Primarily, in the negotiation of drug prices, South Africa has a multi-tier negotiation process in dealing with the multinational drug companies regarding the supply and cost of drugs. This is consistent with the experiences of countries world wide. At the onset, there is the first order negotiation with the national health authorities. Health authorities, in many countries, represent the largest purchaser of drugs and in many cases use their monopsonistic leverage to drive down their purchase price of the drug. South Africa is no exception to this scenario. The second and subsequent tiers of negotiation involves negotiations with the private sector (as is the case in South Africa) or with provincial health authorities.

[14] This is an assumption that Anderlini and Felli use to demonstrate their model.

South Africa is faced with a particular set of circumstances in that the negotiations that are concluded may not be considered efficient in the Coasian sense and as such, may not be socially efficient. Revenue losses on the part of the drug companies may result in less being spent on drugs that are important to the southern African region, namely, malaria, HIV/AIDS, tuberculosis and cholera. The inefficient solution would result in drug companies tending to concentrate on products that result in the favourable return on investments.

A similar situation occurs with the granting of compulsory licenses. If one agent does not recoup potential *ex ante* costs, then the negotiation for a Coasian solution would not take place, even if the negotiation is socially efficient. This is the arrangements that the TRIPS agreement attempts.

2.3.1 The description of the firm

Transaction cost economics sees the firm in terms of its governance structure, rather than the production function described in classical economics. Williamson believes that efficiencies of a firm be considered by its ability to align with different governance structures. Furthermore, the manner in which business was conducted changed drastically through the 1970's and 1980's and that change had a significant impact on the firm. Organisational structures, remuneration packages, job definitions and information flows have all undergone complete makeovers. During this period, there appeared to be a trend of governments to deregulate and privatise, especially in capitalist economies resulting in businesses having to rethink their operational models. A common thread is that business now has to seek out new opportunities in order to remain functional and this has encouraged companies to look toward each other to establish competitive advantages. Businesses have identified complementary activities that enhance the effectiveness of their operations. Furthermore, once a need for change is created, it tends to grow organically, creating an environment where the lines of demarcation are blurred.

2.3.2 The main purpose of the economic organisation

Hayek argued that economic problems arise "always and only in consequence of change" (1945, p. 523) and added that the economic problem of society is mainly one of "rapid adaptation to a particular circumstance of time and place" (1945, p. 524). In introducing their book, Williamson and Masten (1999) observe that Barnard (1938) made a similar assertion on the importance of adaptability of an economic organization. Moreover, Barnard observes that the two assertions

mentioned above are in fact complementary. Hayek goes on to explain autonomous adaptation where individuals respond to market opportunities as signalled by price changes, while Barnard refers to cooperative adaptation, which is the internal mechanism of a firm (Williamson, 1998). Critically, transaction cost economics recognises adaptation as the central problem of a firm or economic organization.

The organisation has been described as a 'nexus of contracts' by a number of theorists, most notable Eugene Fama (1980a, p.6) in his well known 'nexus of contracts' lecture and Alchian and Demsetz (1972, p.781) who also recognised the firm as an independent legal personality or entity. As such, it identifies the organisation as a separate legal identity that is able to bring parties together in order to facilitate exchange or commerce. Without an organisation, there would have to be complex multi-lateral agreements or contracts amongst all the participants (Milgrom & Roberts, 1992, p. 19), something that is logistically unlikely and difficult to effect.

2.4 The Problem of Social Cost

As discussed earlier in the chapter, transaction costs can be defined as the spectrum of institutional costs, including *inter alia* information costs, costs of drawing up and policing contracts, analysing implementation, property rights and negotiation (Williamson, 1979). The dimensions of transaction are uncertainty, transaction-specific investment and frequency of exchange. The Coase theorem states that economic efficiency will be attained as long as property rights are fully allocated and that completely free trade (as long as transaction costs are not too high) for all property rights is possible (Coase, 1960, p. 8). *Ex ante* costs are the expected costs before the transaction takes place. Anderlini and Felli (2004, p.1) explore the impact that *ex ante* costs have on the hold-up problem, as reflected upon earlier in the chapter.

The actions of businesses can have harmful effects on others (*e.g.* pollutants or factory). The traditional approach had been to establish a divide between the private and the social (or public) product of the factory, and has been largely based on Pigou's suggestions in *The Economics of Welfare*. Pigou suggests that by making the 'guilty' party liable for any damages arising from his actions and taking punitive action, such as placing a tax or penalty on the guilty party that would be commensurate with the level of 'damage' caused. Coase asserts that the solutions reached from this analysis are lacking in depth (Coase, 1960, p. 15-19).

Coase challenges Pigou's contentions as being inappropriate and leading to undesirable outcomes. He asserts that the problem is reciprocal in nature in that it attempts to rectify the situation of one party results in a loss for another party. This is a balancing act - trying to do less harm than the arising situation. Is the intervention necessary? He argues that one should consider what is obtained and what is being given up as well as consideration of the total and at the margin. Coase illustrates this point with the famed 'cows or crops' example which occurs in conditions of quasi-competitive frameworks. However, depending on what can be gained or lost, there is room for engagement and negotiation. This is the crux of Coase's argument (1960, p.3-6).

Coase put forth the principle that from an economic perspective, the goal of a legal system should be to establish a pattern of rights such that economic efficiency (as Coase defines it – a wealth-maximising trade rather than the Pareto optimum or perfect competition efficiency) is attained (Medema & Zerbe, 2000, p. 876). The aspect that Coase attempted to highlight is that a legal system has an impact on transactions and that the goal of any legal system should be to minimise these costs in order to permit wealth-maximising behaviour. The issue of transaction costs is expounded upon through the consideration of contracts that could be used by the relevant stakeholders. Such negotiations, according to Coase, would ultimately lead to efficient and invariant outcomes under the conditions of wealth-maximisation and the clearly defined allocation of rights. It is imperative that the extent of the liability of each party be known since, as Coase argues, without the establishment of the initial delimitation of rights there can be no market transactions to transfer or recombine them (Medema and Zerbe, 2000, p.837). The resultant outcome, however, needs to be independent of the legal position if a costless pricing system is implicit.

The so-called Coase 'theorem' was never written up in any formal manner. George Stigler (1996) was the first to recognise the potential of Coase's thinking when he pointed out it asserts that under perfect competition private and social costs will be equal. Moreover, Coase's ideas have raised differing debates. Regen (1972, p. 427), for instance, felt that in a world of perfect competition, of perfect information and of zero transaction costs, the allocation of resources in the economy would be efficient (Coase's assumptions) and unaffected by legal rules regarding the initial impact of costs (social costs are internalised) resulting from externalities. This drives home the point that when parties can bargain and settle their disagreements by cooperation, their behaviour will be efficient regardless of the underlying rule of the law (Cooter & Ulen, 1988, p.105). Hoffman and Spitzer (1982, p.73) are also clear in their reading that a change in a liability

rule will leave the agents' production and consumption decisions both unchanged and economically efficient within the following (implicit) framework: two agents to each externally bargain; perfect knowledge of one another's (convex) production and profit or utility functions; competitive markets; zero transaction costs; costless court system; profit maximising producers and expected utility-maximising consumers; no wealth effects and agents will strike mutually advantageous bargains in the absence of transaction costs.

In the Coasian world, there are two general claims that are evident; the 'efficiency hypothesis' and the 'invariant hypothesis'. The former is the situation where no matter how rights are initially assigned, the ensuing allotment of resources amongst the agents will be efficient. This is also known as the 'weak' form of the Coase theorem. The 'strong form' of the Coase theorem, or the 'invariant hypothesis', describes the situation where the final allocation of resources will be invariant under alternative allocation of rights (Medema & Zerbe, 2000, p.850).

The implication of the Coase theorem is that any analysis done in a classical economics scenario of competitive markets and zero transaction costs, and that subscribes to a Pigouvian solution is not necessarily efficient. Furthermore, if the rights are transferable, then the presence of the legal rules are important, not the specifics of the law. This arrangement will also be efficient, at least according to Medema and Zerbe (2000, p. 861).

The vast majority of literature weighing up the pros and cons of the Coase theorem has done so from a quasi-competitive framework perspective. The areas of criticism levelled against the model include: rents, entry in the long run, separability of the cost functions, non-convexities at the negotiation starting point, plus income, taste and preference effects. The Coase theorem was also addressed from a game-theoretic bargaining perspective and the argument is primarily focussed on non-cooperative game theory.

The argument involving rents asserts that the Coase theorem cannot hold under perfectly competitive conditions in the long run because it considers or gives credence to rents that may not exist. This would also be considered to be an agreement. It has been argued further (Medema & Zerbe, 2000, p.840) that the prior existence of rents must be sufficient to support the externality (such as pollution) in order to keep the players in the fold. This means that both the polluter or the victim should have sufficient recourse to stay involved in the negotiation, or else one of them might exit from the situation. To understand this assertion, one needs to consider the situation where there

are two divergent parties, a polluter (factory) and a victim (citizen). If the polluter pays the citizen for the damage caused, then they have reached an agreement. Alternatively the victim can pay the polluter a bribe in order not to pollute. The situation poses the dilemma of where or on whom does the liability rest. Medema and Zerbe (1999, p.846) conclude that the overall result will be efficient regardless of the allocation of rights.

The issue of liability also impacts entry into the market in the long run, and this challenges the invariance and efficiency hypothesis of the Coase Theorem. Primarily, depending on the allocation of rights, whoever is receiving gratuities (victim or polluter) will experience an increase in the rate of return in that industry. "If one assumes that polluters or victims entering the market are also eligible for compensation, then entry will occur in the long run, leading to an increase in the output of the … industry" (Medema & Zerbe, 1999, p. 841). Two arguments ensue. Firstly the staggered entry affects the legal position of the environment and hence renders the invariance hypothesis unworkable. Secondly, the efficiency hypothesis is rendered ineffective because of the liability issue. If the liability lies with the polluters, then the stream of 'bribe' payments from the victims to polluters results in a excessive victim output relative to what would be considered an optimal solution, and vice versa.

Three steps can be taken to alleviate the efficiency position. Firstly, if we assume that transaction costs are zero, then the agents involved are rational and there are no legal constraints to bargaining, which implies that the long run inefficiency will be addressed through the process of bargaining. This is the same process that resolves the short-run inefficiencies (Calabresi, 1968, p. 68). Secondly, according to Nutter (1968, p. 17) long-run misallocation of resources will be alleviated if a single owner enters the market in order to take advantage of the potential for gain. Thirdly, Medema and Zerbe (1999, p. 842) observe that the above argument assumes that efficient long run equilibrium exists at a single point where efficiency implies invariance. This 'point' need not exist since the long-run equilibria are both efficient, obviating the need for any corrective agent negotiations to validate the efficiency argument. One of the more robust debates emanating from the Coase theorem is the issue of transaction costs, and primarily the assumption of zero transaction costs. Transaction costs are those costs associated with search, monitoring, negotiation and enforcement.

2.5 The Coase Theorem, Wealth Effects and the Value Maximising Principle

Wealth effects, or the change in choice stemming from change in wealth status, tend to influence many economic decisions. Analysis of value-maximising principles, however, can be simplified if no changes in wealth effects in the economies of organisations are assumed. There are three main conditions for the 'no wealth effects' proposal to hold[15] (see Appendix 1). Furthermore if an allocation is Pareto-dominant and the allocation is efficient then the value maximising principle can be summed up thus:

> "An allocation among a group of people whose preferences display no wealth effects is efficient if and only if it maximises the value of the total parties. Moreover, for any inefficient allocation, there exists another (total value maximising) allocation that all of the parties strictly prefer." (Milgrom & Roberts, 1992, p.36).

Coase (1960) proposed that if parties bargain to an efficient agreement (for themselves) and their preferences display no wealth effects, then the value creating activities (y) that they will agree on do not depend on the bargaining power of the parties, or on assets each owned when the bargaining began. Rather, efficiency alone determines the activity choice. The other factors can effect only decisions about how cost and benefits are to be shared (x) (Milgrom and Roberts, 1992).

The transaction cost approach (i.e. transactions under the assumption of no wealth effects) the efficiency principle, and the Coase theorem together imply that all operations are focused on maximising the total value of all stakeholders (since the Coase theorem relates to total social private costs). Simply stated, the firm's system of operations is independent of any dominance in the relationship between the owners of capital and workers. Coase's original thinking (1937) reflected on the monolithic government structures of the former Soviet Union that was influenced by Marxist ideology. The Marxist view, however, holds that organisational composition mirrors the power and

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[15] Milgrom and Roberts (1992, p. 35) indicate that the following three conditions are crucial for no wealth effects to hold:

- Given that there are any two decisions y_1 and y_2 and monetary wealth $\$x$, the first condition states that there is an amount of wealth – $\$x$ – that would be sufficient to compensate the decision-maker for shifting from y_1 and y_2 (or vice versa).
- If the decision-maker was given an additional amount of wealth, then the amount needed to compensate him for the switching from y_1 and y_2 would be unaffected.
- The decision-maker should have sufficient means to absorb any loss in wealth in switching from y_1 and y_2, at least within reasonable parameters.

class structures in a particular society. In another scenario, the practice by firms to limit others in the retail chain to set prices may be viewed as anti-competitive, whereas the transaction costs approach may view it as efficient behaviour.

Hirshleifer and Glazer (1992, p.376) look at the practical application of transaction costs, presenting it as costs of exchange. They distinguish two areas of exchange costs: one, trading of goods and services; and two, the physical movement of turnover. They note that the costs of exchange may depend on the volume of goods traded; the frequency of trades; the number of parties involved in the transaction; and the number of distinct commodities per transaction (1992, p. 379). They further assert that costs contingent on volume of trade are 'proportional transaction costs' while costs contingent on frequency of trade are 'lump-sum transaction costs.' Moreover, they liken transaction costs to taxes on exchange (Hirshleifer & Glazer, 1992, p. 380), as illustrated in **Figure 2.2**, which illustrates proportional transaction costs.

2.6 Concluding remarks on Transaction Costs

In the analyses and designs of economic models, it is possible to present unrealistic assumptions. Some may be valid but others can be untenable. It is assumed, for instance, that firms want to maximise profits and that efficiency is the primary measure to maximise value, although there is a sizeable portion of the market where such principles do not appear to apply. There are inconsistencies, for example, in a situation where there is only one party to a trade: the profit-maximising transaction by the firm need not necessarily maximise the joint wealth for all of the traders in order to come to a settlement where all of them gain from the transaction. Many decisions made by a firm involve situations where spending and investment patterns occur in phases over a period in time, as do the returns. In order to maximise the market value of an investment, it would also be necessary to use insurance and other financial vehicles in order to reduce any risk. Reinsurance is an appropriate tool used by medical schemes to reduce the risk of catastrophe. Such measures occur in complete or competitive markets. There are instances where there is no principal-agent problem, which are not entirely competitive, and may interfere with normal market processes. Some examples include situations where decision makers, who are shareholders, meddle with the flow of returns in order to protect their personal interests, or if they are a supplier to the concern and expect preferential albeit differing price structures.

In developing the theory of joint wealth by the trading-agents (profit-maximising), Milgrom and Roberts (1992) make the assumption that people will seek to maximise their utility

under the guidance of their well-defined utility functions (rationality based theory). This postulation ignores human aspects of self-sacrifice and altruism that could obviate any notion of capitalising on one's utility function. An example of this is the soldier's dilemma in the face of frontline war. Their position, however, accurately reflects general business practice that assumes people are motivated by their narrow self-interests, i.e. the principal-agent relationship is a problem.

Organisation is the composition of how people are co-ordinated and motivated to get things done, what incentives are utilised to encourage employees to show initiative, but also what mechanisms are used to deal with people in an external environment. How to get decision-makers, throughout the establishment to share the organisational objectives and how to delegate authority to those who could use it most effectively, particularly those empowered with the information to make decisions. Finally, to appreciate that giving incentives and delegating authority are complements and to recognise and be able to use this pairing successfully.

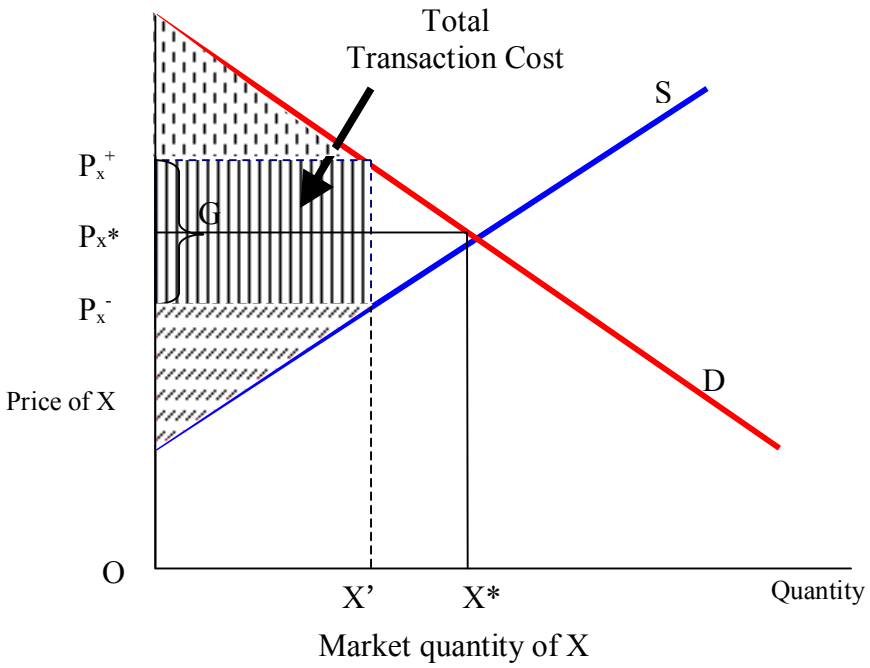


Figure 2.2: **Proportional Transaction Costs** Here there is a proportional transaction charge, in the amount of G per unit of commodity exchanged. In equilibrium, there must be a price gap of this amount between the price paid by the demanders (P_x^+) and the price received by the suppliers (P_x^-). The quantity exchanges is X', and the shaded area represents the aggregate transaction costs (Hirshleifer & Glazer, 1992). The objective for mergers is to reduce transaction costs so that X'=>X* so that the price paid falls and price received rises.

An organisation is a complex structure and can be analysed from various angles. The basic unit of analyses is the transaction, although the basis for evaluation is efficiency: how well has the organisation served the wants and needs of the people it caters to? Efficiency can be used as a positive principle; its value can be verified by the interests, events and actualities being served. An organisation can expand its operations through specialisation and then through individual transactions.

Transaction cost theory is the theory developed on the premise that organisations are designed to minimise costs of commerce (or transacting). These include costs of negotiating and wrapping up transactions including co-ordination costs. Transactions are best managed through the five attributes analysed above, namely asset specificity, frequent similar transactions over sustained periods; uncertainty about circumstances and the subsequent complexity of decisions; costliness of measuring performance and close correlation to other transactions.

The value maximising principle maintains that when individual preferences are free of wealth effects, then the allocations that maximise the total value and divide it amongst the participants are efficient. Similarly, the Coase Theorem states that under a no wealth effects environment, the assets, wealth and bargaining power of the parties do not influence decisions regarding productive activities or organisational arrangements. Firms are not bound by the standards of the profit-maximising principle owing to their variation in structure and objectives and may even be used to serve individual interests or public interests rather than that of the organisation. However, if we look at value-maximising (which depends on the joint wealth maximising from trade) the implications are different. Profit-maximising is the outcome or behaviour of one party and wealth-maximising is the outcome of two (or multiple) parties.

2.7 Conclusions of the Coase Theorem

Coase wrote about the allocation of property rights. He concluded that one or more parties will enter into an agreement that would be beneficial to those all of the parties involved in the negotiation. However, Coase's argument remains largely in the theoretical framework of transaction cost economics and the realm of practical application is still fraught with unwieldy informational asymmetries, bounded rationality and issues of motivation, amongst others, in order for an efficient transaction to develop. With that consideration, Coase offers a strong case for efficient transactions to occur in the design of commerce.

In the area of pharmaceutical study, the viability of patent rights should be balanced against the need to conduct research, to create more efficient drugs and ultimately, advance to a feasible solution that is politically, socially and economically viable. In a broader context, this is the thinking that Coase's work suggests.

Chapter 3 will highlight areas and trade related instances where the scenarios described by Coase arise.

CHAPTER 3

Efficiency in Pharmaceutical pricing? An Examination of Ramsey Pricing and the TRIPS Agreement

The realm of pricing structures of drugs is characterised by many opposing influences: of national governments, socioeconomic disparities, the perils of poverty pitted against the need for efficient drug distribution, research and development, profit motive and commerce. It is about creating a fine balance, adopting a particular pricing policy that would weight the requirements of all of the stakeholders in an equitable fashion. In this chapter the writer will attempt to shed some light on creating this balance through the examination of the economics of parallel trade and imports; the World trade Organisation's (WTO) trade-related aspects of intellectual property rights (TRIPS) agreement ; and finally, Ramsey Pricing (differential pricing) models such as price discrimination, multi-product pricing, and tiered pricing. The latter three focus in on the microeconomics of price theory specifically.

3.1 Ramsey Pricing and Economics of Parallel Trade

Parallel trade can be described as the movement of lower priced products from 'low-price countries' to 'higher-price countries' (Danzon, 1998, p.294). Prices of goods, including pharmaceutical prices, differ across countries and reflect the characteristics of individual economic systems. Healthcare systems fall under this ambit – i.e. prices of medical goods and services differ across countries – reflecting a particular country's need for specific health services and medicines. The movement of these goods and services between countries, including service providers (such as doctors or nurses), has intensified in recent years, suggesting an increasing impact of free-trade agreements and globalisation. The European Court of Justice upheld that parallel trade was consistent with free-trade in the European Union in the case of *Merck v. Primecrown* (C-267/95), even though the exporting country did not offer patent protection (Danzon, 1998, p.296). The resultant situation is a circulation of lower prices. Governments, often challenged to provide cheaper healthcare, tend to benchmark local prices against the lower-end of the spectrum of international prices. It has also been shown that lower prices are not the result of lower production techniques or input costs, but rather the consequences aggressive regulation. There is little economic gain from aggressive regulation because, as Danzon (1998) argues, trade is supposed to

increase welfare. Welfare is not improved where price differentials accrue only to intermediaries, rather than the consumers or producers of the drugs.

Parallel trade negatively impacts welfare by reducing the ability of the manufacturer to recoup costs. Manufacturers need to recoup costs in order to fund further research and development (R&D) which can be used to improve consumer welfare. Parallel trade is sometimes viewed with trepidation by pharmaceutical manufacturers, primarily because it allows for the importation of drugs which may undermine the ability of (locally traded) patented drugs to enjoy the benefits of monopolistic pricing whilst their patents are in effect. Indeed, it has been argued that parallel trade cuts into efficiency gains from trade in general (Danzon, 1998, p.299), and - in turn - has a detrimental effect on the available resources that could be spent on R&D. The core issue is that pharmaceutical R&D is regarded as a 'joint global cost', beneficial to consumers worldwide, and as such, a cost that should be borne by these same consumers. (Refer to page 12 above for analysis)

Ramsey pricing is considered a noteworthy theory of efficient pricing in that it is equitable in assigning overheads in order to minimise deadweight loss. It is a theory that explains how, when consumers have different price sensitivities, a pricing structure would be efficient if it is designed so that there are different prices for different users. An efficient pricing system would, theoretically at least, be able to cover these joint costs. Parallel trade, as indicated earlier, undermines the process of joint-cost recoupment, which is crucial for R&D. One of the more common responses from manufacturers is to resort to uniform pricing, which tends to be higher than the marginal cost, usually to the short-term disadvantage of lower-income countries and consumers. Danzon (1997, p.309) demonstrates the difference between profit maximising price differentials that would be charged by a price discriminating, monopolistically competitive (PDM) firm and welfare maximising Ramsey optimal model (ROP). Moreover, Danzon's conclusion (see Figure 2.3 below) is that although absolute price levels may differ, Ramsey prices are designed to yield specific revenue constraints, usually normal profits for the firm. On the other hand, unconstrained profit maximising prices are designed to extract supernormal profits in the long run and subnormal profits in the short-run.

In the following section, the writer attempts to explore the pricing and cost policies of the pharmaceutical industry that makes R&D susceptible to parallel trade. An assessment of optimal pricing strategies addressing the issue of joint costs will be undertaken and thereafter the impact that parallel trade can have on consumer welfare will be discussed.

3.1.1 Pricing and cost policies of innovative drugs

Innovation or, in the case of pharmaceutical companies, R&D, has its opportunity costs. Estimates indicate that R&D costs amount to approximately 30% of total production costs (Danzon, 1998, p.297). As a cost, it is the same irrespective of the number of users or countries to which it is exported. It is considered to be a joint global cost for this very reason. More importantly, costs are recovered to support further development of R&D and although such costs are not allocated to specific countries, manufacturers or users, they do require a pricing mechanism whereby they can be recovered.

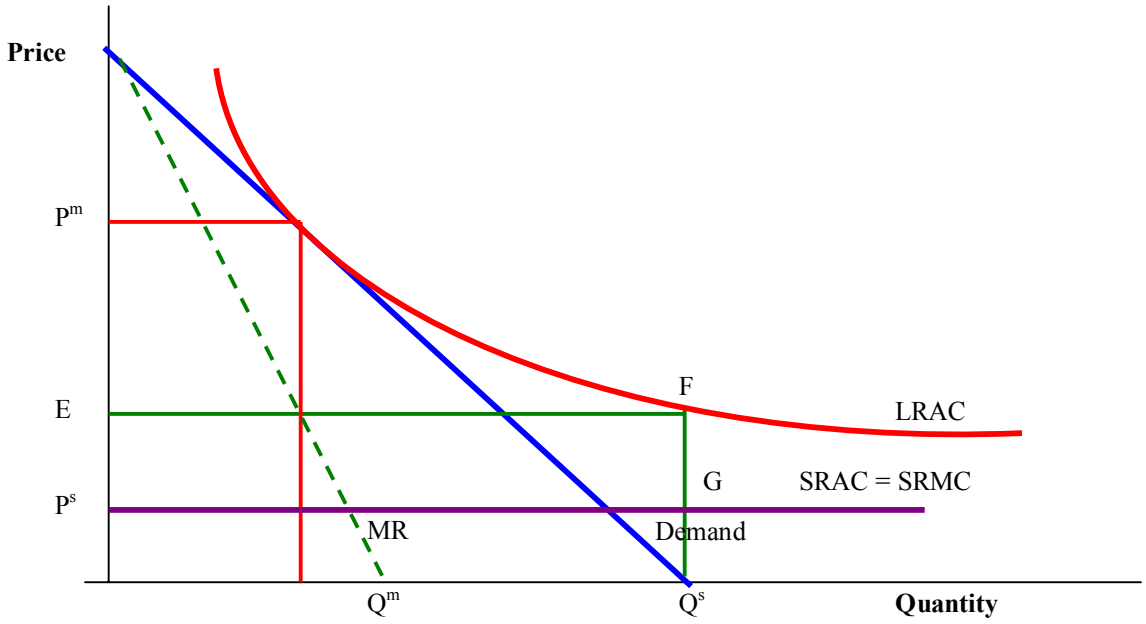


Figure 3.1. Long-run equilibrium with monopolistic competition. "With free entry to R&D business and expectations that are unbiased on average, entry will occur to eliminate excess expected profits at the margin. In the long run, monopolistically competitive equilibrium with the ability to segment markets, each firm sets an optimal price discriminating price structure with price mark-ups related to inverse demand elasticities, subject to a zero expected excess profit constraint. These price discriminating, monopolistic all competitive (PDM) differentials withy monopolistic competition should approximate the Ramsey Optimal Price (ROP) differentials provided that the cross-elasticities are zero." (Danzon, 1997, p. 309).

Source: Danzon 1997.

R&D is a sunk cost and needs to be taken into account in the pricing of the final product, and the bulk of R&D costs are sunk by the time a new drug is launched. Monopsonistic purchasers (or single, large buyers such as government, managed care organisations (MCO's), hospitals or highly competitive markets) tend to drive the purchase price down to the manufacturer's marginal cost in the short-run. Research-based firms would not be in a position to recover the sunk costs.

The granting of patent rights is one mechanism used to enable the developer of a drug to recoup costs by allowing the patent holder to price at a level that is higher than the short-run marginal costs. The patent also bars the production of the drug by generic producers. Moreover, a patent allows the developer of the drug to price-discriminate between countries, and of course to negotiate agreements regarding unauthorised distribution of the drug, including the manufacture and parallel import of the drug (Danzon, 1998, p.299).

The monopoly pricing freedom granted by patent protection is restricted by price regulations in many countries. When a country has a national health system, the health policy effectively becomes entwined with fiscal policy as well. Government control over prices stems from the 'moral hazard' problem explained earlier where citizens become price insensitive to medical services, including drugs. All monopsonistic purchasers will introduce co-payments to alleviate the moral hazard problem, but will also seek to drive the supply price down to the country-specific marginal cost (Danzon, 1998, p.296). Another issue raised is the 'spillover effect'. R&D is heavily reliant on global revenues and lower prices in one region or free trade zone can significantly impact prices in another trading zone (Danzon, 1998, p.302).

The nature of these joint costs make the pharmaceutical industry much more vulnerable to downward pressures caused by government regulation, much more so than other industries (Danzon, 1998, p.300). For example, utility providers invest heavily in capital equipment prior to being able to deliver a product. These are also sunk costs and their pricing structure includes the recoupment of the investment. One of the dilemmas facing pharmaceutical firms is that they cannot tailor prices to recoup some relevant portion of fixed costs from a specific country, because the R&D costs are not explicit in any one country. An illustration of this is that one airline company faces the same price for an aeroplane as another airline company, even though the latter hails from a different land (this does not take into account specific deal-making associated with such purchases).

There is a perception that pharmaceutical firms earn supernormal profits, something that is at least partially fuelled by the accounting practice of treating R&D as an expense, rather than capital (Danzon, 1998, p.303). Accounting measures of capital are underestimated and expenses overestimated giving the impression that returns on capital are higher than they actually are. Although not unique, as demonstrated by the advertising and other industries, this is a case where the pharmaceutical industry does present a grey area or accounting quandary in the current practice.

3.1.2 Optimal pricing strategies addressing the issue of joint costs

Ramsey pricing theory tackles the issue of pricing according to a market segment's price sensitivity. It sets out to address the problem of developing a pricing structure that secures the highest welfare to consumers, while at the same time generating sufficient income to cover all costs, including joint global costs. Ramsey prices *exceed* the short-term marginal cost in order to ensure that all costs are covered. However, consumers who have an inelastic demand curve are relatively price insensitive and face a greater mark-up of prices than consumers with an elastic demand curve. "Such price differentials lead each group to reduce their demand by an equal percentage relative to the hypothetical demand at price equal to (long-term) marginal cost," as Danzon observes (1998,p. 298). If uniform pricing were employed, price sensitive users would reduce their demand significantly, experiencing a greater welfare loss than the price–insensitive users. The latter would not increase their usage since their demand is governed by exogenous factors like sickness and state of health. Highly price-sensitive users would drop out of the market. The resultant situation is a welfare loss to society and a profit loss to the pharmaceutical company.

The economic theory of efficient pricing to cover joint costs, the so called Ramsey pricing, yields the greatest social welfare in that it proposes charging different prices to different users. This is the most efficient means of covering joint costs when the end-users differ in their true price sensitivity or price elasticity (Danzon, 1998, p.295). The level of R&D that can be maintained through Ramsey pricing far exceeds that of uniform pricing structures. In practice, some countries tend to resort to free-riding and not paying a level of pricing as directed by Ramsey pricing principals. Pharmaceutical regulations in South Africa dealing with a single exit price (SEP) are but one example of uniform pricing structures. Similarly, pricing of drugs in France and Italy are examples of governments stepping into the fray and setting uniform prices (Danzon, 1998, p.302).

The distinction between constrained and unconstrained Ramsey pricing is necessary to this discussion. Unconstrained Ramsey pricing is when prices are elevated above marginal cost levels and are inversely proportional to the markets' demand elasticities (hence the inverse elasticity rule). Resource allocation, while maximizing the amount of funds slated for R&D, will be relatively efficient. Constrained Ramsey pricing describes the situation where prices are positioned to a level

that would recover fixed costs (Scherer, 2001, p.2). Professor Scherer, in his presentation[16] "*The Economics of Parallel Trade in Pharmaceutical Products*" at the WTO-WHO Workshop on Differential Pricing and Financing of Essential Drugs, challenges the notion that Ramsey pricing is necessarily requisite in order to recover R&D costs and asserts that calls for Ramsey pricing are often motivated by rent-seeking behaviour. " My belief that unconstrained Ramsey pricing may be 'good enough' is rooted in the assumption that when firms compete for market position and profits by investing aggressively in R&D (a phenomenon which could be known as rent-seeking), pricing behaviour that maximises the profit pool also maximises the stimulus to R&D investment, which, again admitting possible exceptions, is on the whole to be encouraged" (Scherer, 2001, p. 2).

However, given that parallel trade arbitrages price differences, it can undermine any attempts to maintain Ramsey-style price differentials. There are three distinct instances when Ramsey pricing may be undermined; firstly, parallel trade may erode profits in high income markets thereby hampering the attempts to recover fixed and sunk costs. This could prompt profit-maximising firms to reduce their supply to low income markets or not supply to these markets at all. The downside is that many multinational companies may view this as a political risk and continue to supply the drugs at lower discriminatory prices (Scherer, 2001, p.2). Secondly the applicability of Ramsey pricing is undermined in a situation such as a developing nation that has segmented income groups and a multi-tiered healthcare system (Scherer, 2001, p.2). Consider a situation like South Africa where the presence of an affluent minority, covered by private health insurance, with a low price elasticity of demand, and the another group which is the low-income majority, without private insurance and a high price elasticity of demand. Scherer (2001, p.2) asserts that many multinational companies prefer to supply to the affluent classes (minority) since that would be more profitable, but their prices would be too high for the poorer majority. Finally, national reference pricing can also undermine the effectiveness of Ramsey prices (Scherer, 2001, p.3), primarily because the selling price of the drugs are regulated. The latter two occurrences reflect the prevailing situation in the South African healthcare system.

A common misconception is that differential pricing leads to firms selling in low-income countries so that they can cover costs that could not be recouped from higher priced countries, behaviour that is know as 'cost–shifting'. Supporters of the 'cost–shifting' argument, however,

[16] Scherer, F.M. (2001). "The Economics of Parallel Trade in Pharmaceutical Products." Short paper presented at the WTO-WHO Workshop on Differential Pricing and Financing of Essential Drugs. For the transcript see Appendix 3.

ignore the 'jointness' of costs issue. Expressing this proposition differently, the 'cost–shifting' argument ignores the fact that a firm cannot consistently sell below its own variable cost of manufacturing the drug. Pricing in low-income countries should be structured to be able to cover the marginal costs of R&D (which are fixed) and this implies that higher priced countries would pay less leading to an overall drop in prices in the long run.

3.1.3 Impact that parallel imports has on consumer welfare

There are two conditions under which consumer welfare is increased by trade. The first is when lower prices from an exporting country are a result of superior production techniques that lowers the cost of production, or from lower input costs. The second is when lower prices lead to increased consumption in the country that imports the drugs. Parallel imports of pharmaceuticals often go against the principles of efficiency because of stringent regulatory intervention, rather than economic efficiency. Price regulation of pharmaceuticals introduces an exogenous regulatory presence or body, which tends to distort production efficiencies and may even actively reduce efficiencies (Danzon, 1998, p.293). Parallel trade exploits regulated price differentials and does not signify real cost differences. Danzon (1998, p.290) asserts that parallel trade may even increase societal costs because of additional transport and administrative costs. A number of associated problems are related to parallel imports and include, *inter alia,* intermediaries capturing profits; lack of regulatory control over the quality of the product; problems with language on the packaging; or inconsistent standards.

3.1.4 Uniform and Ramsey prices – a Static and Dynamic perspective

In the long run, the manufacturers' profit-maximising strategy in a parallel trade environment is to attempt to set a single uniform price across markets or free-trade zones. Usually the price lies between the expected parallel price floor and the discriminatory price that would have originally been set by the manufacturer. This is an attempt by the manufacturer to pre-empt parallel trade and it signifies the threat of parallel imports to manufacturer profits. In practice, however, it is generally impossible to quantify the impact of parallel trade and the motivation it has toward the move to uniform pricing.

The standard analysis of prices relating to consumer welfare deals with commodities and does not adequately reflect the situation of joint costs. Scherer is of the view that under uniform pricing, there would be a welfare loss only if there is a reduction in consumption (Scherer, 2001,

p.5). The analysis of the joint costs of pharmaceuticals, and in particular Ramsey pricing, shifts away from this analysis by proposing that a reduction in consumption can increase consumer welfare. Economic analysis does however make the point that both Ramsey and uniform pricing structures reduce consumption relative to the prices which cover fixed costs. Both Reekie and Danzon observe that price differentials which relate inversely to demand elasticities allow for higher consumer welfare than uniform pricing (Danzon, 1998, p.300; Reekie, 1997, p.26).

Reekie distinguishes between two aspects of price theory, static and dynamic, and raises the issue of the practical aspect of price setting, citing that it is not as simple as using the elementary textbook construct of price equal to marginal cost (*P=MC*) in perfect competition. The setting of a price is difficult because of the subjectivity of the costs combined with perfect competition, and is emphasized by Reekie (1997, p. 26):

> "These suggest that the phenomenon (and its associated condition of price equal to marginal cost) is an *ideal*. In fact the concept is merely a *predictor*. And in an innovative industry, where unit variables costs are relatively small (as in drugs) but fixed costs as in R&D expenditure are relatively high, the problem of correctly defining marginal cost (even if it can be presumed to be objective) is well-nigh insuperable. Unless this is understood, we are in the hypothetical elementary textbook abstraction of homogenous products where no improvement or innovation can bring extra profits exclusively to the supplier." (Reekie, 1997, p. 26):

Ramsey pricing proposes that all products should be priced at the long run marginal cost and that joint costs should be set in a manner so as to minimise social losses (thereby increasing social welfare) by ensuring that the prices are also higher than the variable cost (Reekie, 1997, p.27). These joint or common costs are also factored into the measurement of optimality, which occurs when the social benefits that accrues from all the products, measured by the markets willingness to pay the price, is equal at the margin per Rand (or $) of deadweight loss that had to be given up in order to accommodate the joint costs.

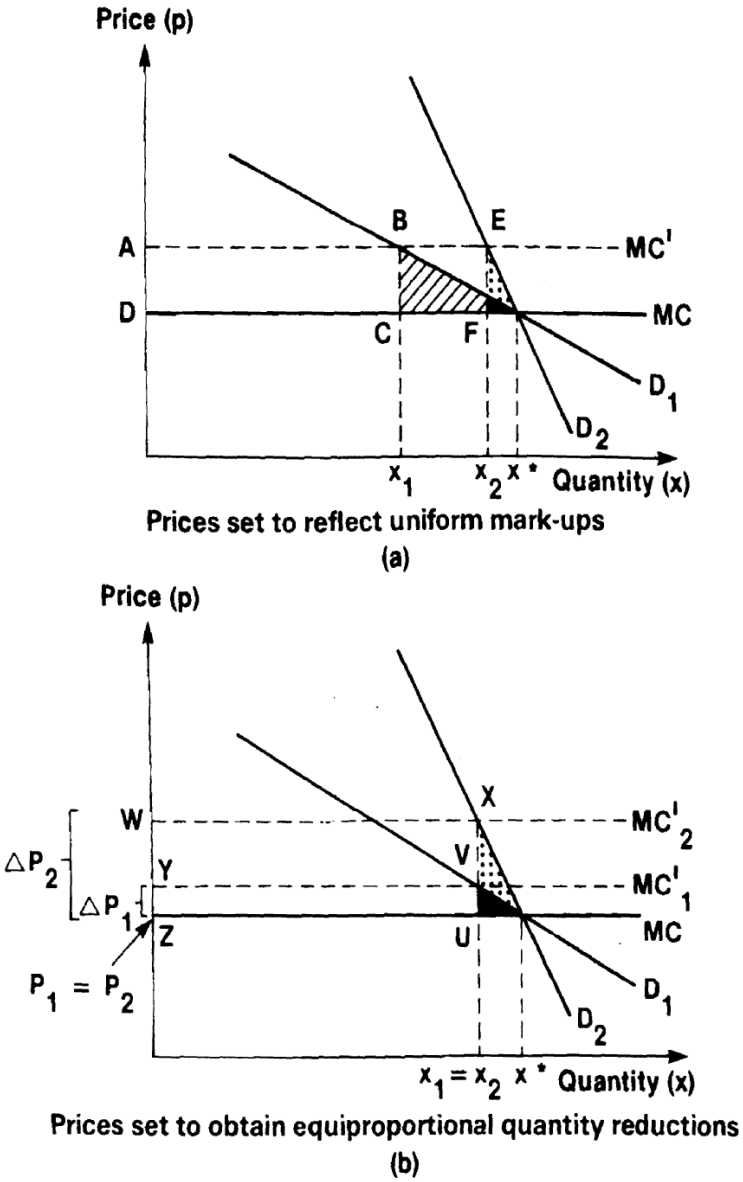
In view of the static theory, Reekie (1997, p.27) considers the issue of optimality by considering the following diagram (see Figure 3.2), which is an adaptation of the illustration originally proposed by Schankerman. Suppose that we are working with two drugs, D_1 and D_2, where the demand curves are D_1D_1 and D_2D_2 respectively and the marginal production cost is equal to MC in both cases. Consider a joint cost such as R&D. If such a cost (this applies to all joint costs) is allocated amongst all of the participants equitably, then the MC would rise to MC^1 and the original output levels of X* would fall to X_1 and X_2 corresponding to the relative deadweight loss in each case. The amount of joint costs that a product incorporates should reflect in its price-elastic demand. By comparing the two situations in 3.2*(a)* and 3.2*(b)*, it is evident that the products with a

relatively price-elastic demand should carry a smaller load of the joint costs than those products with an inelastic demand. In figure 3.2 *(a)*, the total revenue required to handle the joint costs is given by the areas ABCD and AEFD. These areas are equal to the areas WXUZ + YVUZ in Figure 3.2*(b)*. The crux of the argument is in the realisation that under Ramsey pricing structures (when there are equi-proportional quantity reductions shown by the shaded areas BCI + EFI compared to XUI + VUI) the deadweight loss is markedly smaller. As Reekie (1997, p. 28) points out, no other pricing policy would result in a smaller aggregate deadweight loss.

Socially optimal pricing can utilise the inverse elasticity rule, i.e. where the product with the greater inelastic demand displays a greater percentage deviation from marginal cost. Reekie (1997, p.29) explores this idea in Figure 3.2*(b)* where he shows that the optimal allocation of joint costs should be where P_1 and P_2 are increased by ΔP_1 and ΔP_2 respectively and that the output is reduced by equal proportions where X* would fall to $X_1 = X_2$.

The situation in South Africa can be particularly tenuous with the original Medicines and Related Substances Act (Act 90 of 1997) getting the go ahead in 2005 as the Amended Act 101 of 1965. The Act appeals to the uniform mark-up of prices which does appeal to the notions of fairness in the eyes of the stakeholders and certainly in the public arena. The net effect may however be a greater loss of social welfare in future pricing systems and patent drug accessibility. As Reekie observes (1997, p.30) a uniform mark-up on short run marginal cost implies that overheads can be met. In a situation where there are different demand elasticities, the reduction in quantity caused by the uniform mark-up would be greater with the more price sensitive consumers, and the relative amount of deadweight loss would be substantial. However, under a system of Ramsey prices, the joint cost can be recouped through a series of different mark–ups that are contingent on the price sensitivities of the respective consumer groups.

Demand Curves for Drugs with Differing Price Elasticities



Source: Adapted from Schankerman, M.A., *op. cit.*

Notes:
1. This analysis could also apply to the same product sold in different markets.
2. Prices are set so that:
   ABCD + AEFD = WXUZ + YVUZ
   i.e. so that total incremental revenue equals common costs.

Figure 3.2 Source: Reekie (1997, p.46)

Pricing policy, however, is not a static intervention and is often influenced by short-term economic and political influences that may not be the most socially sound path to follow. On the other hand, the pricing policy followed by a profit maximising firm may result in an efficient (Pareto) manner yielding the most socially beneficial outcome, even in the midst of provocative political discussion. Both situations however are contingent on the particular circumstances at hand that need to be considered.

Given the competitive and dynamic nature of the market economy, pricing policy tends to be in itself dynamic in nature. Reekie, in his treatment of dynamic pricing theory, explores the role of the Cocks modification on the Clemens article (Reekie, 1997, p. 31). Cocks supports the idea that competition takes place in more than one dimension, and that a number of other factors need to be considered. Furthermore, he bases his arguments on the following five premises:

i) to attain a preferred market position through the development of new products is the primary incentive of many firms;

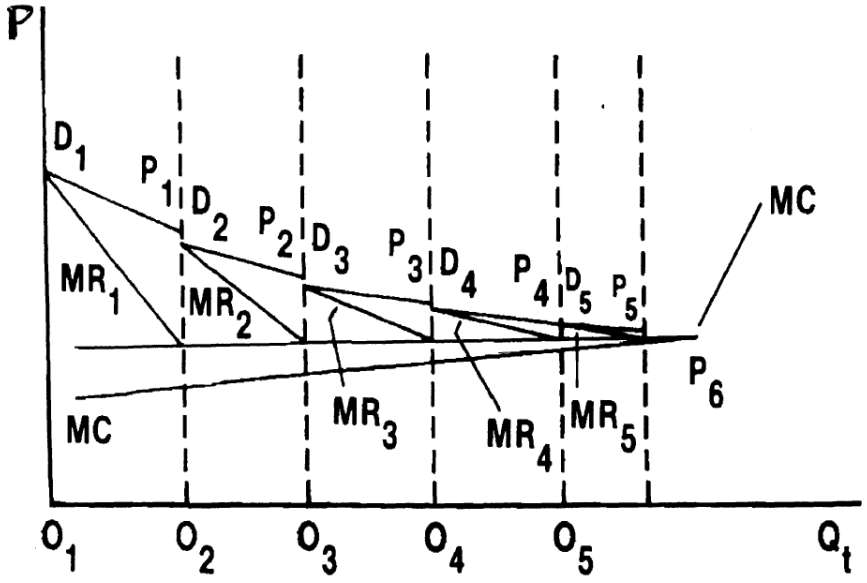
ii) firms will expand output to a level where the least profitable unit will be produced at a marginal cost equal to price. Additionally, firms gravitate toward meeting unfulfilled demand of newer drug treatment through the continuous innovation and changes to its existing products, be they major or minor modifications;

iii) the high degree of cross-elasticity of supply between R&D and pharmaceutical production in the therapeutic markets allows for a heterogeneous range of outputs to be produced when the demand curves under review are considered as commensurate units;

iv) a firm's demand curves tend to be focussed on different therapeutic spheres and this implies a low cross-elasticity of demand between a firm's products;

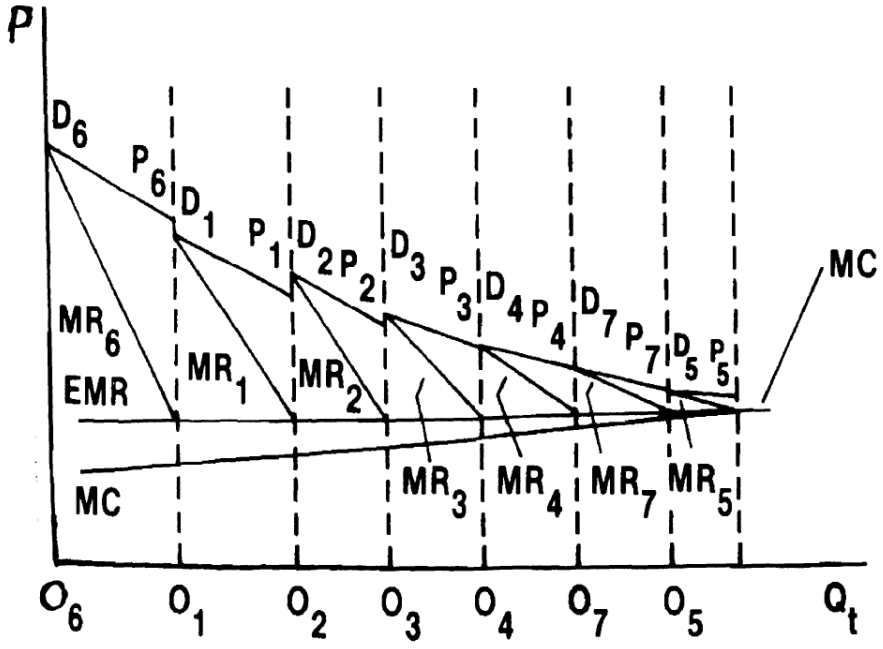
v) a firm's products have a broad spectrum of market positions, ranging from strong market vigour (pertaining to new innovative products, e.g. Lipitor, Crestor) to a situation of perfect competition (as in generic and multi-source commodity type products, e.g. Zocor, Aspirin, multi-vitamins)

Consider Figure 3.3 and Figure 3.4 below. The Clemens model, showing five separate demand curves for one firm, reflects the profit-maximising position where the



Source: Clemens, *op. cit.*

Figure 3.3



Source: Cocks, *op. cit.*

Figure 3.4

Figure 3.3 and 3.4 Source: Reekie (1997, p.47)

marginal revenue in each of the five situations is equated to the limits set by the respective perfectly elastic demand curves. This figure is then compared to the lower diagram, Figure 3.4 which represents the same firm in a subsequent business cycle after it has successfully introduced a new drug that is significantly better than any of the existing drug therapies. In both diagrams, according to Cocks, the price competition reflected by the progression toward greater elasticity and is indicated by a shift in the demand curves from D_1 through to D_5. Of significance in Figure 3.4 is the meaning attached to these demand curves. The demand curve D_6 represents the new drug or drug therapy; the demand curve D_7 represents the firm's entry into the productive areas of its competitors. In this scenario, while the firm is in the development stages of D_6, its competitors want a share of the profit potential associated with the firm's products (and vice versa). Also, if the price of the product represented by demand curve D_5 is higher than its marginal cost, then the competitors' effort to enter their own products into the market would increase the elasticity of D_5. This phenomenon can be witnessed with the introduction of 'me too'[17] drugs and generic drugs into the market. Furthermore the introduction of D_6 signals to competitors the profit potential associated with the new product. This may result in starting the cycle, described above, in a subsequent business cycle.

The equilibrium that this situation moves toward is one where the price reflects the marginal cost in every therapeutic market that is characterised by innovation. Furthermore, as Reekie observes, if the price: marginal cost ratio reflects the differences in R&D cost of producing a New Chemical Entity (NCE) for the intra-marginal markets, then the hypothetical outcome would be an true indicator of a perfectly competitive equilibrium.

Reekie (1997, p. 32) asserts that in a static analyses, the pricing conduct of the industry implies that there is a competitive process with a welfare loss or monopoly rents. This welfare loss is the source of funds used for R&D projects and developments for the future. In a purely competitive environment, these rents are considered to be a social opportunity cost in the sense that this is what society gives up when prices are higher than marginal costs. In order for newer NCE's to be produced in the future, society must forego the benefits of lower prices at present. If this 'welfare loss' to society is added to 'production costs', it may result in the ratio P: MC being equated, i.e., the product price may be close or equal to the total marginal cost. The series of events

[17] 'Me too' drugs are drugs that are modified mimics of existing drugs. It is widely considered that they undermine the profits generated from the blockbuster or patented drug and that the R&D that goes into the development of me-too drugs is thus a social waste. It does not add any social value, but is focussed on seizing a share of profits from other drug companies.

described above is recursive in that new products must be introduced over the continuum of time in order to extract funds for R&D purposes. Furthermore, it is exacerbated by the fact that the component of total production costs is eroded over time with the introduction of 'me-too' drugs and expiring patents.

Reekie (1997, p. 33) points out that the static model of perfect competition is largely an inappropriate tool for the analysis of an innovative industry in that it does not account for the "…richness and complexity of real life variables that determine product price and quality." Citing Schumpeter's theory of 'creative destruction', Reekie stresses that a theory that is dynamic with respect to price and quality and defines marginal cost in a way that sufficiently includes innovative expenses. Much of the analysis that we do regarding perfect competition is not congruent to the real situation at hand because of the fact that it is devoid of the incentive for innovation.

Uniform pricing has a negative impact on consumer welfare where consumers in relatively low-price countries would face higher prices for medicines than they would have paid under a country-specific Ramsey price structure. The broader picture is that small, low-price countries tend to lose access to medicines if manufacturers do not find it profitable to supply medicines to these countries.

Certain policy options are open to discussion regarding manufacturers dealing with parallel trade. First, manufacturers can apply to government to protect their products by excluding competing products that enjoy patent rights from parallel trade. Governments can also be more aggressive regarding the protection of intellectual property and patent rights. Second, country-specific contracts can be established which allow for a rebate system targeting the end-user. Rebates would allow price-sensitive users to enjoy lower prices than users who are less price-sensitive. All buyers would face the same *ex ante* prices, but price-sensitive users would have lower degrees of *ex post* prices (Danzon, 1998, p.302). It would also prevent the distributor or intermediary from exploiting the price differentials.

A key aspect of Ramsey pricing is that rebates reflect the true price sensitivity of users and would yield a normal rate of return. Contract prices should approach Ramsey pricing principles. The issue with a company that enjoys patent protection is that it would priced as a price-discriminating monopolist, yielding returns that could be higher than competitive levels and thus

encouraging other firms to enter the market. The resultant situation is that returns would be driven down to competitive levels.

A common debate (Danzon, 1998; and Scherer and Watal, 2001) is that healthcare has both economic and social implications. In light of this, the question is whether or not pricing should be structured so as to reflect the value to the user, or the cost to the producer. The difficulty in trying to regulate prices that are based on cost of production is that the adequate level of R&D cannot be ascertained. One reason, although not unique, has been that accounting methodologies do not take into account the full costs of the development of a particular drug, a process which often stretches over several years, nor is the opportunity cost that is associated with the development of that drug fully taken into account.

3.2 Concluding remarks on Ramsey Pricing

The issue of Ramsey pricing and patent rights challenges the Coasian argument that if the parties involved are left to their own devices (where transaction costs are low and property rights are specified) they would conclude a contract that is beneficial to both of them and also efficient, given the set of circumstances. Drug companies, when guided by regulation to sell at a specified price, will tend to acquiesce to the level of their country-specific marginal cost. If both parties gain from the relationship, according to the Coasian interpretation, they can hold this arrangement indefinitely. The issue is whether they see any benefit in continuing with this contract or not. A Coasian solution might be, for instance, to sell drugs to Canadian buyers if, and only if, they agree not to resell the drugs to the USA.

However, it can just as easily be concluded that Ramsey pricing and patent rights confirms the Coasian argument given that property rights (patents) are fully specified and that trading is voluntary. Argument against this type of solution is inherent in the fact that patent rights are not fully specified since they are often confused with transaction costs, thereby violating the conditions for the Coasian argument to come into play.

A salient aspect would be to use the arguments presented by a number of writers (including Reekie, Scherer and Danzon) that the methodologies used in the analysis in order to support a particular viewpoint are lacking in depth. Elementary analyses are often used to leverage particular viewpoints. Healthcare is an emotive issue, often mired in politics and socio-economic circumstance, and the issue of substantial profit on behalf of the pharmaceutical companies would

appear to be predatory. In order for issues to be settled, a level of transparency and good faith, on both the supply and demand sides, is important.

3.3 The Impact of the Trade Related Aspects of Intellectual Property Rights (TRIPS) Agreement on Access to Drug Prices in Developing Countries

The agreement on the Trade Related Aspects of Intellectual Property Rights (TRIPS) came into being in 1995 with the establishment of the World Trade Organisation (WTO). Even though there was a formal acceptance of the agreement, developing nations have experienced some difficulty in implementing the final provisions (Watal, 1999, p.105). The implementation of intellectual property rights (IPR's) met with resistance in some developing countries, and this even at the risk of jeopardising direct foreign investment. It was through no fault of their own since they were originally given ten years to change their laws to meet with the compliance, but in reality they had to begin implementation of the IPR's immediately, particularly in areas involving pharmaceuticals and agriculture.

The most significant aspect of the TRIPS agreement is that intellectual property rights, such as patent rights, are private rights that should be enforced by member states. This is the system that is designed to provide protection to patent holders. It is also important to note that American pharmaceutical companies led the international business coalition that called for the TRIPS agreement (Ostry, 1999, p. 196). The issue of parallel imports raised the question of where the limits of property rights were exhausted. Article (6) permits a World Trade Organisation (WTO) member to use parallel imports in a manner that best suits its needs (Ostry, 1999, p. 201). Needless to say, some very strong and eloquent points of view were raised from those in favour of restrictive measures and those in favour of permissive measures regarding parallel trade. One of the arguments favouring restriction was that the positive dynamic benefits that would accrue from the multinational enterprises (MNE's) expertise at customising production and to price differentially would eclipse the benefits from static efficiency losses characteristic of restrictive trade. The argument against restriction focussed on the fact that the WTO sought to liberalise trade, yet supported the concept of protectionism. The Coasian concept that trade arrangements will be made that are beneficial to both parties comes into play here, particularly around the allocation of property rights. The European Union allows free-trade, including parallel trade of patented goods, amongst its member states. However, no external trade of patented goods occurs without the consent of the patent holder. The EU has a monitoring mechanism that could observe such trade.

The interpretation of the patented criteria can vary somewhat. There are three classes:

i) novelty;

ii) non-obviousness (or inventive step); and

iii) utility (or industrial applicability).

These are designed to create transparency in negotiations (Watal, 1999, p. 107 and Ostry, 1999, p.196). The rights of patent holders are strictly protected under this agreement. However there are deliberate 'loopholes' that spell out limited exceptions to the patentee's exclusive rights. One of the subsections of the agreement, Article 30, does not list the specific circumstances where patents could be used without authorisation. In addition, developing countries could use non-voluntary licences to make patent inventions available at more competitive prices (Watal, 1999, p. 110).

Patents are important to the inventors or developers of pharmaceutical products because it allows them to maximise potential profits from trade for the length of its patent life or until superseded by a new patent. Pharmaceutical product patents, in conjunction with government enforcement, are particularly effective in protecting the rights of the patentee. Danzon (1998, p.295) has raised the issue of the recoupment of costs for R&D expenditure. The public policy question is how to balance the desire of national health systems to provide new drugs at an affordable level, and yet retain strong incentives for R&D (Scherer and Watal, 2001, p. 4).

India changed its patent law in December 2004 by presidential decree in order to meet a January 2005 deadline to allow patents on the chemical molecules used in drugs. The decree came into effect on January 1st, 2005. Why would this be significant? One reason is that India[18] is the one of the largest pharmaceutical manufacturing countries in the world, primarily of generic drugs and two is that two-thirds of its drug exports are intended for developing countries. The policy change will cost the Indian economy over $700 million each year, while creating only $57 million in profits for multinationals (James, 2004). However, the real issue for the multinationals is the poor-country examples and not the financially small poor-country markets. One way of looking at the situation is that how can people in rich countries be persuaded to accept death from cancer and other diseases because they cannot pay the tens of thousands of dollars a year that a new generation of drugs and treatments will cost, if companies in India could manufacture and sell the same medicines for a small fraction of the price?

[18] Nature Medicine, December 30, notes that India is the fourth largest producer of pharmaceuticals in the world [some say it is the third largest], and two thirds of its exports go to developing countries

Parallel trade leads to the importation of generic products; there is evidence from nations with patent protection that the prices of pharmaceutical products fall substantially with the entry of generic products into the market (Scherer and Watal, 2001, p. 5). For a country like South Africa, which may be considered a semi-industrialised, middle income country (World Bank Report 2000, p.315), the pertinent question regarding patent protection is whether the market exclusivity provided by patents would encourage R&D investments. One of the areas to consider is whether the market is sufficiently large to provide the purchasing power to justify the higher prices provided under patent protection. Would this market be substantial enough to sustain expenditure on R&D in terms of total or *pro rata* global outlay?

R&D costs are recovered from a relatively small number of commercially successful drugs (Scherer and Watal, 2001, p. 12). The issue facing developing nations in the new TRIPS environment is how to best enhance their access to the newest drugs within their budgets. There are a number of policy options available that would not run afoul of the TRIPS agreement including compulsory licenses, enforcing price controls, donations or financial assistance of medicines and participating in international drug procurement ventures. The writer will discuss compulsory licences as it deals directly with national pricing policies. The other influencing factor is parallel trade.

3.4 Compulsory Licensing

One option available to developing nations that allows for affordable access to patented drugs in the TRIPS environment is compulsory licenses. A compulsory license is the authorisation by permitting a third party to make, use or sell a patent or invention without necessarily seeking the patentee's consent. Article 31 of the TRIPS agreement stipulates that the prospective licensee should have tried for a reasonable period of time, and have been unsuccessful within this period, to obtain authorisation from the patent holder. This requirement can be waived in the event of an emergency or extreme urgency or if the drug is used for non-commercial use (Scherer and Watal, 2001, p. 14). It is understood that non-commercial public use of drugs might occur when health authorities distribute drugs through public health outlets such as clinics.

Compulsory licence regimes have been used to restore competition in the realm of antitrust violations in the United States. The German Federal Cartel Office addressed the issue of monopolistic pricing by dominant firms, in some cases based on patent rights. The most high

profile case, and most litigated, was the case brought against Hoffman-La Roche, manufacturers of Valium (Scherer and Watal, 2001, p. 18).

The TRIPS agreement is important for global trade to be conducted in a fair and open manner. Its interpretation however may result in extreme hardship for less developed nations. The agreements do afford participating nations some level of flexibility in their negotiations. The TRIPS agreement also limits the developments of generic drugs by giving credence to the patent right of the drug's inventors. It also requires that governments play a role in ensuring fair play does exist and not to free-ride on the inventions of other. However the compulsory licence issue and parallel trade gives rise to two areas that threaten the transparency in relationships; firstly, WTO members cannot free-ride on R&D of other nations and secondly, international trade involves comparative advantages with the result that developing countries with small economies may not find it in their interest to uphold the TRIPS principles. Furthermore it might be more advantageous for them to engage in unauthorised economic activities in the short run.

3.5 Concluding Remarks on TRIPS

The Coasian solution in light of these disparities is to highlight the fact that multinational companies will engage each other in order to resolve their conflicts regarding property rights, compulsory licences, generic substitution and parallel trade. One consideration is that the issue of compulsory licenses allows for flexibility in the trade agreements that would allow for nations to develop their own unique set of trade agreements. These agreements would deal with issues concerning production standards in drug manufacturing, pricing, quantity and also some form of payment to the patent holder (if agreed to), reflecting the Coasian solution.

3.6 Conclusion

There are a number of issues at hand regarding compulsory licences and parallel trade. When would be viable to issue compulsory licences? The most recent high profile case could provide some answers[19]. There is a current debate regarding the threat of the avian flu strain (HV51) becoming a pandemic and the efficacy of the drug Tamiflu to treat it. The patent holder Roche purchased the patent from Gilead Sciences Inc in 1996. The debate is centred on the inability of Roche to meet worldwide demand for the drugs and its initial refusal to allow for compulsory licences. Taiwan, Korea and Argentina have already issued compulsory licences for

[19] The Boston Globe editorial (November 11, 2005) and the San Francisco Chronicle (October 19, 2005) reported on this issue.

local production and the Indian generic manufacturer, CIPLA, has announced that it has mastered the manufacturing technique to produce the drug.

Reekie (1997, p. 36) raises the pertinent issues regarding this issue and Ramsey pricing;

i) "How can governments strengthen the demand side further to foster competition?

ii) How can it encourage an informed environment rather than a directed one?

iii) How can patients and prescribers be empowered so that their individual wishes and wants are responded to by suppliers?"

This approach has its critics and supporters. Primarily, depending on the method of analyses used, one can come up with 'scientific evidence' to supports one's view.

The question remains whether the obvious profit motive, regardless of the analyses used, is more valuable than the current lives lost or is the possible future lives lost more important. This line of thinking can be distilled into a Coasian argument of who holds the most important right.

CHAPTER 4

A History of Pharmaceutical Price Regulations

4.1 Introduction

Now that a sound theoretical framework has been established in the preceding two chapters the author intends to focus on the history of safety legislation in the pharmaceutical sector and its implications or lessons for pricing policy. A number of international case studies that are relevant to the South African experience and can be used to inform current policy thinking on price and pricing structure. At the same time, there are international experiences that directly impact – and even limit – the thinking on pharmaceutical pricing in South Africa today. In the chapter presented here, two specific cases have been identified: one in the United States of America (USA) and one in the United Kingdom (UK). The section will open with a discussion of the influential Kefauver-Harris Amendment, which deals with the development of drug safety championed by Senator Estes Kefauver, a member of the USA senate sub-committee on anti-trust and monopoly activity (see Wang, 2002). The impact and continuing ramification of the amendment for drug-pricing, particularly in the USA, will also be assessed. A similar discussion will examine the findings of the Sainsbury Committee in the UK, which outlined the UK experience of drug safety and high drug prices. The work of Towse (1997) will be used to ascertain lessons from Australia and Canada, and whether or not these lessons can be effectively applied in the South African market. Two significant inquiries that were held in South Africa focussed on the high cost of healthcare and the perceived high drug prices. Both these inquiries, the Snyman Report (1962) and the Steenkamp Report (1978) made observations similar to those of their international counterparts. The Melamet Commission (1993) went beyond the existing debate and made recommendations on reviewing and changing the tax structure. Primarily, people paying for insured medical benefits (medical schemes) received a tax break on the amount that they contributed for this cover. The situation resulted in a greater benefit to those employees who fell into the higher tax brackets and they benefited from the then current tax laws.

4.2 International Developments

Costs to patients and reimbursements incurred when paying for medicines has given rise to many investigations including those conducted by the Hinchcliffe Committee in 1959 by the Department of Health (DoH) in the UK; the Douglas Committee, also in 1959, by the Scottish DoH, These commissions may have made it feasible for weightier investigations, which will be discussed

below, to take place; importantly the Kefauver Senate Committee hearings in the US, which were instituted in 1960, and brought out both a majority and a minority report (Snyman Report, 1962, p. 104) and the Sainsbury Report in1965-7.

4.2.1 The Kefauver Hearings in the United States of America (USA)

The Kefauver hearings focused on strengthening the drug provisions that were originally promulgated in the Federal Food, Drug and Cosmetic (FDC) Act of 1938 and signed by President F.D. Roosevelt. In the USA, prior to the FDC Act, there was an ongoing problem with perceived dangerous drugs because drugs were being introduced into the market without significant testing (Hamilton, 1997, 14). The issue received national attention when more than a hundred people died after taking a preparation called 'Elixir Sulphanilamide', a drug distributed by the manufacturer Massengill. The preparation contained diethylene glycol, which Hamilton (1997, p.14) described as "a chemical analogue of antifreeze" (1997, 14). In June 1938, the FDC Act was signed into law and required that new drugs be tested for safety before being distributed onto the market. The results of these tests had to be submitted to the Food and Drug Administration (FDA) in what was called a 'new drug application' or NDA. The law also required adequate labelling for information and safety purposes.

Notably, Senator Estes Kefauver of the Sub-committee on Antitrust and Monopoly, which fell under the Committee on the Judiciary, chaired these hearings. One of the outcomes of the hearing was Bill No. S3815, which among other measures proposed that stringent manufacturing standards be instituted. It also expanded antibiotic certification to cover all antibiotics. The bill was explicitly aimed at protecting public health (Hamilton, 1997, 14).

Whilst the Kefauver hearings were in progress, the FDA received a new drug application for a brand of thalidomide, called Kevadon, from the William Merrell Company. The application was however not supported by sufficient data and analysis from safety trials. William Merrell Company undertook trial runs of the drug. By 1962, the disastrous effects of thalidomide on newborn babies became evident and the drug had to be removed from its limited distribution channels. Subsequently, the application was not approved. In light of this development, Senator Kefauver re-introduced his Bill, which came into effect when President John F Kennedy signed the Drug Amendments of 1962 into law. These became known as the 'Kefauver-Harris Amendments'. The Amendments were far reaching. They required that drug manufacturers prove to the FDA the safety and efficacy of their products prior to the products being marketed; that all antibiotics be

certified; and that the FDA area of control be expanded to encompass drug advertising. In the wake of these amendments, the FDA's approval of new drugs became increasingly risk averse and rigorous. The FDA extended the processing times for new drugs typically by almost two years (Gieringer, 1985). The cost of development was also impacted as a direct result of the 1962 Amendments, increasing to $24 million by 1976 which was about 20 times that prior to the Amendments being enacted. Furthermore, the amendments ensured that the full details of clinical investigations be submitted to the FDA and that all drugs be tested on animals prior to any human trials (Hamilton, 1997, 14). Although the 1962 Amendments did not directly address the price of drugs, it put into place drug safety requirements that needed to be met. It was the process of ensuring that a particular drug was safe that impacted on the final costing of the drug. Elements such as development times, safety and efficacy standards resulted in the higher prices of drugs.

Ruwart (2004a, p.1), in trying to assess the impact of the Kefauver-Harris Amendments on prescription drug expenditures by consumers used published data to show that the Amendments had both a monetary and human life cost, the latter being beyond the scope of this paper. The results showed that drug development time increased by an additional 9.8 years, primarily due to the Amendments. After the amendments the rate of R&D costs increased by 13-fold. A comparison was drawn between pre- and post-amendments trends. Had pre-amendment trends continued, the capitalised cost of putting a drug on the market would have been approximately 8% of the cost in 2004. Ruwart also shows a strong correlation between R&D/NCE[20] and prescription drug expenditures which suggest that there is a significant link between excessive drug prices and amendment-driven increases in drug development costs.

The significance of what Ruwart highlights is that the additional costs of drug development which are amendment-induced add significantly to the structuring of the price of the drug. This means that manufacturers spend more on R&D in order to compress development times. Additional development costs will be captured into the final selling price structure. Further impacts on manufacturing, labelling and advertising would also tend to increase the final selling price.

Finally, it is common business practice to price products as a multiple of costs. R&D is the largest cost factor in the development of NCE's and hence becomes an expedient measure in which to price new pharmaceuticals. The reduction in development costs would imply that there would be a proportionate reduction in the selling price and hence in total drug expenditures (Ruwart, 2004a,

[20] New Chemical Entity (NCE)

p.1). Ruwart estimates that, in the USA, reported drug costs in 2003 were $162 billion, whereas they could have been as low as $24 billion (15% of what they are today) had pre-amendment trends continued. The Amendments had the effect of imposing additional fixed costs which impacted on the final cost of the drug, and which had a knock-on effect of increasing the selling price to the consumer.

4.2.2 The 'Sainsbury Committee' Investigation in the United Kingdom (UK)

In 1966 the British government, under pressure to investigate alleged spiralling drug cost to the National Health System (NHS), charged a committee of inquiry under the chairmanship of Lord Sainsbury to inquire into this process. This Committee, known as the 'Sainsbury Committee' was tasked with examining the relationship of the pharmaceutical industry in Great Britain with the NHS. Their agenda included the consideration of and inter-relationships between, the structure of the industry, the commercial policies of the respective firms in the industry, pricing practices, marketing practices, the impacts of patents, the relevance and value of any research that was conducted and finally to make recommendations regarding its findings. This Committee made thirty-three recommendations and in doing so set the ground rules relating to pharmaceutical trade for a number of countries, many of whom were in strong trade relationships with the UK. The recommendations were broken down into four sections, two of which are of relevance to this paper, "Future Pricing Arrangements and The Medicines Commission" and included;

i) The Ministry of Health (Ministry) should be entitled to obtain from a manufacturer of any medical speciality product a Standard Cost Return in prescribed form.

ii) That the Standard Cost Returns should be prepared on the basis of a stated anticipated annual volume of sales and each return should show the proposed margin of profit and the proposed selling price.

iii) That the Ministry should compare their own estimate of cost with the Standard Cost Returns and should negotiate prices of medicines on this basis and in the light of successive Financial Returns of the firm concerned.

iv) The attention of the British tax authorities should be drawn to the transfer prices of pharmaceutical raw materials or intermediaries, and that the Ministry, in assessing the Standard Cost Returns of foreign-owned manufacturing companies, should make use of the ability of chemical

engineers to form reasonable assessments of the production costs of chemical materials.

v) That the ministry should calculate capital employed on the basis of historical cost provided the limitations of this basis are borne in mind.

vi) That, since the negotiation of prices may sometimes fail to result in agreement, a procedure must be available to which the ministers may have recourse and that the ministers should consider amendment of the National Health Acts to bring the General Medical and Pharmaceutical Services within definition of 'services of the crown' for the purposes of Section 46 of the Patents Act, 1949.

vii) That the Commission should prepare a 'control document' for a product on the basis of information submitted in prescribed form by the manufacturer. The Commission might also introduce an abbreviated control document to facilitate the control of advertising.

viii) That all advertisements for licensed medicines should be wholly consistent with the control document.

ix) That no product subject to the licensing procedure should be advertised until a copy of the control document has been sent out to all practising doctors and pharmacists.

x) That as soon as the Commission has established procedure for dealing with advertisements relating to new pharmaceutical preparations, it should consider to what extent they should apply to existing products advertised to doctors. (Sainsbury Report, 1967, p. 1-3)

The Committee gathered information from diverse sources including the pharmaceutical industry, research houses, factories and specialists and general practitioners from the UK, USA and Switzerland. The primary focus was whether or not drugs were unreasonably priced resulting in drug companies making excessive profits. Furthermore the Committee sought to establish whether the industry's research effort is relevant and viable and whether the methods employed in the sale and distribution of drugs are appropriate (Sainsbury Report, p. 5)

The profitability and operational aspects of firms were scrutinised and a robust stance was adopted against companies who reflected substantially high profits. In one instance, a severe view was taken against the drug manufacturer Beecham because of their high drug prices and large

profits (Corley, 1997, p 21). Furthermore, the Committee were resolute that Beecham had spent relatively little on scientifically based R&D compared to that of marketing and sales.

The Committee also argued against the government control of drug profits, as observed by Earl-Slater (1967), who also points out that the concept of reasonable price is an ongoing discussion. Moreover, he identifies seven problems which are endemic with the pharmaceutical regulations ranging from lack of robust reasoning, theoretical basis, empirical basis, transparency, due process and an impact analysis.

The Committee considered a policy of nationalising the pharmaceutical and healthcare industry but abandoned the idea. However they did recommend that a Medicines Commission be set up in order to supervise the manner in which drugs are introduced, promoted and marketed. The findings of the Committee revealed that the "industry was out of control, that the market was 'flooded with undesirable drugs', and that the NHS was paying for them" (Rawlins and Medawar, 1998, p.1). The recommendations played a vital role in promulgating the *Medicines Act of 1968* in Britain. This Act was a first step in the regulation of the pharmaceutical industry in a constructive manner.

In retrospect, it is beneficial, at least to British society, that the Sainsbury Report did not have any legislative muscle to completely entrench its recommendations since its impact on prices would have been profound. The focus tended to rely too heavily on controlling the prices of drugs through regulation. Danzon (2000) has showed, albeit subsequently, that the prices of innovative drugs tend, in the long-run, to be cheaper in countries that have free pricing as opposed to countries that have restrictive pricing regulations.

The Sainsbury Commission did impact positively in some ways. Primarily it set the foundations for the formation of the Voluntary Price Regulation Scheme (VPRS) which subsequently became the Pharmaceutical Price Regulation Scheme (PPRS). This body regulates profits. It permits new drugs to be freely priced provided total company or specified product profits remain within a range of 17.5% to 22.5% of sales which are not normal profits. Ramsey pricing structures are the implicit basis of these recommendations.

Despite the Kefauver-Harris Amendments and the Sainsbury report, the USA does not and the UK does not impose stringent control on drug prices. The UK has moderate controls- which

results in profits from constrained Ramsey pricing. Competition is buoyant, the market forces of demand and supply would settle on pricing levels and R&D would be encouraged. The control of prices through regulation (Italy, France, and Japan) can also keep prices at a sustainable[21] level in the short run. It does, however, imply that there would be fewer funds deployed to R&D by the manufacture's because the return on investment is low. As Ruwart concludes, there is also a social welfare need that has to be addressed

4.3 The South African Experience

As in the US, pharmaceuticals as a cost factor in the healthcare equation have received a great deal of attention from both health authorities and users in South Africa. As mentioned earlier in this dissertation, a number of commissions have investigated the pharmaceutical industry in recent years. The SA pharmaceutical industry has had its share of investigations, too, including: the *Report of the Commission of Inquiry into High Cost of Medical Services and Medicines* in 1962 (the Snyman Report); the *Report of the Commission of Inquiry into the Pharmaceutical Industry* in 1978 (the Steenkamp Report); the *Interim Report on Pharmaceutical Services* in 1985; the findings of the Melamet Commission; and *the Medicines and Related Substances Act (Act 90 of 1997),* which was eventually promulgated as an amendment to the *SA Medicines and Related Substances Act, No. 101 of 1965*.

4.3.1 The Findings and Recommendations of the Snyman Report (1962)

The authors of the Snyman Report conceded that the pharmaceutical industry had made great strides towards building the health of SA, in particular with the introduction of new and innovative medicines. The report also noted that there had been a remarkable decrease in the number of deaths from infectious diseases, as well as earlier recovery of patients, and lower demand for hospital beds (Snyman, 1962, p.188). The commission furthermore identified the following factors in the price structure of medicines:

i) Export prices, where control is beyond that of the importer;
ii) Customs tariffs, which amounted to about 20% of the normal wholesale price. The commission concluded that there was no justification for import duty on essential medicines that could not be manufactured in South Africa;

[21] The healthcare systems from these countries draw up budgets regarding what can be spent annually on various medical interventions. The amount spent on drugs has an annual limit. Through regulation and price controls, these healthcare systems are amongst those that attempt to get the most value in the short run, which in this case is considered to be one year.

iii) Local transport costs, which fluctuated between 5% and 25% of the drug;

iv) Importers profit margins, which were set overseas;

v) Wholesale profit margins, which amounted to 15% of the retail price; and

vi) Retail trade prices, estimated at about 50% of the retail price.

The commission noted that it was concerned about the multiplicity of identical compounds on the market and called for this practice to be curtailed. Among the recommendations made by the commission, the following are pertinent to the discussion here:

Recommendation 32

The Central Board of Control of Medicines should fix and limit the permissible number of identical preparations. This issue had implications in that it could impact on the development of generic medicines and keep upward pressures on innovative drug prices high. The board was eventually established in terms of the Medicines and Related Substances Act, Act 101 of 1965 and called the Medicines Control Council.

Recommendation 33

The commission devoted attention to better siting of pharmacies within communities and considered the contribution of pharmacists by canalizing medicines through pharmacies, which could only be achieved if no other business other than a pharmacy is allowed to sell medicines within a certain distance of an established pharmacy. The decision had implications for the amendments of Act 101 in 2004, where the issue of doctor dispensing licenses was dealt with as well as that of the single exit price (SEP) and capped dispensing fee for pharmacists. A detailed discussion of the 2004 amendments will be undertaken in Chapter 5 of this paper.

Recommendation 41

Patent rights on medicines should be maintained for a period not exceeding five years and when a patent is granted only the generic name of the preparation, followed by the name of the company concerned in brackets, should be granted. There is a clear indication that the issue of patent rights of manufacturers was seen as a problem by the commission. Patents, at that stage, were held for sixteen years and it was viewed that manufacturers exploited this patent in order to employ monopolistic pricing.

Recommendation 46

The commission recommended that all white (taxable) citizens, regardless of income, should join existing or future schemes providing medical cover.

Recommendation 47

Compulsory membership of funds for all employees should be made as a condition of service of the various public authorities.

These final two recommendations called for mandatory cover of white income earners. Mandatory cover is currently being touted as a progressive step in some quarters of the medical schemes industry.

4.3.2 The Findings and Recommendations of the Steenkamp Report

The Steenkamp commission deliberated on a number of different issues regarding the pharmaceutical industry but its primary purpose was to assess the manufacture of drugs in SA and analyse the requirements for enabling this manufacture. Aspects of the investigation included raw materials required, patent legislation, exports, prices and associated factors and finally, joint purchasing of public requirements. The commission also discussed the possibility of reducing the rate of increase in medicine and developing a domestic industry, suggesting that measures should address the healthcare situation as a whole, rather than considering a single aspect in isolation (such as pharmaceuticals).

The commission considered the physical possibilities of developing a local manufacturing industry. Although it felt that South Africa was on the verge of significant progress in this area, the commission pinpointed a number of economic factors that could hinder the process. A lack of a strong domestic market was one such concern, particularly because of highly skewed income distribution patterns in the country as evidenced by the Gini Coefficient. A measure of health and income inequality, the coefficient takes 0 to mean perfect income equality and 1 to mean perfect inequality. The Gini Coefficient for SA reached 0.68 at its peak. Local demand for high-cost drugs was thus limited to a small group of people. The fact of a higher local price (compared with international prices) meant that exports would be limited.

One of the commission's most pertinent observations was regarding patent rights. The commission quotes healthcare economist Duncan Reekie in saying that patent rights encourage innovation (Steenkamp, 1977, p. 44). The observation is made that no company can sustain the costs (*e.g.* research or marketing) of introducing a new and innovative drug when a competitor can simply copy the drug and recoup its profits. The commission went on to support the view, widely held at the time, that patent protection should be extended to twenty years depending on the product. The proposals were in line with then-contemporary thinking in Europe. Another recommendation (internally inconsistent) that was made in the Steenkamp report was the introduction of price controls, to limit monopolistic behaviour on the part of manufacturers and distributors. It went so far as to suggest that a statutory body be established to investigate monopolistic conditions (Steenkamp, 1977, p. 48).

A desirable policy measure was that government policy should be encourage market transparency, rather than intercede with price. The follow-on effect would be an improvement in competition. The report findings supported the need for more market transparency via the restriction of 'non-market' related practices. Examples included 'sampling and bonusing', a practice where 'free' samples are given to practitioners in order to 'encourage' them to prescribe a particular manufacturers' product. Add to that, the excessive promotion material produced by the manufacturing companies allegedly reduced both transparency and competition in the marketplace. This perception does create a moral dilemma; Does one allow for more advertising which would invariably dissipate more information? More information creates a greater level of understanding and subsequently a greater level of transparency. In an ideal economic paradigm, perfect competition occurs in a situation where there is perfect information. One can thus infer that greater transparency is synonymous with greater competition.

Coase surmised that for parties involved in a negotiation for exchanging their respective property rights, the parties involved need to be fully informed about the situation at hand, both in terms of *ex post* and *ex ante* costs. To restrict the flow of information through restrictive advertising practices would imply that consumers would not have the requisite amount of information in order to make an informed choice, thus compromising social welfare. A simple example would be when a physician prescribes a certain drug for a patient to use. If the patient has an allergic reaction to that particular drug, then the patient can inform the physician who can change the prescription. Had the patient not been informed and developed an allergic reaction, there would have been a welfare cost to society. The Steenkamp Reports recommendations in this area, consistent with that of the Sainsbury and Kefauver recommendations would ultimately, in the long run, lead to structural inefficiencies in the purchases of medications.

The purchase of generic products by the state and provincial departments was also highlighted by the commission (Steenkamp, 1977, p. 65). Although the commission supported this proposal, it felt that the matter required further investigation.

The relevance of the Steenkamp report to the discussion at hand is primarily its acknowledgement that patent rights do encourage innovation and thus should be promoted, although weighed-up against the need to reduce costs for the patient. The commission was likewise aware of the ability to adopt monopolistic pricing that patent protection permits.

For the research here, the key question is whether or not the findings of the Snyman and Steenkamp commission are relevant for a Coasian approach to pharmaceutical pricing. Bear in mind that a Coasian solution presupposes agreement between parties to a transaction. The *ex post* costs associated with supplementing the supply of drugs by encouraging local discovery of innovative drugs would arguably lead to a failure of the Coasian solution. If discovery of innovative medicines were to occur in South Africa under a licensing arrangement, then the costs of the associated R&D would likely be prohibitive such that it would not be a viable option to undertake such an endeavour. There is currently a lot of work done in HIV/AIDS research, but the primary source of innovative medicines still remains America, Asia and Europe. South Africa has substantive production facilities and has been sufficiently competitive to be able to enter the export market in pharmaceuticals.

4.4 The evaluation of pharmaceutical pricing methods - experiences from Australia and Canada

The SA commissions discussed above made the point that information on efficient drug pricing is crucial for policy-makers to design a healthcare system in line with the country's healthcare objectives. This is where the Coasian and Williamson arguments regarding transaction costs (as described in Chapter 2) can best be demonstrated. They believed that in trying to ascertain which of the available drugs work most efficiently, money would need to be spent to achieve an efficient outcome.

Towse (1977) however argues from a more traditional point of view. He disaggregates the idea of 'efficiency' into two categories: *allocative* and *productive* efficiencies (1997). Allocative efficiency is achieved through a mix of outcomes that is based on what society wants, i.e. how consumer valuation is reflected in product prices. Productive efficiency is simply achieving the outcomes at the most cost- effective manner, i.e., the prices that permit profit over costs. Towse, in an attempt to measure the value and quality of life, uses the concept of the Quality-Adjusted Life Year (QALY). It was useful in ascertaining the success of an intervention through measuring the outcomes based care.

Outcomes from treatments and similar health-influencing pursuits comprise two basic components: the quantity and quality of life. Costs are measured per Quality-Adjusted Life Year (QALY), which is designed to combine both the quality and quantity of life. QALY however is undoubtedly a crude measurement. As Towse himself explains, " …costs per QALY thresholds and

QALY maximization objectives will, if met, lead to productive efficiency (for a given drug), but only to allocative efficiency if the sole objective of the healthcare system is to maximize health gain, irrespective of whether some patients or diseases are left untreated as a consequence", (Towse, 1997, p. 64).

Furthermore, health policy – to be allocatively efficient – needs to assess *inter alia* economic observations, social values, advocacy, views of lobby groups and political expediency. Economic evaluations for instance could be used to enhance productive efficiency, which in turn yields production efficiency, and could add value by supporting allocative decision-making. Measures to enhance productive efficiency gains in the short-run may also be employed, including an increase in generic prescribing, or reducing repeat-prescription. The short-term implications of reducing pharmaceutical prices may be attractive to payers, as proposed in the current legislative paradigm in South Africa, but brings up the possibility of sacrificing longer-term 'dynamic' benefits for short-term 'static' gain. Towse describes *static* efficiency as realising productive and allocative efficiencies from available resources. *Dynamic* efficiency he defines as realising the best outcomes over time.

The use of economic evaluation of pricing structures raises two issues. The first is the efficient pricing in pharmaceuticals and the second is the timing of economic evaluation. A product can be priced in a range bounded by the 'bottom' end and the 'top' end, where the bottom-end is a range of prices approximately equal to the marginal cost of production. Pricing can be considered cost-effective if it is skewed towards this lower end. Under this scenario however the manufacturer would not realise sufficient returns on its sunk costs, and particularly its investment in R&D. The top-end is where prices equate to the value of health benefits that society pays the manufacturer. Ideally, the price of a drug should be bounded by these two extremes. The precise setting of the price is a judgement call between balancing society's willingness to pay for the drug and the importance of encouraging pharmaceutical innovation. Simply put, it can be seen as a trade-off between static and dynamic efficiencies. Ultimately the trade-off is determined by the willingness of patients to purchase more expensive drugs because of perceived better outcomes, in addition to the degree of competition (Towse, 1997, p. 65). Efficiency in pricing can be used to influence the economic evaluation and favour a policy of lower prices to maximise static efficiency.

The second issue for dynamic efficiency stems from timing – specifically when the economic evaluation is conducted in the continuum of the drug pricing procedure. In addition,

cost-effectiveness may differ from clinical practice to results achieved in the clinical trials, as the drug could be used for different patient groups or for different treatments than originally intended (Towse, 1997, p.64). The quantum of cost-effectiveness may differ in real life from those of the clinical trials for two reasons:

i) The cost-effectiveness could deviate from cost-efficacy because of inconsistencies between actual experience and drug trials, caused by a number of factors including accuracy of diagnosis or patient compliance; and

ii) The constant evaluation of the drug could result in additional patient responses being collected, thus reflecting a different outcome.

Such inconsistencies highlight the fact that healthcare decision-making about price occurs in a second-best situation where guidelines intended to achieve efficient results can be constrained because other areas of the healthcare system are inefficient.

4.4.1 National healthcare systems in Australia, Canada and the United Kingdom – ascertaining value for money in pharmaceuticals

Australia, Canada and the UK each use the economic evaluation of pharmaceuticals in order to determine what the payment of drug therapies by their national healthcare system would be. Although such methods are typically used in the public sector, they have significant implications for the private sector in South Africa because of the dual healthcare system with both public and private streams. Drugs are sold at public sector prices to the government via a tender process and at a supposedly marginal cost level. The same drugs are sold to the private sector at higher prices in order to recoup sunk costs, as it is claimed (Appasamy and Riding, 2004, p. 1), to private sector buyers. Private sector prices are directly linked to public sector prices. It may be useful to consider the methods of reimbursement used in other paradigms.

4.4.1.1 The Australian Experience

Australia requires that companies provide an economic evaluation of any new medicine if they want to be listed on the Pharmaceutical Benefit Scheme (PBS), which is a public reimbursement scheme that handles about 90% of the Australian prescription pharmaceutical market (Towse, 1997, p. 65). Guidelines for information on a specific drug are published by the government. Based on this, and economic evaluation, the drug may be listed for reimbursement

purposes by the PBS. Economic evaluation further assists in establishing a price for the particular drug when it is listed. The evaluation and related price-setting exercise are the primary mechanisms used by the Australian model to arrive at a 'value for money' level.

Drummond and Aristides (1997, p. 34) point out that possible delays and restrictions in getting a drug listed may result in preventable healthcare costs being incurred. They note that the PBS process is weighted toward static cost-effectiveness, rather than innovation and those new, innovative products are sometimes denied listing because they are not sufficiently cost-effective.

Towse refers to a study on the Australian pharmaceutical industry conducted by the Industry Commission Inquiry, an organisation that has published data on price trends. It shows that prices of new products in Australia are about a third lower than the world average. Further, it shows that the best-selling products in Australia are, on average, approximately two-thirds below world prices (Towse, 1977, p. 68). It has been argued that the use of economic evaluation as part of the price-setting process helps benefit the industry by rewarding innovation (Freemantle, *et al*, 1995). Economic evaluation has been responsible for pushing up prices in this environment compared to that in a more arbitrary regime; however, there was also the concern that economic analyses could be used as a cost-containment tool rather than an efficiency tool.

There are, however, a number of problems associated with this approach. Drummond and Aristides (1997, p.36) point out that if thresholds are used to calculate payouts, there would be an attempt to rule out expensive drugs for chronic ailments, even where these drugs could result in higher levels of health gain. The current medical scheme environment demonstrates this thinking. The medical scheme, under pressure to contain costs, would opt for cheaper, albeit less cost effective drugs and procedures, in order to maintain reserve levels[22]. An informal threshold furthermore could be manipulated. Higher-priced, newer products could be listed but may not be as cost-effective, or only be cost-effective at lower prices. The process is also susceptible to delays in market access for companies while the analysis is in process, thereby imposing a substantial cost to both the PBS and the applicant. The process falls short in its monitoring of the drug once it hits the market, especially in terms of competition from generic drug producers, parallel imports and

[22] In a conversation with a principal officer of a large open medical scheme, the point was made by the principal officer that it was not the schemes responsibility to see to social welfare. Rather, if the physician, employer or patient was of the opinion that an alternate drug or procedure (which usually has a higher initial and absolute price) provided a faster recovery time and greater social welfare, then those parties should pay for the higher priced alternative intervention.

provider prescribing practices. Towse nevertheless emphasises that there is no evidence that the rate of growth of pharmaceutical prices is slowing down.

4.4.1.2 The Canadian Experience

An economic evaluation in Canada needs to take cognisance of the guidelines developed by the Central Coordinating Office of Health Technology Assessment (CCOHTA). Although the guidelines are not prescriptive, they do require that funding and stakeholder details be disclosed, as well as ensuring that the project team has a certain level of independence (Buxton, 1997, p. 19). CCOHTA does however commission its own studies. There is also a national health technology assessment unit in each province and the CCOHTA liaises with the provinces in this matter.

Canada has a publicly-funded health system that includes a limited pharmaceutical benefit. The national prices are capped at a maximum set by a separate national body, the Patent Medicine Pricing Review Board (PMPRB). The board likewise sets prices for both the public and private sectors, usually setting the maximum price in both environments.

The *modus operandi* of the CCOHTA is that it requires an applicant of a new drug to submit an economic evaluation as a prerequisite to obtaining listing and subsequent reimbursement price of the drug to each province is based on a provincial formulary (Towse, 1997, p. 66). Canada has a federal system of government and each province gets reimbursed a portion of the provincial spending on each drug.

Buxton (1997, p. 23) concludes that economic evaluation will continue to have a significant influence on the pricing process in Canada, albeit in specific situations. Good economic evaluation will generate information that is relevant to local needs but in order to achieve this goal, the guidelines – as in the case of the CCOHTA (which is province specific) - need to be context-specific. Buxton (1997) goes on to say that even though the differences are unique in each situation, the CCOHTA guidelines encourage a culture of including economic evaluation in order to develop a price directive.

4.4.1.3 The UK Experience

The UK's National Health Service (NHS) controls approximately 95% of the UK prescription drug market (Towse, 1997, p. 66) and it lays down guidelines for economic evaluation (of new drugs) to be undertaken by those companies wishing to trade with the NHS. However,

companies are able to set their own prices for new drugs in their negotiation with the NHS. A profit control scheme, the Pharmaceutical Price Regulation Scheme (PPRS), regulates profits, permitting firms to freely set the price of new drugs, and hence, potentially compensate for lower-priced drugs if the company has no innovation. It allows for given, controlled profits for manufacturers and (what is perceived to be) affordable prices for users.

A cost to the consumer is a function of frequency and severity. The control mechanism for keeping medicine costs in check is to monitor the prescribing budgets of the general practitioner (GP) and this is accomplished through a series of reports reflecting budget comparisons. The alternate approach used is to give the budget holding GP's to GP's who will retain surpluses. GP's are also influenced by an NHS programme of research, review and dissemination of information relating to economic evaluations (Towse, 1997, p. 66). The budget approach is similar to the mechanism used in France where each provider group is provided with a national budget. Similarities can also be drawn with the medical schemes in South Africa using the medical savings account.

The introduction of budgets passes the responsibility of cost containment and risk-sharing to the GP. The NHS system appears to be succeeding in getting the message across, as seen in the growth of prescribing of generic medications across the national healthcare system. The budget holders reduced their drug costs more than the non-budget holders as reported by the GP group (Towse, 1997, p. 66). Towse notes that one of the key concerns is that prescribers often do not see the value of economic studies and this could partially be due to the fact that there is a lack of relevance to the local situation, or a view that cost effectiveness is not an important decision making criterion. This is the revered doctor-patient relationship, one that requires the best healthcare at all costs.

The pricing of pharmaceuticals, primarily if it is positioned above the short-run marginal cost level, is contingent on the public sector costing structures - as has been illustrated by the Towse discussion above and the Reekie discussion in the previous chapter. This occurs in many countries that operate on a government run public healthcare system. The government's involvement in healthcare (as in Canada) allows it to become a monopsonistic purchaser of drugs. Economies of scale would dictate that the selling price to this purchaser would be as close to or equal to the marginal cost of production. This issue of Ramsey pricing is raised in the Canadian market, which has a large, affluent middle class who are able to afford the price of drugs. The

uniform price structure, although lower than what manufacturers would like to price their products at, would still tend to alienate the less affluent pockets of the population. Ramsey pricing is non-existent.

4.4.4 Concluding remarks

In summary, the legislative concern of drug pricing began in earnest with the Kefauver recommendations to the US Senate, and gained *gravitas* with the Sainsbury Committee report to the British Parliament in the 1960's. Arguably, these were two of the more prominent markets regarding drug pricing regulations in the world and their actions did spill over into and subsequently influence other markets. South Africa had its experience with a number of investigations into pharmaceutical pricing, including the Snyman Report in the 1960's and the Steenkamp Report which were discussed here. It is important to note that many of the issues, including the single exit price and dispensing fee control, investigated by these commissions (such as the Snyman and Steenkamp Commission) were primarily driven by pressure from the higher income groups who dislike paying more for health services and drugs than the lower income groups.

More legislative issues will be examined in Chapter 5 including the pricing of drugs being dependent on factors including the markets, the public sector infrastructure, and patent protection. The Coasian Theorem stipulates that for an efficient solution to exist there should be an exchange, a critical level of harmonisation or agreement between these parties. It is therefore important to appreciate the forces that influence pricing structure.

CHAPTER 5

A Review of the Regulatory and Environmental Constraints on Pharmaceutical Pricing

5.1 Introduction

Building on the theoretical and historical lessons gleaned in the preceding three chapters, this chapter turns to the market that includes both the private and public environments within which drugs are priced in South Africa. An initial priority will be to explore the competition agenda in South Africa, with specific reference to price collusion. The market dilemma is whether collusion on any level is regarded as anti-competitive. Examples include price parallelism, price uniformity, pricing transparency and specific price differences. The letter of the law appears to lend support to the interpretation that most forms of information sharing is collusion and hence anti-competitive. Previous research suggests that two mechanisms play a role in the regulation of prices: namely, competition and legislation. Price structures are built on a web of relationships between various stakeholders in the healthcare industry. In the prevailing environment, the Competition Commission uses the Competition Act (Act No. 89 of 1998) to investigate price collusion between private sector stakeholders, including inter alia bodies such as the Board of Healthcare Funders (BHF), the Hospital Association of South Africa (HASA), and the South African Medical Association (SAMA). The effects of the Competition Act (Act No. 89 of 1998) on drug pricing will be explored.

Apart from the risk and monitoring of collusive behaviour, the healthcare industry faces a changing regulatory environment that impacts the pricing of drugs. South Africa's public sector healthcare policies in the past decade have been strongly influenced by the Department of Health's initial White Paper (1997), which sets out the broad-based long term goals of the ministry. The proposed reforms were substantial, the goals and objectives are listed below:

i. to unify fragmented health services at all levels into a comprehensive and integrated National Health System;
ii. to promote equity, accessibility and utilisation of health services;
iii. to extend the availability and ensure the appropriateness of health services;
iv. to develop health promotion activities;

v. to develop human resources available to the health sector;
vi. to foster community participation across the health sector; and
vii. to improve health sector planning and the monitoring of health status and services.

The critical aspect of the policy is that it overlooked a basic economic tenet - the scarcity of resources. In attempting to fulfil its noble and admirable reforms, the opportunity cost of such reforms needs to be considered. Primarily, the more accessible healthcare becomes, the greater the size of the financial burden is on the government. The Minister of Finance, the Hon. Trevor Manuel, has indicated that this is a problem when he was speaking about changes to the private healthcare system (BHF conference, Namibia, 2002). Moreover, the national budget for healthcare has been progressively reduced over the past four years and as such presents a double-pronged dilemma – less money and more people to treat.

The question as to how this situation impacts upon pharmaceutical prices is somewhat perplexing. The Department of Health, faced with smaller budgets and greater number of patients to sustain, would be placed in a position to obtain resources from other areas; either negotiate the purchases of goods and services at a lower price using its monopsonistic leverage or cut back on its range of services and introduce a minimal 'co-pay' for all services rendered. The department has, as the pharmaceutical manufacturers allude to, chosen to intensify its negotiation around the purchases of drugs. In turn these manufacturers increase the price of drugs to the large purchasers of drugs in the private sector, i.e., the hospitals and the pharmaceutical retailers. This is a world-wide phenomenon and both Scherer and Danzon have referred to the role that the government plays in influencing the price of goods. An indirect (and simplistic) interpretation would be that the greater the pharmaceutical manufacturers' cut is to the national purchaser (above marginal cost), the higher the selling price to the private sector purchaser – which is the free market price since the public goods are not traded.

The past ten years has also seen private healthcare undergo some dramatic changes, not least because of the Medical Schemes Act (1998) which resulted, *inter alia*, in the advent of the Prescribed Minimum Benefits (PMB's), in the enforcement of the previously unenforceable, the minimum reserve levels that schemes need to hold and the introduction of the new investment guidelines for schemes. These factors all need to be scrutinised and applied to the question of how price structures are influenced by the regulatory environment. The writer also intends to explore the link between market regulation and innovation by assessing the effect of government price

regulations on drugs on the cost and quality of healthcare such as incentives for R&D in drugs, and the problem of indirect impact, as researched by Kessler (2004).

Another component of the discussion around drug price regulation in South Africa is the development of national health reference price lists and, critically, the impact these could have on free market operations (Magennis, 2004). As has been pointed out, relationships between private sector stakeholders, prior to the intervention of the competition authorities, were characterised by each trade organisation, the South African Medical Association (SAMA), the Hospital Association of South Africa (HASA) and the Board of Healthcare Funders (BHF) producing their own negotiated price lists. These relationships have subsequently shifted as the competition authorities charged that these negotiated price lists were anti-competitive. The writer will analyse the issue of how these shifting relationships drive prices. An additional area of analysis is the delivery costs of medical services, mainly in the private sector (BHF, 2004; CMS, 2004) and their role within the wider *milieu* of factors affecting pricing and possible policy directions.

5.2 The Medical Schemes Environment

Perfect competition occurs in an environment where there is availability and access to perfect information. The healthcare industry has, in many instances, exhibited non-competitive behaviour. In the patient-practitioner relationship, the patient is in a weak bargaining position (the patient would tend to follow the advice of the practitioner) because of informational asymmetries, and this is particularly true in a fee-for-service (FFS) environment where there is a principal-agent relationship between the patient and the physician. It is not in the interest of the physician to limit medical interventions. Another case would be the medical scheme-private hospital scenario. The informational asymmetries allow the hospital to charge as it pleases with very little rebuttal from the medical scheme. This scenario forces the medical scheme into a position of a price-taker as opposed to that of a price-setter. Reekie (1997b) describes it as an *agency problem* (emphasis added by writer). In the long-run, the medical scheme would be regarded as a cash cow by large enterprises such as hospitals. In order to maximise the amount it receives from a medical scheme, it is imperative that these enterprises charge the same fee for services so that any form of bargaining on the part of the schemes is obviated.

Furthermore, there are two key reasons why the patient does not challenge the charges of the service provider: firstly, the patient is in a weaker bargaining position and secondly the patient

enjoys third party payer status in that the medical scheme would settle any outstanding payments. There appears to be no perceived value in challenging the system. Such a situation creates the circumstances for monopolistic pricing structures to emerge, replacing any competitive price structures and ultimately allows for oligopolies and cartels to develop. The most overt example of this is the rapid growth and development of the private hospital sector in South Africa. The cost of this falls back to the patient through the cyclical relationship which warrants that the patient (consumer) ends up paying for these charges through increased medical scheme contributions. Baumol[23] raised the argument in his dual economy theory- the service sector and the production sector. Increases in the production sector occur steadily whilst that of the service sector tend to lag behind because of time constraints. With the service sector lagging behind the production sector, a threshold is reached resulting in the service sector increases being substantially more than that of the production sector. This is the phenomenon that we are currently seeing in the healthcare sector. This will continue as long as the production sector becomes more efficient.

The Competition Commissioner (CC) needed a cause to investigate the private healthcare sector and the spiralling prices gave the Commission the reason. The Commission was established in 1999 by the Competition Act, No. 89 of 1998. The Commission, armed with this Act, began to flex its muscle regarding anti-competitive behaviour. The private healthcare sector displayed an endemic problem of steep price increases. The BHF Annual Survey of Increases reflected that medical scheme contribution increases were literally double that of headline inflation for the years 2001 to 2004 (Appasamy, 2001b, 2002b, 2003b, 2004b). A number of practices in the healthcare industry were not seen to be in the interests of the consumer. The Medical Schemes Act 131 of 1998 introduced a number of the concepts that were originally mooted in the National Health Plan such as open enrolment and community rating for members of medical schemes. It introduced the first set of Prescribed Minimum Benefits[24] (PMB's) that schemes had to offer as part of their benefit options, and also introduced the date that medical schemes had to achieve a minimum solvency level (25% by 31st December 2004). In addition, these regulations reversed the schemes ability to manage risk in the manner that they have previously done. The restriction on investments and the restriction on medical savings accounts leading to the current proposals to phase out medical savings accounts. The medical schemes reaction to the burgeoning benefit structures and

[23] In discussions with Professor Reekie who broached the issue of service sector salaries.
[24] The Prescribed Minimum Benefits (PMB's) are a group of 270 treatment pairs that each scheme has to offer all of its members. Furthermore, these conditions have to be paid for from the explicit risk pool and not from the medical savings accounts (MSA). The PMB's are a community and not an individual risk, hence all medical schemes need to offer then as part of any benefit package and pay for them out of the schemes risk pool rather than from an individual's MSA.

greater fiscal restraint was to increase premium contributions at rates that exceeded any inflation index (see Table 1 below).

The medical scheme quandary is exacerbated by the agency problem and the price-taker status. In a fee-for-service environment, the provider of service has no incentive to save costs, neither does the patient who enjoys 'first-rand cover' (cover without any co-payments or deductibles) and the administrator to the scheme also has no incentive to cut back on cost since their business model is structured on the number of claims processed (Reekie, 1997, p. 297). Add to that the increasing spend on private hospitals (approximately half of which is in the form of pharmaceutical charges) and pharmaceuticals, also creates upward pressure on contribution increases.

Table 1

Medical Schemes			Private Hospitals			Pharmaceuticals		
Year	Contribution Increases	CPIX	Annual Spend	Year on Year % Change	Percentage of Total Spend	Annual Spend	Year on Year % Change	Percentage of Total Spend
2000	10.54%	7.80%	R 8,260,725	8.70%	30.42%	R 7,311,690	5.00%	26.92%
2001	19.60%	6.60%	R 8,987,929	8.80%	29.12%	R 7,929,897	8.50%	25.69%
2002	16.40%	9.30%	R 11,436,297	29.40%	35.70%	R 8,656,021	5.60%	24.28%
2003	12.50%	6.80%	R 13,283,344	15.80%	34.33%	R 8,617,709	-4.00%	22.27%

Source: Council for Medical Schemes, Annual Report 2004

Pharmaceutical companies, prior to the introduction of the single exit price (SEP), engaged in a system of sampling (the free supply of medication from the manufacturer to the dispenser) and bonusing (a rebate or bonus system). This was a case of anti-competitive behaviour, particularly when it became the *modus operandi*[25]. It was this behaviour that drew the attention of the architects of the ANC's document on the National Health Policy and subsequently motivated the Medicines and Related Substances Control Act of 1965, as amended in 2001.

Table 1 above also highlights the point that the pharmaceutical and hospital spend make up the bulk of the total spend in the industry. The demand for first generation innovative drugs and what the hospital industry considers 'first-world hospital services of the highest standards' is primarily induced by the supply of these services. The system of referrals by the primary physicians to specialists associated with a particular hospital shows that there are unnecessary

[25] In an interview with Ms Maureen Kirkman in 2003, the then CEO of the Pharmaceutical Manufacturers Association (PMA), Ms Kirkman indicated that she had received complaints that one of the private hospital groups used its oligopolistic power and demanded these rebates. If these rebates were not forthcoming, then the hospital group refused to see these manufacturers' representatives and also refused to make any purchases from them. Such a situation could be considered as anti-competitive behaviour.

services being rendered. One example is the rate of Caesarean procedure births (C-Section) being performed. The South African private sector has a rate of approximately 63% of birthing being done in the C-Section compared to an average in North America and Western Europe (similar socio-economic homogenous populations) is approximately 19% (World Health Report 2000). Another example are newspaper reports in June 2000 of pathology laboratories giving kickbacks to general practitioners for higher volumes of blood tests (*The Star*, June 2000,). Given the situation of supply induced demand, these two areas have traditionally been regarded as the primary drivers of high prices in the private sector (Appasamy and Riding, 2002, p.14).

An important consideration when discussing prices is that the private sector accounts for approximately 60% of the total healthcare budget (BHF 2002, CMS 2002). The disparity could be partially explained by the fact that there is a level of cross subsidy of state purchases by the private sector, and this cross-subsidy is reflected in their pricing structure[26]. The State, through the National Department of Health, purchases approximately 70% of the medicines used in South Africa. The State uses its monopsonistic capacity to purchase drugs at a price level that equates to the current levels of the marginal cost of production. Drug companies, in order to recover some of their 'losses', inflate their selling price in the private sector. This may be considered as a form of Ramsey pricing, however according to Danzon (1998), this form of pricing does not seek to extract monopolistic profits but rather to make normal profits. Hence the pricing structure may be considered to be monopolistic pricing, but in actuality it is a form of Ramsey pricing.

The practice has come to the attention of the Competition Commission and its ensuing action highlighted the issue of abuse of market dominance. The Commission investigated a complaint by the Ms Hazel Tau and ten others, including the Treatment Action Campaign (TAC) against GlaxoSmithKline (Pty) Ltd (GSK) and Boehringer Ingelheim (BI) pertaining to anti-retrovirals in 2003. GSK is the world's largest producer of AIDS medicines and has 50% of the world market (Baker, 2003). The Commission found that the two companies abused their dominant positions in their specific anti-retroviral markets (CC, 2004) and referred the case to the Competition Tribunal. The Competition Commission has found that pharmaceutical firms GSK and BI have contravened the Competition Act of 1998. The firms were found to have abused their dominant positions in their respective anti-retroviral (ARV) markets. "The Commission found that the firms engaged in the following restrictive practices:

[26] Interview with Ms Maureen Kirkman, CEO of the Pharmaceutical Manufacturers Association (PMA), in 2003.

i) Denied a competitor access to an essential facility;
ii) Excessive pricing;
iii) Engaged in an exclusionary act."

The Commissioner, Menzi Simelane, said that, "Our investigation revealed that each of the firms has refused to license their patents to generic manufacturers in return for a reasonable royalty. We believe that this is feasible and that consumers will benefit from cheaper generic versions of the drugs concerned. We further believe that granting licenses would provide for competition between firms and their generic competitors."… Simelane said these practices violate the Competition Act of 1998's prohibitions against excessive pricing (section 8(a)), refusing access to essential facilities (section 8(b)) and exclusionary acts that have an anticompetitive effect that outweighs technological, efficiency or other pro-competitive gains (section 8(c)". (Competition Commissioner Press release, October 2003 – see Appendix 5).

Both GSK and BI, facing the prospect of litigation from the Competition Tribunal, agreed to negotiate voluntary licences with generic manufacturers rather than face the possibility of compulsory licences (Baker, 2003). Seven licences were issued to generic manufacturers and the new licences will have the effect of significantly increasing access to these medications.

The finding of the Competition Commission represents acknowledgment of the Doha Declaration on TRIPS and Public Health. The Doha Declaration is a World Trade Organisation (WTO) agreement reached in Doha, Qatar that gave more consideration to public health concerns as opposed to absolute patent protection. Baker (2003) asserts that the decision by the Commission endorses three significant competition theories:

i) That the monopolistic pricing structures used by drug companies (for primarily patent protected drugs) can and will impede access to necessary drugs even if these prices are discounted.[27]
ii) The reluctance of the drug companies to issue voluntary licenses to generic manufacturers impedes competition.
iii) The refusal to grant voluntary licences has, particularly for treatments that require combination therapies, hinders the production of fixed dose therapies.

[27] Access is however contingent on the size of the discount.

Patents, by their very nature are anti-competitive, since they are exclusionary - they tend to impede or prevent firms from coming into, entering or growing the market. However, patents do not automatically mean that the patentee would enjoy monopolistic profits because the patented product could face competition from similar products already on the market. Furthermore, the product could be used to treat conditions, such as pandemics, where the afflicted population may not be able to afford the treatment. Baker (2003) asserts that whilst reaping the benefits of a patent might not be considered exploitative, excessive pricing policies and the refusal to licence may be considered anti-competitive behaviour in some situations. He contends that the "most encouraging pro-competition/public health arguments focus on both exclusionary and excessive pricing doctrine and on a resulting access/affordability gap for the product" (Baker, 2003, p.6). In the South African situation, the competition regulations are designed to discourage exclusionary acts. It is possible to argue that exclusivity, coupled with higher 'oligopolistic' prices, deny access to those who need the drugs. The resultant situation could be used as a justification for compulsory licenses. The case-in-point is that of the anti-retrovirals ruling made by the Competition Commissioner. Simple economic theory holds that generic drugs, when introduced in a market, would tend to be competitive and as such drive down the price of all drugs in that particular therapeutic class. The surrender by GSK and BI meant that cheaper, locally produced generic drugs have significantly influenced the timing of the ARV rollout in the public sector. A further consideration is that although GSK agreed to the compulsory licences, it had already made its patented drugs (for the treatment of HIV/AIDS) available at a price lower than the suggested UNAIDS prices. The South African government initially did not want to purchase these drugs from GSK, citing budgetary constraints and policy direction, but now appears to have no reason not to purchase the drugs.

Stakeholders of the private healthcare sector have enjoyed a longstanding, if somewhat consultative, relationship with each other. This relationship has grown organically, resulting in annual negotiations regarding tariffs or price. However, the three large medical trade associations, the Hospital Association of South Africa (HASA), the South African Medical Association (SAMA) and the Board of Healthcare Funders (BHF) were all investigated by the Competition Commission in 2003 and 2004 for price collusion in the setting of tariffs. This action changed the relationship between these groups. The Commission argued that the negotiations done on behalf of each group was tantamount to price collusion. Free market principles were being undermined by this negotiation process. Arguments from the stakeholders that a tariff was needed in the industry to ensure stability appeared to have gained some sympathy from the Commission; however, they recognised that a price guideline is necessary in the industry. This and this is called the National

Health Reference Price List (NHRPL) and is published by the Council for Medical Schemes (CMS). The associations agreed to refrain from publishing price lists. HASA were charged and found guilty of price collusion and had severe penalties imposed on it, including being fined, and similarly with SAMA. BHF, whose primary focus is the consumer, got off without a large fine and an agreement to investigate the economic impact of price collusion.

The reasoning behind the actions taken by the Competition Commissioner was too simplistic. Primarily, the Commission appeared not to have taken cognisance of the transaction costs involved in the healthcare situation that it was addressing. The purpose of the price negotiations between these associations was to facilitate a common price that would agreeable to all of the participants of the negotiations. A Coasian solution would have considered the *ex ante* costs of the negotiation and ascertained whether they were too expansive or not. A Coasian solution is not possible because the perceived added welfare to society may not materialise.

The action of the Commissioner, however, has had a minimal impact on the pricing structure of hospital prices in the short term. Even in an environment where direct collusive behaviour has been curtailed on the surface, the oligopolistic nature of the hospital industry has not resulted in any significant reduction in the total amount spent on hospitals in the short run. Some aspect of this is that cost is a factor of price as well as volume. The basic economic dilemma is that as prices fall, the quantity demanded for these services (goods) will increase, recreating the quandary that it originally set out to address. In an oligopolistic market, it is extremely difficult to establish a competitive pricing structure if oligopolists enter into some sort of collusive behaviour. It does however, set the base for a more transparent pricing structure going into the future. This policy creates a situation of greater information to the consumer (both medical schemes and patients) and may, theoretically at least, create a situation where the consumer does not have to be in a weaker bargaining position.

Consider the development of drug regulation in the current paradigm and the relative impact that it has had on the stakeholders involved. The framework of the current environment had been laid down by the African National Congress's (ANC) National Health Plan for South Africa (1994). The thrust of the ANC document was to re-focus the direction in which healthcare was delivered – to concentrate on health of the nation as opposed to medical care – and the healthcare approach was to be based on a Primary Healthcare Approach (PHA). There also appears to be a move away from the reliance on the form of treatment in favour of the PHA and in particular

moving away from drug therapy as is evidenced in "The National Drug Policy (NDP) will incorporate strategies for the effective application of drugs within the framework of the National Health Service (NHS). The promotive, preventative and rehabilitative aspects of healthcare will receive proper emphasis and will not be made subservient to the curative aspect, with its reliance on the use of drugs." (NDP, p. 23). This is an important aspect because it does influence the amount of *gravitas* the drug issue sustains in the legislative environment.

The proposed tenets of the drug policy included the increased use of generic drugs in both the public and private sectors, the development of the essential drug list, the promotion of the local drug industry and the procurement of drugs by the government at the best possible prices. Furthermore, the mechanisms that were mooted in order to translate the policy principles into regulations included the setting of a maximum drug price, non-discriminatory drug prices, parallel importation and a review of all drug prices. In addition, the proposals put forward a suggestion to investigate the feasibility of a National Health Insurance (NHI), a construct of health insurance of which medical schemes would form the basis.

The proposals addressing the broader healthcare environment impacts on pharmaceutical prices as will be demonstrated later in this chapter. The writer wishes to show that there have been endemic problems in the spectrum of healthcare delivery, and that the current regulations, at least to this stage, have tended to destabilise the industry, allowing for opportunistic pricing leading to monopolistic gains from trade in some sectors, particularly in the private hospital sector (as discussed above) and the specialist and pharmaceutical sectors.

In May 1997, the Department of Health under the leadership of Dr Nkosazana Dlamini Zuma, presented the White Paper on the Transformation of the Health System in South Africa (White Paper). The White Paper should be considered in conjunction with the NDP since together they form the basis of the healthcare programme for South Africa, and offer guidelines as to how pharmaceutical services in the country will be managed. In addition, the tenets of the White Paper and the NDP are in line with the guidelines published by the World Health Organisation (WHO: 2nd edition on National Drug Policy, 2001).

The White Paper attempts to deal with two major issues; First, it outlines a number of steps in the addressing the inadequacies created by the apartheid regime's delivery of healthcare. Second, it introduces the building blocks toward moving to a national healthcare system. In laying down the

foundation of the way forward, the NDP outlined specific objectives, categorised into the three areas of health, economic and national development objectives. The former two areas put forth the notion of an accessible and available essential drug[28] list would be made available to all citizens. It also requires that the rational use[29] of drugs by prescribers be promoted. Furthermore, the objective that the cost of drugs in both public and private sectors should be lowered is also considered.

Reekie, in his presidential address[30], commented on the essence and viability of the White Paper from an economist's perspective, focussing on the study of exchange. He espouses a Lockean view that natural rights are generalisable and non-contradictory (Reekie, 1997b). Healthcare, according to this benchmark, is not a natural right, since it pre-supposes that another individual needs to supply the requisite healthcare and as a result lacks that right to healthcare. The only rights that can be generalised are life, liberty and estates, primarily because they are available to all.

The thrust of the White Paper is to provide healthcare for all citizens, healthcare being considered to be a basic human right in the New South African Constitution. It is this idea or concept that is termed a 'positive' right. Reekie (1997b) raises the issue of the alleviation of socio-economic inequities, or the mechanism purported by the notion of 'positive' rights that the wealthy should give to the less affluent to the best of their ability. The dilemma still remains, 'Where is the threshold?'. Reekie (1997b) proposes four counter arguments to the 'positive' rights view, as follows:

i) The traditional view of healthcare should be refined, people strive for the best (and not second-best) that they can give themselves and that inequities are a result of successive (generations) voluntary trade decisions;

ii) The "…view that health care is a merit good, implicit in the positivist view, should be challenged." (Reekie, 1997, p.287). People do not have a choice regarding a merit good; it is made available by the governments for any of its citizens to use. An example being a system of highways for transport, public health systems or the police force;

[28] Essential drugs, as defined by the World Health Organization, are drugs that are required to treat the majority of conditions that are prevalent in a particular country. Since these drugs would be provided primarily by the public sector, they should be made available in a cost-effective and efficient manner. Furthermore, these drugs would predominantly be used by the bulk of the population in that country, requiring that their availability should be uninterrupted and dosages forms should be correct.

[29] Rational use of drugs refers to the use of drugs that are therapeutically sound and cost-effective when compared to other alternatives.

[30] Prof W Duncan Reekie, during his term as President of the Economic Society of South Africa 1995-97, September 1997.

iii) Externalities such as 'free-riding' impacts on 'positive' rights. Reekie argues that there would be no externalities if the provision of healthcare is treated as a public good. If there are free-riders, then there can be no efficient provision of the public good; and

iv) He argues that "…some minimum level of health-care provision is one where the political process as opposed to the market process has a role to play." (Reekie, 1997b, p. 290).

Furthermore Reekie makes the point that the objectives of 'equity' and 'access' fall within the confines of available resources and may not be possible at the margins since different diseases require different interventions, and hence different cost structures. He raises the dilemma that we could have equal outcomes, equal inputs and equality of care at the margins. The latter would maximise health outputs but the second situation of equal inputs is far more politically attractive. Hence it is easily concluded that the three situations are incompatible.

One can argue that a Coasian solution is possible in a market where one would be able to negotiate the value of one's healthcare package, particularly if it is not a merit good. This could be the direction in which Reekie appears to be heading.

The submission for rationalisation of price structure of pharmaceuticals included the establishment of a Pricing Committee that would investigate the viability of price transparency across the supply spectrum, including that of a single exit price. The Pricing Committee would also explore the feasibility of a non-discriminatory pricing system (non-Ramsey pricing structures), regulated price increase of drugs, state supply of certain high priced drugs to the private sector and a system where the single exit price and dispensing fee would replace the wholesale and retail percentage mark-up for drugs (NDP, p. 8). Moreover the NDP proposals also recommend the use of "…interchangeable multi-source pharmaceutical products (IMPP), using non-propriety name (INN), or generic name…" drugs in order to reduce drug costs and expenditure (NDP, p. 10).

Generic names will be used to draw up the Essential Drugs List (EDL). The EDL is designed to meet the needs of the bulk of the population, and has a default to the drug with the best cost advantage and the best locally manufactured drug amongst other criteria (NDP, p. 11). The NDP also proposes the strengthening of the role of the pharmacists in the dispensing of drugs, particularly in their role of informing and educating patients regarding their choices.

The *White Paper* resulted in a number of healthcare related Acts being introduced by the Department of Health through Parliament, some of the more significant being the National Health Act (Act No. 61 of 2003), the Medical Schemes Act (Act No. 131 of 1998) and the Medicines and Related Substances Control Amendment Act (Act No. 101 of 1965, as amended in 2001). These Acts can be seen as building blocks toward building the structures ultimately leading to a national health system. Although Act 101 (as amended) deals primarily with the pharmaceutical industry and the pricing structures, the sequence of legislative changes stemming from the White Paper need to be considered in their entirety.

Act 101 (as amended) introduces the EDL as a concept that will be compiled and published by the Department of Health at predetermined intervals. It also addresses the need for more affordable retail drug prices. The Act proposes a number of interventions that could be used by the Minister, the Director-General or the Department of Health:

i) by empowering the Minister to revoke the patent specific drugs that are required to protected the public should the health of the public be threatened and the specified drugs are required for treatment (s15C(a), (b), (c)); and

ii) by allowing the Minister to grant permission for parallel importation of these specified patented drugs (s15C(a), (b), (c)).

Furthermore Act 101 also addresses the bonus and sampling schemes that was endemic in the supply of medicines (s18A and s18B). There have been arguments in the pharmaceutical industry that this practice led to higher prices at the retail level.

Finally, one of the more litigious issues has been that of establishing a single exit price (SEP) by manufacturers and a dispensing fee for pharmacists as a percentage of this SEP (s 22(g) of the Act). The regulations have been challenged by a group of pharmacists and hospital groups who believe that the regulations are unconstitutional as they limit the right to earn a living on the part of the pharmacists. At the time of writing, the case was being heard in the Cape High Court where the Department of Health (DoH) was challenged by a consortium of corporate pharmacies that included New Clicks Pharmacies, Netcare Holding on behalf of their pharmacies and the Pharmaceutical Society of South Africa (PSSA). The Cape High Court ruled in favour of the DoH in September 2004. This decision was appealed by the complainants and in December 2004 the case then went to the Supreme Court of Appeals, which upheld the application by the complainants. The matter was subsequently heard by the highest court in the land, the Constitutional Court of South Africa in

March 2005. At the time of writing, the Constitutional Court ruled that the legislation is valid, but it has referred the legislation back to the DoH for re-writing. [31]

The broad-based challenge to the regulations is that it interferes with the normal market related economy in medicines and challenges the basic ethos of trade. Furthermore the advantages gained from economies of scale and economies of scope have been compromised by the regulations. The impact, its critics claim, would be that drug prices would tend to face an upward pressure since there are no discounts available.

At the initial stages of the proposals, the Competition Commission's Annual Report for 2002 also raised concerns regarding the issue that the SEP. The Competition Commissioner felt that the SEP might facilitate collusive price setting by manufacturers and a complex reimbursement structure further down the supply chain. There might be some truth to this.

HASA, in its submission document to BHF in August 2004, raised its concerns regarding price setting issues. Concerns centred on the unintended consequences of the price-setting regulations, specifically production distortions and limited access. HASA cites research from an article in the Economist magazine that draws from a Bain and Company study (Gilbert & Rosenberg, 2004) that Europe is a significant loser in R&D in healthcare and economic terms primarily because of price controls. The USA has grown into a far more dominant force in pharmaceutical R&D, creating greater economic spin-offs. Furthermore, price regulation impacts on access to drugs and tends to get to the market much more slowly. The resultant situation is that people spend longer periods in hospitals, have higher absenteeism rates in the workforce, and higher rates of mortality (Gilbert & Rosenberg, 2004). The Bain and Company study also makes assertions that price regulations have an indirect impact on innovation and tends to discourage competition.

The principal objective of price regulation is to reduce the price of the drug primarily in order to reduce the expenditure on healthcare delivery. Price regulation has two fundamental effects on the price of medicines. Furthermore, this effect may impact the cost and quality of

[31] It has been inferred or speculated that the Constitutional Court might adopt a 'wait and see' stance in order to allow for some sort of negotiation to take place between the various stakeholders in the industry at the time of the Constitutional Court proceedings. The decision reached by the Constitutional Court is that the legislation is valid, but it has given it back to the DoH for re-writing.

healthcare in two ways, and in each case the impact of price regulation on the well being of the patient is not fully understood (Kessler, 2004).

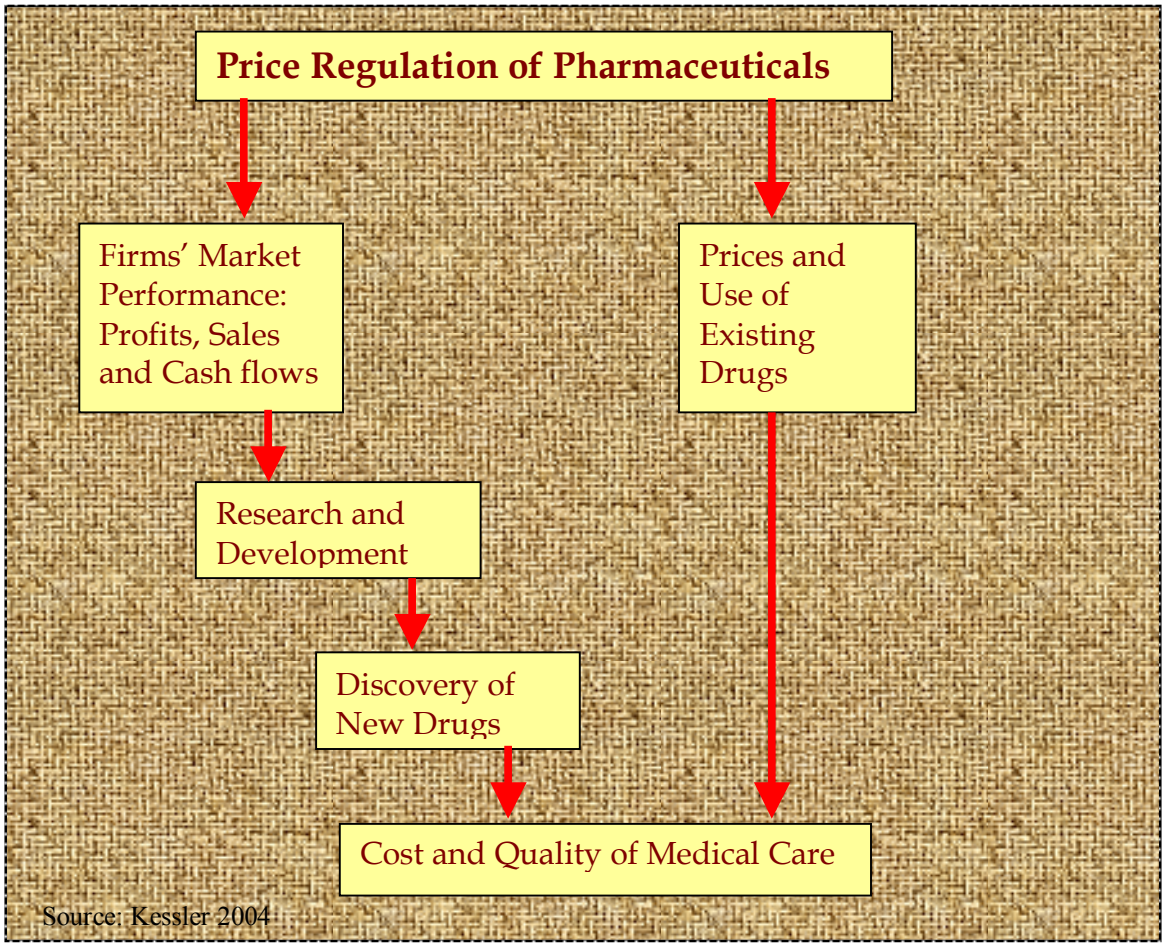
First, the immediate impact of regulation on drug development happens at the R&D project stage – that is projects that are being undertaken by the drug company. There is a general series of events. Regulation-induced reduction in pharmaceutical expenditure leads to lower profits and reduced cash flows for the pharmaceutical companies. This means lower profits and lower cash flows for the pharmaceutical manufacturing firm. Kessler (2004) refers to a study by John A. Vernon that suggests lower expected profits translate into a reduced supply of external capital which in turn means lower investment. This significant analysis indicates that if profits are held constant, "…then the lower expected cash flows translate into a reduced supply of internal relative to external capital, which may independently reduce investment, to the extent that the external markets are imperfect." (Kessler, 2004, p. 3).

A decline in investment into R&D may result in fewer new products being developed a basic linear relationship. Danzon (1997) is of the view that most price regulations result in fewer products being expanded. Furthermore, regulators are inclined to focus on the more prominent drug expenditures which tend to be those attracting higher prices or volumes. Danzon (1997) further asserts that many of these drugs are apt to be innovative or ethical drugs (that is, they are not generic drugs). In addition, a 'reference pricing' system – where a drug is costed and regulated at a certain level – tends to be biased against innovative drugs. Reduced R&D has two implications. It could lead to more or less cost-effective healthcare. The latter is the situation that results in higher mortality, morbidity and more healthcare expenses. The former occurs when the reduced spending on R&D exceeds the associated costs of not spending.

The second implication of price regulation is that the regulation may affect the quality and cost of healthcare through the use of existing products. Kessler (2004) contends that lower regulated prices may lead to lower per unit costs and therefore lower total healthcare costs. However, the inverse may also occur: Regulation could have unintended consequences for drug prices that may nullify intended benefits. Prices may actually increase: An obvious example is when the single exit price was introduced in South Africa, the associated regulations (Amendments to Act 101 of 1965) abolished the system of bonusing and rebates that were inherent in the pharmaceutical supply system. The implementation of the regulations resulted in the prices of many drugs increasing, particularly for chronic medication. Danzon, Wang and Wang (2003) point

out that firms may delay their launch of new drugs in regulated markets because of the threat that it may, through parallel importing, 'spillover' into unregulated markets at a cheaper price thereby undermining the price which the drug company expected to sell it.

Figure 5.1
The Effect of Government Price Regulation on Pharmaceuticals on Cost and Quality



One of the more divisive debates is the one that relates price regulation, market performance and the innovation of pharmaceuticals. Vernon (2003) investigates the relationship between price regulation and profit margins. In his study involving a sample of twenty large pharmaceutical firms over a five year period (1994-1999), Vernon found a significant negative correlation relationship between a firm's sales in a price-regulated environment and its pre-tax profits. He compared the level of sales from outside the USA to that within the country. He demonstrated that a ten percent increase in sales in price-regulated environments outside the USA

resulted in a 2.7% to 3.5% decline in the profit margin in the USA. In his later paper, Vernon (2004) expands his original analysis to show that declines in profit margins resulting from exogenous factors such as price regulation outside the USA leads to reduction in R&D spending by the pharmaceutical company. In a model developed to simulate how global pharmaceutical R&D spending would react to a price-regulated regime, he demonstrated that the impact decreased the amount spent on R&D by 23.4% to 32.7%. This is however an obvious argument. The profit (net or pre-tax) is contingent on the sales volume and the price. Intrinsically, there would be very little variation in sales volume of an innovative, volume held constant, the level at which the price is set in the primary influence on the profits earned by the drug firm. In a situation where other factors are kept constant, the drug firm would have more resources available to spend on R&D at higher rather than lower prices. In a simple linear relationship, the more resources that are put towards R&D would usually result in a greater number of innovations.

Interventions using newer improved drugs are initially more costly than the conventional approaches but tend to have a greater efficiency in the long run with regard to the actual health outcomes. In his argument regarding this issue, Kessler states that there is a substantial body of evidence linking the discovery and use of pharmaceutical leads to lower long term medical expenses and improved outcomes after treatment interventions. This is especially true of newer and novel[32] drugs. In particular, he refers to the work done by Frank Lichtenberg (2004, 1996) and Miller and Frech (2002) regarding treatments and outcomes for 100 disease profiles between the years of 1979 and 1998. The findings are predictable: An increase in the availability of drugs leads to an increase in the mean age of the patients studied. Furthermore, the fraction of people dying before the age of 65 is also reduced. Lichtenberg also finds that the number of inpatient bed-days is reduced by the increased use of novel drugs, and in particular there is a reduction in mortality. Improved short-term outcomes from these interventions necessitate more spending on ambulatory care. Kessler (2004) also makes the observation that the use of drugs does impact the cost and quality of healthcare. In particular, he draws on the point that there is significant association between a national budget or expenditure on novel medicines and the quality and length of life. The pertinent questions involve the conditions under which these drugs extend the length of life, primarily what is the quality of life in that extended period and at what opportunity cost?

[32] Novel drugs are drugs used for a specific purpose – they are highly effective drugs with few side effects – and are developed primarily using the genetic coding of the parasite that infects the host.

CHAPTER 6

Statins in South Africa: A Cost-Minimization Investigation

6.1 Introduction

In undertaking a pharmacoeconomic analysis the writer wishes to investigate how do the pricing structures of drugs relate to the Coasian Theorem explored in Chapter 2. One needs to consider the dilemma in terms of *ex ante* and *ex post* costs. Anderlini and Felli (2001) argued that the Coase theorem would not hold in cases where the potential or anticipated *ex ante* costs are expected to be substantially higher than the *ex post* costs. They examine the basic 'hold-up problem' that arises whenever agents to a Coasian negotiation have to pay *ex ante* costs for the negotiation to take place. Developing this theory would lead to a conclusion that rising healthcare costs that are unsustainable.

The investigation will study the pricing of statins relative to each other. The reason for pursuing a comparative study of statins was that the level and availability of drug price data was overwhelming in the international arena. However data relating to the use of statins in South Africa still appears to be sparse. Furthermore multinational drug companies are making a number of assumptions in their marketing literature with regard to the efficacy of their drugs. Often local conditions and attitudes toward newer drug regimens are ignored. On the other hand, if the drug companies are not freely allowed to market their drugs because of restrictive regulatory oversight, then the space for new drugs to enter the market might not be sufficient to accommodate newer, technologically superior products. The potential welfare gain from the products would be the welfare loss to society. A secondary reason was that there was insufficient data available to conduct an independent analysis into another drug class because there is very little work being done in South Africa and many of the drug trials are being concluded in foreign countries.

Pressures on healthcare resources, in developed and developing economies, emanate from both the supply and demand side. Informational asymmetries, inequities, regulatory intervention and unchecked provider and administrative costs are examples of supply side pressures (Appasamy and Riding, 2004). The situation is exacerbated by higher demands stemming from aging populations, lifestyle diseases and an increasingly high level of supply-induced demand. This is a classic economic problem of scarcity and resource allocation resulting in an emergence of a

different class of healthcare purchasers (Wessels, 2004, p. 2) including pharmaceutical benefit managers (PBMs), formulary managers and district health authorities (DHAs). Furthermore, Appasamy and Riding (2002, 2003, 2004) note that the largest component of healthcare spend in the privately insured market in South Africa is on pharmaceuticals[33]. This constitutes the in-hospital spending that includes the surgical disposables and consumables and out-of-hospital spending which is from pharmacies. The hospital dispensed drugs and direct pharmaceutical spend is in excess of 45% of the total benefits paid for in the private market. This is the backdrop to the pharmacoeconomic investigation undertaken in this chapter.

6.1.1 An Introduction to Statins – lifestyle 'wonder drugs'

One of the classes of drugs is called statins and these drugs are used to treat symptoms associated with vascular diseases such as hypercholesterolemia, asymmetric dimethylarginine (ADMA), heart attack, stroke and revascularisation. Statins are a class of enzymes called 3-hydroxy3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase inhibitor. They tend to reduce coronary mortality and morbidity in certain types of high-risk individual by limiting the amount of low-density lipoprotein cholesterol (LDL-C) produced by the liver. The statins achieve this by slowing down HMG-CoA reductase, an enzyme responsible for cholesterol production. Moreover, statins enhance the liver's facility to eliminate LDL-C from a person's bloodstream. This has been shown in a number of clinical trials, particularly with the impact of statins in the reduction of heart attack and stroke. Statins are generally well tolerated by most patients. The most prescribed drug in the world is the statin called LIPITOR®[34]. However, myopathy-muscle aches and pains is one of the major side effects of statins and may subsequently lead to kidney damage. Conversely, the frequency of myopathy is rare, and is more likely to occur in individuals with complicated medical conditions or in the elderly. Another side effect is that statins could lead to an increase in liver enzymes, which necessitates additional costs in that liver tests may need to be conducted. All statins are effective in lowering total and LDL-C and increasing HDL-cholesterol, but have differing rates of reduction. The newer, more developed statins tend to be more potent than the older statins, a consequence of ongoing research and development by the pharmaceutical companies and also a testament to the advantages of newer, albeit more expensive, technologies. The precept is that a

[33] Pharmaceutical spending usually constitutes in-hospital and out-of-hospital spending and is usually around 45% of total healthcare spending.
[34] Lipitor is made by Pfizer and is often acknowledged by the medical industry as the drug that sets the 'golden standard' amongst statins.

lower blood concentration of LDL-C is associated with lower cardiovascular disease (MRC/BHF Study, 2002, 2005)[35].

Coronary heart disease (CHD) is one of the leading causes of mortality amongst the South African population and in many of the industrialised nations of the world. HD prevalence is high, with South Africa having one of the highest rates in the world amongst certain race groups. However, despite the high prevalence rate of CHD, mortality associated with CHD declined in the decade from 1988 to 1998 (Hay and Sterling, 2005, p. 134) in the United States. A number of studies have confirmed that this decline is evident in many countries with populations that suffer from CHD related diseases, including South Africa. The primary reason is because of the development of drugs, such as statins, that are used to treat plasma lipid disorders. These drugs and the associated treatments are the fundamental aspect of the improvement in the mortality rate associated with CHD. Furthermore, Hay and Sterling (2005) note that there is a substantial body of evidence to prove that HMG-CoA reductase inhibitors A (statins) have reduced the number of CHD events by approximately 31%. In addition, these reductions are *independent* of patient age, gender, ethnicity, diabetes, pre-existing CHD or any other risk factor.

South Africa faces a situation where CHD is endemic in the more affluent sectors of society. It is a disease that has a strong linear relationship with lifestyle factors such as eating foods that have a high fat content, smoking and a sedentary way of life. Add to that, the market penetration of insured or private medical cover tends to be fairly high in this sector when compared to the less affluent quarters (BHF website, Statistics South Africa (STATSSA) 2001 census). It is therefore plausible that it becomes extremely important for medical schemes and third party payers that the drugs they are paying for are efficient and cost-effective.

What could be considered the *ex ante* and *ex post* cost for someone on a drug therapy? The *ex post* costs are the costs associated with using the drug after therapy has begun, including the cost of the drug and the payment of any adverse reactions to the drug. The *ex ante* costs would be the cost of developing the drug and making it available on the market. In order to reduce potential *ex post* cost (such as adverse reactions to the drug therapy), a greater amount of *ex ante* spending needs to be undertaken.

[35] MRC/BHF Study – are the acronyms for the United Kingdom Medical Research Council (MRC) and the British Heart Foundation (BHF) and should not be confused with the South African Medical Research Council and the Board of Healthcare Funders.

When considering the efficiency, efficacy and cost of a particular drug regimen, it is important to take a number of different factors into consideration such as the impact of a particular intervention (such drug regimens are considered chronic medication) in both the cost and life-changing scenarios in the medium- to long-term. Chronic medication generally needs to be taken over relatively long periods in order to be effective. In a Coasian world this would entail the consideration of *ex ante* and *ex post* costs. If the *ex post* costs are too high, i.e. the drug is not effective in the short term, or that cost would continue in perpetuity, then the intervention is not one that would be considered favourable. However, if *ex ante* costs are relatively higher and result in a shorter period that the insured remains on the drug, then the *ex post* cost would tend to be minimised.

It is with this understanding that the writer approaches the pharmacoeconomic study of the various statins available in South Africa. Whilst individuals and providers of service may have individual nuances pertaining to each treatment event, the broad based analysis is drawn from a number of randomised controlled drug trials (the Comparison of the Efficacy and Safety of Rosuvastatin versus Atorvastatin, Simvastatin and Pravastatin across doses (STELLAR) trial; the Myocardial Ischaemia Reduction with Aggressive Cholesterol Lowering (MIRACL) trial, the Scandinavian Simvastatin Survival Study (4S study) group, the Current Lipid Management and Low Cholesterol Goal Attainment in Common Daily Practice in Spain (REALITY) study, the Open Label Primary Care Study: Rosuvastatin based Compliance Initiatives to Achievements of LDL Goals (ORBITAL) study and finally, the Smith and McBurney's paper, 'An Economic Analyses of the Atorvastatin Comparative Cholesterol Efficacy and Safety Study (ACCESS) based on the ACCESS study. The last study is an economic analysis of statins and can easily be adapted to accurately reflect the South African scenario. Furthermore permission has been obtained from the primary researcher on the ACCESS study, Dr Dean S Smith at the University of Michigan, United States, to use the modelling exercise that they developed in the study. In consideration of the discussion up to this point and by using this model, it is possible to address the four questions raised by Summer *et al* (1998) that deals with the specifics of undertaking a pharmacoeconomic study.

The initiation of any drug therapy is dependent on a number of factors, The obvious one is choice. Choice is subject to both clinical and financial considerations. The former is developed along the lines of safety, efficacy and patient preferences (particularly when there is a possibility of some form of adverse reaction), whilst the latter is largely a function of affordability. The overriding reason is that if the patient cannot sustain long term-costs in the event of insured benefits

running out, the likelihood of non–compliance to the treatment regimen is high, thereby compromising the treatment of the disease. The same scenario is true of most chronic treatments. Price, out-of–pocket payments for drugs, restrictive benefit plans in the medical scheme arena, and a desire to control costs are all factors that need to be considered when making such a decision.

The ACCESS study was designed to address the different factors that could influence the manner in which a particular drug regimen is developed, and especially the factors that could impact the choice of HMG-CoA reductase inhibitors. Its design constituted a depth and range that includes the features of the South African market. Salient features include a range of five comparators, a large number of patients (3600), and the goal of achieving the NCEP-II guidelines for cholesterol targets in a 54 week program.

6.2 Methodology

The methodology employed is broken up into two components, primary and secondary. The primary methodology consists of a review of the literature pertaining to statin drug trials for the reduction of LDL-C and selecting an appropriate model. An understanding of the initial methodology used the understanding of the subsequent part of the methodology. The secondary methodology will be to use the results of part one and convert that to reflect the South African experience as closely as possible, taking into account the local pricing structure including generic drugs. This can be done because clinical drug trials, unlike economic drug trials, can be applied to different populations that have a similar profile. Moreover, the statins available are those that are currently used in South Africa. It is also important to observe that there are two endpoints in such a study – a clinical (or efficacy) endpoint and a financial (or economic) endpoint – and these needs to be adapted to meet South African guidelines.

6.2.1 Study Description

The study's objective was to compare the efficacy of atorvastatin to that of other statins on the market. A randomisation of approximately 4:1:1:1:1was used with atorvastion at 1800 patients: fluvastatin, lovastatin, pravastatin and simvastatin all at 450 patients each. This was conducted in 153 centres across the United States and 3916 patients. Amongst the eligibility criteria, patients had to have an LDL-C level that was at least 30mg/dL (0.8mmol/L) higher than the NCEP LDL-C target, have a fasting tri-glyceride (TG) level of less than 400mg/dL (10.26mmol/L), and also had to give their consent for taking part in the study. Patients were provided with one of the five study medications listed in Table 5.1 below. These study medications were dispensed at six-week

intervals during weeks 0, 6, 12, 18 and 24. At weeks 30 and 42, a 12-week supply was dispensed. Patients were started on the lowest possible dose that was titrated up to the requisite dosages as recommended by the NCEP guidelines in the subsequent weeks.

This study was pivoted around two endpoints, efficacy and economic. The former is informed by the number of patients reaching the NCEP targets, and hence the objective of the study by measuring the impact of these various drugs. The targets are 160mg/dL (4.13mmol/L) for patients with less than two risk factors, 130mg/dL (3.36mmol/L) in patients with two or more risk factors and 100mg/dL (2.59mmol/L) in the higher risk groups, i.e., those patients with a history of CHD.

Table 6.1 Study Medications

Drug	Dosage per day
Atorvastatin	10-80 mg per day (2x40mg for 80 mg dose, twice daily)
Fluvastatin	20-80 mg per day (2x40mg for 80 mg dose, twice daily)
Lovastatin	20-40 mg per day (2x40mg for 80 mg dose, twice daily)
Pravastatin	10-40 mg per day
Simvastatin	10-40 mg per day

Source: ACCESS Study 2003

The economic endpoint was the cost associated with each of the interventions in achieving the NCEP II LDL-C targets. Third-party payer (health insurance companies, HMO's) costs were taken into account. Furthermore, only direct medical costs were considered and not indirect costs such as out-of-pocket payments and loss of productivity. The secondary economic endpoints included the relative cost-effectiveness of patients achieving their targets.

The costs were calculated by adding the absolute costs of treatment, and these included the standard cost of services provided to patients during the course of the study. Costs were adjusted for those patients who achieved their targets sooner than the required timeframe. The total costs comprised the cost of study medication, recommended physician visits to review lipid level concentrations, costs associated with lipid level measurement, and costs to accommodate for adverse reactions and contra-indications.

6.3 Results of the ACCESS Study

6.3.1 Patient demographics

The patients had similar profiles in each of the groups. The objective was to compare the cost effectiveness of atorvastatin with the other statins. The atorvastatin group comprised of 1944 patients; fluvastatin had 493 patients; lovastatin had 494 patients; pravastatin had 478 patients and simvastatin had 478 patients. A total of 3887 patients were randomised into one of five statins. The descriptive statistics of each group is summarised below in Table 6.2.

Table 6.2 Risk Status and Demographic Characteristics of Patients

Status/target	Atorvastatin (n=1944)	Fluvastatin (n=493)	Lovastatin (n=494)	Pravastatin (n=478)	Simvastatin (n=478)
< Two risk factors/4.13mmol/L (%)[a]	12.6	12.4	9.7	12.1	10.9
> Two risk factors/3.36mmol/L (%)[a]	20.3	20.3	21.1	21.5	24.9
CHD or PVD/2.59mmol/L (%)	67.1	67.3	69.2	66.3	64.2
LDL-C target (mean)[a,b]	1.83mmol/L	1.78mmol/L	1.85mmol/L	1.85mmol/L	1.75mmol/L
Mean age at randomization (years)	61.2	62.4	61.4	61.1	60.8
Gender (female) [%]	39.0	37.55	39.9	38.5	42.3
Race (non-white) [%]	11.8	11.6	8.9	11.3	11.1
Weight (kg)	83.1	83.6	83.5	82.8	83.1
Systolic Blood Pressure (mmHg)	133	133	133	133	134
Diastolic Blood Pressure (mmHg)	80	80	79	80	81

Source: ACCESS Study 2003

CHD – Coronary Heart Disease; **PVD** – Peripheral Vascular Disease; **LDL-C** – Low-density lipoprotein cholesterol
a - converted from 160 and 130 mg/dL respectively **b** – the mean point reduction in LDL-C necessary to achieve LDL-C target, calculated from risk factors and LDL-C target concentration

6.3.2 Efficiency Analyses and Results

The number of patients reaching their LDL-C targets in the atorvastatin and simvastatin groups was significantly higher than in the other three groups. These response rates were similar to clinical trials that were previously conducted. One of the reasons for the difference in the numbers reaching their targets could be the higher atorvastatin sample size, which may have influenced the variance of the group. Furthermore, the number of people who left the study as well as those who did not reach their targets from each individual statin group may have had a significantly larger impact on the smaller sample groups. The clinical efficiency analysis is summarised in Table 6.3 below.

Table 6.3 Clinical Efficiency Analysis of Ethical Statins

Statin Ingredient	Percentage of Patients Reaching LDL-C Target
Atorvastatin	88%
Fluvastatin	48%
Lovastatin	66%
Pravastatin	44%
Simvastatin	76%

Source: The ACCESS Study 2003

6.3.3 Economic Analysis

The quantum of medications required to reach the NCEP II LDL-C targets are presented in Table 6.4 below. The concern that was raised by the investigators was that the consistency with which the medication was dispensed varied for a number of reasons including wrong dosages and wrong medication. However this was low (n=50 or 1.3%) and followed a similar pattern amongst all of the treatment groups. Hence this impact was considered to be minimal. From the table below it is evident that the number of treatment visits varied substantially. Primarily, a high variance would be expected in a sample that has a low number of visits over the treatment period, as would be expected. The variance can be explained by the number of patients opting out of the study after they began treatment (611 patients), patients missing scheduled appointments and then picking up the slack (9 patients) and patients reporting adverse reactions to the medication (241 patients).

A total of 9707 adverse events were reported during the study. It was indicated that 1327 of these events were directly related to the study medication. The majority of these reactions concerned previously recognised complaints associated with this class of drug, including that of the digestive system, the musculoskeletal system and the body as a whole. A number of these events were treated in the scheduled study visits and did not incur any additional costs. All of the statins experienced a similar percentage of complaints with the exception of fluvastatin, which was somewhat higher. However, the smaller sample size may impact on the interpretation of the results, indicating a higher variance for fluvastatin. The patients' experiences are reflected in Table 6.4 below.

Table 6.4 Resource use to achieve National cholesterol Education Panel (NCEP) II low density lipoprotein cholesterol (LDL-C) targets.

	Atorvastatin	Fluvastatin	Lovastatin	Pravastatin	Simvastatin
Mean number of treatment visits	2.94	4.85	3.98	5.03	3.49
Standard Deviation	1.47	2.31	2.18	2.43	1.93
Difference vs. Atorvastatin		1.91	1.04	2.09	0.55
p-Value of the difference		<0.01	<0.01	<0.01	<0.01
Number of Patients with medicine related adverse events (%)	317 (16.3)	99(20.1)	77(15.6)	64(13.4)	93(19.5)
Difference vs. Atorvastatin (%)		3.8	(0.7)	(2.9)	3.2
p-Value of the difference (%) ANOVA		0.05	0.07	0.12	0.10

Source : ACCESS Study 2003

The ACCESS study calculates the cost of treatment for each statin. The resource use (summing of the unit values associated with medication, study visits and adverse events) is multiplied by the price of each component. This exercise yielded the total treatment costs. The ACCESS study also concluded that medication costs in this study amounted to almost half of the total costs. Furthermore the investigators concluded that total treatment costs associated with atorvastatin are significantly lower than the other statins.

As previously mentioned, the secondary methodology calls for these clinical results, *inter alia*, to be used in a South African setting to ascertain whether the same conclusions will hold there. It is also vital to attempt to explain the relevance to South Africa. A demographic review of South Africa indicates a society that is segmented in terms of socio-economic level, race, health and accessibility to healthcare (BHF website, census 2001 - STATSSA website). A small part of the population, approximately 16%, has access to privately insured healthcare (Appasamy and Riding, 2003, 2004). This subgroup also enjoys, subject to benefit constraints, access to the most technologically advanced drugs on the market. Drug trials involving statins may not necessarily be conducted locally because the target population that is likely to afford the drug is not significant when compared to high-cholesterol sufferers in other parts of the world. It becomes imperative that any drug trial be 'reinvented' in order to reflect local conditions. South Africa's high-cholesterol sufferers are concentrated in two specific segments of the population, namely, Afrikaner and Indian males. These two groups have also tend toward a high degree of diabetes and high blood pressure in their later years.

A number of considerations would need to be taken into account: the ACCESS study did not use generic drugs; the advent of the single exit price (SEP) brought on by regulations in the South African market may have changed the relativities between the price of the drugs; pricing structure may differ substantially from the United States because of patents regulations; multinational relationships and other significant differences; the development of newer, more potent drugs that have come onto the market since the study was undertaken , and finally, there may be different treatment protocols that could impact on the cost minimisation analysis. Table 6.5 to Table 6.8 illustrates the number of scripts that were used to calculate the total amount of tablets required for each strength of medication in order to achieve the NCEP II LDL-C targets. The number in the top grid corresponds to the number in the lower grid (it is simply multiplied by 42 which is the number of days in-between the prescription collection points. The 80mg dosage of fluvastatin and lovastatin were doubled to accommodate for the consumption of a 40mg dose twice a day whilst the same dosage for atorvastatin remains as is because the price is the same for both the 40mg and 80mg strength tablet. The prices of the drugs at the various dosages, used in this analysis, were taken from the local reference price files for drugs (NAPPI) that reflect the single exit price (SEP) of the medication. The SEP is made up of the ex-manufacturers cost (the manufacturers selling price) plus the logistics fee (the agreed upon distribution cost). Under the current regulatory framework, all scheduled drugs have to have a transparent pricing structure that is consistent across the country thereby obviating any regional price differentials. More importantly, it negates the use of discounting and rebates in the pharmaceutical supply chain. However, it obviates the opportunity to engage in a contract that may involve Ramsey pricing or even a Coasian solution. Table 5.7 reflects the local price per tablet that was utilised in the study, and following a similar process that was used in the ACCESS study, the cost of the medication, at each dose used in the study, was calculated. The cost per patient was calculated by dividing the total number of patients in each statin group by the total cost in each group. This was the cost that was borne by the third-party payers.

Table 6.5 Number of scripts used in the ACCESS Study

Total Amount	Atorvastatin	Fluvastatin	Lovastatin	Pravastatin	Simvastatin
10mg	2966	n/a	n/a	560	659
20mg	1278	575	639	449	400
40mg	724	492	429	1061	357
80mg	649	1140 (x2)	780 (x2)	n/a	n/a

Source: The ACCESS Study

Table 6.6 Number of Tablets at each dose level

Total Amount	Atorvastatin	Fluvastatin	Lovastatin	Pravastatin	Simvastatin
10mg	124572	0	0	23520	27678
20mg	53676	24150	26838	18858	16800
40mg	30408	20664	18018	44562	14994
80mg	27258	95760	65520	0	0

Source: The ACCESS Study

Table 6.7 Local prices of medication

Total Amount	Atorvastatin	Fluvastatin	Lovastatin	Pravastatin	Simvastatin
10mg	R 5.35			R 5.65	R 2.63
20mg	R 8.30	R 3.91	R 2.38	R 7.03	R 2.96
40mg	R 9.39	R 5.22	R 2.69	R 8.41	R 3.78
80mg	R 9.39	R 6.00	R 2.69		

Source: The NAPPI Code and Price File for medications using the Single Exit Price (SEP) as supplied by MediKredit June 2005.

Table 6.8 Price of medications used in Study

Total Amount	Atorvastatin	Fluvastatin	Lovastatin	Pravastatin	Simvastatin
10mg	R 666,460.20	R 0.00	R 0.00	R 132,888.00	R 72,793.14
20mg	R 445,510.80	R 94,426.50	R 63,874.44	R 132,571.74	R 49,728.00
40mg	R 285,531.12	R 107,866.08	R 48,468.42	R 374,766.42	R 56,677.32
80mg	R 255,952.62	R 574,560.00	R 176,248.80	R 0.00	R 0.00
Total Drug Cost	R 1,653,454.74	R 776,852.58	R 288,591.66	R 640,226.16	R 179,198.46
Cost per Patient	**R 850.54**	**R 1,575.77**	**R 732.47**	**R 1,339.39**	**R 374.89**

Source: The ACCESS Study and NAPPI Code Price File as supplied by MediKredit June 2005.

The second part of this equation is to calculate the cost of the medical interventions utilised to achieve the NCEP II LDL-C. This comprises the cost of the physician's consultation, of dispensing the drugs, of conducting lipid tests and the additional cost of adverse reactions that the patients may have had to the medication. This segment of costs can be subjective and driven from a supplier-induced demand in the world of real practice. However in the tightly defined clinical study, the number of visits to the physician tends to be higher than usual[36]. Table 6.4 above summarizes these interventions as reflected in the ACCESS drug trial.

A comprehensive analysis is presented in Table 6.9 on the development of the economic understanding of the efficacy of drugs and the development of a cost effective and cost

[36] In a conversation with Dr Rajesh Patel, Head of the Benefit and Risk Department at Board of Healthcare Funders, Dr Patel indicated that clinical studies tend to have a higher proportion of physician intervention than in practice.

minimisation analyses. The actual cost of treating a patient over a period of 54 weeks will be substantially less if the generic form of simvastatin was used. Simvastatin is R272.77 less than atorvastatin and R512.28 less than lovastatin. The other two statins, at higher absolute prices, are substantially more expensive.

Furthermore, dividing the minimum cost amount by the efficacy of the drug can deepen the analysis. This exercise yields the cost effective value, which is the actual cost of treating a patient over the period of a year. Atorvastatin and simvastatin are virtually identical in terms of their cost effectiveness and these two statins are substantially more efficient when compared to the4 other three statins in the study.

This conclusion is in line with that of the economic analysis of the ACCESS study that atorvastatin is the more cost effective drug. However, when compared to simvastatin, it does not appear to be all that more cost effective. On cost minimisation comparison, it appears that atorvastatin is about R272-78 more expensive than simvastatin. However when the consideration accommodates for the effectiveness of the drug, then the difference between the two drugs is less than two Rands (R1.93, to be precise).

Table 6.9. Cost Minimization and Cost Effective Analysis for Statins

Cost Minimisation **Analysis**	Atorvastatin (n=1944)	Fluvastatin (n=493)	Lovastatin (n=494)	Pravastatin (n=478)	Simvastatin (n=478)
Mean number of Visits	2.94	4.85	3.98	5.03	3.49
Cost of Physician's Consult	R 154.70	R 154.70	R 154.70	R 154.70	R 154.70
Cost of Lipid Measurement	R 191.12	R 191.12	R 191.12	R 191.12	R 191.12
Dispensing Fee (Legislated)	R 26.00	R 26.00	R 26.00	R 26.00	R 26.00
Medical Intervention Charges	R 371.82	R 371.82	R 371.82	R 371.82	R 371.82
Total Medical Intervention Cost	R 1,093.15	R 1,803.33	R 1,479.84	R 1,870.25	R 1,297.65
Medicine Costs	R 850.54	R 1,575.77	R 732.47	R 1,339.39	R 374.89
Medicine and Physician Intervention Cost	**R 1,943.69**	**R 3,379.09**	**R 2,212.31**	**R 3,209.64**	**R 1,672.54**
Adverse Reaction Adjustment (R)	3.47%	3.05%	1.73%	2.33%	3.93%
Adverse Reaction Adjustment (%)	R 67.42	R 102.94	R 38.31	R 74.73	R 65.80
Cost Minimisation Analysis Total Cost per Patient	**R 2,011.12**	**R 3,482.03**	**R 2,250.62**	**R 3,284.37**	**R 1,738.34**
Efficacy from Clinical Assessment	0.88	0.48	0.66	0.44	0.76
Cost Effective Analyses	**R 2,285.36**	**R 7,254.23**	**R 3,410.03**	**R 7,464.48**	**R 2,287.29**

Source : The Access Study, Council for Medical Schemes, Lancet Laboratories,

6.3.4 Sensitivity Analyses

The two drugs, atorvastatin and simvastatin have virtually the same cost-effectiveness; this means that a slight change in any of the factors used in the progression toward the total cost would

be reflected as a change in price and result in either one of the drugs being more cost-effective. They have a seesaw relationship with the pivot being the number of visits to a physician in one relationship and the other pivot being potency of the drug. Any adjustment to these two areas impacts the cost effectiveness one-way or the other. In conducting the sensitivity analysis, one component is adjusted whist the others are kept constant. This has been done for four factors that reflect quite succinctly the effect of such an adjustment would have (Table 6.10). An increase in the price of drugs would have a greater impact on a higher priced drug and in the situation of a delicate balance would forego advantage to the lower priced drug, as in the case of simvastatin. In the event of such an increase, the relative cost-effectiveness of the drug could be made less attractive when compared with a competing compound. As shown below in Table 6.10, this impact can vary from 1.96% to 8.68%, depending on the rate of increase.

Table 6.10 Increase in the Price of Drugs results in an efficiency gain for simvastatin

Percentage Increase	Rand value	Efficiency Gain (%)
10%	R 46.80	1.96%
20%	R 95.54	3.84%
30%	R 144.28	5.58%
40%	R 193.01	7.19%
50%	R 241.75	8.68%

Source: The ACCESS report, own study

Similarly, the increases in the non-drug costs would have a greater impact on the lower priced items such as a generic lower priced drug as in the case of simvastatin. The factors that influence the lower priced drugs are contingent on these externalities, which fall outside the ambit of drug manufacturers. The three tables below (6.11, 6.12 and 6.13) support this assertion. The tables reflect different scenarios where the external factors are increased, and this impacts the lower priced drug adversely, making it less cost effective.

Table 6.11 Increase in the Number of Physician Visits results in an efficiency gain for atorvastatin

Percentage Increase	Rand value	Efficiency Gain (%)
10%	R 50.86	2.10%
20%	R 99.79	3.92%
30%	R 148.72	5.57%
40%	R 197.00	7.06%
50%	R 246.58	8.42%

Source: The ACCESS report, own study

Table 6.12 Increase in the Cost of Physician Visits results in an efficiency gain for atorvastatin

Percentage Increase	Rand value	Efficiency Gain (%)
10%	R 22.29	0.94%
20%	R 42.65	1.75%
30%	R 63.01	2.51%
40%	R 83.37	3.23%
50%	R 103.72	3.90%

Source: The ACCESS report, own study

Table 6.13 Increase in the Dispensing Fee for Drugs results in an efficiency gain for atorvastatin

Dispensing fee increase	Rand value	Efficiency Gain (%)
R 29	R 5.88	0.26%
R 30	R 7.20	0.31%
R 33	R 11.15	0.48%
R 37	R 16.41	0.71%
R 40	R 20.36	0.87%

Source: The ACCESS report, own study

6.4 Conclusion

The manner in which prices of drugs is pitched is contingent on a number of factors, both internal and external. It appears that when looking at a comparative drug study such as the ACCESS study, there may be an inclination to draw too much on the conclusions as opposed to examining the assumptions that the study is based upon.

The original study concluded, beyond a shadow of a doubt, that atorvastatin is a much more cost-effective drug. However, one of the tenets of the study is that it looked at branded products. The situation is a little different in South Africa in the sense that there is a strong legislative presence when compared to the United States (the ACCESS study setting). The single exit price legislation, generic drugs and monopsonistic purchasers (Department of Health) would all tend to influence the pricing structure of the drug. When these influences are taken into account, there is virtually no difference in the cost effectiveness between atorvastatin and simvastatin.

Technology has introduced a number of newer drugs onto the market, including a statin that is not currently locally available, rosuvastatin. It may be prudent to accommodate for the current impasse in the dispensing fee legislation and the single exit price debate when undertaking a pricing structure for the drug. Recent analyses in the United States placed rosuvastatin's potency at reducing LDL at 63%, atorvastatin at 57%, and simvastatin at 47%[37]. However the circumstances

[37] Caremark publication, article by Maribeth Bettarelli, available on www.caremark.com, accessed on 16th June 2005.

in the real world treatment, such as the REALITY Study conducted in a number of European countries, indicated that the drugs actually achieved a lower level of success. The externalities would include lifestyle factors, up titration of drugs, and the use of combinations of drugs. One such combination would be the use of the statin with a fibrate, such as Ezetimibe, which works to reduce the amount of cholesterol that the body absorbs.

In concluding, compliance with the drug regimen is more important than the drug potency. Compliance is a dynamic result of price, availability, acceptability and simplicity of the dosages. Looking back at the dilemma posed at the beginning of the chapter, the Coase Theorem applies in the sense that if *ex ante* (the cost of drug development) or *ex post* costs are too high (the costs of complying with the drug regimen), then the transaction would not be concluded. Newer drugs would not enter the market if the drug manufactures' are not guaranteed of a certain return on investment.

CHAPTER 7

Regulations, Competition and Price - Observations

7.1 Introduction

Pharmaceuticals are the focus of much of the price control regulation geared toward reducing the cost of healthcare delivery. There are two schools of thought on the topic of price control. One that favours regulation to limit or to restrain the price of drugs, the other proposes that competition be allowed to govern the level at which prices are set. Moreover, there is a substantial body of evidence supporting both points of view.

Danzon and Towse (2003, p.1-2) identify three unique economic questions relating to the pharmaceutical environment. First, the substantial capital investment related to research and development, patent protection, and technical advances raise weighty positive and normative concerns regarding the industry structure, prices and broader healthcare policy.

Second, the industry is heavily regulated and its tenets have been born out of a regulatory environment that was initially set on safety and marketing ethics (Sainsbury Report, 1966, Kefauver-Harris Amendments, 1962), but subsequently enhanced its role to include the efficacy of drugs, to a more recent attention to areas deemed to be non-healthcare costs (Appasamy and Riding, 2002, p.12). These concerns are driven by the need for budget-conscious governments to control healthcare cost in order to minimise spending on their national healthcare budgets.

Third, major drugs are globally sold products and the cost of the development of those drugs should ideally be shared globally. Under the current paradigm, there exists the incentive for countries to have national free-rider strategies for drugs that required by their populations. On the other hand, regulators are under pressure to limit the total healthcare expenditure in order to support the burgeoning need for healthcare. Ironically increased demand for healthcare stems from the lower prices of healthcare interventions and drugs and reflects a classic economic problem of the scarcity and the allocation of resources. The issue of moral hazard (as explained in Chapter 2) also emerges in this situation. The lower cost of healthcare increases demand for healthcare thereby placing a larger burden on limited resources (in this case both the public and private healthcare budgets). Ultimately the objective to provide sustainable healthcare services to all tends to be compromised.

In South Africa, the introduction of the single exit price (SEP) may be indicative of this development and implies further regulatory and structural expansion in the future. It is ironic that the government policy on the SEP and pharmacy dispensing fee issues are directed exclusively for the benefit of the middle class purchaser, which constitutes primarily the medical scheme member. On the surface it appears that this policy is not designed for the benefit of the public sector health departments. However, the development of Social Health Insurance is a signal that the government intends to substantially increase its role in the private healthcare market, a directive that is in line with the White Paper proposals – in order for that market segment to support the public sector infrastructure.

The dilemma, in light of this paper, is whether these developments will be efficient in a Coasian sense. Furthermore, there is also a question as to the measurement of efficiency of the changes. How can this be measured? One suggestion is that there is currently a wealth of multi-variate information, both in the public and the private sectors for an information baseline to be established. It can be seen that this baseline can be used as a measurement tool against which to measure future experiences.

This and the final chapter will review the literature of some of the thinking in this area and make recommendations regarding the development of healthcare policy with specific reference to pharmaceutical pricing. Weighting of the costs against the benefits of any regulatory intervention would be ideal as a simplistic measurement. However, the impact of any such regulation is subjective and contingent on a myriad different factors including the socio-economic target group, the level of out-of-pocket payment for the patients with insurance cover, the behaviour of the prescribing physician as to whether or not they are acting as true agents for the patients, the likely presence of a national social insurance, and the penetration of generic drugs into the market.

7.2 The Costs and Benefits of Regulation

Part of the role of regulation is to protect the public, control the manner in which commerce is conducted, and to establish a transparent basis for trade; which includes protecting the public from the incidence of dangerous drugs and drug therapies being used by its citizens. Secondary is the function to provide services that add value or simply put, services that increase the welfare to society. The latter function usually means that the regulatory framework might opt for a delivery method that fits its budget – its focus is to deliver a certain level of healthcare to as many people as

it possibly can at the lowest price. Governments also use their monopsonistic purchasing power to negotiate for better prices. There have been attempts to quantify the impact of regulations on pharmaceutical prices (Peltzman, 1987, Ruwart, 2004), especially by researchers in the United States, but there is very little literature available that deals specifically with this issue.

In a similar manner, attempts have been made to try and quantify the cost of regulatory interventions. One well known study by Grabowski *et al* (1978) compares the changes in the United States after the Kefauver-Harris Amendments of 1962 to the situation in Britain, where, at that stage, there had not been considerable regulatory change. Studies dealing with the cost of regulation counted the cost in lives of not having the drug on the market because of the regulatory processes that needed to be adhered to.

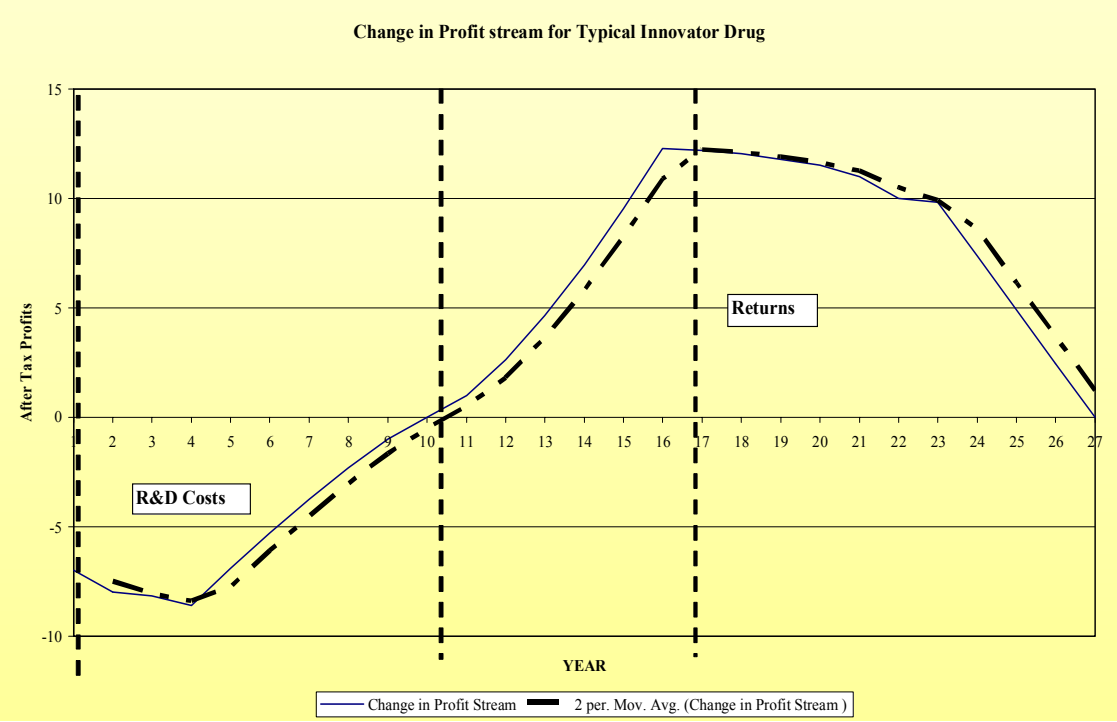
7.3 Pricing and Competition

An obvious approach to the issue is to look at competition in the pharmaceutical market, including the relationship between the innovator drugs and the generic drugs. Mathews (2000) observes that there are two pharmaceutical industries, one that manufacturers generics and over the counter (OTC) drugs fairly cheaply, and the other that spends billions of dollars in R&D in order to develop new compounds that are more effective that current therapeutic drugs – the 'pharmatech industry'.

Competition in this area comes in three forms: between drugs in the same therapeutic class, such as the branded statins; between *innovative* and *generic* drugs in the same class (simvastatin versus the other statins); and finally amongst the generics themselves such as the aspirin producers. The world market for innovative pharmaceuticals is largely governed by developments in the United States market. This was clearly evident in the Uruguay Round of the World Trade Organisation talks concerning intellectual property rights. Those countries that have robust pharmaceutical manufacturing industries, particularly Switzerland, the United Kingdom, France and the United States, pushed hard for agreements on patent protection. Furthermore it was made clear that pharmaceutical companies in the USA invest heavily in R&D with the intent of recouping such 'capital investment' from the drugs' users. India, widely considered the largest producer of generic drugs in the world, has ratified the 2001 TRIPS agreement on patent rights effective from January 1st, 2005. This would most likely intensify the pro-patent nations in their call for further patent protection, particularly amongst the Oriental nations, India and China. The method used to protect these innovative drugs is to register a patent that is effective for a certain period of time.

The Waxman-Hatch Act of 1984 extended the length of time[38] that an innovative drug is patent protected, but also made it attractive for generic drugs to enter the market at a greater rate. This Act is credited with the dramatic rise of generic products since 1984 worldwide. Such action resulted in lower prices of drugs, primarily because average prices fall when consumers switch to the cheaper generic. Generic manufacturers compete quite heavily on price (Caves, CBO study 1998, MediKredit 2005).

Figure 7.1



Source: Ruwart (2004a p. 1, http://www.ruwart.com/AAPS.pdf)
According to Ruwart, the profit reaches a peak at the end point of patent protection, 17 years, and signalling the decline of profits over the following ten years. (See Appendix 4)

The holding companies of innovator drugs require a certain time before they can recoup their investment. This is provided for in the patent protection period. The price of an innovator drug includes the cost of drugs that do not make it to the market, the cost of waiting for a return on the drug, the cost of capital, and cost incurred in conducting the requisite clinical trials. These expenses were heightened and expanded by the requirements put forth by Senator Estes Kefauver in 1962. It is often argued that these regulations did more harm than good (Ruwart, 2004a, p. 1).

[38] The Waxman-Hatch Act extended the period that a drug enjoyed patent protection to 20 years. This however, was not a straight-forward extension. The time that that drug spent being assessed for safety and efficacy is also included in the 20-year period. The Act did allow for some flexibility to enter into the market by easing regulatory conditions (proposed by the Kefauver-Harris Amendments) for manufacturers.

Competition amongst innovative drugs[39] is characterised by the breakthrough innovator drug with 'me-too'[40] drugs and generic drugs following in its path. When an innovator drug reaches the market, it is protected by a patent for a period of roughly seventeen years. Although patent protection prevents competing companies from producing the exact compound, it does not prevent the competitors from producing slightly different drugs that are functionally similar. The statin example illustrates this state of affairs. Zocor, with its active ingredient simvastatin was the first broad-based statin on the market to achieve a level of success. Lipitor[41], using a similar mechanism to block the production of cholesterol production in the liver, was developed using an active ingredient called atorvastatin. The later drug set a new standard in cholesterol treatment and can be referred to as a 'me-too' drug, newer examples include the drug Crestor.

The competition between a generic drug and an innovative drug has intensified somewhat, primarily to the number of innovative drugs coming off-patent, but also due to a peculiar effect that Kong (2004) referred to as the 'generic competition paradox'. The typical economic situation is in the result of a generic drug entering the market: more innovator drugs are being substituted for in prescriptions, driving the average price of a prescription down. These generic drugs quickly gain a large share of the market.

The generic competition paradox can be explained by considering the role of the consumer, particularly the consumer's behaviour. Those consumers who are price sensitive or covered by health plans will more likely purchase the generic product. As this purchasing pattern continues the demand for the innovative drug falls. At this juncture, the remaining consumers who still continue to purchase the innovative drug are likely to have an inelastic demand for the drug and hence less sensitive to the price of the drug. Given this situation, the price of the innovator drug could rise rapidly over a short period of time in order to take advantage of the inelastic demand for the drug. The manufacturer can only do this because of the influence of the generic drug in segmenting the market. The CBO (Caves, CBO study 1998) paper lists a number of studies that support this phenomenon. Two considerations are important in the generic competition paradox: the

[39] Innovative or ethical drugs are newer drugs that still enjoy patent protection. In other words, they are not generic drugs.
[40] 'Me-too' drugs are drugs that capitalize and build on older drugs and technologies. It is often the case where the 'me-too' drug performs at a much higher efficacy than the original drug.
[41] Lipitor was recently reported as the world's top selling drug with sales of 10.86 billion dollars (USD) with Zocor in second place with 5.17 billion dollars in sales. Both drugs maintained their 2003 standing of 1st and 2nd most popular drugs in 2004. Med Ad News, May 2005

substitutability of the brand name with that of the generic product and the market share of the non-price sensitive patients.

Table 7-1

Box 7-1. Calculating the Impact of the Replacement Effect and Generic Competition on the Returns from Innovation						
Calculation of Returns from Innovation When New Products Replace Old Ones						
Present Discounted Value (PDV) of Profits from Innovation	=	PDV of Returns from New Product	-	**[** PDV of Returns from Currently Marketed Product	x	Share of Current Market Replaced by New Product **]**
Calculation of How the Rise in Generic Entry Since 1984 Has Affected Returns						
Change in PDV of Profits from Innovation Caused by Increased Generic Entry	=	Change in PDV of Returns from New Product	-	**[** Change in PDV of Returns from Currently Marketed Product	x	Share of Current Market Replaced by New Product **]**

That relationship can be expressed mathematically, as follows. Assuming that:

t = number of years a product has been on the market

t_g = year of generic entry

T = number of years of product life

h = year in the life of the currently marketed product when a new, competing product is introduced by the monopolist

α = share of the current product's market that is absorbed by the new product

$\Pi^M(t)$ = monopolist's profits in year *t* with no generic entry

$\Pi^G(t,t_g)$ = monopolist's profits in year *t* with generic entry

$\Pi^C(t,t_g) = \Pi^M(t)$ if $t < t_g$; $\Pi^G(t)$ if $t \geq t_g$

Source: Caves R (1998), p.74

Competition amongst generic drugs is characterised by price wars. The CBO (Caves, CBO study 1998) study indicated that the price of a generic is inversely proportional to the number of generic manufacturers in the market. Primarily all of the generic producers manufacture the same compound (that of an off-patent drug). The result is that these producers compete on price. Caves (1998, p. 65-71) found that when the number of manufacturers increased from 1 to 10, the average generic drug fell down from 60 percent to 34 percent of the brand name drug.

7.3 Regulatory Interventions

In many national healthcare delivery models, the largest purchaser of healthcare products tends to be the government. This presents a problem to drug manufacturers because of the monopsonistic nature of the contact that they enter into. The situation is further exacerbated by the presence of generic manufacturers who may have more appeal to the purchaser. Governments control prices in a number of ways (as discussed in Chapter 3); reference pricing, limiting the level of reimbursement to the patient necessitating out-of-pocket payment and ultimately running the risk of non-compliance.

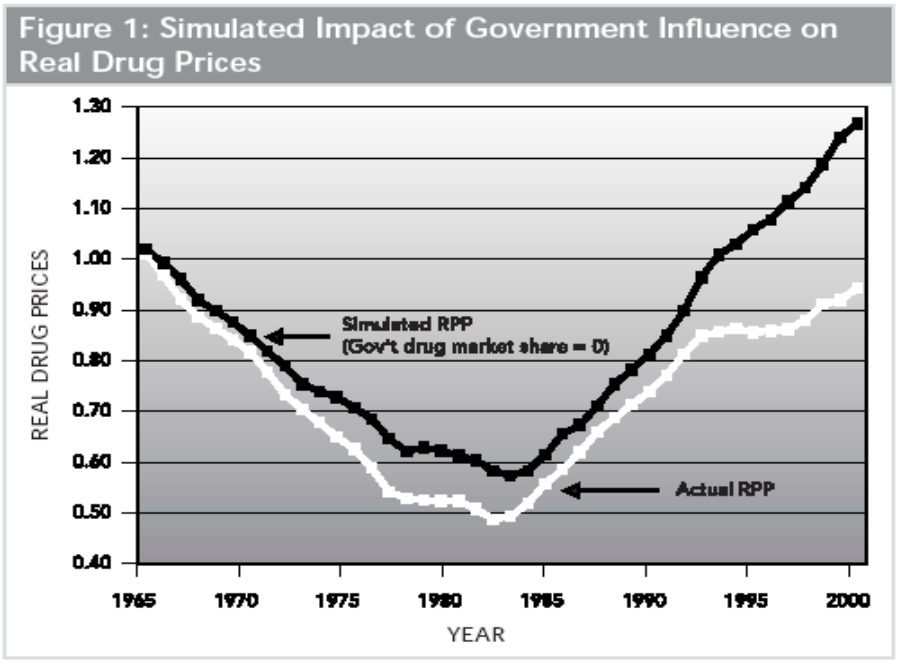
The state of affairs presents a dilemma in that drugs are targeted to specific populations and it is important to the manufacturer that sufficient recoupment of capital costs take place. The impact of monopsonistic purchasers tends to reduce income because the purchaser tends to want the product at the marginal cost. This does not leave sufficient monies to invest in R&D.

Vernon, *et al* (2004, p.2) indicate that new drugs generate immense social benefit, mainly by obviating older, more time consuming and painful treatment protocols. Newer drugs tend to have a higher success rate at treating certain conditions, and in some cases, obviate the need for surgery – as in the case with stomach ulcers. Economic theory, according to Vernon *et al* (2004, p.2), is clear in its prediction that price controls will reduce biotechnology and pharmaceutical R&D by reducing cash flows, thereby decreasing expected revenues streams. This situation reduces the incentives to develop new drugs. In their study they infer, through the use of retrospective data, that governments impact through regulation and purchasing has a negative impact on biotechnology prices and pharmaceutical R&D (see Figure 7.2 and Table 7.2 below).

Danzon's (1999, p. 352) analyses of drug pricing in seven countries supports Vernon's view and goes further in postulating that countries with a relatively free pricing system (such as the USA, Canada and Germany) are much more susceptible to the impact of generic pricing. Countries

that have a stringent drug pricing policy (such as France, Japan and Italy) do not gain the benefits of generic pricing structures.

Figure 7.2



Source (Vernon et al, p. 5). One series identifies the trend in actual real drug prices over time, whereas the other series shows how drug prices would have trended in the absence of any government influence. Notice that real drug prices actually dropped by roughly 50 percent from 1960 to 1980. Also notice that after 1980, real drug prices continued to increase but never quite obtained in 2001 the same level observed in 1960.

Anecdotal evidence (Danzon, 1999, p.352) suggests that generic manufacturers in countries with stricter regulations tend to be licensed co-marketers of drugs that manufacturers introduce in order to get a price increase. This differs markedly from the situation where in a free market system, generic manufacturers enter the market, competing on price. The price of the product is inversely proportional to the number of generic manufacturers in the industry. Volume discounts and competitive pricing are also reflective of this environment. Danzon's analyses suggest that "…regulation of both manufacturer prices and retail pharmacy undermines competition in the off-patent sector and that potential budgetary savings from post-patent competition are not fully realised in countries with strict regulatory systems." (Danzon, 1999, p. 355)

The extreme view is that regulations take lives instead of saving them (Ruwart, 2004b, p. 3). The aspect known as 'regulatory creep' is cited as a major cause of the increase in the cost of healthcare to the patient. A number of issues are raised, one of them being the impact that regulations have on drug development time and the negative impact of cost-cutting legislation.

Table 7.2

Figure 2: Estimates of Lost R&D Because of Government Influence on Drug Prices

Year	Predicted R&D as a Percentage of Sales (Government Share = 0)	Actual R&D as a Percentage of Sales	Cumulative Lost R&D Dollars (Millions of Capitalized 2000US$)
1960	8.19%	8.15%	$340
1965	9.36%	9.14%	$9,541
1970	9.80%	9.32%	$27,370
1975	9.91%	9.02%	$68,074
1980	9.82%	8.86%	$107,362
1985	13.54%	12.90%	$127,749
1990	15.27%	14.44%	$140,161
1995	18.91%	16.70%	$157,534
2001	19.79%	16.67%	$188,310

Source Vernon *et al* (2004, p. 7). "The key estimate from this simulation exercise is, of course, the measure of cumulative forgone R&D investment. We estimate this amount to be $188 billion as of 2001. This figure represents the amount of R&D that the federal government, through its influence and constraint on real drug prices, disincentivized firms to undertake."

As mentioned in Chapter 3, the Kefauver-Harris Amendments of 1962 required that manufacturers test drugs for efficacy. Ruwart's contention is that no drug treats everyone equally and hence even testing the number of people that will be affected would not decrease substantially. Furthermore, the 1962 regulations increased the drug development time from 4.4 years to 14.2 years on average (Ruwart, 2004b, p.1). Using the number of lives that the average drug saves, the number of lives saved compared to the number of lives lost is in the region of 4.7 million lives lost from 1962 to 2004 compared to 90 000 lives saves. This reasoning is extended to the amount of money spent on R&D costs and the additional amounts required because of the regulatory requirements. A similar situation was seen in South Africa in the medical schemes environment where roughly a third of the annual increase was attributed to the regulatory requirement of holding a mandatory reserve comprising of 25% of gross contributions (CMS, 2005, p.111).

7.4 What lies ahead for the South African Pharmaceutical Industry? Questions?

How does South Africa fare in this arena? South Africa's national health policy is driven fairly rigidly along the lines of the White Paper on health. Add to that, South Africa has a strong regulatory arm which tends to run against the grain of the healthcare community. The introduction of the single exit price (SEP) has, in the short-run, attempted to restrict the free movement of the price of drugs. Does this necessarily risk the public's access to modern drugs in the long run? Or does it necessitate that all drug development will be stopped. The southern African region has been significantly affected by the HIV/AIDS pandemic and is reliant on the development of newer drugs

to help ease the afflictions of this disease. Most drug trials, as mentioned earlier, are conducted externally, very few compounds are tested locally. The fact of the matter is that any research based organization (like a pharmaceutical manufacturer) will throw its resources behind an R&D project that has a fair return to investment.

7.5 Concluding notes

However, the reasoning presented above regarding regulatory heavy handedness appears to defeat the purpose that the regulation was intended for and one can assume that South African prices for both innovative and generic drugs will be higher than elsewhere in the world, particularly for the private sector patient.

The research problem is focussed on whether a Coasian relation can exist within the current healthcare paradigm. Furthermore the paper undertook to inform the reader about the significant relationships that exist in the healthcare arena. In particular we considered a number of questions posed in the introductory chapter were addressed, including:

i. whether the nature of the relationships between the stakeholders in the healthcare industry was efficient?;
ii. if any aspects of the industry can be changed in order to create greater levels of efficiency?;
iii. whether the lessons learned from other healthcare systems are useful? How can alternate healthcare systems inform the issues at hand?;
iv. are there any efficient pricing structures that can be utilised?; and
v. ultimately the main thrust of the hypothesis would be whether an efficient relationship can exist between the supply and usage (demand) for medicines.

It is clear from the discussion that an efficient relationship between demand and supply is governed by endogenous and exogenous factors and a multiplicity of relationships. One way of examining this issue is to consider the overarching problem and then cascade it into more localised issues.

Can an efficient solution exist between the supplier and the purchaser of pharmaceuticals? This was answered theoretically by a number of writers including Reekie (1997), Vernon (2004) and Danzon (1999). Would this solution be a Coasian solution? If all of the agents are informed and are happy with their respective agreements, then the solution is Coasian.

The paper also dealt with systems used in other parts of the world that have important lessons for South African policy-makers. The recent legal impasse regarding dispensing fees and the high cost of pharmaceuticals prompted a number of calls from the Department of Health for expansion in the use of generic drugs. The empirical study in Chapter 6 showed that the innovative drug, although more expensive per unit price, was more efficient than a generic. Innovative drugs build on the R&D and success of the older drugs (some of which already have generic versions on the market). Thus it is vital that R&D continue for such advances to be made.

Medical schemes, under regulatory pressure to offer more benefits and reduce contributions, have responded by defaulting to generic versions of the prescribed drug in their benefit plans. If a generic version of the particular prescribed drug is not available, then the next choice would be a generic of another drug in the same therapeutic class. This may be considered as inefficient behaviour, particularly in the case of coronary disease where the likelihood of a person getting worse is high.

Healthcare systems vary in structure, funding and efficiency. The public healthcare system is regarded as far more efficient than the private healthcare system (WHO Report 2000). Why? Outcomes are similar and yet the public system costs far less to treat specific conditions – albeit in far more dubious circumstances. Could the use of generics allow for healthcare systems to become more efficient? Reekie (1997) argues for higher prices and more profits, which in turn, would allow for more R&D and hence, innovative medicine. This is the initial welfare loss to society given up for future gain. This would allow for a Coasian solution, if the agents involved could agree on what would be spent today for the sake of improved health tomorrow. The agents would have to agree on a principle of whose rights are more important.

Efficient pricing can also take the form as suggested by Ramsey price structures. South Africa is divided, quite distinctly, along the lines of income earnings. The affluent groups can be subject to one price and the less affluent groups to a lower price. One would venture that this situation already exists. However, if one assumes that both groups are 'insured' against healthcare interventions in the broadest sense, then a situation of Ramsey pricing does not exist. An investigation into the specific impact of Ramsey pricing would be useful.

This leads to the final question of how the supply and demand of drugs in healthcare services can be made more efficient? Specific policy recommendations are listed in the following

chapter. However, assessing the broad based scope of the sector, one would assume that encouraging the established pharmaceutical industry to expand through a series of localised inventions, the use and encouragement of the use of traditional medicines, and a greater use of pharmacoeconomics in the assessment of prescribed drugs.

The role of R&D in pharmaceutical companies is core to their operations and profitability – which makes it important for these companies to compete on an R&D basis. Drug companies depend on new drugs because such drugs, if successfully launched, yield the highest percentage returns (which increase profits). Furthermore, newer drugs are much more efficient than their previous counterparts. Add to that, there are differing pressures put onto healthcare infrastructures, such as HIV/AIDS in southern Africa; cholera, dengue and typhoid in south east Asia; SARS in China; avian flu in northern Asia, south and central Europe. Viruses and viral strains change and research has a constant battle to come up with antidotes. Such situations need to be addressed with newer drugs since the older methods are no longer effective. Malaria, one of the constant health issues in South Africa, being a prime example.

The twentieth century has indicated that there are many new strains of disease but many of them can be treated quite successfully with new generation drugs. However, what is the cost of bringing these drugs to the market?

Stated differently, the role of R&D is core to the efficiency of healthcare systems and it would be efficient, in a Coasian sense, if the cost of R&D was borne by these healthcare systems. This does not imply that individual patients should bear the brunt of their own medications, but patients as a collective group would enjoy a level of cross subsidy for the (more expensive) drugs that they use.

CHAPTER 8

Conclusion and Recommendations

8.1 Discussion of Salient Points

The study highlighted the proposition that economic efficiency can be attained if property rights are fully allocated. However there are myriad additional costs that are involved, all encapsulated under the banner of transaction costs. A useful approach would be to address the different transaction costs.

A motivation cost is one type, and in particular one of its subsets called informational incompleteness. One area where this cost is widespread is that the patient is in a weak bargaining position when it comes to making decisions about their own health; a typical principal-agent problem. Secondly, the discussion that involved the restriction on advertising would also tend to exacerbate this problem. The resultant situation would be a society that is totally dependent on what is being told to them regarding their health.

Coase raised the issue of social cost. If parties bargain to reach an efficient agreement for themselves, and that they display no wealth effects, then efficiency alone determines the agreement. The question asked in the introduction is whether this type of solution is possible in the healthcare arena. A Coasian solution is possible in the South African healthcare environment. This will be expounded upon in the final section of this chapter. However the solution may appear to be far more complex that the theoretical grasp presented here.

Ramsey pricing for pharmaceuticals is currently being touted, in certain quarters, as the solution to many of the problems in the South African healthcare system. However the issue of Ramsey pricing and patent rights challenges Coase's argument that efficient solutions can be reached without the influence of externalities. Multinational drug companies will price according to their country-specific marginal cost. However, the multi-national agreement on TRIPS is indicative that nations are willing to work together, at least on paper. Mechanisms expounded by TRIPS include compulsory and voluntary licence agreements that parallel trade restrictions. These arrangements show that agreements can be effectively and efficiently reached if the parties to the agreement do not display any wealth effects.

Medicine prices have been the bone of contention for decades and governments, in their desire to protect their nations, often resort to heavy-handed regulation in order to restrict the free movement of prices (drug prices in this instance). All four Commissions surveyed in the study recommended punitive restrictions on the free movement of pharmaceutical prices. Support for this viewpoint comes in the form of the World Health Report 2003 that ranked France as having the most efficient healthcare system in the world. There are, however, measures that go beyond the usual fiscal assessments and that comes in the form of opportunity costs and efficient usage of resources.

Experiences from other countries can inform and help bridge the divide between the manufacturer and the patient in an environment characterised by diverging perspectives. The PPRS in the UK is an example of how to address the needs of both sides of the issue. The manufacturers get what they want because they make a normal profit and the payer gets lower prices.

Some regulatory controls take the form of competition legislation. The CC ruling against industry trade organisation is short-sighted since it ignores one of the basic tenets of microeconomics, namely transaction costs that were obviated by collusive bargaining. The ruling led to a reference price list for services rendered. Although this does not impact the pharmaceutical pricing policies of individual drug manufacturers, it does play a role in defining the selling price to large purchasers such as hospitals. Indirectly, the manufacturer must sell at a certain price level. The advent of the SEP enforced a transparent selling price. The level of transparency can be argued in the sense that it is possible for a company to make supernormal profits which is enforced by government regulation.

8.2 Gaps, Anomalies and Deviations

Assessing the social impact lacks the robustness of a controlled scientific study, hence much of what is proposed cannot be accurately measured. *Ergo*, even though are limitations, the debate regarding prices should not be lost. Regulations do have consequences and not all of them are intended.

The pharmacoeconomic exercise was not done on original evidence but based on an assessment done elsewhere. This may not be a true reflection of the local conditions. If original research were undertaken, results might differ.

The results of the cost-effectiveness study deviated from the results of the original study. A number of factors may have contributed to the deviation, price differentials, the inclusion of generic drugs and different treatment protocols.

8.3 Significance of Results

The cost-effectiveness study demonstrated there are a number of factors that need to be taken into account when making a decision regarding which drug to use. Often decisions are made purely on the basis of price – true of some players in the medical schemes industry.

Two significant factors come into play when looking at the results of the cost-effectiveness study, firstly, the study differs in its conclusion to the original study that it was based upon using the same clinical trial data, and secondly, the impact of the externalities on the cost effectiveness study is significant. All factors need to be considered.

Management care organizations tend to favour the least costly intervention, and this is true in their selection of drugs. In South Africa, the drug of choice when treating patients suffering from CHD is a generic drug with the active ingredient simvastatin. The cost-effectiveness study supports this decision on the surface. A closer examination of the assumptions and the sensitivity analyses leads to a different conclusion. Firstly, if the dispensing fee increases for pharmacists and dispensing doctors, then the innovative drug Lipitor becomes more cost effective. Secondly if another generic comes onto the market, then the generic drugs would compete on price alone. Finally, compliance to a drug regimen is far more important than efficacy. Compliance is a function of price, availability, simplicity of dosage and acceptability. If the *ex ante* costs are too high, then the transaction would not be completed. The innovative drug scores higher on all of these areas and hence would be the favoured choice, as is evidenced in the MED AD News (May 2005).

8.4 Policy and Other Recommendations

Recommendations pertaining to the private sector;

i. A body is formed, similar to the PPRS, in order to negotiate prices on behalf of the consumer and the manufacturers. A Coasian solution can be found since the negotiating parties would necessarily want to find an agreeable solution.

ii. R&D should be a joint cost, but in a *pro rata* manner. If a drug company develops drug that afflicts one nation more than the other, CHD for instance, then the purchasing nation should necessarily pay more for the greater usage of the patent.

iii. If this is not a possibility, then a free market pricing system should be adopted in order to allow for competition to prevail and that the innovative drugs compete within and between classes. Furthermore the role of generic drugs will be enhanced to compete with each other and also, in some instances, with the innovative drugs if they fall in the same therapeutic class (e.g. simvastatin competing with the innovative drug Lipitor).

iv. For patented drugs, the patent holders can issue compulsory licences for a limited period in order to meet local demand, if the need arises. This however should be a last resort.

v. Advertising of drugs carry as much information as possible in order to inform the public regarding their efficacy. The primary aim should be that of informing rather than that of giving the wrong impression.

vi. The private hospital industry, which trades in pharmaceuticals, should adopt a more transparent pricing structure that is made available to the public and done in a manner that would not compromise their competitive advantage.

vii. The public sector hospitals should identify (as they have previously attempted to do) a number of premium hospitals that would be able to compete with the private sector hospitals. The advantage that they gain in their monopsonistic purchasing ability can be used to fund the upgrade of other hospitals in the area and to pay their staff higher salaries. This would create a level of competition within the hospital sector and also enhance competition amongst the drug producers since these stakeholders are the major clients.

viii. A philosophical argument leads to the notion that advances in medicine, particularly in pharmaceuticals, are outstripping their value to society in the long-run. This viewpoint contends that the rate of mortality is insufficiently high for the population to accommodate the current birth rate. The net effect is that although the drugs are effective in the short-run, they ultimately have the effect of increasing the population so that the impact on sustainable resources is endemic. Furthermore, there is an impact of the environment as

more and more people compete for less and less resources. Many of the institutions that were set-up to cater to various sectors of society, pension funds being one example, require major structural changes in order to remain functional. The contention is that drug companies would eventually also not be able to compete at this level.

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APPENDIX 1

Wealth Effects and the Value Maximising Principle, a summary of the Milgrom and Roberts proposals in Economics, Organization and Management (1992)

There are three main conditions for the 'no wealth effects' proposal to hold (Milgrom and Roberts, 1992, p. 35):

i) Given that there are any two decisions y_1 and y_2 and monetary wealth $\$x$, the first condition states that there is an amount of wealth – $\$x$ – that would be sufficient to compensate the decision-maker for shifting from y_1 and y_2 (or vice versa).

ii) If the decision-maker was given an additional amount of wealth, then the amount needed to compensate him for the switching from y_1 and y_2 would be unaffected.

iii) The decision-maker should have sufficient means to absorb any loss in wealth in switching from y_1 and y_2, at least within reasonable parameters.

These three conditions are fairly restrictive and do not hold all of the time. A reasonable assumption is that the sizes of the wealth transfers should be relatively small to the overall wealth of the decision-maker for the conditions of no wealth effects to be somewhat accurate.

The utility function of the decision-maker, under these conditions, can be taken back to first principles. When used for group decisions, a value index of all the stakeholders can be developed to measure the total change in the group's welfare. Assume x represents the decision-maker's monetary wealth, and y represents all the characteristics associated with the decision-maker's preferences (*e.g.* societal influences, job category, performance bonuses, *etc*). Now x can be seen as the amount of money that will be received and y is the uncertain or risky component. Under normal conditions the utility function of any decision-maker can be expressed as $u(x, y) = x + y$. However under the no wealth effects conditions, a cash equivalent value $v(y)$ can be assigned to y allowing the utility function to be re-written as $u(x,y) = x + v(y)$, thereby obtaining a personal value index for the decision maker. Moreover the total utility for the group can be addressed to each individual through,

$u_i(x, y) = x + v_i(y)$, with $i=1, 2, 3$ representing a particular individual. This utility function can represent satisfaction – $P(y)$ – gained from investments, wealth, or whatever is defined by y (Milgrom & Roberts, 1992, p.37).

The concept can be further developed to demonstrate the logic of value maximising. Assume $P(y)$ represents the total cash income generated by the total of individual investments under consideration. For the sake of simplicity, assume that there are only two investors, i_1 and i_2. The total investment income $P(y)$ is divided on a pro rata basis to each of the investors, i.e., $P(y) = x_1 + x_2$. Now for any allocation ($x1, x2, y$), the total utility can be stated as $[x_1 + v_1(y)] + [x_2 + v_2(y)]$ which is equal *to* $P(y) + v_1(y) + v_2(y)$. This implies that the total utility depends on the variable y and not on the certainty x. In addition, the total value or utility is not contingent on the distribution of wealth between the stakeholders. If an allocation is Pareto-dominant, it can be inferred that the allocation is efficient if and only if y maximises the value of $P(y) + v_1(y) + v_2(y)$. The value maximising principle can be summed up thus:

An allocation among a group of people whose preferences display no wealth effects is efficient if and only if it maximises the value of the total parties. Moreover, for any inefficient allocation, there exists another (total value maximising) allocation that all of the parties strictly prefer (Milgrom & Roberts, 1992, p.36).

APPENDIX 2 Detail of Retail Prices for Statins as supplied by MediKredit

NAPPI Code	NAPPI Suffix	Product Name	Product Strength	Dosage Form	Pack Quantity	INGREDIENT	Retail Excl Tax	Retail Tax	Retail Incl Tax	Effective Date
701226	3	Adco-Simvastatin 10mg	10mg	TAB	30	Simvastatin	69.3	9.7	79	2002/01/05
701229	3	Adco-Simvastatin 20mg	20mg	TAB	30	Simvastatin	78.07	10.93	89	2002/01/05
701231	3	Adco-Simvastatin 40mg	40mg	TAB	30	Simvastatin	99.5	13.93	113.43	2002/01/05
806634	4	Lescol 20mg	20mg	CAP	28	Fluvastatin	96.1	13.45	109.55	1995/12/13
806672	7	Lescol 40mg	40mg	CAP	28	Fluvastatin	128.13	17.94	146.07	1995/12/13
709963	2	Lescol XL 80mg	80mg	TAB	28	Fluvastatin	147.47	20.65	168.12	2002/09/12
831484	5	Lipitor 10mg	10mg	TAB	500	Atorvastatin	234.54	32.83	267.37	1997/07/28
831484	6	Lipitor 10mg	10mg	TAB	30	Atorvastatin	140.79	19.71	160.5	1997/07/28
831492	7	Lipitor 20mg	20mg	TAB	28	Atorvastatin	203.85	28.54	232.39	1997/07/28
831492	8	Lipitor 20mg	20mg	TAB	30	Atorvastatin	218.42	30.58	249	1997/07/28
886615	7	Lipitor 40mg	40mg	TAB	28	Atorvastatin	230.69	32.3	262.99	2001/05/14
886615	8	Lipitor 40mg	40mg	TAB	30	Atorvastatin	247.18	34.61	281.79	2001/05/14
704166	1	Lipitor 80mg 80mg	80mg	TAB	30	Atorvastatin	247.18	34.61	281.79	2005/04/01
703996	1	Lovachol 20mg	20mg	TAB	100	Lovastatin	20.9	2.96	23.86	2004/10/29
703995	1	Lovachol 40mg	40mg	TAB	100	Lovastatin	22.6	3.24	25.84	2004/10/29
783345	16	Prava 10mg	10mg	TAB	30	Pravastatin	148.7	20.82	169.52	1992/05/08
783753	27	Prava 20mg	20mg	TAB	30	Pravastatin	185.06	25.91	210.97	1993/04/07
839955	2	Prava 40mg	40mg	TAB	30	Pravastatin	221.29	30.98	252.27	1998/05/18
704253	1	Simvahexal 10mg	10mg	TAB	28	Simvastatin	64.68	9.06	73.74	2005/03/30
704254	1	Simvahexal 20mg	20mg	TAB	28	Simvastatin	72.86	10.2	83.06	2005/03/30
704255	1	Simvahexal 40mg	40mg	TAB	28	Simvastatin	125.26	17.54	142.8	2005/03/30
704174	1	Simcard 40mg	40mg	TAB	30	Simvastatin	99.5	13.93	113.43	2005/03/01
705159	1	Simvacor 10mg	10mg	TAB	28	Simvastatin	65.49	9.17	74.66	2003/07/16
705520	1	Simvacor 20mg	20mg	TAB	28	Simvastatin	74.38	10.41	84.79	2003/07/16
705520	2	Simvacor 20mg	20mg	TAB	30	Simvastatin	78	10.92	88.92	2003/07/16
703525	1	Simvotin 10mg	10mg	TAB	28	Simvastatin	64.68	9.06	73.74	2004/09/13
703526	1	Simvotin 20mg	20mg	TAB	28	Simvastatin	72.86	10.2	83.06	2004/09/13
703527	1	Simvotin 40mg	40mg	TAB	28	Simvastatin	125.26	17.54	142.8	2004/09/13
783351	19	Zocor 10mg	10mg	TAB	28	Simvastatin	90.5	12.67	103.17	1992/09/28
783398	6	Zocor 20mg	20mg	TAB	28	Simvastatin	100.46	14.06	114.52	1992/09/28
836325	9	Zocor 40mg	40mg	TAB	30	Simvastatin	149.16	20.88	170.04	1997/11/24

APPENDIX 3

THE ECONOMICS OF PARALLEL TRADE IN PHARMACEUTICAL PRODUCTS
Revised Summary for WTO-WHO Workshop April 2001 Presentation, Prof FM Scherer.

This contribution summarizes a longer paper by the same title which is drawn from a more comprehensive manuscript, "Post-TRIPS Options for Access to Patented Medicines in Developing Countries," written jointly with Jayashree Watal. Copies of the complete parallel trade paper will be available at the workshop. The conclusions in this version are my own and not necessarily those of Mrs. Watal.

Let me begin by addressing a semantic muddle. Various workshop contributions speak of "equity pricing," "tiered pricing," and "differential pricing." There is a century-old tradition in economics of calling the subject on which we focus "discriminatory pricing." I prefer to be precise but politically incorrect and abide by that tradition. I will also refer to a special case known as Ramsey pricing (named after British economist Frank Ramsey, 1903-30) and propose that there are good reasons for using that term, since the concept characterizes the kind of pricing that, we shall see, is in a particular sense ideal for international price formation in pharmaceuticals.

Parallel trade occurs when a product covered by intellectual property rights in Nation A is exported to and re-sold in another Nation B without the rights holder's authorization. The incentive for its occurrence is a sufficient difference in prices between the two nations to cover shipping and transaction costs and still offer gains to both the shipper and the Nation B buyer. It is therefore a form of arbitrage. For it to occur, there must be underlying monopoly power and/or market imperfections, among which patent protection figures most prominently, exploited by the original seller through a strategy of price discrimination. Adjudicating parallel trade disputes using WTO's disputes resolution procedure was expressly excluded in the compromises struck when the Uruguay Round Treaty was concluded, so the legality of barriers to parallel trade depends upon national laws, which are only required to confer most-favored nation treatment.

My longer paper shows in detail why, in two nations that are identical except in incomes per capita, the demand curves for a pharmaceutical product can differ because of what economic theory calls an income effect. The demand curve in the rich nation is steeper and (admitting possible exceptions) less price-elastic than the demand curve in the less affluent nation. Assuming similarity

of production and distribution cost functions, this difference in demand curve elasticities leads a profit-maximizing firm with some monopoly power to charge a higher price in the rich nation than in the poorer nation. If forced to charge the same price in both nations, the firm's profits will be lower, and under conditions that plausibly mirror the distinctions between rich and poor nations, the firm required to quote uniform prices may choose to set its price so high that there are no sales in the less affluent market. Thus, discriminatory pricing facilitates selling pharmaceutical products in less affluent markets at lower prices than would otherwise be charged, and it may make the difference between having the product available in the developing country market and not having it at all. It cannot ensure that sales will occur in the less affluent nation, for if demand is so weak that no feasible price is high enough to cover production and distribution costs, the market will implode to a zero - supply equilibrium. In such cases, charity or government financing of drug purchases are the only viable alternatives. Watal and I have shown in our Post[a] TRIPS paper that certain interpretations of the U.S. federal income tax laws make it profitable for pharmaceutical companies to donate free supplies to charitable organizations.

For those who are concerned with ensuring that the citizens of less-developed nations have affordable access to patented pharmaceuticals, discriminatory price-setting is intrinsically attractive. But economic analysis makes a stronger statement. When a large block of fixed costs must be recovered -- in the case of new pharmaceutical products, the costs sunk for research, development, and clinical testing -- setting prices lower in high[a] elasticity markets (i.e., in low-income nations) than in low[a] elasticity markets confers the further advantage that those fixed costs can be recovered with minimal distortion to the efficiency of resource allocation. That is, with so-called Ramsey pricing, the fixed costs can be recovered with the smallest feasible reduction of the summed surpluses retained by consumers and producers. In the case of constrained Ramsey pricing, prices will be elevated only enough to ensure recovery of the desired fixed costs. With unconstrained Ramsey pricing, i.e., with the elevation of prices above marginal costs being proportional to the inverse of the affected markets' demand elasticities, resource allocation will be relatively efficient while maximizing the amount of funds inducing future research and development. Such pricing comes about as close as one can hope in an imperfect world to having one's cake and eating it.

The distinction between constrained and unconstrained Ramsey pricing is an important one. Professor Danzon appears to believe that the profits of pharmaceutical firms are constrained by price competition among themselves. Wholly apart from the fact that such competition was not the sort of constraint Ramsey and his followers had in mind, I am skeptical of the Danzon argument for

two reasons. For one, the detailed market structures within which pharmaceutical firms find themselves competing vary enormously, from situations (such as with Diflucan) in which there is no good substitute therapy for certain indications, to those in which several different patented molecules offer essentially the same therapy, and from there to those in which good generic alternatives exist. It is impossible to know whether the "right" degree of constraint arises from such a heterogeneous set of market structures. Also, economic theory and studies of actual pricing strategies reveal that competition among substitute patented products with differing characteristics may lead to price increases, rather than the price restraint assumed by Professor Danzon. My belief that unconstrained Ramsey pricing may be "good enough" is rooted in the assumption that when firms compete for market position and profits by investing aggressively in research and development (a phenomenon known as rent-seeking), pricing behavior that maximizes the profit pool also maximizes the stimulus to R&D investment, which, again admitting possible exceptions, is on the whole to be encouraged.

My longer paper then explores three cases in which Ramsey pricing will fail, or at least, fail to have these desirable properties. All are related to parallel trade.

Because parallel trade arbitrages price differences by diverting products from low-price to high-price markets, it can undermine attempts to maintain a system of discriminating prices. This has two adverse consequences. First, it will erode profits in the higher-price markets, lessening the contribution those markets make to the recovery of fixed (i.e., research and development) costs. Second, profit-maximizing firms will react to the diversion of products from high-elasticity, low-price markets by reducing their supply to those markets, raising prices there and perhaps (depending upon demand curve shapes and the magnitude of parallel trade) choosing not to supply them at all. Since this works to the disadvantage of low-income nations, one might reasonably support national laws or international covenants that prevent parallel exportation of pharmaceutical products supplied at low discriminatory prices within less-developed nations.

Second, the attractive logic of Ramsey pricing may vanish if the market for pharmaceutical products within a low-income nation can be segmented into two (or more) groups: an affluent minority, often well-covered by health insurance, with a low price elasticity of demand, and another group (comprising the majority of low-income nations' population) with little ability to pay and high price elasticity of demand. Multinational pharmaceutical companies may find it more profitable to supply only the affluent minority, in which case prices in the low-income nation will

be much higher than one would expect under Ramsey pricing with homogeneous demand. To deal with such cases, nations characterized (e.g., under United Nations criteria) as less-developed should not be denied the opportunity to engage in parallel importation from other nations in which prices are lower.

Third, national price controls can undermine the logic of discriminatory world market pricing. Then nations may be the origin of parallel exports not because prices have been kept low under a Ramsey pricing rationale, but because local governments have exerted their price-restraining power. When this happens, individual nations will end up paying less than their Ramsey[a] optimal contribution to cover research and development costs. In addition, the pharmaceutical manufacturer may react to the diversion of product from the price-controlled market by reducing its supplies into that market. If parallel exports continue nevertheless, there will be welfare-reducing product shortages in the market from which the parallel exports originate. Recognizing these difficulties, it might be necessary to prohibit parallel exports from national markets subjected to price controls, especially when the receiving market is an affluent industrialized nation.

Further complications can arise under so-called "reference price control" regimes that take as the benchmark for setting controlled prices the lower price charged in some other nation. If discriminatorily low prices in low-income markets are the external reference, pharmaceutical producers will respond rationally by reducing the supply of drugs to the low-income markets and increasing prices there, or perhaps discontinuing supply to those low-income markets altogether. Since this is plainly undesirable, price control systems using low-income nations' prices as an external reference benchmark should be strongly discouraged. Because this may conflict with the narrow national interest of the price-controlling jurisdiction, such a prohibition is likely to be accomplished only through an international accord.

There appears to be considerable uncertainty as to whether pharmaceutical manufacturers actually try to set their prices across diverse national markets in conformity with the idealized Ramsey pricing guidelines. If they did, we should expect to see lower prices for a given product in low-income markets than in high-income markets, other conditions being held equal.

Jayashree Watal and I have assembled a database providing insight into this hypothesis for certain drugs used in combating AIDS. From the leading collector of data on pharmaceutical product sales, we have obtained information on sales revenues and quantities sold for 15 AIDS anti-retrovirals in

18 nations with low or intermediate per-capita incomes over the years 1995 through 1995. The nations or national groupings comprise Argentina, Brazil, Central America, Chile, Colombia, the Dominican Republic, Ecuador, French West Africa, India, Indonesia, Malaysia, Mexico, Peru, the Philippines, South Africa, Thailand, Uruguay, and Venezuela. For most of the nations, the sales covered are at the wholesale level to retail outlets, but for four of the nations, sales to hospitals are also included. Excluded from the data set are donations or other sales at especially low prices to national procurement authorities. Average wholesale prices for each of 586 nation-product-year triplets could be derived by dividing sales revenue by the number of units sold, the latter expressed as standardized daily dose quantities. These standardized prices were then expressed as a ratio of the Red Book wholesale list prices for the same products in the United States. The ratios derived in this way are called U.S. price relatives.

Figure 3 attached plots the price relatives for 461 nation-product-year triplets attributable to multinational pharmaceutical companies. (The average price relatives for the 125 triplets from companies not known to be multinationals were on average 14 percent lower than those of the multinationals plotted in Figure 3.) In 98 of the 461 cases plotted in Figure 3, price relatives were higher, and sometimes much higher, in the less-developed nations covered by our sample than the unit value implying parity with U.S. wholesale list prices. The average of all 461 price relatives was 0.847, suggesting that on average, prices in our sample of low- and medium-income nations were lower than wholesale list prices in the United States. This finding must be amended by recognition that there is extensive discounting of actual transaction prices in the United States below published Red Book values -- assuming typical current experience, in the range of 15 to 25 percent off list. Thus, prices of AIDS anti-retrovirals in the 18 nations were on average at about the same level as those prevailing in the much more affluent United States.

A regression analysis of the multinational drug product price relatives yielded two noteworthy further insights. First, there was a systematic tendency for the price relatives in our sample nations to fall over time -- by about seven percentage points per year. Thus, in 1995, prices in our sample of 18 low- and medium-income nations were on average above those prevailing in the United States, assuming that discounting in the United States then was of about the same magnitude as it has been recently, but by 1999, they had been reduced to average levels below those prevailing in the United States. Second, there was a weak overall tendency for price relatives in the lowest-income nations to be below those for the high-income members of our sample. However, that tendency eroded with the passage of time so that by 1999, the correlation between per-capita

income (measured in purchasing power parity terms) and price relatives was close to zero. Since the Ramsey pricing hypothesis predicts that price relatives should rise systematically with income per capita, it would appear that the multinational pharmaceutical companies have moved away from finely-tuned discriminatory pricing strategies toward cruder but more extensive discounting relative to the United States in less affluent nations. Nevertheless, the main impression conveyed both by the scatter diagram presented as Figure 3 and the regression analysis is one of enormous unsystematic variation reflecting idiosyncratic pricing policy variations not adequately explained by our data. Absent evidence to the contrary, these unsystematic variations would appear to suggest that the pricing of AIDS drugs by multinational pharmaceutical companies conforms at best poorly to the Ramsey strictures we have suggested as a rough ideal.

To be sure, our data set ends with price observations for 1999. Since then there have been important new developments as multinational pharmaceutical companies have offered large price concessions on AIDS drugs in some low-income nations. Frank Ramsey's spirit may yet smile approvingly from its exalted place in economist's heaven.

APPENDIX 4 Presentation to PHrMA by Prof Mary J Ruwart, November 2004.

Is Excess Regulation Responsible For Soaring Pharmaceutical Prices?

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Appendix 5

Competition Commission Finds GSK and BI in Contravention of the Competition Act

16 October 2003

The Treatment Action Campaign welcomes the statement below by the Competition Commission. Just over a year ago, Hazel Tau and 10 others lodged a complaint at the Competition Commission against GlaxoSmithKline and Boehringer Ingelheim for excessive pricing of their antiretroviral medicines. The Competition Commission has now decided to refer this matter to the Competition Tribunal for adjudication.

The 11 complainants are: COSATU, the TAC, CEPPWAWU, Hazel Tau, Nontsikelelo Zwedala, Sindiswa Godwana, Sue Roberts, Isaac Skosana, William Mmbara, Steve Andrews and Francois Venter. Two additional parties joined the complaint in February 2003, the AIDS Consortium and a TAC volunteer who subsequently died of AIDS in June .

For questions on the Competition Commission case, please contact Jonathan Berger on 011 717 8600 or 083 419 5779, or Fatima Hassan on 083 279 9962.

We reprint the Competition Commission Statement below.

Fact Sheet on the Competition Commission case last updated in October 2002.
Price of Life: a booklet by the AIDS Law Project on the Competition Commission case.

MEDIA RELEASE FROM THE COMPETITION COMMISSION

16 October 2003

Competition Commission finds pharmaceutical firms in contravention of the Competition Act

The Competition Commission has found that pharmaceutical firms GlaxoSmithKline South Africa (Pty) Ltd (GSK) and Boehringer Ingelheim (BI) have contravened the Competition Act of 1998. The firms have been found to have abused their dominant positions in their respective anti-retroviral (ARV) markets.

In particular the Commission has found the firms have engaged in the following restrictive practices:

1.Denied a competitor access to an essential facility

2. Excessive pricing

3.Engaged in an exclusionary act

The Commission has decided to refer the matter to the Competition Tribunal for determination.

Menzi Simelane, Commissioner at the Competition Commission, says," Our investigation revealed that each of the firms has refused to license their patents to generic manufacturers in return for a reasonable royalty. We believe that this is feasible and that consumers will benefit from cheaper generic versions of the drugs concerned. We further believe that granting licenses would provide for competition between firms and their generic competitors."

"We will request the Tribunal to make an order authorising any person to exploit the patents to market generic versions of the respondents patented medicines or fixed dose combinations that require these patents, in return for the payment of a reasonable royalty. In addition, we will recommend a penalty of 10% of the annual turnover of the respondents' ARVs in South Africa for each year that they are found to have violated the Act."

Simelane said these practices violate the Competition Act of 1998's prohibitions against excessive pricing (section 8(a)), refusing access to essential facilities (section 8(b)) and exclusionary acts that have an anticompetitive effect that outweighs technological, efficiency or other pro-competitive gains (section 8(c).

"Indeed the very goals of our Competition Act - promoting development, providing consumers with competitive prices and product choices, advancing social and economic welfare and correcting structural imbalances - have been made difficult in this context by the refusal of the respondents to license patents."

The original complaint in this matter was filed by Hazel Tau and others alleging that GSK and BI were charging excessive prices to the detriment of consumers for their patented ARV medicines.

GSK and BI hold patents on certain antiretroviral (ARV) medications used to treat HIV/AIDS. GSK holds patents in South Africa on AZT (branded as Retrovir), Lamivudine (branded as 3TC) and AZT/Lamivudine (branded as Combivir). BI holds patents in South Africa on Nevirapine (NVP) (branded as Viramune).

ENDS

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On behalf of: The Competition Commission

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[ENDS]