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GORDON INSTITUTE
OF BUSINESS SCIENCE
University of Pretoria

AN EXPLORATION INTO THE FEASIBILITY OF A RESEARCH AND DEVELOPMENT CLUSTER IN THE SOUTH AFRICAN PHARMACEUTICAL INDUSTRY

Dr. Rosie Ndhlovu

A research project submitted to the Gordon Institute of Business Science, University of Pretoria, in partial fulfilment of the requirements for the degree of Master of Business Administration.

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ABSTRACT

This pharmaceutical industry faces many challenges and a decision made one way or the other could pave the way for spectacular success or failure. Over the last ten years, the South Africa (SA) government has actively promoted research and development in human health and local diseases through an extensive series of funding and investment programmes. Unfortunately, to date the strategy has not yielded the results hoped for. An exploratory, in-depth interview based study was conducted in order to inform the feasibility of using a focussed cluster strategy that directs investment on only the most critical of national health priorities that have an effective market and potential for global export growth. There were two main areas identified as potential for a cluster strategy fulfilling the requirements listed which have informed the recommendations for collaboration and partnering in the form of a programme exhibiting an appreciation for the tension and ambiguity that exists between the goals for social good and the economic motive of the private sector creating a shared benefits.

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DECLARATION

I declare that this research project is my own work. It is submitted in partial fulfilment of the requirements for the degree of Master of Business Administration at the Gordon Institute of Business Science, University of Pretoria. It has not been submitted before for any degree or examination in any other university.

……. Date: 14 November 2007

Dr. Rosie Ndhlovu

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Always, always the journey is never on your own. There are always hands that hold yours, shoulders that carry you when you can't carry yourself and those who simply stay, silent with you in your quiet despair at times when the mountain seems too high and the journey too long.

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LIST OF ABBREVIATIONS

Bioinformatics – use of computing in drug discovery

BRIC - Biotechnology Regional Innovation Centre

Clinical Trials – clinical testing of new products

CSIR - Council for Scientific and Industrial Research

Disease Physiology – Research on the physiological basis and mechanisms of diseases

Drug Design and Development – rational drug design, combinatorial chemistry and drug synthesis strategies

Drug Testing – analytical or in vitro testing of pharmaceuticals

DST - Department of Science and Technology

DTI - Department of Trade and Industry

Efpia - European Federation of Pharmaceutical Industries and Associations.

GLP - Good Laboratory Practice

GCP – Good Clinical Practice

GMP - Good Manufacturing Practice

HIV/AIDS - Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome

Human Physiology – studies on general human physiology

Protein Production – production of proteins and antibodies for therapeutics or diagnostics

TB – Tuberculosis

Therapeutics – pharmaceuticals for the treatment of diseases or precursors of pharmaceuticals

CHAPTER 1: INTRODUCTION TO RESEARCH PROBLEM.

1.1 Introduction

This pre-emptive quote made by the minister of science and technology could not be more apt to describe the cross roads that South Africa's pharmaceutical industry finds itself.

"In many respects we are fortunate: new advances in biotechnology promise to make the path of progress a great deal easier and shorter. We stand at the crossroads and our response to this opportunity will shape our future".

This industry faces many challenges and a decision made one way or the other could spell spectacular success or failure. Over the last ten years, the South Africa (SA) government has actively promoted research and development in human health and local diseases through an extensive series of funding and investment programmes that are collectively said to have invested about a billion rand.

These programmes introduced in the late 1990s following SA's democratization were in response to a failure to extract value from an industry that had contributed to catapulting other developing nations like South Korea, India, Brazil and China

into accelerated economic growth and created massive spin offs in terms of job creation and industry skills development.

1.2 Motivation For The Research

Through the National Biotechnology Strategy For SA, the Department of Science and Technology (DST) set an ambitious plan that aimed to use research, development and technology transfer, to promote the improvement of the health and the quality of life of the population through institutions like the Medical Research Council, Council for Scientific and Innovative Research. The high-level research strategy was based on three key drivers for health research priorities namely, the burden of disease and health profile of the country, strategic priorities in health and development, and the need for the training and capacity building in health research and hoped to capture the profitability and extended benefits of a successful pharmaceutical industry.

The strategy directed R&D investment into a broad set of areas ranging from infectious diseases burdens such as HIV and AIDS and Tuberculosis to lifestyle diseases such as cardiovascular, metabolic diseases and mental health disorders rights through to initiatives in genomics, proteomics and computational biology.
At the time it was important to build capacity and thus investment in almost 12 distinct disciplines in human health as well as an extended portfolio of research in food security and environmental sustainability may have been a prudent strategy.

Further, the strategy acknowledged that the model for a successful network that supports R&D had already been mapped out by preceding countries and so it would seem it was optimistically sensible to have a broad approach to research.

1.2.1 Room for Improvement

Unfortunately, to date the strategy has not yielded the results hoped for. For example a comparison of the level of biotechnology patenting among seven developing countries indicated that SA had both the second lowest number of patents and patent ownership among the countries studied Cloete T E, Nel L H and Theron J (2006). This disappointment is further contextualized by the absence of a single marketable product that is as a result of R&D in SA.

Others argue that, government's strategy has tended to focus on developing SA's indigenous sector and contrary to other nations has not focused nor pursued a mutually beneficial relationship with multinational biotechnology and pharmaceutical companies which has been identified as a key driver to building up an industrial profile that can attract FDI, Kuermmelle (1999), Johnston, Henry and Gillespie (2006). One could almost argue that the events of the past ten years, Kahn T (2007, 12 July) have achieved the exact opposite and resulted in a tenuous and conflict riddled relationship between government and foreign industry. As a consequence, current performance is not encouraging. SA has failed to produce what others would call tangible results in the form of a patentable

medicinal drug from the investment made, nor has all the research activity emerged SA as an attractive location for multinational biotechnology and pharmaceutical companies worldwide as would be expected, Kuermmele (1999). Granted there are other economy wide considerations such as a shortage of skilled and specialized labour as well as the cost of labour that have hampered development, but the impact has been quite destructive in the pharmaceutical industry in SA. Consequently, the first reason for study is to provide contribution to the direction at the crossroad considering that a huge investment in time, financial and human resources has already been made in developing this industry.

1.2.2 Critical To Economic Growth

The second reason this study is important is because this industry has been flagged as critical for economic growth under Accelerated & Shared Growth Initiative for South Africa, ASGI-SA (2006) the national effort for faster and shared growth proposed by the office of the presidency. This recommendation of the pharmaceutical sector as one of priority sectors to achieving high growth aims to further diversify SA's economic performance which is currently based mainly on strong global demand especially from China & India for primary products. This strategy is to be further sharpened and informed by industrial strategies from industry proposals.

According to a report by Genesis Analytics consultancy, Kahn (2007) the industry is said to be in need of a serious intervention. This report confirms that the global

trend in disinvestment and rationalization has hugely impacted the SA industry in the last ten years. Less that 15% of pharmaceutical companies registered in SA today manufacture and produce locally, 35 production plants have closed since 1994, and the import by the majority of raw materials has created a trade imbalance last reported in 2005 of $830 million, Taylor (2007). More that just an industry audit the report, intends to drive debate about what kind of pharmaceutical industry SA needs, how to achieve it and whether to accord the sector priority status.

1.2.3 Health Priorities

Thirdly because of the significant impact of health problems that South Africa faces, R&D into these diseases must become more focussed on producing products that can be used as interventions. Infectious diseases accounted for more than half of healthy years lost in Africa in contrast to only 3 percent of healthy years lost in developed countries, Ridley, Grabowski and Moe (2006). Further estimates of the burden of disease help us appreciate the broader impact that diseases such as TB, Malaria and HIV-Aids have not just on individuals, but on collectives—families, communities, nations. Because of this impact, an exceptional response is required. Clever solutions have to be found in order for efforts in public health programmes to be useful. The need to develop needs based research and development (R&D) in the developing world is underpinned by the continuing

lack of access to essential drugs or vaccines that form the foundation of any advance that is to be made of any country.

Ensuring the sustainability of this industry should be a part of this exceptional response making this industries success a matter of utmost importance and it is now becoming clear that innovation based solutions for health problems in developing countries are both appropriate and feasible, Thorsteinsdóttir, Sáenz, Quach, Daar & Singer (2004).

All three of these motivations demonstrates the tough task of balancing the competing aims of health policy which strives for self sufficiency and local R&D and production in order to provide affordable medicines for South Arica and industrial strategy which aims to generate accelerated growth by strategic investment. If this industry is to remain a focus, it will have to generate quick wins and begin to show a return on the investment made.

1.3 The Purpose Of The Research Study

The purpose of this study is to explore the feasibility of using a focussed cluster strategy that directs investment on only the most critical of national health priorities that have an effective market and potential for global export growth.

The reason for this choice in topic was based on preliminary review of aspects of this industry had been researched. This initial review showed that a relatively good understanding of the barriers to the development of a R&D based pharmaceutical

industry had been explored by Ridley, (2006); Webber (2003); Cloete (2006) Thorsteinsdóttir (2004); Ferrer (2004); Zhenzhen (2004); Abdelgafar (2004) and these could largely be grouped into financial and infrastructural, human capital, the role of domestic collaboration and linkages and government prioritisation which includes regulatory review policy and the political will.

Further, an assessment of the local manufacturing capacity confirmed that manufacturing as a capability is present although the capacity remains limited. Based on these assessments and the relevance to current debate the topic of this study was chosen to look at how all these factors could be effectively employed in a successful industry.

1.4 The Scope Of The Research Study

The pharmaceutical industry includes companies undertaking research, development and the manufacture of medicinal products and because it is difficult to draw a clear line between the pharmaceutical industry and other industries classed biotechnology, for the purposes of this study pharmaceutical will include the traditional pharmaceutical and the biotechnology sector. The scope of this study will be limited to the SA Pharmaceutical industry as a developing country.

1.5 The Aims And Objectives Of The Research Study

The aim of this study is founded on the assertion that based on the investment made to date in this industry and the difficulty the industry finds itself in, without

changes in public policy it will probably continue to weaken and lead to despondency. This means the industry can't afford to not do anything, but needs to find out where there is a market. The aim is thus to provide an industry perspective as to where the growth opportunities are. The objectives are thus to: Assess if SA research institutions, academia and pharmaceutical firms have competencies across the value chain required to conduct pharmaceutical R&D and to determine where these R&D capabilities should be deployed i.e. what nature of research cluster should SA organizations and policy makers encourage for a competitive and pragmatic entry into R&D in the pharmaceutical industry?

These questions will consider how a cluster strategy can improve the performance of this industry.

This study hopes to make the argument that with directed and focused investment in very specific areas that can generate both social benefits and economic results, this sector should remain a priority and recipient of fiscal focus. Consequently, this study seeks to understand if R&D technological capabilities exist in the South African context and could be used to encourage entry into a research based pharmaceutical industry.

The layout of this report proceeds as follows:

This next section is Chapter 2 which is a literature survey, and will begin with a discussion of the pharmaceutical industry, the research and development process and the relevance of this industry in today's global economy, followed by a review of pharmaceutical R&D as a tool for development as well as the economic and societal benefits derived from a research based pharmaceutical industry. After that an exploration on the theory of clusters and how they promote economic development will be presented.

Chapter 3 will present the precise purpose of the research and the research questions to be asked to address the research objectives.

In Chapter 4, the research design will be detailed and the appropriateness of the proposed design discussed based on methodology used in similar studies. The research instrument used, the details of how the data was collected and the process of data analysis are described and discussed. This chapter concludes with a description of the key data analyses performed in this study.

Chapter 5 reviews the results of the research which will be clustered around the research questions.

Chapter 6 is an evaluation and critique of the results, emphasizing the implications for practice and also discussed in terms of the research questions including recommendations to stakeholders. The limitations of the research will be presented in this chapter.

Chapter 7 will be a conclusion chapter highlighting the main findings of the research, and a brief discussion of the implications for future research..

The results of this study will be useful for a wide range of audiences. Stakeholders include government policymakers as they are the people best positioned to consider and possibly implement some of the recommendations identified. Researchers and academia may find this paper useful to further direct the R&D occurring in their departments. Departmental heads at the DST, DOH DTI and Treasury may making the recommendations regarding strategic direction may also find this report a useful input. Finally the entrepreneurs and venture financers who commercialise R&D and aim to market products produced from the research may find this a useful input to their business plans.

In the most, the study findings and recommendations are directed at the SA government and its associated public sector institutions such as science councils and universities.

CHAPTER 2 - LITERATURE REVIEW

2.1 Introduction

The purpose of this chapter is to provide a discussion of the pharmaceutical industry, the research and development process and the relevance of this industry in today's global economy. Next the body of literature that encourages pharmaceutical R&D as a tool for development explores the economic and societal benefits derived from a research based pharmaceutical industry. Subsequently, an exploration on the theory of clusters and how they promote economic development and national competitiveness is discussed, followed by a conclusion on the lack of work examining the specific clusters that a developing country, like South Africa could focus on based on current capabilities in order to develop a research based pharmaceutical industry.

2.2 The Pharmaceutical Industry

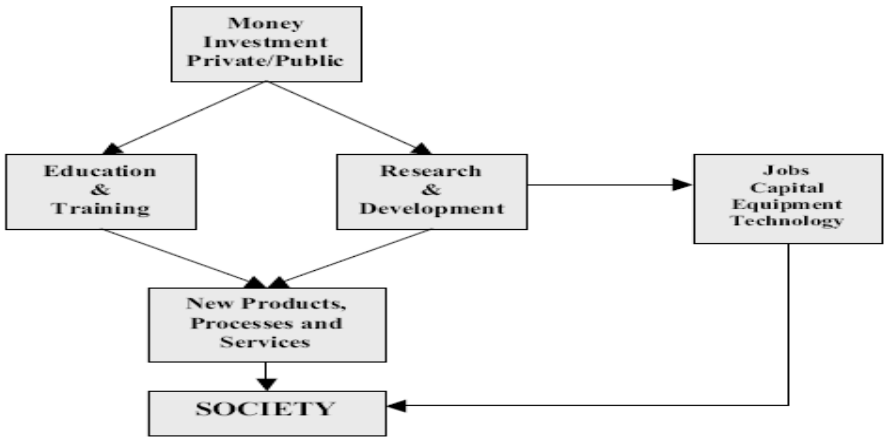
The research-based pharmaceutical industry's key intention is to turn basic research findings into novel medicinal treatments that are widely available and accessible. Its successes in researching and developing new medicines have helped in the fight against previously fatal diseases and has spurred medical progress in the treatment of others, Brännback, Malin, Hyvönen , Raunio , Renko

and Sutinenl (2001) and nowhere has that been more evident than in the benefits that modern technology have offered to improve health care, Pecoul B, Chiraq P, Trouiller P and Pinel J (1999); Thorsteinsdóttir (2004); Winters (2006) and Webber (2003).

Over and above driving medical progress and improving health, the research-based pharmaceutical industry is a key asset to contributing to country economies. As a hotbed for innovation, the R&D in the industry is a potential catalyst (Webber 2003, pg 5) for economic growth and employment in developing countries as it has been in the developed world , and understanding its impact and any factors preventing or enabling its speedy development is important.

A nation's economic success depends on its capacity to carry out R&D, develop human capital built through training and skills development and financial investment in the industry Figure 1. This improvement brought about by technological advance incrementally creates long-term economic growth because it is translated into new products and processes that will stimulate, drive and create new markets, which is fundamentally how the pharmaceutical industry contributes to economic growth, employment creation, health improvement and development, Webber (2003).

Figure 1. The relationship between Research, Product Development, and wealth creation. Webber (2003)



Because of the potential significance of this industry, it is important to understanding the barriers preventing the development of such an industry. The literature demonstrates the barriers to research and development are largely in the areas of finance and investment, patent and regulatory law, human capital and government commitment and leadership as in Table 1, Ridley (2006); Thorsteinsdóttir (2004); Webber 2003; Ferrer (2004); Zhenzhen (2004); Abdelgafar (2004) and Motari (2004).

Table 1: The Barriers To Development Of The Pharmaceutical Industry

Low levels of venture capital leading to limited commercialization.	There is a relatively low levels of venture capital or angel investors investment both for early- and late-stage R&D in health biotechnology. South Africa only has one venture capital firm, Bioventures dedicated to funding local biotechnology companies. This combination of inadequate levels of public funding and low levels of private investment creates a serious barrier for bridging the gap between research ideas and commercialization. [Thorsteinsdóttir (2004); Webber 2003; Motari (2004) and Zhenzhen (2004]
Lack of human resources.	The lack of skilled human resources is further exacerbated by an academic overemphasis on teaching and curiousity driven R&D as opposed to applying science. Most relevant in developing countries is the loss of skills and migration of professionals to developed nations. [Ferrer (2004); Motari (2004); Thorsteinsdóttir (2004)) Abdelgafar (2004) and Zhenzhen (2004]
Inefficient regulatory systems with protracted time lines	To enhance competitiveness and productivity, the sector needs to make improvements, for example, by speeding product development so that therapies, vaccines and other applications can enter the market more rapidly. [Thorsteinsdóttir (2004) and Ferrer (2004)]
Limited domestic collaboration and linkages	The lack of collaboration / intellectual linkages and lack of sharing of resources among biotechnology firms -"dispersed dynamic individuals," "isolated islands"- is seen as one of the major barriers to R&D. Cooperation between firms and the actors most active in health biotechnology research, such as the universities and research institutes, would be the basic tenet of the cluster co-opertion theory to drive innovation and competitiveness. [Thorsteinsdóttir (2004); Ferrer (2004) and Zhenzhen (2004)]
Lack of governmental policies or political will	To promote industrial development in the health biotechnology sector, governmental policies must be more decisive, development has to be identified as a national priority that contributes toward development. [Ferrer (2004)]

Contrary to the significance highlighted by the benefits above, the role of pharmaceutical companies in the developing world is a matter of some debate, ranging from concerns regarding the limited R&D conducted on behalf of the developing world, to those critical of the use of the poorest in human clinical trials.

There is however consensus and acknowledgment on the role science and technology based solutions have to play in improving the quality of life and in addressing the health needs of those not only in the developed world but also in the developing countries around the world, Winters (2006), Pecoul (1999) and Bale (2002).

For improved development and access to new improved medicines, affected countries need to acquire and harness relevant and applicable technological capabilities, develop local capacity and competence towards R&D. For countries that do not have an established presence in this industry, there are many viewpoints to consider before regarding how to further develop and become competitive in this industry.

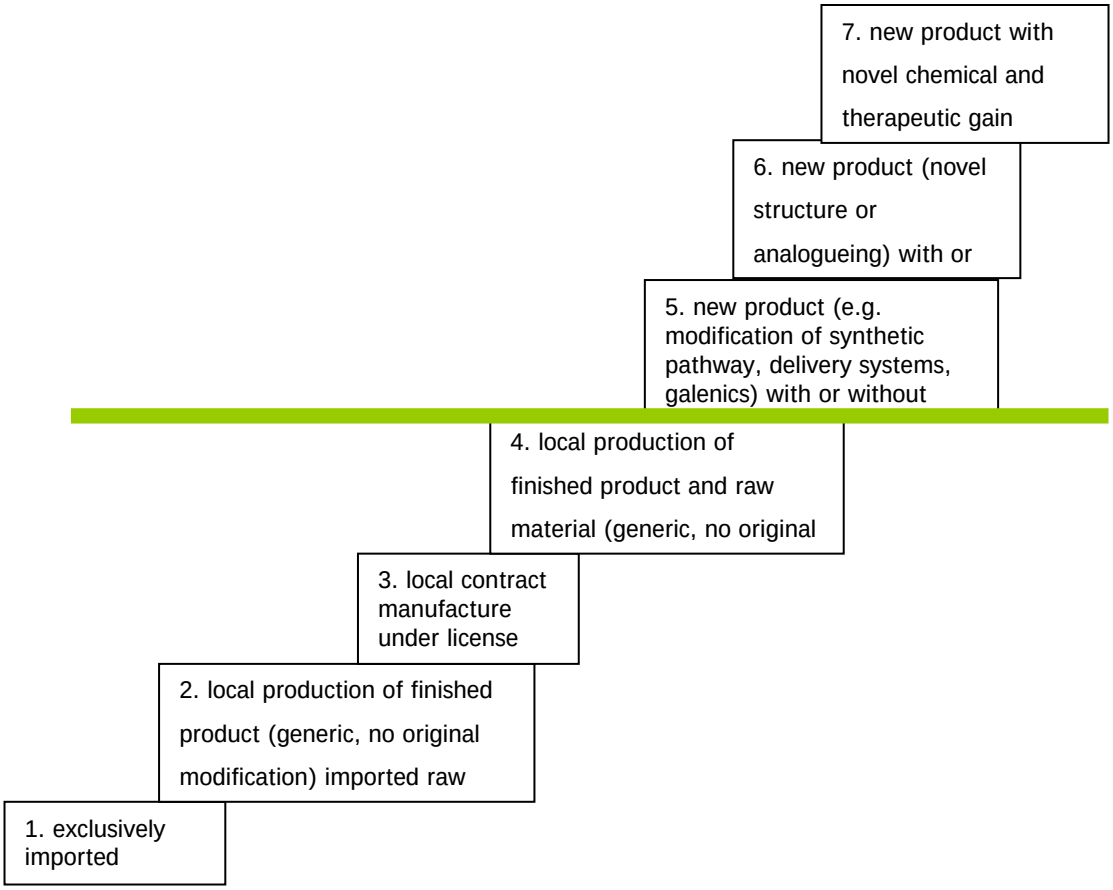
2.2.1 Entry into The Pharmaceutical Industry

The development of an R&D-based industry within a developing country, like South Africa, could be based on models proposed by Webber(2003). An essential

part of developing an industry cluster requires participation by mnc to facilitate knowledge and capability transfer.

A prominent approach, is for domestic firms to back-integrate and expand to include R&D activities (Roscigno 2002), which is encouraged based on the successes of several developing nations, China, Brazil, Egypt and India, who increased local production as a focal point for a knowledge and skill creation, Thorsteinsdóttir, (2004). Following this stage a transition into value added manufacturing (Figure 2) progresses until product development research.

Figure 2. Back Integrate Manufacturing into New Drugs R&D. Roscigno 2002



The biotech approach is useful in an environment of high academic research which can spin off 'start-ups' to commercialise the biotechnology products. The biotech approach is supported by the disintegration currently occurring in the pharmaceutical industry Bell,(2002), which allows emerging participants to exploit this opportunity by concentrating on a few therapeutic areas or components of the pharmaceutical value chain(Figure 2). This model is further supported by the increasing trend to partner with other firms along the chain to bring a drug to market thus sharing costs, risks and rewards.

This disintegration decreases the barriers to entry for those choosing to compete is very specific parts of the value chain or R&D and provides an opportunity for developing countries to focus and apply R&D to high burden health needs in their local markets and outsource any other components it may not have the capability to perform.

These two approaches – manufacturer backward integration and pharmaceutical area specialists - seem to be a valid means that an emerging industry like South Africa, could participate in the benefits of local R&D and production as well as leverage technology to leapfrog into competitive R&D. These alternatives are an efficient model to compete, which facilitates entry without competing with countries like Ireland and Singapore who have enabling environments to attract

MNC R&D investment, and are intensifying their efforts, Skehan (2002) and Webber (2003).

An important question to understand then is how could an industry like South Africa apply these two approaches and in what area could SA establish a competitive advantage? By focusing resources that are available on an integration of the local manufacturing and biotech strategies could create an ideal basis for participating in the benefits of this industry. In order to propose such a strategy, it would be informative to ensure that capabilities exist across the value chain in SA.

2.2.2 The Pharmaceutical Research And Development Value Chain.

The pharmaceutical R&D value chain is a streamlined funnel-like process aimed at identifying the most promising drug candidates out of thousands early in the drug discovery process and put them through a series of tests to eventually find and produce compounds that can be used to fight diseases and can be profitably marketed.

Typically the pharmaceutical value chain (Figure 3) progresses through four major phases, over a period of between eight to twelve years, in drug development namely drug discovery, pre-clinical testing, clinical research and development and manufacturing before commercializing. The range of professionals(Table 2) needed in R&D are extremely varied and of a high proficiency which contributes

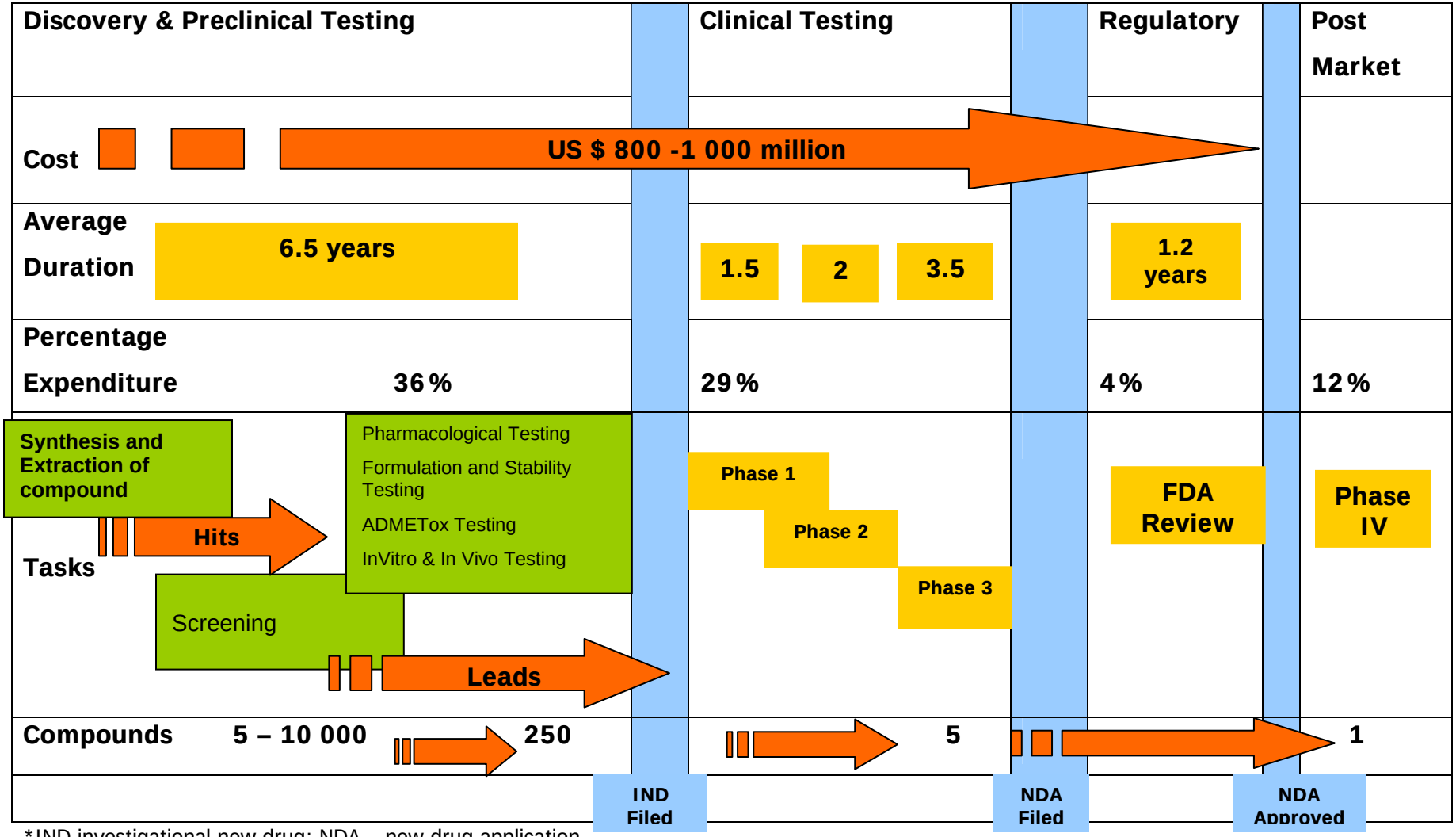
significantly to the estimated billion dollars in average research costs required to bring one drug to market, Brännback (2001). As an ever-smaller number of new drugs is able to pass through the process, this investment makes this a high risk game.

These costs and risk are clearly prohibitive for most developing nations firms even with fiscal interventions. What is clear however is that a strategy that focuses resources in a strategic and articulated area, leverages technology and innovates to possibly shorten development times, cut costs and improve the quality and reliability of drugs is an area of great potential competitive advantage, Brännback (2001).

Table 2. Academic professionals needed in the drug development process. Brännback (2001).

Discovery	Biochemists Pharmacologists Pharmaceutical chemists Molecular biologists Professionals in data capture and mining Analytic & synthetic chemists
Preclinical Testing	Professionals in animal experiments Biopharmacists and Toxicologists Professionals in pharmaceutical development and manufacture
Clinical phases	Biostatisticians and Clinical scientists Clinical research associates (CRA) Professionals in data management and Pharmacoeconomists
Registration Procedures	Professionals in registration and regulatory strategies
Manufacture	Production and Process Engineering Professionals in manufacturing

Figure 3. The Drug Discovery Chain. Medical Research Council of South Africa (2007)



*IND investigational new drug; NDA – new drug application

Unfortunately, despite year-to-year increases in R & D budgets and efforts to structurally support R&D, the SA sector has yet to see either a potential or a successfully commercialized medicinal product, which has been attributed to the fragmented, non market-focused approach to R&D cited as "general lack of cohesion in research programmes", Mulder and Torsten (2003, pg 3).

In conclusion, modern economics condones fiscal policy interventions to promote R&D in the business sector but it would seem the most prudent way of doing this considering the high risk, cost and resource requirements of this industry, could be in a focused area of potential competitive advantage. This approach to government intervention is the case in many countries who until two to three decades ago did not have a pharmaceutical industry to speak of, such as the case of Ireland's biotechnology strategy that focused on investment and development of world-class pharmaceutical research platform, thus allowing Irish firms to build up an industrial profile, Johnston (2006).

It would therefore seem that should a R&D capacity platform exist in SA, a particularly useful approach would be to focus and harness it in a specific area. This study further argues that to justify further investment in R&D, SA must make a strategic choice in a specific area of high unmet need in order to make efficient use of capacity and limited financial resources.

Thus far this study has reviewed the economic benefits that could be generated from a successful industry, the capability requirements of this industry and the mechanism through which entry into this industry could be gained. But a rather crucial question still remains unanswered. This is why any developing nation would want to embark of such an expensive and risky strategy to development. Why not focus on other low cost sectors, and simply buy in pharmaceuticals.

2.2.3 The Benefits Of The Research Based Pharmaceutical Industry

The benefits of R&D can only truly be appreciated by a consideration of the burden of disease and the impact it has on SA.

This section will review the burden of disease in SA and therefore put into context the potential benefits of a successful R&D industry. The potential rewards of products or processes are manifold especially considering the socio-economic spin-offs and form the fundamental reason why any developing country would want to sustain an industry in spite of the technological and resource intensity required, Webber D (2003).

2.2.3.1 Key Country Challenges

The pharmaceutical sector should be of strategic value to South Africa, mainly because of the country's ever growing need for a supply of medicines to treat

illnesses of a high burden such as HIV/AIDS, tuberculosis and malaria (Figure 4). The HI Virus (HIV) has caused one of the most severe global epidemics and SA is the epicenter of this epidemic with close to 25% of the population affected. Further challenges in other communicable diseases including malaria, tuberculosis, and others, among others that collectively account for an estimated thirty four percent of deaths in SA, Ridley (2006).

More than the fatality caused by these diseases, is the societal and economic ruin that they are said to have. The deaths from HIV have created the rapid emergence of orphans and a social phenomenon of child headed families in South Africa at an unprecedented rate, MDG Report (2006).

From an economic perspective, these diseases are estimated to threaten microeconomic potential and stability, and firm operations due to the increase in absenteeism, turnover and reduced productivity, Neilson (2006) and Daly (2000) and contribute at the macroeconomic level to an increasing trade deficit because SA is a net importer of products required to manage and monitor these diseases, Health Policy Unit Report (2007).

Figure 4: Cause of death according to categories, South Africa 2000. Bradshaw (2003)

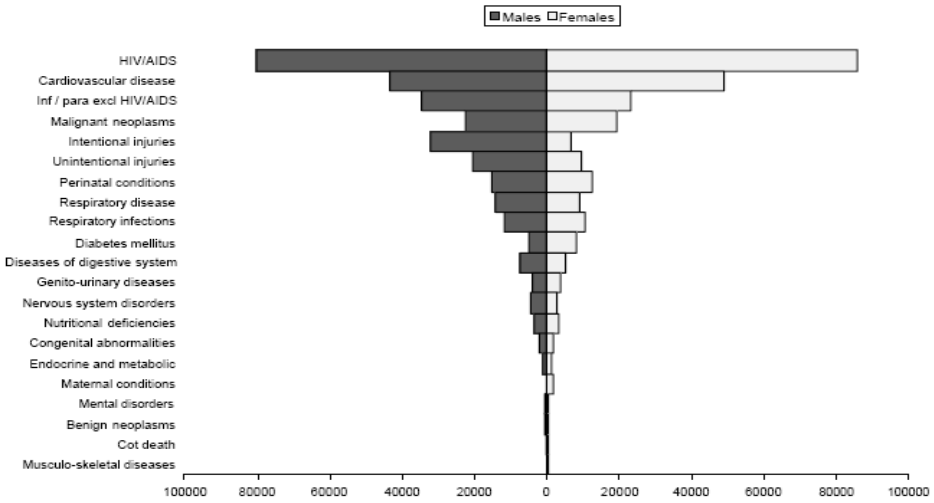


Figure 2: Cause of death by category, 2000

To improve the nation's health and quality of life will require a massively accelerated prevention and treatment effort requiring better and improved drugs which are also cost effective.

Over and above addressing these health needs an R&D based pharmaceutical industry has a multitude of social and economic benefits.

2.2.3.2 The Societal Benefits Of The Research Based Pharmaceutical Industry.

Returns to R&D come not only from economic benefit but also from the benefits to society. These benefits are reportedly very high and were quantified by Odagiri H (1999) in Webber (2003) as being almost twice the financial rate of return. This is as a result of the direct and indirect benefits that accrue through improved healthcare.

a. In a social context such as SA, the obvious benefit from a successful industry are in the ability to tackle country-specific disease /medical problems. By directing investment in R&D on issues specific to the population, rapid solutions are gained by adopting known technology or novel ideas to the problems faced may be developed as indicated in various country case studies of Cuba, Brazil and India Thorsteinsdóttir (2004), Ferrer (2004) and Kumar Thorsteinsdóttir, Quach, Singer and Daar (2004).

b. Furthermore, major health benefits are gained as relatively cheaper access to newer and improved medicines is gained.

c. The knowledge spill over that occur benefit local academia, research institutions and biotechs because of the increasing collaboration that occurs with multinationals and the learning opportunities gained for local researchers. Kuemmerle (1999) demonstrated that foreign R&D activities rises as commitment to R&D by local private and public entities increases in a country.

d. The other factors that were demonstrated to influence R&D investment included the quality of the human resource pool which is another spillover from investment in R&D because a local knowledge based industry would improve the build human capital.

2.2.3.3 The Economic Benefits Of The Research Based Pharmaceutical Industry.

The economic benefits of this industry address the aim of efforts such as AsGiSA to create employment and accelerate growth.

a. The contribution to economic growth through employment, FDI investment on research & development, investment in social responsibility programmes and procurement of goods and services from companies in SA each year is calculated to the value of five billion rand.

b. Further international trade would create a strong and enduring export potential trade surplus from exports into the rest of Sub-Saharan Africa. Currently South Africa is a high commodity market with a current account deficit close on 7% of GDP, Kahn (2007). With a locally successful industry and value adding activities, a significant contribution could be made to balance of payments.

c. The investment in local production would have indirect spillover effects and substantial positive externalities that supports related industries and suppliers ultimately creating a 'trickle-down' effect and building capacity and infrastructure.

d. A successful industry would provide quality jobs which would deploy graduates and PhDs from university which ultimately would create the type of sectoral dynamism that would hopefully lure some of the departed professionals back to South Africa and begin to address the brain-drain concern, MIHR Report to CIPIH (2005)

e. Establishment of a high technology, high value-added sector encourages further research, in a self-perpetuating way that fuels long-term economic

growth, better access to modern technology through technology transfers from collaborations with multinational companies (MNC).

These societal and economic benefits highlight the value that could be extracted from an industry such as this one and create an argument for ensuring an integrated and balanced strategy in developing policy to direct this industry. By making a strategic choice on where to compete the likelihood of being able to capture the social benefit while extracting the economic benefits is heightened.

A fragmented research approach to R&D would require a much greater critical mass of skills, infrastructure and investment than is currently available in South Africa. Ridley (2006); Webber (2003); Cloete (2006). Furthermore, research target selection must also be strongly influenced by financial considerations. In an industry where there are such high risks and high investments, consideration must be given to what the best way of utilizing that investment would be.

It is important to note that economic prospects of a successful industry may precipitate a pressure towards research that is profitable which may not necessarily always be driven by local market needs. This type of focus may create the impetus to conduct research in areas that could support mnc and thus generate income. By adopting a cluster strategy, the generated success could

still satisfy the financial return requirement while catering for local needs and begin to address the potential of an either or solution.

These critical limitations of resources validates a cluster strategy to concentrate and rationalize the skills that are currently present in the South African R&D environment to create success in the industry. The decision regarding what the focus of the cluster would be can be made much like selecting a research target, which is the process to making a choice to focus on finding an agent with a particular action in a particular disease area, Knowles and Gromo (2003).

This approach of focusing on high un-met medical needs and focusing all available capacity on could be deemed a type of 'needs based' cluster strategy. By giving direction through policy, R&D can begin to address the medico-social needs of the country.

2.3 The Theory Of Clusters

Competitiveness is linked to a nation's prosperity because it is based on the productivity, efficiency and profitability with which the nation produces goods and services, Garelli (2006). Porter (1990), said that the competitive advantage of a country was not naturally endowed and inherited but a man-made, created outcome which could thus be partly managed by "creating a business environment, along with supporting institutions, that enable the nation to productively use and upgrade its inputs", Porter (1990, pg. xii.)

Garelli (2006) furthered this definition by elucidating that competitiveness, analyses how nations and enterprises manage the totality of their competencies and fully exploits all its resources to achieve prosperity by developing a comparative advantage solely in an "area of specialization" where it can outperform others in light of the fact that success and a high level of competitiveness in all areas undertaken by a nation is highly unlikely.

2.3.1 Clusters And Economic Development

The Principles of World Competitiveness Report proposes that to generate this competitiveness nations should support a cluster approach that confines state intervention to creating competitive conditions, infrastructure development and an environment that champions adaptation of existing technologies, Garelli (2006).

Ultimately, competitiveness could be described as an action plan to be the best in what one chooses which highlights the importance of cluster theory within the context of policy decisions that will drive the strategic choices that Knowles asserts must be made in order to have success in R&D in the pharmaceutical industry.

2.3.2 Clusters And National Competitiveness

Sainsbury (1999), expanded German economist Albert Hirschman in 1958 philosophy that initially proposed clusters to one that describes clusters as geographic concentrations of firms or industries that compete, collaborate, and are complementary and interdependent. These cluster frms do business with each other or have common necessities of talent, specialized technology, and shared physical and human infrastructure.

In 1998, Porter expounded the cluster theory with his paper on Clusters And The New Economics of Competition when he clearly demonstrated how the world had come to be dominated by "*clusters"* - critical masses in one place of unusual competitive success in **particular fields**, based increasingly in "cluster resources", made up of the local knowledge, relationships and motivation, that made it difficult for competitors or new entrants to match.

Often these clusters may extend through to include governmental and other institutions such as "universities, standards-setting agencies, think tanks, vocational training providers, and trade associations that provide specialized training, education, information, research, and technical support, which are the fundamental components of a R&D driven pharmaceutical industry.

As globalization might appear to make geography irrelevant, cluster theory puts emphasis back on the notion that of competitive advantage resting on making more productive use of inputs available.

2.2.3.1 Cluster Impact on Competition

Typically clusters impact on competition in three broad ways, Porter (1998):

1. They increase the productivity of companies based in the area by allowing companies to operate more productively in sourcing inputs; accessing information and technology, and coordinating with related companies; and motivating improvement.
2. They drive the direction and pace of innovation, through their access to specialized information regarding the market, employees, suppliers and specific technology which accumulates within a cluster. This would be of great benefit and valuable in the case of a local pharmaceutical cluster, as a wide range of academic professionals are required to drive research and development (Table 2) and in this way they could effectively be “shared” in a cluster.
3. They stimulate the formation of new businesses, as in many cases, clusters are a better alternative to vertical integration, which would thus expand and strengthen the cluster itself creating a reinforcing effect, jobs and economic contribution. The peer pressure within a cluster

simultaneously intensifies competitive pressure which may be highly motivating among companies.

Clustering sets into motion a range of benefits that can have direct effect on a developing nation's imperatives. The local collaboration and cooperation promotes a "collective capacity" in the desired area, which strengthens the ability of the cluster to compete in markets, by sharing costs and by engaging in joint tasks such shared research, development, marketing and distribution. The consequent innovation due to the employment of advanced technology as a result of the three broad benefits of clustering is the reason this research project proposes a cluster approach to building competitive advantage in the South African pharmaceutical industry.

In contrast to Porters assertion that the aim of cluster policy is to reinforce the development of *all* clusters and not to abandon others, we would argue that for the purposes of speeding delivery and performance, a choice must be made initially to generate traction and early success.

Similar to Israel's irrigation equipment cluster which developed as result of the nation's strong desire for self-sufficiency and scarcity of water, clusters may also arise from unusual local demand. The same type of proactive focus may be applied by choosing a pressing local issue and supporting it through national

policy as opposed to a self organizing cluster that emerges around already exixting competencies.

Smith (2004, pg 987) points out what was initially highlighted by Massey in 1988 and others that the traditional processes by which an industry begins to spontaneously cluster and a favourable environment develops, may not necessarily be spontaneous and may be prodded along through national investment decisions and strategic policy decisions on the kinds of research undertaken in particular institutions which in turn affect the strength of activity in that locations.

By preferring a government motivated policy to this cluster, the limited fiscal investment can be focused on a particular niche with high local need, Motari (2004). And though the local demand and market is reported to be limited, successful clusters can grow far beyond that limit by adopting a global and thus exporting attitude as seen with some of the global clusters in the US.

2.3.3 Pharmaceutical R&D Clusters

Life sciences demand three basic inputs: specialized labour, appropriate facilities, and knowledge spillovers between research and development supportive networks among linked businesses, research centres, and individuals, Walcott,

(2001). As a result, life science firms cluster because of the need to share and exchange knowledge in order to gain competitive advantage. The proximity between research centres and a development site results because of the "propensity for knowledge spill-overs to remain sticky, Walcott (2001, pg 5).

The performance of clusters demonstrates how small companies or nations can compete with the majors if they focus on a limited number of areas and does not require the huge capital investments typical of the multinationals to foster the formation and growth of R&D based companies.

2.3.3.1 Biotechnology Cluster Case Studies

There are many cases of countries where a biotechnology industry has been nurtured in the past century to a currently successful industry through a cluster approach that also integrated a focused policy intervention.

The Case of South Korea

The healthcare biotechnology sector in South Korea is competitive with that in many developed countries. To reduce the inherent risks in the biotechnology field, South Korean industrial policy makers, along with private sector investors, focused on creating enterprises that could most effectively use the country's existing industrial competitive advantages in fields like pharmaceuticals and

information technology. South Korea became an example of a country that was able to leverage technology, despite being a late entrant into the life sciences field, and make its mark in biotechnology innovation, following commitment to the 'Biotech 2000' plan established in 1994, signed by seven government ministries with an aim to make South Korea one of the world's top seven biotechnology producing countries by 2010. By increasing total R&D spending to nearly three percent of GDP, almost tenfold what is was during the early 1970s, leadership helped to focus and directed R&D through fiscal policy.

This has assured South Korea as a player in the global biotechnology scene rapidly catching up with other Asian countries, such as Japan, and keeping pace with regional competitors like Taiwan, Singapore and China, Wong (2004).

The Case of India

Given its limited resources for R&D in the past, the government encouraged process, rather than novel product innovations and based on these successes India now has the twelfth most successful biotechnology sector in the world as measured by number of companies but also based on its actually producing a commercialisable product, which was developed within four years, and costs approximately one thirtieth of the original cost. Although India has yet to introduce a novel product, the local generic products have been as a result taking full advantage of local strengths, focusing on low-cost processes and relatively simple

vaccines, therapeutics and diagnostic products, that primarily address Indian health needs. The projects undertaken by India's extensive public R&D network are prioritized based on public health needs.

The Case of Cuba

Cuban health biotechnology is said to have reached its relatively advanced stage of development because of the vision of its political leaders and their continued commitment to promote the sector. Cuba's health biotechnology sector focused on relatively, well-defined fields, such as immunology, tropical medicine, immunoassays or vaccines which had been established in the research capability from the late 1980s to the mid-1990s.

Thorsteinsdóttir (2004) illustrates the key to the Cuban success as being the government's long-term policy coherence, promotion of cost-effective treatment options based on the needs of the Cuban public.

Based on the multiplicity of research aims of the national strategy, we would argue that South Africa currently does not possess the capability to address these areas.

This highlights a particular area which has a lack of work examining the specific niches that could be feasible based on current capabilities and competencies and commercialisable based on a reachable market that are aligned with national imperatives, market demand and regional expertise.

We would argue that as recommended in other reviews, Thorsteinsdóttir (2004), a good starting point would be to identify a problematic disease prevalent in the community and focus government policy to support R&D in that area to address urgent local needs and ultimately for expanding the local science base in a way that leads to economic development.

Thus this research paper aims to elucidate which therapeutic or value chain niche South Africa could rationally develop and establish a competitive position in the short to medium term over the next ten to fifteen years.

2.4 Chapter Summary & Concluding Remarks

This chapter began with showing that technology has resulted in remarkable advances in the past century and now where has that been more evident than in the benefits that modern technology have offered in improved health care. developing infrastructure addressing urgent local needs. However the remarkable sums invested by the pharmaceutical industry in R&D to bring a potential molecule to market, pose a potentially insurmountable challenge. The collective African market, as well as the broader global market if a competitive advantage can be built in a niche area of R&D represents a significant opportunity for nations that can establish competitive advantage.

The current review of the research into the important areas of opportunity recognition and exploitation has shown that pharma industry is fragmenting and

holds much opportunity for a biotech strategies that has a focused and narrow research-based product line with potential for commercialization.

A growing body of research seems to support that in the context of developing nations, clusters offer an efficient way to gain access to specialized labor, appropriate facilities, and knowledge spillovers required in life sciences R&D to overcome barriers to R&D in oreder to gain competitive advantage.

Because of limited resources for technological development, it is important that developing nations like South Africa prioritize specific areas and rely on their existing strengths for health biotechnology development.

From this review it can be seen that there is a lack of work examining the specific niches that could be feasible and so the present research addresses this gap by asking the following questions:

1. Do South African research institutions, academia and pharmaceutical firms have competencies across the value chain required to conduct pharmaceutical R&D?
2. Where should these R&D capabilities be deployed in order to efficiently make use of them in SA? What type of research cluster should SA encourage for a competitive participation in the pharmaceutical industry?

CHAPTER 3: RESEARCH QUESTIONS

3.1 Introduction

The purpose of the research is then to answer the primary question addressing what types of research and development are the most desirable for development in the South African pharmaceutical industry. Which sector cluster could easily be developed based on the market need and demand as well as R&D institutions' capability and capacity. Can South Africa realistically aim to begin to provide solutions for the health ailments of its population?

Research Question 1

Do South African research institutions, academia and pharmaceutical firms have competencies across the value chain required to conduct pharmaceutical R&D?

Research Question 2

Where should these R&D capabilities be deployed ie what nature of research cluster should the South African organizations and policy makers encourage for a competitive and pragmatic entry into R&D in the pharmaceutical industry?

CHAPTER 4- RESEARCH METHODOLOGY

4.1 Introduction

Research methodology constitutes the overall programme of the research, and so in this chapter we begin by describing the rationale for collecting the data, then we explain how this research project will be conducted and argue for the proposed methodology that has been used. The population and sampling methodology are then defined, followed by a review of the research instrument. The details of data collection and an explanation of the analysis method used have been are offered followed by a the anticipated limitations of the research.

4.2 Research Design

This purpose of this study is to explore the feasibility of developing a pharmaceutical industry sector cluster based on the capabilities, capacity and market needs of South Africa that can be globally competitive. In order to do this an exploratory, in-depth interview based approach was chosen as the best method that could provide the depth of opinions and perceptions about the possibility of success with this type of strategy.

Qualitative research methods are said to be gaining in popularity, Mack, (2005), particularly in public health and international development research because they provide valuable insights into the local perspectives of study populations.

Furthermore, the contextual richness of qualitative has proved critical in the design of public health solutions in developing countries Mack (2005).

This type of research consists in general terms of an investigation that seeks to systematically apply a predefined set of questions, collect evidence and produce findings and ideas that provide an understanding of a given problem and form the basis of future research.

It was not anticipated that this research would provide conclusive evidence and thus subsequent research is expected to test and further develop the ideas generated from this paper of the concept of a directed policy driven cluster strategy. However, this research is expected to provide a textured review of the issues that should be considered in future stages.

Similar research conducted in the development of a research based pharmaceutical industry in South Africa has been conducted using exploratory research including stakeholder surveys and semi-structured face-to-face interviews, Pharmaceutical Manufacturing Sector Study July (2000), Motari (2004) and Webber (2003), Brännback (2000); Walcott (2001) which corroborates the proposed methodology of this research.

The strength of qualitative research is its ability to provide rich, complex textual descriptions and has the ability to evoke responses that are meaningful and relevant, specifically with reference to the slow development of a research base.

The added advantage of using a qualitative framework is that it is a more flexible, iterative style of eliciting responses that allowed the order of questioning to be slightly modified during data gathering, which facilitated the investigation of important new issues as they arose and the removal of unproductive areas from the original research plan.

From a structure perspective, the qualitative method used was a semi-structured free flowing approach will allowed respondents to describe their individual experiences. Although resource intensive from the point of view of the time required for fieldwork and the analysis process, captured nuances that would not have been possible to capture with a quantitative research method.

4.3 Discussion Of Literature Search For Secondary Data

The secondary sources used to identify literature for Chapter 2 were retrieved from EBSCO source a repository of published peer reviewed journals, as well as internet sources. This secondary data provided a deep reference of industry reports, scientific papers, and government publications of the health, pharmaceutical and biotechnology sector, to firstly gather a contextual understanding of the South African industry and also to identify foundations to proposed solutions to questions asked in this research paper.

None of the publications directly addressed the question of which area of specialization South Africa should adopt though some, Pharmaceutical Manufacturing Sector Study July (2000), Motari (2004) and Webber (2003), Bagchisen (2004), did suggest areas such as HIV-AIDS, TB, Malaria among the most pressing of diseases. It was thus probable that one of these areas would emerge from the survey as an area of high unmet market need.

4.4 Discussion Of Data Required

Based on secondary data collected it was determined that a series of open ended questions would be the best way of collecting primary data. The initial question posed was to try to create rapport and open the discussion by determining respondents opinions as to the reasons why a research based industry had not emerged and developed in South Africa. It was determined from secondary literature review that the barriers to this industry and similar in developing countries was an area of research that had been explored already.

Subsequently an understanding of the manufacturing capacity in South Africa was tested as possible area of exploration based on the back integration into R&D model, however an in depth survey had already been conducted Pharmaceutical Manufacturing Sector Study July (2000), and thus the next useful area of research was in identifying feasible niches as a platform of entry for R&D. This was proposed by works of Motari et al and Thorsteinsdóttir et al in 2004.

4.5 Data Collection

The primary data for the purposes of this research was collected using semi-structured, in-depth expert interviews with representatives of each stakeholder group representing interest groups of the pharmaceutical industry from senior executives of biopharmaceutical firms, directors of academia and research institutions to policy makers in the office of the presidency(Table 2).

These interviews were conducted through a series of face-to-face and/or telephone interviews with the identified stakeholder incumbent. In-depth interviews were deemed best for collecting data on individuals' personal histories, perspectives, and experiences, which elicit a vivid picture of the participant's perspective on the research topic,. Although telephone interviews do not offer as much interaction as do face to face interviews, they were still deemed appropriate in cases where stakeholders could not be physically reached.

An interview guide, a general outline of the topics to be discussed, was used to ensure that the same general areas of information were collected from each interviewee on capacity present in the R&D value chain. The respondents were interviewed once and on average from one to two hours because of the depth of discussion that was reached during each interview.

An alternative method of data collection is a structured survey type of questionnaire such as was used by Webber, (2003) who collected data by asking all members of the sample to respond to the same questions. The advantages of questionnaires or surveys is the cost and time effectiveness, ease of analysis and potential to reduce bias by means of uniformity.

Interviews also help to overcome response rates because they are less intrusive and time restricting on the respondent, however the inability to probe responses makes this methodology inflexible and unable to capture the salient opinions, gestures and visual cues that are not available with written questionnaires.

Another alternative method of collecting data may have been to conduct focus groups which are a qualitative data collection method effective in helping researchers learn about a range of perspectives of a community or subgroup, defined in this case as the biopharmaceutical community representatives. Focus groups are useful in that they determine what is important to a particular population.

The prime advantage of focus groups would have been their ability to elicit a large amount of information over a relatively short period of time and their ability to access a broad range of views on a specific topic. This method could also have been effective, because the type of information required for this interview is not of a highly personal or socially sensitive nature which is one of the key limitations

of focus groups. Focus groups are however, more prone to elicit group norms and opinions which was a key reason for not using this type of collection method. For this type of study, eliciting individual experiences and opinions on the matter was more relevant which is a format more suited to in depth interviews.

Based on the questions asked and the conclusions developed from the literature it was determined that an appropriate method of asking this information would require a questionnaire grid identifying all stages in the R&D process - research discovery, preclinical research, clinical research and commercialization limited to regulatory review and manufacturing, Tonkens (2005); Ginsburg (2001) and Bhattacharya *et al* (2005)- and cross tabulating this with suggested areas of focus from suggested during the interview (Appendix A). It was envisaged that this would be disease area specific but also possible that other suggestions could emerge that were not initially thought of.

The second part of the interview involved asking the second research question questions regarding the strategy of a policy driven cluster as a way to drive to success of this industry.

4.6 Proposed Population And Sampling

Sampling is that part of research methodology concerned with the selection of individuals in order to derive some knowledge about a group that has common

criteria. According to Webster(1985) in Mugo (2004), it is a limited part of a larger group / population, that can be studied in order to gain understanding about the whole. A population is a group of people, objects, or items from which the sample may be taken.

4.6.1 Population

The population of relevance consisted of senior expert representatives of the stakeholder groups identified above who have been involved in R&D and in other parts of the pharmaceutical value chain.

4.6.2 The Sample

Sampling itself is that process that someone conducting research would use to gather the people or the things to be studied. The sample thus has important implications for the conclusions and generalizations that can be drawn from a study.

As qualitative research does not attempt to generalize, but rather aims for depth of understanding regarding the relevant issue, the sampling method usually requires a flexible, practical approach in order to access the subset of the total relevant population. Marshall (1996) further contextualizes qualitative research

by clarifying that “an appropriate sample size for a qualitative study is one that adequately answers the research question” and thus it is typical in qualitative investigations for samples to be smaller.

In practice, the number of required subjects usually becomes apparent as the study progresses through its iterative process and thus requires a sampling technique that can support this iteration.

Based on the stakeholders, it was anticipated there would be a population of approximately 15 interviewees, however the final sample was 12 interviews. These were high quality interviews with respondents who possessed a depth and breadth of knowledge about this industry. Research shows that determining an adequate sample size in qualitative research is a matter of judgment and experience, Sandelowski (1995), based on the intended use. Sandelowski (1995, pg 179) argued that “a sample size of 10 may be judged adequate for certain kinds of homogeneous sampling”. Furthermore, in qualitative research, people are sort out because of their attributes, in this case deep in-depth knowledge regarding this industry. We would argue that based on the caliber of respondent that the quality of data collected would outweigh the quantity that could have been achieved with respondents of a lower position with less precise and deep knowledge regarding the industry.

Further it is acknowledged that this research was not conducted with the purposes of generalizing but with the intention of drawing greater understanding could be extracted from a smaller sample size. Sandelowski (1995) also refers to Trost (1986) who proposed the notion of an “infomationally representative” sample comprising of data that was obtained from persons who could essentially represent others with similar characteristics. We would argue again that the people interviewed in this sample, were informationally representative and formed a cross spectrum of stakeholders who were relevant to this issue (Table 3).

Table 3: Stakeholder Groups of Interviewees

Stakeholder Group	Organization Interviewed
Government Institutions And Policy Makers	Department Of Trade And Industry Policy Co-Ordination And Advisory Services In The Office Of The Presidency
Research Institutions And Academia	Medical Research Council Council For Scientific And Industrial Research
Biopharmaceutical Industry	Local Manufacturer Local Clinical Research Organisation
Biotechnology	Biotechnology Startups Biotechnology Regional Innovation Centre Biotechnology Funding Firm

There are two basic approaches, probabilistic and non-probabilistic, to sampling based on the desirability of making conclusions or predictions about the larger, broader population from which the sample is selected. In this report, we do not wish to make specific conclusions that can be generalized to the broader population, but simply an in-depth understanding on the issue at hand. As

proposed, this research would form the basis for future research and thus would not require generalisability.

4.6.3 Sampling Method

A non-probabilistic judgment or purposive snowball sampling method was selected. This sampling method identified participants based on the selected criteria i.e. their membership to the identified institutions in Table 1. The difference making this sample usable was its base on the researcher's own understanding and knowledge of the area and began with subjects that were known by the researcher to have specific experience and expertise in that domain selected by non probability judgement method. This group subsequently recommend further candidates to include in the study, which created a network of reference and increases the sample size as new contacts were added.

Snowball sampling is often used to find and recruit “hidden populations,” groups not easily accessible or known to researchers through other sampling strategies and such hidden groups emerged from the chain referral. Zikmund (2003, pg 384). Furthermore, due to the researchers established familiarity with the industry, this form of sampling was deemed as appropriate.

Of the alternative non-probability sampling techniques, convenience, was not chosen as it is noted to be the least rigorous technique, involving the selection of the most accessible subjects and thus prone to result in poor quality data and

quota sampling, was not chosen as sampling everybody within the defined parameters of this population would have proved extremely difficult if not impossible as not all members of this population were known upfront.

4.7 Data Management

The data was collected during interview using an interview guide and was collected in the form of interviewer's notes made during the interview and transcribed notes of recordings of audiotapes. Part of the data management was to interpret any immediate impressions regarding the respondent's responses, body language, language used and any other softer aspects that may enrich the meaning derived from the interview.

Data management was simplified and designed to preserve as much of the respondents conversation as possible, capture any added information from observation and to permit ongoing analysis. Therefore the process proceeded as follows:

- During each interview, the interviewer wrote notes in a notebook and captured answers to the interview guide as well as made audio recordings of the interview. These field notes were gathered from responses, quotes and direct observations during and after the interview.

- Immediately post the interview, any additional notes, or observations deemed relevant, or which time did not permit to record during the interview session, were added to the notes.
- Transcription of recorded notes were made after the interviews.

4.8 Data Analysis

The data analysis technique used in this research was a traditional qualitative data analysis (QDA) model of noticing, collecting, and thinking about the aspects mentioned in the interview, Seidel (1998). As illustrated by Figure 5, the QDA process is a simple, non-linear, iterative and progressive process that keeps repeating the cycle of thinking about the data and noticing new things in the data.

Figure 5: The Data Analysis Process (Seidel, 1998)

It can be achieved by using a variety of aids that help one process and derive meaning from large amounts of data such as thinking aids, display methods and coding.

The first part of the data was already prepared for analysis due to its grid structure and so the coding and counting process could occur immediately.

This process allowed an easy transition to a structured, content analysis of the second half of the data, involving, Zikmund (2003) coding , sorting according to the frequency of use of certain words, categorizing, and counting and cross tabulating of common themes, which allowed specific responses to be located with relative ease to facilitate the identification of emerging patterns. The appropriateness of this method is that common themes were easily identifiable and clusters of common recommendations were recognizable which made this method of analysis highly suitable. A preplanned analysis based on stakeholder groups to establish any commonality of industry perspectives and recommendations was included in the analysis plan.

4.9 Possible research limitations

The following aspects are possible research limitations to this research:

- ⇨ The research may minimally confirm already intuitively known areas of focus and clustering such as HIV-AIDS which would have simply reiterated current assumptions and not proposed alternative areas

⇨ The findings are subjective and not generalisable to other developing country which is an acceptable limitation as this study is intended for the South African context.

4.10 Chapter Summary & Concluding Remarks

This chapter began with a description of the research methodology which was of an exploratory, qualitative nature, said to be gaining in popularity in public health and international development research due to its contextual richness. The discussion then focused of describing the process and plan for the required data and its collection, followed by a description of the type of data collection tool of in-depth, expert interviews aided by a two part interview guide with both structured and open ended questions. The snowball sampling strategy used was discussed and the chapter concluded with a description of the key data analysis methods performed in this study. The next chapter reviews the results of the qualitative data analyses followed by chapter 6 which provides a discussion and interpretation of the results.

CHAPTER 5 - RESULTS

5.1 Introduction

This chapter presents the results from 12 interviews with experts in South Africa that indicate that there is strong scientific R&D base from which to further develop though a cluster strategy. These results are derived through a qualitative content analyses conducted from the in depth interviews achieved. The presentation of results follows the structure of the research questions put forward in chapter three by first presenting the results regarding the capabilities required in the pharmaceutical value chain that are present in South African organizations according to interviewed respondents.

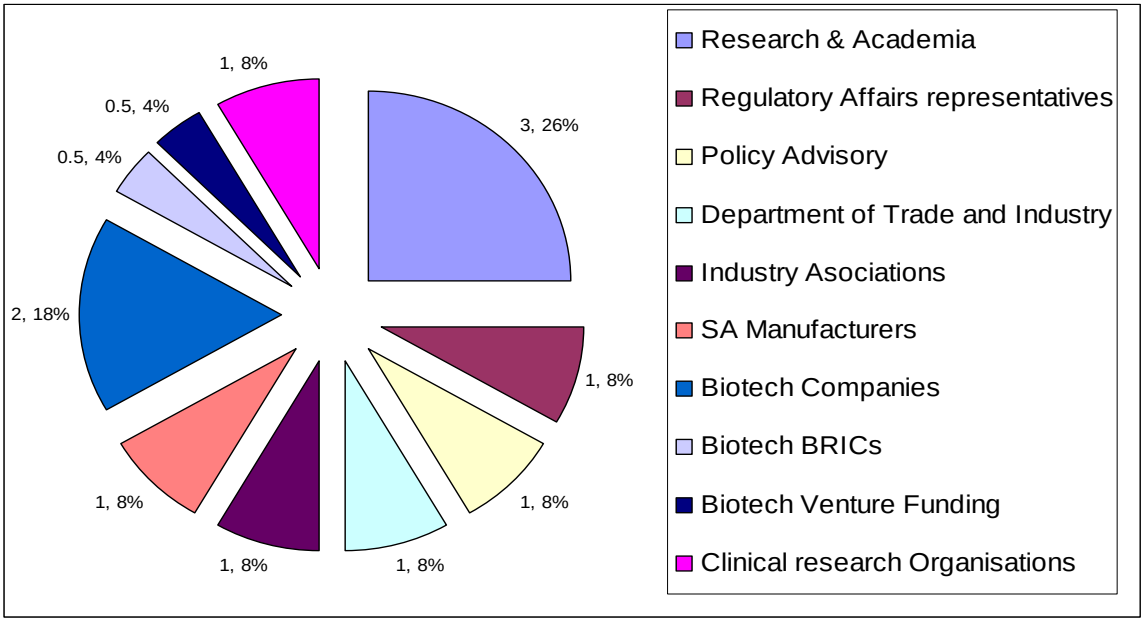
Next, the results identify the main areas of focus regarding the proposed cluster approach, based on unmet medical need, market potential and potential competitive advantage could be encouraged in South African organizations.

Finally, a summary of the results and a summary of the key insights are presented, followed by some concluding remarks.

5.2 Capabilities Present In South African Organisations That Is Required In The Pharmaceutical R&D Process

In order to begin the debate regarding which area to compete in, as the process of target selection requires, scientific and medical consideration should be given to the presence or absence of such highly specialized skills. The final sample comprises of individuals highly knowledgeable about this industry, who represent wide stakeholder interests with a depth and breadth of knowledge which gives this study credibility and value (Figure 5).

Figure 6: Stakeholder Representation Of Respondents .



5.2.1 Overview of Results

From these interviews this study was able to confirm that the skills and capability required in the R&D process “definitely do exist although limited in quantity” as mentioned by one of the respondents. From this study it can be confirmed that capability is believed to exist across the entire value chain although there are very specific areas where there is an obvious gap (Figure 7). It is important to note that the general tone of responses explains that these skills exist in a context of general research which is not always tied into producing marketable products or processes. So in order to drive towards commercialisable outputs, closer collaboration is encouraged with MNC and international research institutions and universities, “big-brothers of sorts” as recommended by one respondent, that can assist that can assist local capacity towards an output driven research approach to take a potential candidate through the value chain.

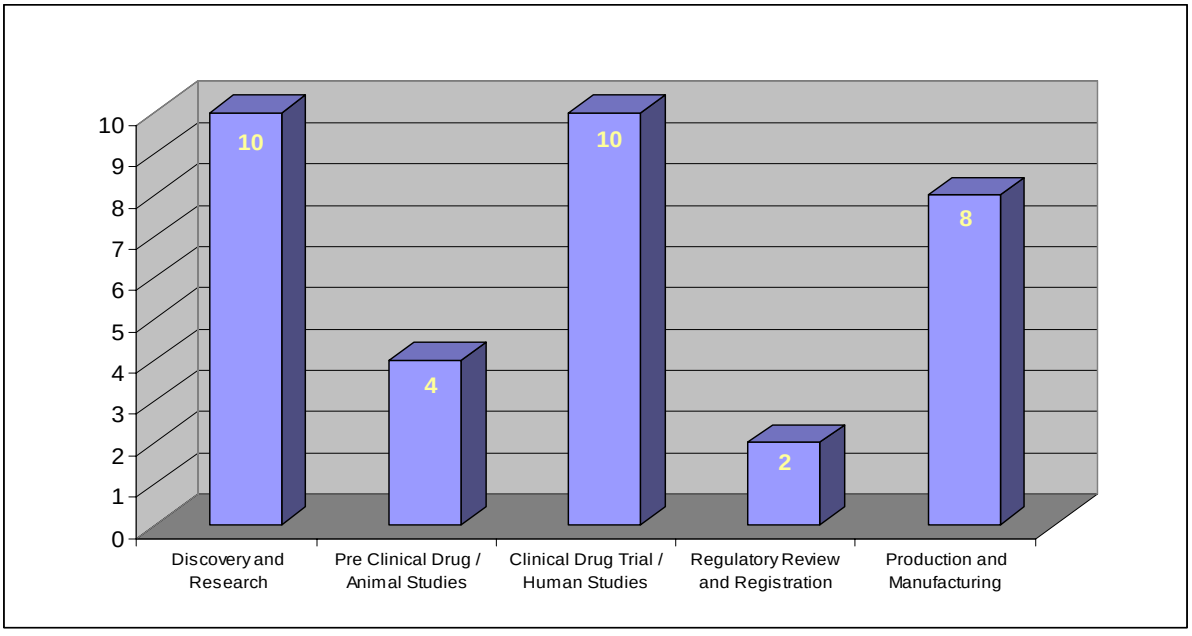
5.2.2 Capability Results by Value Chain Stage

5.2.2.1 Discovery

In the discovery stage, which is the first step of the research process which tries to link the “targets”, which are the vital processes of the human body especially during illness that can be attacked with specific therapies, ten (83%) of the twelve respondents, assessed the capabilities present in the South African pharmaceutical environment to be very good capability of a world class standard.

This quality was further highlighted by an anecdote shared by one of the respondent in which they state that a large number of scientists leave South Africa because there is “very little work for them and end up in the US or Europe working in the laboratories of MNC earning salaries probably three to four times” what they could in South Africa. Further corroborating this position was highlighted by one of the respondents who mentioned that much of the output from research at this stage conducted in South Africa is licensed out to foreign firms and “big pharma” who have the deep pockets to invest in developing these discoveries. These discoveries are then registered in patent offices as discoveries originating from other parts of the world and South African scientists do not receive the acknowledgement for their work, which is highlighted as a key driver of scientific innovation.

Figure 7: R&D Capabilities According To Respondents



5.2.2.2 Pre-Clinical Testing

The next stage of the pharmaceutical R&D process involves testing the drug candidates that can attack the identified “target”. This process involves testing the drug candidate on animals and in medical labs and was highlighted as the first “serious bottleneck” in R&D. One respondent went as far as to say that “we most certainly do not have this capability” and another mentioned that “this is the point of a spectacular blockage which prevents candidates going forward …” and “nips creativity in the bud”.

Only four (30%) of the respondents thought that this capability exists in South Africa at a reasonable standard to support further development of candidates identified in discovery and deliver them to clinical development. Preclinical research is described to not exist in the private sector and that current capacity is mostly in state institutions which is not directed at sustaining private research and most appreciably where it does exist, is not GLP standard compliant.

Of note and particularly interesting was that, of the interviewees that worked in discovery research, none felt that the standard of pre-clinical work was what it needed to be to in order to support discovery. The respondents who deemed the stage to have adequate capacity were often in the later stages of the value chain which may reflect a less precise knowledge of the earlier stages of the R&D process. One particular respondent did however explain that in their business they require work from this stage and do not have a problem acquiring it. This

may confirm and agree with the early stage discovery scientists who state that, although this stage represents a significant bottleneck, there are “some pockets of some capability and activity” which could be further developed with investment in order to close this gap”.

Overall all respondents agreed that although little, some capability does exist and is present at this stage and requires directed investment by government to stimulate it further which may be followed by private funding. One of the respondents did caution that “it would increase the pressure on the pre-clinical centres which may drive them to conduct research in a fragmented but high margin environment”, contrary to supporting any focused area of research chosen as a cluster. In contrast, another respondent highlighted an alternative development approach of partnering with a global facility to allow skills transfer and improve access to a global outsourcing market as befits of developing preclinical capacity.

5.2.2.3 Clinical development

The area most well developed, funded and with the greatest capability in this value chain lies in clinical drug trials development, which is not surprising considering that this area is largely developed and funded by MNC. This is as a result if the diversity of disease and racial representativity of the patient

population found in South Africa. The infrastructure, coupled with excellent medical practitioners who are well trained in clinical trial processes, is able to support world class and regulatory standard compliant research. This was described to be because the investment directed to South Africa has kept pace against India and China because they currently have “questionable quality.

These two nations were however pointed out to be serious competitors who are rapidly catching up because they also have the diversity of disease and patient numbers. A respondent in the clinical research area stated that “South Africa can still compete in terms of quality and some level of cost effectiveness because the costs are in-between Europe and lower cost centres like China and India. A development programme can still be conducted in South Africa for a third less than it would in the developed nations so we remain competitive. We also have capability to write and develop protocols so could easily support activity” aimed at developing and commercialising a product through the value chain. The only limitation cited to this stage is the impact of the regulatory review and registration process which has a direct impact on the global competitiveness of this component.

5.2.2.4 Regulatory Review and Registration

The most cited stage of limited and restricting capacity is in the regulatory review and registration process. This traditionally involves a review of the

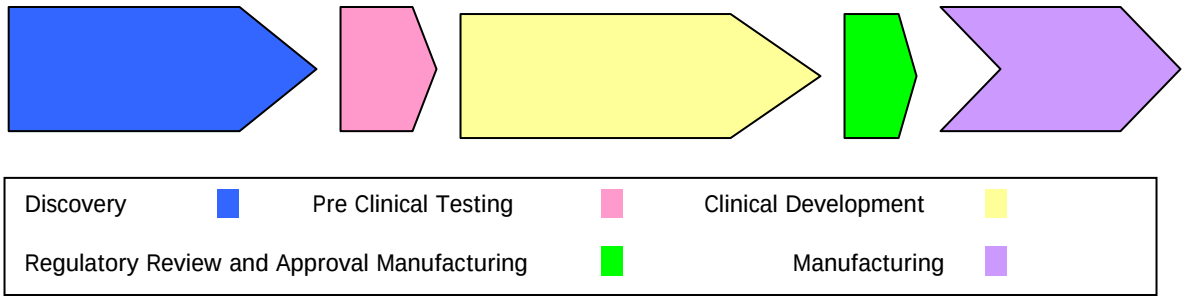
candidate/medicines safety, quality, and efficacy and is the last major development hurdle that must be passed by a new medicine before it reaches the market. In an R&D context, regulatory functions extend to include pre-submission assistance. In both these areas the majority of respondents cited the South African process as a “grave bottleneck”, which in an industry where being the first on the market gives competitive advantage, posed a serious challenge to R&D. Only two of the twelve respondents considered the capability and most importantly the capacity that exists in the South African regulatory body to be enabling of the industry. What was further highlighted was that a regulatory body requires a separate skill set in the case of R&D to assist and have an open dialogue between the firm developing the drug and the regulatory body, to give advice on scientific and administrative issues before an application is submitted. The study respondents in this study did not feel the South African body to have these capabilities.

5.2.2.5 Production and Manufacturing

The last stage of the R&D value chain which may also run parallel to clinical development, requires that candidates that have proven to be effective and safe be produced and manufactured in bulk for mass utilization. According to the respondents South Africa also has reasonable ability in production and manufacturing. Of the respondents, approximately eight (67%, Figure 8)

assessed the manufacturing capability to be present in South Africa. The critical challenge pointed out was the decline in manufacturing output highlighted in the interviews. All respondents highlighted that the capacity in South Africa has been declining over the past few years to a point where one respondent pointed out that "ninety percent of the locally used pharmaceuticals are imported which contributes significantly to the (trade) deficit". The focus in this part of the value chain was collectively on ensuring that South Africa increases the scale of production and also invests in making local production facilities compliant with standards ie Good Manufacturing Practice (GMP).

Figure 8: Capabilities and Bottlenecks in R&D Value Chain in South Africa according to study respondents



In summary with respect to the first question of capabilities available in South Africa, this study concludes that the capability in the R&D process in South Africa are limited and asymmetrically developed. The most well developed segment of the R&D value chain is in clinical development (29% of capability available) which has been assisted by the development programmes of mnc. The are two

main stumbling blocks drawn attention to are in preclinical development which would require investment to mature and in the regulatory review process which is assessed to require development in skill and competency.

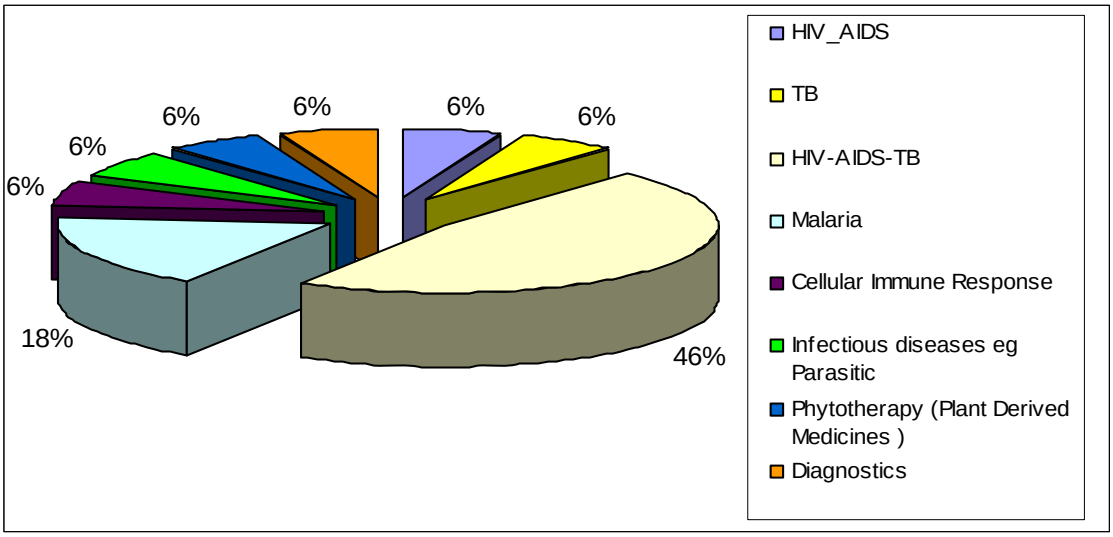
5.3 The Cluster Recommendations For Pharmaceutical R&D Focus

5.3.1 Cluster Results Overview

The results identifying the main areas of cluster focus based on unmet medical need, market potential and potential competitive advantage identified the therapeutic area of HIV-AIDS-TB and API manufacturing as the key fields to be encouraged in South African organizations.

The results for all the interviews are presented in Figure 9 confirming that the area of most pressing public need is currently in HIV-AIDS which is increasingly associated with TB.

Figure 9: The Therapeutic Areas Recommended As A Cluster For Pharmaceutical Research And Development Focus Based On Public Need



A cluster strategy was encouraged and acknowledged as an approach that could optimize the limited resources available to develop this industry into one that is "fully integrated and competitive'. In the words of one respondent, "South Africa has an obligation to make products that are for our people…, must industrialise in a sensible way… and take a long term approach".

5.3.2 Leadership In A Cluster Strategy

But several respondents highlighted that before asking the question of where to focus, it is firstly important that the industry, which includes the policy makers and politicians, realise that "a bold and courageous thought leadership" will be required to make these "difficult decisions". It would necessitate that acknowledgement be made of the "great strides that had been made by the investment that has created the broad knowledge base and R&D platform present today", and then "show the political will to chose to focus and make deliver tangible results" on the investment made over the past years. For this type of strategy to succeed the R&D community would need to bring to a close working in silos on their own "little pet projects", focus on the big picture and collaborate. This collaborative clustered approach would stop self motivated research that encourages competitiveness with science objectives and promote research that generates needed products to generate profits that create jobs and economic prosperity.

An example cited of this type of focus is illustrated by a conversation one of the respondent had with director at a Cuban R&D centre who said, “here no one works on a project unless its research that works to create a product that leads to the betterment of people.

5.3.3 Disease Area Recommendations

The second aspect to consider in order to make the choice of where to direct resources, policy makers are encouraged to ask questions that others like India, Japan and Cuba have asked – “what do people here need and what can the people here do profitably”. The former question is highlighted as the most important and likely to inform the choice for South Africa because of its social and economic implications. Based on these implications and the “sheer scale of unmet medical need” almost 50% of respondents voted for focusing R&D capacity on HIV-AIDS-TB. One respondent really contextualized the tension that emerges from asking the question of market economic potential in the following statement, “the problem with this magnitude of question is that it is difficult for any developing country to make. There are so many problems that need to be

addressed so we tend to do a little bit of everything, but the decision must be based on the impact that disease could have on the population, so my choice would be HIV-AIDS & TB as they become increasingly integrated.

This therapeutic area is repeatedly mentioned to be where South Africa has the largest inbuilt market extending into Sub Saharan Africa which addresses the question about the ability to profitably develop a cluster. An analysis by stakeholder groups showed a preference in all groups for focusing research in the area of HIV-AIDS-TB (Table 4).

Table 4: Proposed Therapeutic Area by Stakeholder Group

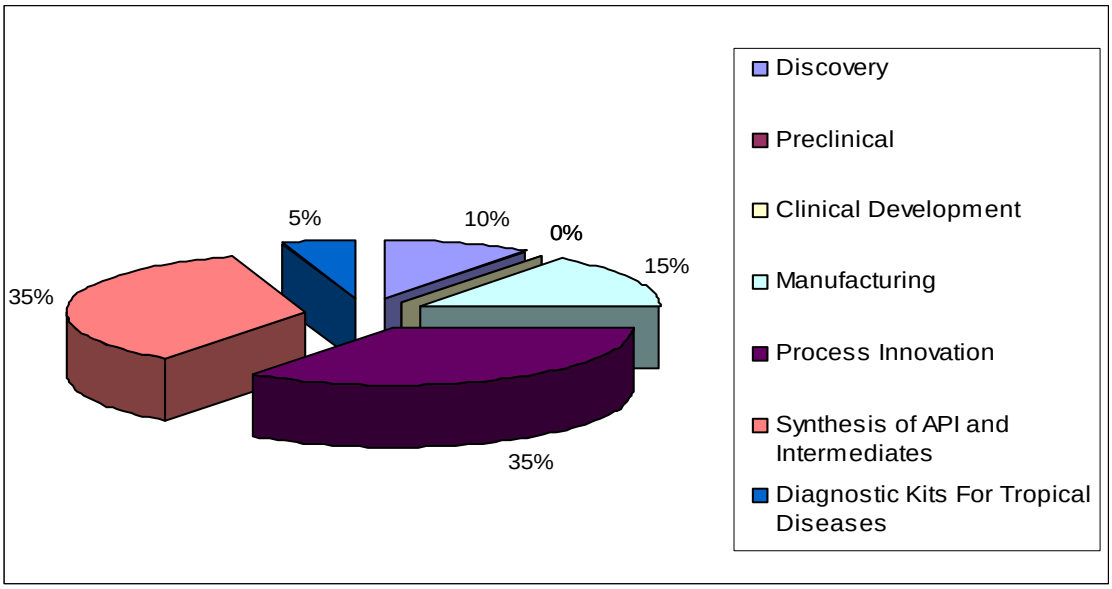
Disease area recommended	Research & Academia	Biotech Companies	Regulatory Review and Registration	Policy Advisory	DTI	Industry Asociations	SA Manufacturers	Biotech Companies	Biotech BRICs	Biotech Venture Funding	Clinical research Organisations
HIV_AIDS	0	0							1		
TB	0	0								1	1
HIV-AIDS-TB	3	2	1	1	1	1	1	2			
Malaria	1	1		1				1			
Cellular Immune Response	1	1						1			
Infectious diseases, parasitic	1	1						1			
Phytotherapy (Plant Derived Medicines)	1	1						1			

Other possible therapeutic areas mentioned (Figure 8) are Malaria (eighteen percent) based on the significant health burden of that disease. Cellular Immune Response research was mentioned because it facilitates understanding of the failure of immunity which is the basis of many diseases especially infectious diseases. This would build capacity that would be relevant because of the developed insight into disease processes and allow this knowledge to be applied across various diseases with overlapping bodily processes.

5.3.4 Value Chain Cluster Recommendations

Additional areas of focus proposed in this study are in a component of the pharmaceutical value chain and applying this capability across a variety of diseases (Figure 10). The production of Active Pharmaceutical Ingredients (API), emerged from thirty five percent of respondents, followed by Manufacturing Process Innovation which was suggested by twenty nine percent of respondents as other alternatives from a value chain derived cluster. These two recommendations could essentially be combined to represent a cluster focused on using technology-enabled innovations to the processes of manufacturing.

Figure 10: Value Chain Pharmaceutical R&D Based Cluster



The respondents in this study believe that by strategically choosing products in the proposed disease areas above with “high market need, local manufacturing has important industry spin-offs” in the form of local job creation, contribution to the balance of payments through profitability derived from scale economies, and most importantly becomes the driver of process innovation. One perspective is that by basing the choice of what to produce on products with similar production processes, firms become as efficient as possible until they learn how to innovate the process so as to manufacture cheaper and faster. This iteration creates a manufacturing platform which can build “a meaningful industry that can in time, through reinvesting profits, backward integrate into R&D”. The merit of this approach is captured by one of the respondents’ synopsis, “R&D is a high risk

game and you may never produce tangible result. Manufacturing helps you start like other nations and learn to crawl, then walk then run".

One caveat to focusing on manufacturing is that there ability to process innovate may be restricted by the insufficiency of production and process engineering skills, although these specialized skills could easily e developed by partnering with countries like India or Brazil. Further most respondents suppose that success and development in this part of the value chain would respond to success in early stages of R&D because "if you have a block buster drug candidate the investment will follow and drive manufacturing capacity. The current challenge is in driving early research and developing and taking products across the value chain".

5.4 Chapter Summary & Concluding Remarks

This chapter has presented the results from experts interviews that indicate that there is a fundamental scientific R&D platform of R&D capability in South African organizations although limited in some areas and restricting in others. The results identify the main area of focus regarding the proposed cluster approach to be mostly in favour of HIV-AIDS-TB as a combined diseases area based on unmet medical need and market potential and a manufacturing strategy based

on the economic profitability that could enable the early stage research as a result of reinvesting profits.

The next chapter discusses these results in the context of the literature.

CHAPTER 6: DISCUSSION OF RESULTS

6.1 Introduction

This chapter discusses the results outlined in Chapter Five in light of the reviewed literature in greater detail. It begins with a summary of the findings of the capabilities required in R&D presented according to the key themes of the process. Next, a discussion of the proposed cluster in light of the recommendations from the literature is presented. Finally, additional considerations that are linked to the proposal emerging from the results are discussed and a discussion of the achieved research objectives is offered.

6.2 Capabilities Present In South African Organisations That Is Required In The Pharmaceutical R&D Process

As discussed in chapter 5, qualitative analysis found that, the skills and capabilities required in the R&D process "definitely do exist although limited in scale' and unequally developed in SA. From this study it can be confirmed that capability is believed to exist across the entire value chain although there are very specific areas where there is an obvious gap. Furthermore the R&D capacity is said to exist more in a general scientific research context and not in a mind-set that tries to create marketable products or processes. This is consistent with Thorsteinsdóttir (2004) who indicated that South Africa possesses excellent

researchers and facilities, a strong biomedical research base which represents a promising future for the country and Mulder (2003) who asserts that capability to conduct R&D does exist, except it has been fragmented and Webber (2003) who observed SA' research base and highlighted the need for detailed country analysis to identify country assets and gaps.

6.2.1 Capabilities in Value Chain Stages

In the four major steps of research - drug discovery, pre-clinical testing, clinical development and regulatory review and manufacturing – this study confirmed that the R&D value chain is unevenly developed in SA (Table 5). Encouragingly though some steps are of a world class standard such as discovery research and clinical development is reportedly the area most well developed, funded and possessing the greatest capability and capacity based on the available infrastructure and trained skills. Notably discovery research is currently confined to the public sector in universities and research academia, whereas clinical development capacity is found in both public and private organisations.

6.2.2 Capability Bottlenecks in The Value Chain

A previously undocumented bottleneck identified in this study is in pre-clinical animal testing which is an area where capability is "most certainly" not as well developed as it should be and is noted to be a "*point of spectacular blockage preventing candidates going forward*". Current capacity is mostly in state institutions which are not directed at sustaining private research and most appreciably where it does exist, is not always GLP standard compliant. A minority of study respondents assessed this capability to be at a reasonable standard in SA. It is informative though that this study is able to show that there are "*pockets of capability*" which respondents believed could be further developed with investment in order to close this gap in R&D".

Some components of the value chain, specifically regulatory review and approval represents a "*serious and grave bottleneck*", which is contradictory to Thorsteinsdóttir's (2004) assertion that SA possesses a sound regulatory system and needs to make improvements and enhancement of competitiveness and productivity so as to speed product development. Most respondents in this study cited this stage as the limiting and restricting capacity which in its current format would not be able to assist product development. In an R&D context, regulatory functions extend to include pre-submission assistance requiring the body to possess a separate skill set that encourages open dialogue and consultation

between the firm developing the drug and the regulatory body and to give advice on scientific issues before an application is submitted. Accordingly this would be an area requiring significant restructuring and capacity development that is currently underway.

Encouragingly, the manufacturing capability in SA is also assessed as reasonable and a critical challenge pointed out was the decline in manufacturing output highlighted in the interviews. All respondents highlighted that the capacity in South Africa has been declining over the past few years with up to ninety percent of the locally used pharmaceuticals being imported. This is in agreement with Kahn (2007) who reported that the industry is in need of a resolute intervention to slow the impact of the global disinvestment and rationalization trend and has hugely impacted the SA industry in the last ten years with almost 35 production plants having closed since 1994.

Back-integration into R&D activities which is encouraged based on the successes of several developing nations that increased local production, Roscigno (2002), may be threatened if this gap is not addressed. As initially proposed in the literature by Webber (2003), this backward integration approach is a valid means that an emerging industry like South Africa, could participate in the economic benefits and production as well as adopt technology to enable R&D. Although this decline in country specific manufacturing by MNC is a global trend,

increasing local production should be an urgent point of intervention to maintain this part of the value chain.

Table 5: Respondents Assessing Capabilities Required As Available

R&D Stage	Respondents Assessing Capabilities Required As Available	Level of skill (defined based on commentary)
Discovery	Yes (92%)	Comparatively well developed and somewhat of a world class standard
Pre Clinical Research	Yes (33%)	Poorly developed with "pockets of knowledge"
Clinical Research	Yes (100%)	Most well developed World class infrastructure and capacity
Registration Procedures	Yes (17%)	limited and restricting capacity and represents major development hurdle
Manufacturing	Yes (67%)	Relatively well developed however currently in need of investment and in decline

() proportion of respondents who assess capability to be available and of a standard complying with international standards such as GLP- Good Laboratory Practice. GCP- Good Clinical Practice. GMP- Good Manufacturing Practice

6.2.3 The Role of Collaboration and Close Linkages

The results highlight the importance of closer collaboration and partnering with mnc and international research institutions and universities "big-brothers" who can assist local efforts to take a potential candidate through the value chain. This

is consistent with the recommendation to partner and generate closer intellectual linkages locally as well as sharing of resources to promote cooperation between firms and the actors most active in health biotechnology research, Thorsteinsdóttir (2004). This is further confirmed by Webber (2003) who asserts that successful commercialisation of public sector research and development requires strong linkages between public and private sectors, with ready access to business, financial and legal, and a good network between the academic domain and the commercial world is the basic tenet of the cluster co-operation to drive innovation and competitiveness. The multi-disciplinary activities required in R&D necessitate the establishment of these links and partnerships.

Manufacturing back-integration provides an alternative and efficient model to compete and enter the industry without competing with countries like Ireland and Singapore who have enabling environments to attract mnc R&D investment, and are intensifying their efforts, Skehan (2002) and Webber (2003).

6.2.4 Conclusion to Research and Development Capability Findings

This study concludes that the capability in the R&D process in South Africa is present although asymmetrically developed and thus limited in certain parts of the value chain.

Further, the findings of this study supported focusing these skills as they currently do not warrant a broad approach is consistent with Webber's (2003) conclusion that no single developing country, company or government institution could hope to cover all areas and or be at the leading edge of all interesting R&D developments. This conclusion is in support of a cluster approach.

6.3 Cluster Strategy Findings

In many respects the responses from the interviewees confirm the sentiments expressed by the Minister of DST, "we really do stand at the crossroads and our response to this opportunity will shape our future" as some went as far as to suggest that discussion is currently occurring on how to structure R&D going forward.

The National Biotechnology Strategy had aimed to use research to try to address the burden of disease, national strategic priority for development and the need for training and capacity building which based on the results of this study can be achieved by following a focused cluster strategy. This is echoed by the Accelerated & Shared Growth Initiative for South Africa, ASGI-SA (2006) which flagged this industry as critical for economic growth. This is consistent with the respondents who believe that choosing where to focus the industry will have important spin-offs" that contributes to these goals.

We have to use clever solutions that ensure the sustainability of this industry so it can form part of this exceptional response making this industry's success a matter of utmost importance and it is now becoming clear that innovation based solutions for health problems in developing countries are both appropriate and feasible, Thorsteinsdóttir (2004).

6.3.1 Disease Area Cluster

The results identified the therapeutic area of HIV-AIDS which is increasingly associated with TB and therefore grouped HIV-AIDS-TB as the key fields to be encouraged in South African organizations, consistent with the two diseases of highest burden, Bradshaw (2003).This is consistent the collective deaths caused by these diseases, Ridley (2006), the impact on microeconomic potential and stability, firm operations and productivity, Neilson (2006) and Daly (2000) and because collectively this is a growing need for medicines. It could therefore be deduced that the participants of this industry are mindful of the environmental impact and most importantly are motivated to tackle this problem.

Based on these implications and the "sheer scale of unmet medical need", the respondents who proposed focusing R&D capacity on HIV-AIDS-TB, contextualized the tension that could emerge if another areas is chosen based only on economic potential in the following statement, "the decision must be

based on that disease the could have the largest impact on the population, so my choice would be HIV-AIDS, as well as TB as they have become increasingly integrated.

Another possible therapeutic area mentioned of interest is in Cellular Immune Response research because it provides an understanding of the failure of immunity which is the basis of many diseases especially infectious diseases. This understanding and knowledge could be applied across various diseases with overlapping bodily processes.

6.3.2 Proposed Therapeutic Area by Stakeholder Group

The most interesting results are the analysis conducted according to stakeholders who believe that research should be focussed on HIV-AIDS-TB. Only two stakeholders groups recommended addressing these issues as separate entities which highlights the collective appreciation of the burden of these diseases.

Furthermore, a therapeutic area approach is repeatedly mentioned to be where the SA industry would have the largest inbuilt market which could also extend into Sub Saharan Africa. This would begin to address the need for multiple nations to provide the returns required on any R&D project which is inconsistent with the assertion that government-controlled R&D is likely to suffer from an

intrinsic set of problems due to the conflict of societal vs. economic needs balancing act that tampers with these market-based dynamics, Webber (2003).

Contrary to the caution that the economic prospects of a successful industry may precipitate a pressure towards research that is profitable but not necessarily always driven by local market needs, the stakeholders in this study have verified that there could be a middle ground that balances both by addressing problems that have scalability. Similar to the current model of the pharmaceutical industry with privately conducted research, where R&D is financed from sales across many markets, Kremer (2001) in Webber (2003), products for high burden diseases have a multinational market in Sub Saharan Africa. Further a rapidly increasing market is in India, China and Eastern Europe thus creating a point of entry for a potentially innovative solution.

Some respondents in this study proposed that balancing the competing aims of health policy striving for self sufficiency, science policy for local R&D and industrial policy which aims for local production and accelerated growth was indeed feasible by following a cluster type of approach. If this industry is to remain a focus, it will have to generate quick wins and begin to show a return on the investment made.

This study hopes to make the argument that with directed and focused investment in very specific areas that can generate, social benefits and economic results, this sector should remain a priority and recipient of fiscal focus. Consequently, this study seeks to understand if R&D technological capabilities exist in the South African context and could be used to encourage entry into a research based pharmaceutical industry.

6.3.1 Value Chain Cluster

An interesting proposal that emerged from the interviews is to focus on a component of the pharmaceutical value chain and to apply this capability across a variety of diseases. This proposal proved interesting for two reasons. Firstly it highlighted that the local production costs were still high due to an absence of local suppliers of Active Pharmaceutical Ingredients (API). A third of interviewees proposed this because by producing and sourcing locally much of the input costs could be reduced.

Manufacturing Process Innovation which was suggested by twenty nine percent of respondents as another alternative of a value chain derived cluster. As one respondent framed it, China and India are the low cost competitors, therefore SA needs “a smarter, clever strategy that addresses local and regional needs and innovate the process”. This is directly consistent with Winters (2006), Pecoul (1999) and Bale (2002) who put forward the role science and technology based

solutions have to play in improving the quality of life and in addressing the health needs of those in the developed and in the developing countries around the world. Further they proposed that by acquiring and harnessing relevant and applicable technological capabilities and by developing local capacity and competence towards R&D, affected countries could improve access to new improved medicines.

6.3.2 A Value Chain Based – Disease Directed Cluster

As suggested in the previous chapter, these two recommendations could essentially be combined to represent a cluster focused on developing and therefore using technology-enabled innovations to the processes of manufacturing. This would assist local suppliers to begin manufacturing API as which would begin to improve local knowledge capacity and increase the manufacturing capacity which is an area current concern, Kahn (2007). This strategy helps the industry to “start like other nations and learn to crawl first, then walk, then run”.

Manufacturing strategically chosen products with “high market need, would have considerable industry spin-offs” especially local job creation, and in addition become the driver of process innovation so that firms become as efficient, cheap and fast as possible. This iteration creates a manufacturing platform that can in time build “a meaningful industry and by reinvesting profits, backward integrate

into R&D", in agreement with Roscigno (2002) and Porter's assertion that local collaboration and cooperation promotes a "collective capacity", an ability of the cluster to compete in markets, sustain competitive success because the enduring competitive advantages become the "cluster resources" made up of the local knowledge, relationships and motivation, that made it difficult for competitors or new entrants to match, Porter (1998).

This benefit of enduring success of competitive clusters can be achieved by directing and focusing government investment. By limiting fiscal investment and focusing it in the particular niche with high local need identified in this study, the collective capacity of knowledge that already exists can be leveraged. Relationships and linkages between research institutions, academia and other stakeholders may be strengthened to overcome the barrier of "dispersed dynamic individuals operating as isolated islands, in silos on their own "little pet projects" and focus on the big picture forming the cluster, collaborate and partner, Thorsteinsdóttir (2004); Webber 2003; Ferrer (2004); Zhenzhen (2004); Abdelgafar (2004). This collaborative clustered approach would stop self motivated research that encourages competitiveness with science objectives and promote research that generates needed products to generate profits that create jobs and economic prosperity.

The third cluster resource, motivation, may be assumed from the unison of stakeholder responses in this study to be present and as accordingly will be intensified by the local rivalry and peer pressure that builds within a cluster.

6.4 Additional considerations

6.4.1 Investment

One caution to focusing on manufacturing identified in this study is that the ability to process innovate may be restricted by the insufficiency of production and process engineering skills would have to be addressed not only in capacity building, skills development but also in education of specific professionals geared towards providing human capital for that cluster.

An important proposition in the literature regarding entry into the pharmaceutical industry involved the choice between backward integration as a form of pull strategy and R&D as a form of push strategy. This was knowingly integrated and balanced by one of the respondents who proposed that the two approaches need not be separated out, because “if you have a block buster drug candidate the private investment will follow and drive manufacturing capacity. The current challenge is to drive early research and development and take products across the value chain”.

And so from an investment targeting perspective it would seem that an either or is not really the question but rather the sequence. Over ninety percent of

respondents in this study believed the discovery capability to be comparatively well developed and clinical development to be of a world class standard. To establish a competitive advantage, investment needs to plug the gaps in order to unlock the value chain, consistent with Webber (2003) who proposes that specialised players can move up the learning curve, build critical mass, and potentially expand to incorporate other parts of the value chain.

A strategy that focuses resources in a strategic and articulated area, helps build competitive advantage, Brännback (2001), provides for local demand and can grow far beyond that limit by adopting a global and exporting attitude.

6.4.2 Leadership and Political will

This industry faces many challenges and a decision made one way or the other could spell spectacular success or failure. The study findings put forward that “a bold and courageous thought leadership” will be required to make these “difficult decisions”. This leadership could acknowledge all that the achievements made as a result of the investment thus far that has created the broad knowledge base and R&D platform present today”, and then “demonstrate the political will to chose to focus that can deliver tangible results”.

This is in accord with Webber (2003) and Thorsteinsdóttir (2004) who identified political will and conclude that to promote industrial development in the health

biotechnology sector, governmental policies must be more decisive, and development has to be identified as a national priority e.g. Egypt's National Strategy, which outlined short and long-term goals with specific disease targets and technologies and the US government who has played an important role in almost every stage of its biotechnology industry's development. One remark cited as an example of this type of focus is illustrated by a conversation one of the respondents had with director at a Cuban R&D centre who said, "no one here works on a project unless its research that works to create a product that leads to the betterment of people". In a democratic society this type of direction can certainly be provided by using policy instruments such as funding, incentives etc.

6.5 Conclusion

The potential rewards of products or processes are manifold especially considering the socio-economic spin-offs and form the fundamental reason why any developing country would want to sustain an industry in spite of the technological and resource intensity required. A fragmented research approach to R&D is cited to require a much greater critical mass of skills, infrastructure and investment than is currently available in South Africa, Ridley (2006); Webber (2003); Cloete (2006).

The objectives of this study were to explore if SA organizations posses the capabilities across the value chain required to conduct pharmaceutical R&D and if

these exist to determine where they could best be deployed to serve market need and demand these objectives have been reached. From this study it may be concluded that a platform for R&D exists although unequally developed and not of a large scale. This study argues that to justify further investment in R&D, SA must make a strategic choice in a specific area of high unmet need in order to make efficient use of current capacity and limited financial resources.

These societal and economic benefits highlight the value that could be extracted from an industry such as this one and create a further argument for a strategic choice to direct this industry.

These critical limitations of resources validate a cluster strategy to concentrate and rationalize the skills that are currently present in the South African R&D environment that promotes a “collective capacity” to generate success in the industry. The decision regarding what the focus of the cluster should be is proposed by this study to be the disease area of a combined HIV-AIDS-TB and or in the value chain to focus on manufacturing and specifically process innovation to improve manufacturing efficiency.

CHAPTER 7 – CONCLUSION AND RECOMMENDATIONS

7.1 Introduction

Over the last ten years, the South African (SA) government has actively promoted research and development in human health and local diseases through an extensive series of funding and investment programmes which are said to have failed to extract industry economic value. However by directing future investment in areas such as those identified in this study, SA could possibly raise the R&D platform that currently exists and truly participate in the fruits of R&D based pharmaceutical industry.

Through the National Biotechnology Strategy For SA, an ambitious plan that aimed to use research, development and technology transfer to address strategic priorities in health and development and the need for the training and capacity building in health research was set. This plan placed a broad set of almost 12 research disciplines to be pursued and can be credited for the R&D capabilities and platform that exists in SA. However after after investments said to be over a billion rand, SA has failed to produce what others would call tangible results in the form of patentable medicinal drugs, nor has all the research activity emerged SA as an attractive location for multinational biotechnology and pharmaceutical companies FDI.

Considering that a huge investment in time, financial and human resources has already been made in developing this industry the first reason for this study is to contribute to providing direction regarding the form further investment in this industry should take. Secondly as one of the industries that can diversify SA's economic performance and flagged as critical for economic growth under ASGI-SA, industry insights from this study on how to proceed at this crossroad would be valuable for industry decision makers. And thirdly but probably most importantly because R&D into diseases of the greatest impact in South Africa must become more focused on producing much needed interventions, this report intends to drive debate about what kind of pharmaceutical industry SA needs, how to achieve it and whether to accord the sector priority status.

7.2 Research Aims

Therefore the purpose of this study was twofold - to survey the breadth of R&D capability in SA across the pharmaceutical R&D value chain and to explore the feasibility of using a focused and directed cluster strategy that directs investment on only the most critical of national health priorities that have an effective market and potential for global export growth to improve the output performance of this industry.

These questions would inform the answer addressing which types of research and development are the most desirable for development in the South African pharmaceutical industry and should be encouraged. As a result this study hopes

to make the argument that with investment directed and focused in very specific areas that can generate social benefits and economic results, this sector should remain a priority and recipient of fiscal intervention.

The findings were determined using twelve semi-structured, in-depth expert interviews with representatives of stakeholders representing various interests of the pharmaceutical industry and possessed a depth and breadth of knowledge about this industry. These experts ranged from senior executives of biopharmaceutical firms, directors of academia and research institutions, biotechnology investors to policy advisors who were a smaller “informationally representative sample but from which greater contextual understanding could be extracted. This group not easily accessible was identified using non-probabilistic judgment snowball sampling method.

7.3 Main Findings Of The Research

The qualitative analysis achieved the objectives outlined and found that the skills and capabilities required in the R&D process “definitely do exist although limited in scale’ and unequally developed in SA. From this study it can be established that capability is believed to exist across the entire value chain. The strongest areas are in drug discovery and clinical development and where there are obvious gaps is in pre-clinical testing, previously an undocumented bottleneck

identified in this study, and regulatory review. Furthermore the R&D capacity is said to exist more in a general scientific research context and not in a mind-set that tries to create marketable products or processes.

The manufacturing capability in SA posed as particularly interesting area of discussion which, although the literature suggested decline, the study found there was still a reasonable platform to make local manufacture a reasonable goal that could with further investment arrest the current decline and in time facilitate back-integration into R&D activities which is proposed as an alternative and efficient model to compete in the industry.

On the second objective, the results identified the grouped therapeutic area of HIV-AIDS-TB because these areas are increasingly as the key fields to be invested in and encouraged in South African organizations, which is consistent with the two diseases of highest burden. This therapeutic area approach is repeatedly mentioned to be where the SA industry would have the largest inbuilt market which could also extend into Sub Saharan Africa possibly addressing an urgent need for multiple nations and provide the returns required on any R&D project which is inconsistent with the assertion that government-controlled R&D is likely to suffer an intrinsic set of problems due to the conflict of societal vs. economic needs.

An interesting and potentially economically attractive area also indicated in this study is to focus on Manufacturing Process Innovation, a component of the pharmaceutical value chain and to apply this capability across a variety of diseases. This proposal proved interesting it would overcome the high input costs currently indicated as limiting cost efficient local production because the deficiency of local suppliers of API dictates that local manufacturers still import this important component which kept production costs high.

Innovating the manufacturing process of key API inputs was suggested as an example of the “a smarter, clever strategy that addresses local and regional needs” upon which SA could compete. This is would represent a harnessing of relevant and applicable technological capabilities that can address the health needs of those in the developing countries and developing local capacity and competence towards R&D directly consistent with the role science and technology based solutions have to play in improving health outcomes.

Fortunately, these two recommendations can be combined to represent a cluster focused on developing and therefore using technology-enabled innovations to the processes of manufacturing medicines for the indentified therapeutic areas which would begin to improve local knowledge and capacity as well as increase the manufacturing capacity which is an area current concern. This strategy helps the industry to “start like other nations and learn to crawl first, then walk, then run”. Manufacturing strategically chosen products with “high market need, would

have considerable industry spin-offs" especially in the national strategic imperatives to create jobs and economic prosperity.

7.4 Recommendations to Stakeholders

A few aspects to be considered before specific recommendations are made:

1. The results highlight the importance of closer collaboration and partnering with MNC and international research institutions and universities who act like "big-brothers" who can assist local efforts to take a potential candidate through the value chain.
2. The fundamental characteristics of this programme must exhibit an appreciation for the tension and ambiguity that exists between the goals of government policy makers for social good and the economic motive of the private sector. Unless this tension is managed and there is agreement that pharmaceuticals are as much commercial goods as they are public goods, then any type of incentive offered in this industry will remain ineffective to drive the productivity and results desired. This conclusion encourages non traditional ways of thinking about the industry that test current assumptions.
3. A fundamental yardstick of feasibility and shared benefit is offered here which was used to measure the proposed recommendations and may be used to measure future interventions and initiatives. This framework is

based on the “Thinking Hats” principles of De Bono (1985) and considers the different stakeholder motivations.

4. An important insight captured in the study is that in making investment decisions, it would seem the question is not really an either or but rather of sequence. Based on Figure 8 pre clinical development and regulatory review are the key bottlenecks inhibiting development and this study proposes that initiatives aimed at improving these two are addressed first. As mentioned it would seem efforts are underway to restructure and rejuvenate the regulatory review stage already.

7.4.1 Recommendation 1 - Address the key bottlenecks in order to support outputs from R&D (Appendix B for framework)

In the medium term a reasonable goal in this stage of the value chain would be capacity development to support discovery projects. This should be guided by a long term aim to create a world class pre clinical centre by consolidated the existing pockets of knowledge an expertise and infrastructural investment to develop capacity. A proposal offered to gather skills initially from MNC or international research organisations is based on a Skills Exchange Sabbatical programme which would benefit from visiting lectures, capacity consulting etc by experts who would be motivated by a holiday package which could be offered in conjunction with other departments like SA Tourism. Furthermore a skills offering

preferred partner programme could be the motivation by to tap into skills in MNC. This programme is further explained in the Appendix A and B.

7.4.2 Recommendation 2 – Focus On Key Strengths In Discovery Research And Clinical Research To Drive R&D Into HIV-AIDS-TB (Appendix C for framework)

Local R&D may be focussed in the identified areas (Innovating manufacturing process for HIV-AIDS-TB therapeutics) by using fiscal research funding as a vehicle to direct specialisation. This study appreciates that a dictatorial approach would not be feasible however by gradually increasing funding towards all research in the identified area- therapeutic, diagnostic, preventative etc, a majority of research could be channelled in this area of high need through the development of R&D Centre's of Excellence. This may be an effort contributed to by business, local and MNC, and based on the principles of the open source software research model which promotes the sharing of basic discoveries as proposed by Munos (2006).

The potential disadvantage to this method may be the perceived inability to produce patentable products which are a key driver of success in this industry. Munos (2006) counters this perception and concludes that with clearly articulated goals, stewardship from pharmaceutical MNC this model may work to tackle unmet medical needs, and consistently with this study proposes that there would be economic benefit from the “flourishing coopetition" with traditional R&D.

7.4.3 Recommendation 3 – Use Partnering Model To Develop Capacity Building Across The Value Chain (Appendix C for framework)

As is recommended in the above, public private partnerships should be a foundation of all interventions put in place in order to further develop the capacity that exists in both sectors and jointly strengthen the collective resources of this proposed cluster.

Furthermore, this study recommends public-private-MNC partnerships (PPMP's) as a key relationship that must be nurtured, harnessed and leveraged in order for this industry to survive and benefit. As cautioned by Webber (2003) no government or private or public firm can achieve this on its own. However as demonstrated by Kuemmerle (1999) foreign R&D activities will rise as commitment to R&D by local private and public entities and create knowledge spill overs because of the increasing collaboration and learning.

7.5 Limitations Of The Research

The following research limitations of this study pertain to a preindentified possibility that the findings would confirm already intuitively known areas of focus and clustering such as HIV-AIDS. This was balalnced however ny the recommendation of a new possible cluster focus area which ahs now been incorporated into the final proposal.

The second limitation of this study is that the findings are subjective and not generalisable to other developing countries. This however is an acceptable limitation as this study was intended for the South African context.

Finally, this research did not engage the respondents on possible incentives that could be used to support the industry cluster which may have been useful in making recommendations to various stakeholders. Furthermore the motivation that could compel MNC's and local industry to invest in discovery research in SA could is an important aspect not investigated in this study.

7.6 Recommendations on Further Research

Based on the stated limitations, further areas of study recommended include:

- The motivation that would compelling MNC's to invest in discovery research in SA
- A quantitative analysis of the return on investment from the fiscal investment in SA R&D in the past 5yrs. This study would be interesting to quantify the platform that has been created in order to make or disprove that argument that the investment has not borne results.

7.7 Concluding Remarks

In conclusion, this study reached it objective to firstly conduct a capability assessment across the value chain and to identify an area where R&D in SA could be focussed in order to address market needs and to provide a potential market for organisations adopting this strategy. By providing input on this debate, this study represents an important step in the ongoing effort to provide direction for the future of this industry.

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APPENDICES

APPENDIX A: Research Interview Grid

R & D Stage/Step	Answer
Based on your industry experience, which particular therapeutic area of research do you believe the pharmaceutical industry in SA (industry firms, research institutions and academia, policy makers) could & should focus its R&D efforts on based on market & public need and potential competitive advantage ? **Disease Or Therapeutic Area** E.g. HIV, TB, Infectious Disease (Please note these are examples and not an exhaustive list)	
Discovery and Research	
Based on the drug discovery process, do you believe that South African firms, research institutions and academia have competency and capability to conduct these R&D steps?	
1. Gene Sequencing And Identification 2. Target Identification and Target Validation 3. Lead Identification And Discovery 4. Lead Optimisation 5. Lead Development	1. ❒Yes ❒ No 2. ❒Yes ❒ No 3. ❒Yes ❒ No 4. ❒Yes ❒ No 5. ❒Yes ❒ No

Pre Clinical Drug / Animal Studies	
1. GPL toxicology 2. ADMET – absorption, distribution, metabolisms, excretion testing 3. Safety pharmacology	1. ❒Yes ❒ No 2. ❒Yes ❒ No 3. ❒Yes ❒ No
Clinical Drug Trial / Human Studies	
1. Clinical phase 1 2. Clinical phase 2 3. Clinical phase 3	1. ❒Yes ❒ No 2. ❒Yes ❒ No 3. ❒Yes ❒ No
Commercialization	
1. Drug Authorisation and Registration in an R&D context 2. Production and Manufacturing incl scaling up to manufacture commercial quantities	1. ❒Yes ❒ No 2. ❒Yes ❒ No

APPENDIX B: Framework To Address The Key Bottlenecks To Support Outputs From R&D

Test Framework				Investors (Local and Foreign MNC)	Researchers	Policy makers
				What are the benefits - economic and social		
Pre Clinical Research	1	What do we know now / Where are we now	Poorly developed with "pockets of knowledge"	Preferential partnerships with MNC willing to invest in cluster development specifically in areas requiring improvement i.e. pre-clinical. Preferential partnering leverages a key driver of the industry - Speed to Market- by providing expedited review vouchers to preferential partners.	Skills development initiative	Capacity and human capital development
	2	What is our desired outcome	Medium term capacity development to support discovery projects with long term aim to be world class pre clinical centre			
	3	What are the next steps - Proposal and Suggestions	Existing pockets should be consolidated, infrastructural investment to develop capacity, Skills Exchange sabbaticals (lectures, capacity consulting etc) in partnership with SA Tourism can offer working holidays and exchange programmes with preferred partner MNC			
	4	Disadvantages	This may be perceived as a punitive measure however this would not be the intention of the intervention in that companies choosing to not participate would be subject to normal regulatory review timelines.			

APPENDIX B: Framework to Focus On Key Strengths In Discovery Research And Clinical Research To Drive R&D Into HIV-AIDS-TB

		Test Framework		Investors (Local and Foreign MNC)	Researchers	Policy makers
				What are the benefits - economic and social		
Discover Research	1	What do we know now / Where are we now	Comparatively well developed and somewhat of a world class standard, scientific research platform with capability	A combination of market incentives as well as R&D derived from the open source model would be the business motivation to participate in this COE. Preferential vouchers may again be used with preferred MNC gaining priority review vouchers to facilitate speed to market. Based on the principle that for every month you delay market entry in this industry, this may prove a beneficial economic motivator for MNC to contribute human resources in PPP model.	To encourage academics from international institutions to participate in a knowledge and expertise sharing portion to drive the COE, a working holiday / sabbatical model may be applied similar to one adopted now by the surgical community who offer holiday packages	Capacity and human capital development, increased potential for incremental and radical innovation in products and process of treatment options in identified disease area
	2	What is our desired outcome	Increased product aimed at HIV-TB disease area			
	3	What are the next steps - Proposal and Suggestions	Local R&D may be focused by using fiscal research funding as a vehicle to directed specialisation. This study appreciates that a dictatorial approach would not be feasible however by subsequently increasing funding towards all research in this area- therapeutic, diagnostic, preventative etc, a majority of research could be channeled in this area of high need.			
			Develop R&D Centre's of Excellence based in current hubs (CSIR, MRC). This may be an effort contributed to by business, local and MNC, as well as fiscal investment. The basis would be based on the principles of open source based on the open-source software research model sharing basic discoveries as proposed by Munos (2006).			

	4	Disadvantages	The potential disadvantage to this method may be the perceived inability to produce patentable products which are a key driver of profitability and thus success in this industry. Munos (2006) counters this perception and concludes that with clearly articulated goals, stewardship from pharmaceutical MNC this model may work to tackle unmet medical needs, and consistently, this studies proposes that there would be economic benefit from the " flourishing coopetition" with traditional R&D.		linked to surgical procedure in association with SA based tour and holiday operators.	