MIHR report to CIPIH, April 2005
WHO Ref. CIPIH Study 10d (DGR)

INNOVATION IN DEVELOPING COUNTRIES TO MEET HEALTH NEEDS

EXPERIENCES OF CHINA, BRAZIL, SOUTH AFRICA AND INDIA

Country Reports for submission to the

Commission on Intellectual Property Rights, Innovation and Public Health

CIPIH

A contribution to a study on

DEVELOPING INNOVATIVE CAPACITY IN DEVELOPING COUNTRIES TO MEET THEIR HEALTH NEEDS

prepared by

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DEVELOPING INNOVATIVE CAPACITY IN **SOUTH AFRICA** TO MEET HEALTH NEEDS

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Foreword

This paper is part of a collection of publications that provide an overview of key issues that impact on the ability of developing countries to stimulate and sustain innovative capacity to meet critical health needs and benefit from an innovative culture through active R&D. The study, commissioned by the World Health Organisation Commission on Intellectual Property Rights, Innovation and Public Health, first examines the strategies and policies that shape health innovation in South Africa. Over and above government involvement in promoting innovation; global treaties, investment support, trade and market conditions, science and technology (S&T) infrastructure and R&D networks also have a significant influence and impact on health innovation, and are necessary to build, regulate and sustain systems of innovation for health development. To define or measure innovative capacity is not a simple task[1]. This paper therefore focuses on understanding the drivers of innovative capacity and their potential impact on access to and the availability of health technologies. The paper largely makes use of existing sources of information and pulls together material to provide a broad assessment of the drivers of local innovative capacity.

The local health technology and services sector is evolving rapidly as a result of a variety of interventions taken by the South African government and industry to address economic growth, poverty alleviation and access to health. The full impact of the interventions designed to promote health innovative capacity can only be determined some time after this paper has been written.

[1] Lorentzen J, The *Nolegde* of Numbers: S&T, R&D, and Innovation Indicators in South Africa, 2004

Executive Summary

This paper reviews and discusses the current state of innovative capacity in South Africa. It identifies sets of policies at national and international level that have contributed to the promotion of innovative capacity in health R&D and establishes the indicators and drivers of innovative capacity. Policies that contribute to building a system of innovation to meet the health needs of developing countries are examined and proposals to improve the system of health innovation are presented.

The study begins with an overview of the health biotechnology sector in South Africa. It introduces key national strategies and identifies the main players in the biotechnology arena. Critical issues relating to biotechnology are reviewed and the constraints and strengths of the industry are discussed.

Before one can analyse the status of local innovation, it is important to understand the drivers of innovative capacity. Chapter one first focuses on examining what constitutes innovative capacity and then presents the various measures and approaches used to evaluate innovation.

Chapter two presents key data on the health industry and reports on existing local technical services and scientific and technological infrastructure that contribute to health innovation. The analysis is limited to understanding the dynamics of specific areas of biotechnology including R&D infrastructure, entrepreneurship, and manufacturing capacity.

Chapter three is an overview of the health innovation system and takes a closer look at the range of factors that contribute most to driving innovation and health outcomes. The impact of interventions aimed at promoting and stimulating biotechnology research and its development into marketable products is discussed. The broad policy areas reviewed in this chapter include Intellectual Property, Regulatory Controls, Government Funding, Business Affairs, Human Resources and Trade.

The role of regional and international partnerships and collaborations and their function in stimulating innovative capacity is addressed in chapter four. Here, the paper draws from local examples of South-South and North-South collaborations to determine their role in advancing policy, human capacity growth, and infrastructure development and funding.

The paper ends with brief concluding remarks and key recommendations from a health sector perspective.

Background

The importance of biotechnology in the economic transformation of South Africa is evident through the range of policies, strategies and initiatives promoted and implemented by national government. The National R&D Strategy[2] provides for all stakeholders to participate in the National System of Innovation. The Strategy introduces a framework for "the establishment and funding of a range of technology missions that are critical to promote economic and social development". Biotechnology is one of five missions identified in the R&D strategy. The National Biotechnology Strategy[3] identifies gaps in South Africa's biotechnology industry and seeks to address resulting problems, especially in the areas of human health, food security and environmental sustainability. The Strategy draws attention to the contribution that biotechnology can make to national priorities, namely[4]:

- accelerated economic development
- sustainable development for poverty alleviation
- rural development
- small business development
- human resource development
- infrastructure development

South Africa's competitiveness in biotechnology and ability to address issues of economic and social development is dependent on its capacity to research, develop and trade in new biotechnology goods and services. To an extent, South Africa has an established first and second generation biotechnology infrastructure. However, the industry as a whole has not been efficient in exploiting or extracting value from the emergence of third generation or "modern" biotechnology. The Biotechnology Strategy focuses on stimulating, strengthening and diversifying the local biotechnology industry base by adding to the existing biotechnology infrastructure. This has resulted in the establishment of biotechnology regional centres, a bioinformatics network and biopharmaceutical resource centre. South Africa's biotechnology knowledge base and expertise is spread across a number of disciplines that include the biosafety, chemical, environmental, food, medical, plant and veterinary sectors. Furthermore, the HIV/AIDS, tuberculosis and malaria pandemics that is wrecking havoc in Africa in terms of morbidity and mortality force South Africa to take a leading role in the development of therapeutics, diagnostics, phytopharmaceuticals, natural health products and disease physiology[5]. To achieve its objectives, the Biotechnology Strategy addresses primary means by which government can influence development through[6]:

- legal and regulatory frameworks

[2] South Africa's National Research and Development Strategy, August 2002. http://www.info.gov.za/otherdocs/2002/rd_strat.pdf
[3] A National Biotechnology Strategy for South Africa, June 2001
[4] http://www.atpsnet.org/docs/mugabe.pdf
[5] Mulder M, South African National Biotechnology Strategy, September 2003.
[6] Webster J, The Status of Biotechnology in South Africa, AfricaBio, October 2002

- institutional arrangements
- creation of new infrastructure
- development of research capacity
- development of funding mechanisms
- development of business ventures

The main challenges South Africa faces in developing its health biotechnology sector include:

- lack of human resources
- inadequate funding for R&D
- low levels of venture capital investment
- limited private sector partnering with public sector institutions involved in biotechnology research

Public research institutes and universities play a significant role in the development of South Africa's health biotechnology industry. The greater part of human health research is shared between the Medical Research Council (MRC) and the Council for Scientific and Industrial Research (CSIR). In addition, there are some 40 biotechnology companies involved in human health with an estimated 315 projects involved across the private and public sectors [Mulder].

South Africa's experiences in biotechnology offers some lessons for other African and developing countries. Key areas of learning include:

- the formation of an enabling environment for biotechnology to take place
- improving biotechnology capacity through new infrastructure and capacity-building initiatives
- political will and support
- allocation of substantial budget and resources to biotechnology R&D
- appropriate regulations and legal structures that promote biotechnology – namely in the form of Intellectual Property Rights (IPRs) protection and bioprospecting
- a holistic approach to addressing biotechnology

Improved health is critical for South Africa and Africa's efforts to reduce poverty and improve the standards of living. Modern biotechnology offers huge potential in the realisation of national and regional imperatives. The Draft Emerging Biotechnology Roadmap[7] defines a set of activities that will result in the establishment of key technology platforms in genomics, transgenics, cell and tissue culture, process and product technologies, and convergence technologies. The aim is that these key technology platforms should help to build South Africa's competitive advantage in the

[7] Du Preez C, Morris J, Walwyn D and Webster J, Draft Emerging Biotechnology Roadmap prepared for The Department of Science and Technology, Nov 2003.

industry and to realise future market opportunities.

Summary of Key Issues

- South Africa's government is actively supporting growth in the biotechnology industry as demonstrated by the introduction of various national policies and strategies in the past five years.
- The biotechnology industry is diverse, however there are some fundamental challenges that need to be addressed in order for the industry to become globally competitive
- The biotechnology industry is seen as a vehicle which, with the appropriate support, can contribute to addressing public health priorities.

I. An Introduction to Innovative Capacity

R&D is essential to the formation of an effective biotechnology industry that not only can address national health priorities, but in the process stimulate economic growth and employment through innovation. To plan for a promising bio-economy it is necessary to determine and understand interventions that can be used to promote health innovation. Measuring South Africa's innovative capacity is beyond the scope of this study; however the OECD Oslo Manual[8] and Science, Technology and Industry Scoreboard provide guidance on how this can be achieved. Innovation surveys have been developed in response to the need for reliable and systematic data for the design, monitoring and evaluation of policies aimed at promoting technological innovation. They are an attempt to collect data on input to and output from innovation and such data is particularly useful if it enables direct comparisons between countries and over time[9].

The Oslo manual focuses on institutional innovation and views innovation in terms of market opportunities and the institutions knowledge base and capabilities[10]. Innovation surveys based on the Oslo Manual ask institutions information on a variety of topics including products and processes introduced, objectives of innovation, factors hampering innovation, and sources of information for innovation in a given period. The Oslo Manual sets forth methodological standards and provides guidelines for collecting information on various subjects such as the impact of innovation on the performance of the organisation, the diffusion of innovation through the socio-economic system, the use of advanced technologies, patenting, the appropriateness of results derived from innovative activities, and the acquisition and diffusion of technology [Pianta].

Furman et al [11] go further to identify the determinants of national innovative capacity. In their paper, the authors define innovative capacity as the "potential – as both a political and economic entity – to produce and commercialise a flow of innovative technology at a given point in time". Therefore, innovative capacity is not dependent on a single entity but the interplay of a range of factors including technological sophistication; human resource capacity; government intervention through incentives, policies and strategies; public-private sector investment and productivity; and R&D activities and infrastructure. National innovative capacity goes beyond the performance of research and science activities to include the economic application of new technology.

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[8] Oslo Manual: The Measurement of Scientific and Technological Activities, Organisation for Economic Co-operation and Development, 1997.
[9] Muzart G, Description of National Innovation Surveys, Carried Out, or Foreseen in 1997 – 1999 In OECD, Non-CIS-2 Participants and NESTI Observer Countries, 1999.
[10] Pianta M and Sirilli G, The Use of Innovation Surveys for Policy Evaluation in Italy, 1998.
[11] Furman JL, Porter ME and Stern S, Understanding the Drivers of National Innovative Capacity, http://people.bu.edu/furman/html/research/files/Innovative%20Capacity%20-%20Best%20Paper%20Proceedings.pdf

The OECD publication on Drivers of National Innovation Systems[12] makes reference to the complexity of interactions that result in innovation. The paper further emphasises the role of government in influencing innovation processes through the financing and steering of public organisations directly involved in knowledge generation and diffusion. The formation of "clusters" and the act of "clustering" is viewed to be important for diffusing and using knowledge in a manner that stimulates innovation. Clustering is defined as "a process whereby inter-firm linkages and cluster externalities are built up, and so what where hitherto disparate firms gain competitive advantage from their interaction". Because of their capacity to boost innovative performance, cluster policies have become an increasingly popular government tool. To illustrate local use of "clustering" in the area of biotechnology, South Africa established Regional Innovation Centres, "each having separate technology platforms, and a close relationship with technology incubators" [Biotechnology Strategy].

To determine South Africa's innovative capacity would require the selection of data sources and indicators of national innovative capacity[13]. The next requirement would be developing an innovation survey and identifying major stakeholders to provide information on a number of aspects. The final step is the collection and analysis of the data. For a comparative assessment, it would be necessary to identify a set of countries against which South Africa can be reasonably assessed while taking into account the appropriateness of the indicators selected for South Africa and for the countries of interest.

Porter and Stern present a framework for determining national innovative capacity[14]. Based on this framework, the elements of national innovative capacity are:

- *Common IinnovationIinfrastructure* – this is a set of cross-cutting investments and policies supporting innovation throughout an entire economy. Chapter 3 of this paper examines the determinants of national innovative capacity within the South African context. South Africa shows mixed performance in the total set of elements that include public policy development and implementation, human and financial resources availability for S&T, excellence in basic research, the protection of intellectual property, tax-based incentives for innovation, the degree to which free competition encourages innovation-based competition, and the openness of the economy to trade and investment.
- *Cluster-Specific Conditions* – these apply to geographic concentrations of interconnected companies and institutions in a particular field and are characterised by four attributes; namely firm strategy and rivalry, demand conditions, related and supporting industries, and factor input conditions. South Africa has adopted the cluster approach to stimulate a competitive bio-

[12] OECD, Innovative Clusters: Drivers of National Innovation Systems, 2001.
[13] CSIR Policy Group, Research Proposal: A Comparative Analysis of South Africa's National Innovation System and its Relationship to National Competitiveness, 2003.
[14] Porter ME and Stern S, National Innovative Capacity, 1999.

economy. It is yet too early to assess the extent to which the local biotechnology industry has increased the rate of innovation and attracted related industries to get involved in the innovation process.

- *Quality of Linkages* – of interest is the reciprocal relationships between the common innovation structure and a nation's industrial clusters. Collaborations and networks are important for feeding into the common innovation infrastructure, but their real value is realised through the exploitation of scientific and technical advances through technology transfer and commercialisation.

Having introduced a conceptual model of innovative capacity in this chapter, subsequent chapters will contextualise the theory, taking into consideration the elements that contribute to the system of innovation and relating these to the current state of health-related innovative capacity in South Africa.

Summary of Key Issues

- Recognising the complexity of the field, especially in measuring national innovative capacity.
- Setting the focus of the paper, which is to explain the drivers of innovative capacity rather than to measure it.
- Introducing the innovative capacity framework, which comprises:
    - A common innovative infrastructure
    - Innovation clusters
    - Quality linkages

II. An Overview of the Health Industry

South Africa represents one of the most diverse medical markets in existence. On the one hand there are wealthy urban areas that enjoy access to high-quality medical facilities; while on the other the rural areas and townships lack basic health facilities. This two-tier system is further challenged by the scourge of the HIV/AIDS pandemic which is most prevalent in areas of low socio-economic development. This chapter takes a closer look at the facts and data that account for South Africa's health status.

South Africa has a population of approximately 45 million and a GDP per capita of US$2 298. Health expenditure per capita is estimated at US$195 and is 8.5% as a percentage of GDP. When compared to other African countries, South Africa's health status indicators are superior to the majority. However, the health status indicators are poor relative to most other middle income countries[15].

South Africa has the largest pharmaceutical industry in Africa, which in 2002 was estimated at US$1.5 billion. South Africa's sophisticated industrial base is supported by modern telecommunications and transport infrastructure. Labour costs, when compared with western industrialised countries, are relatively low. As a member of the WTO, South Africa generally promotes free trade. Even though the country's fundamental economic base is in place, South Africa has been faced with significant challenges in restructuring its health profile to address the inequities in health care. It is against this backdrop that the economic, policy and development issues that impact on health innovation are analysed.

Despite the many economic and social challenges, South Africa's innovation performance is promising compared to other middle income countries such as Brazil, India and China. While data required for direct country-to-country comparisons of innovative capacity is not available, it is useful to examine common determinants of innovative capacity.

2.1 Innovation Infrastructure

2.1.i Attractiveness of the Natural Environment for Exploiting Science and Technology

South Africa is one of Africa's fastest growing economies with economic growth accelerating to 3.7% in 2004. This expansion is draining South Africa's skilled workforce. There are a number of concerns with respect to the country's ability to build skilled capacity at the rapid rate required, and to retain professionals. A big weakness lies in its education system, where performance in science and maths is generally poor. South Africa's secondary education pupils scored significantly below

[15] World Pharmaceutical Markets: South Africa, Espicom Business Intelligence, December 2003.

the international average in the Trends in International Mathematics and Science Study (TIMSS)[16]. It is discouraging to note that the 2003 TIMSS scores were hardly an improvement on the 1999 scores. Science and maths are required for the study of the biosciences and with such a low rating the education system will struggle to meet the demands by the bioscience sector for skilled individuals.

Statistics show that in the 10 years ending 1999 an estimated 10 000 South Africans engaged in science and technology emigrated, mainly to developed countries[17]. South Africa's brain drain is listed in the 2004 World Competitiveness Yearbook as one of the country's key challenges – it ranks 58th worldwide in terms of the rate at which professionals are emigrating; 60th in the availability of skilled labour; and 50th in drawing on foreign highly-skilled labour[18]. Overall, this indicates that South Africa is in a weak position as far as the availability of skilled labour is concerned. The major cost to the country is in lost production and the export of human capital in the form of education, training and experience [Kaplan]. In addition to the export of human capital, emigration also results in the export of real and financial assets. As a result, this dire situation has forced many employers to leave posts unfilled, finance training programmes, and/or hire abroad.

2.1.ii Intellectual Property (IP) Protection

South Africa has a relatively sophisticated intellectual property system that is in line with WTO's Trade Related Aspects of Intellectual Property Rights (TRIPS) Agreement. The national intellectual property system is supported by sound policy and regulations and it is respected and used by local and foreign parties seeking IP protection in South Africa. Even though South Africa is a member of the African Regional Intellectual Property Organisation (ARIPO), it has its own filing and monitoring system. There are approximately 200 biotechnology-related patents filed by South African inventors between 1979 and 2003 [Mulder]. In addition, South Africa registers about 100 patents per annum with the US Patent and Trademark Office, of which only 65 were awarded between 1976 and 2003. To obtain a patent, inventors are required to prove that the idea or discovery is novel, inventive and has not been publicly disclosed. The application procedure is straightforward and the patent and maintenance costs are reasonable. A complete application is examined by the patent office for correctness and completeness rather than to determine the novelty or obviousness of the subject matter. There is opportunity for individuals to oppose a patent application either during the filing process or after it has been granted.

Intellectual property rights can be protected under a variety of laws and regulations.

[16] http://www.hsrc.ac.za/research/npa/ATEE/timss2003/factSheet3.html
[17] Kaplan D, Meyer J-B and Brown M, Brain Drain: New Data, New Options, South African Network of Skills Abroad, 1999.
[18] El-Agamy H, International Competitiveness: How We Measure Up, South Africa 2014, 2004.

For comparability, Lesser introduces an IP indicator based on 1) protectable subject matter, 2) convention membership, 3) enforcement, 4) administration, and 5) cost of protection. Out of a possible maximum score of 12.36 and minimum of 1.6, Lesser gives South Africa a score of 7.4[19]. Compared to scores of 6.7 for Brazil, 3.6 for India and 7.2 for Chile, South Africa's rating is relatively high for a middle income country. This suggests that overall South Africa has a sound intellectual property protection system that businesses are confident in and can trust for the protection of new inventions and discoveries.

2.1.iii Government Tax Credits and Subsidies for R&D

Tax incentives for research and development are used widely in developed countries for the promotion of science, technology and innovation[20]. They are one way through which governments can influence R&D and its impact. Typical tax incentives include 1) allowing companies to write off R&D expenditure as current expenses, which decreases profit and thereby reduces company taxes, 2) permitting companies to write off capital expenditure for R&D, 3) differential capitals gain tax, or 4) providing explicit tax credit incentives for R&D. South Africa uses a suite of policy incentives designed to encourage business interest in technology innovations. It is intended that the various interventions will help to build the capacity for local businesses to absorb and adopt new innovations, enabling them to become more competitive and economically successful.

Table 1. Range of Government Incentives Targeted at Different Areas of Industry.

	Target	**Purpose**	**Incentive**
Innovation Fund	Industry, academia and science councils	To promote industry, academia and science council co-operation	Support R&D spending of consortium
Support Programme for Industrial Innovation (SPII)	Private sector firms	Promote technology development through the innovation of new products and processes	• Support for up to 50% of qualifying costs • Matching grant of up to R1.5m • Conditional grant repaid by means of levy sales
Technology and	Tertiary	Develop skills in the	Supports private

[19] Intellectual Property Rights in South Africa: An Economic Review of Policy and Impact, The Edge Institute; http://www.the-edge.org.za/pdf/Intellectual%20property%20Rights.pdf
[20] Pouris A, Towards a South African R&D Tax Incentives Scheme: Fiscal Policies and Social Benefits, South African Journal of Science, 99, May/June 2003.

Human Resource for Industry Programme (THRIP)	institutions and industry	higher education system	sector R&D spending to the tune of R1 for every R2 from industry and in certain cases R1 for R1.
Foreign Investment Grant	Private sector firms	Provides cash incentives for foreign investors who invest in new manufacturing business in South Africa	Compensation for the qualifying costs of moving new machinery and equipment (excl. vehicles) from abroad.
Export marketing and investment assistance schemes	Private sector	Various schemes exist to encourage exports and attract imports	Various cash incentives are on offer depending on the scheme

Source: Pefile, 2005

This table shows that South Africa is focusing on three areas, namely:

- capacity building to develop the critical mass of science and technology human capital;
- the stimulation and advancement of innovation; and
- the stimulation of enhanced entrepreneurship and enterprise development through the provision of incentives for the private sector.

2.1.iv Company Spending on R&D

South Africa's R&D capacity is growing at a slow rate. The current R&D spending, as a percentage of GDP, is 0.7% (the current target being 1%). Private industry's share of the total R&D expenditure exceeds 50%. The R&D spend in South Africa's medical and health sector is 9.8% of total R&D expenditure, and only 6.1% is spent in all science fields on research directed at health[21]. The business survey of the National Research and Technology Audit reports that the level of R&D investment is one of four factors that determine the level of overall technological dependency of a given field[22]. The other factors are skills, equipment and competency dependencies.

2.1.v Procurement of Advanced Technology Products

Where new technologies and inventions are concerned, the National Research and

[21] South African National Survey of Research and Experimental Development 2001/02, Department of Science and Technology, September 2004

[22] Survey of the Technology Base of the South African Business Sector (the Business Survey), Project Report, Department of Arts, Culture, Science and Technology, South Africa, 1997.

Technology Audit reveals that South Africa is competing in a highly competitive international environment[23]. While there is high awareness within the business sector of this competitiveness, the awareness of the role that technology plays in maintaining competitiveness is, according to the report, low. One of the major risks the country faces is high reliance on international sources of technology for emerging strategic industries, including biotechnology. South Africa is a net importer of technologies such as diagnostics and medical equipment, for which there is local manufacturing capacity.

2.2 Cluster Specific Conditions

2.2.i Production Process Sophistication

South Africa has developed an established and diversified manufacturing base that has shown the potential to compete globally. South Africa ranked 27th worldwide in the technology management index and 29th in the Innovation Capacity index. The technology management rating suggests that local industries either have a good capacity for innovation or capacity for assimilation, while the innovation capacity index is a rating of overall innovative activity[24]. South Africa needs to build up its pharmaceutical development and production capacity in order to take emerging research and develop it into new products. Competency is also required for local industries to be able to re-design and re-engineer existing technologies for further application in the market.

2.2.ii Extent of Product and Process Collaboration

South Africa's National Research and Development Strategy proposed establishing an entity to promote the economic competitiveness of South Africa through investments in technological innovation that lead to new enterprises and the expansion of existing industrial sectors. The result is the Innovation Fund, which has become a key instrument of government for the development of products, processes and services. The Innovation Fund invests in technologically innovative research and development and preference is given to projects involved within a consortium arrangement of the appropriate combination of research, business, NGO and Black Economic Empowerment partners [25]. In its six years of existence, the Innovation Fund has invested in excess of R0.5 billion in projects and programmes designed to encourage

[23] Technology and Knowledge: Synthesis Report of the National Research and Technology Audit, Department of Arts, Culture, Science and Technology, South Africa, 1998.
[24] Orr S, A Comparison of AMT Strategies in the USA, South Africa and Germany, Int. J. Manufacturing Technology and Management, vol. 4, No. 6, 2002.
[25] Black Economic Empowerment (BEE) is a strategy aimed at substantially increasing participation of Blacks at all levels in the economy. BEE is aimed at redressing the imbalances of the past in South Africa's history by seeking to substantially and equitably transfer ownership, management and proportionate control of South Africa's financial and economic resource to the majority of its citizens.

and sustain product, process and service collaboration.

2.2.iii Local Supplier Quality

One of the strategic objectives of the Biotechnology Strategy is to encourage linkages between large companies and the biotechnology regional centres to stimulate industrial activity. The local biotechnology industry produces high value bio-products ranging from intermediates to high purity substances, most of which are destined for export markets. Quality is a high priority and therefore production and testing processes are under GMP conditions. Most facilities will have also undergone validation of the production site. Despite this, there is room for South African biotech industries to improve on their production efficiency, reliability and continuity of supply.

The extent to which linkages with both local and international production systems and markets have increased biotech productivity and contributed to economic progress and health improvement still remains to be determined.

2.2.iv State of Cluster Development

The Biotechnology Regional Innovations Centres (BRICs) are localised clusters whose business is influenced by the nature of the industries and infrastructure in a given area. The BRICs act as nuclei for the development of biotechnology platforms and each of the four centres established works in close collaboration with academia and business. In addition to setting up the BRICs, a national bioinformatics network has been established for the training, computing and provision of laboratory facilities for bioinformatics. Government has also supported the development of incubators to nurture small and medium enterprises involved in the technology industries. While there are no dedicated biotechnology parks in South Africa, the existing Science and Technology parks provide proximal access to companies active in high technology development.

2.3 Quality of Linkages

2.3.i Absorptive Capacity for New Technology

Big industry in South Africa is largely owned by foreign investors, while infrastructure in the form of energy, mining and agriculture is mainly owned by the national government. Through the use of various policy instruments, the South African government is attempting to manage technology development in a manner that places technological decisions in the hands of local companies, and as a result, decisions on technology transfer are largely prescriptive rather than expansive or

selective.

In 2004, South Africa ranked 40th in the world in the technology index[26]. Technology is at the centre of economic growth and is generally seen as the most critical factor in driving sustained high growth. The Global Competitiveness Report, which is responsible for this ranking system, differentiates countries that are "core" and "non-core" innovators. Countries that fall in the former category produce at least 15 patents per million population. South Africa's patent rate is 2.5 patents per million population and is therefore classified as a non-core innovator. This means it is highly dependent on technological adoption from abroad as opposed to its economic growth being driven by its own capacity to innovate. To get closer to the technological front, South Africa needs stronger political commitment and administrative strength to ensure that technologies imported from abroad are current, appropriate for the needs of the country, are transferred in a systematic manner, and create real opportunities for growth and development.

2.3.ii University/Industry Research Collaboration

The Department of Science and Technology is responsible for integrating and strengthening research in South Africa. The Innovation Fund discussed earlier encourages public/private sector research collaboration on projects that develop key technological platforms and address socio-economic priorities. International partnerships have grown rapidly since 1994[27], and they usually have a developmental component aimed at strengthening South Africa's research capacity[28]. Universities and Universities of Technology are also working increasingly in collaboration with business on applied projects with economic and productive potential. A number of tertiary institutions have set up science networks or innovation centres where applied research is forging ahead in many fields, especially health. South Africa's research sector is by far the strongest in Africa, and the government is harnessing the sector's capacity to support its vision of an African Renaissance and the New Economic Partnership for Africa's Development.

2.3.iii Venture Capital Availability

South Africa has a long history of bringing to market significant medical innovations including the CT scanner developed in the early 70s, the mechanical heart valve, and more recently the new anti-cancer and anti-obesity drugs. While highly innovative

[26] The Global Competitiveness Report, 2003 – 2004, World Economic Forum.
[27] South Africa's first fully elected democratic government came into office in 1994. Before this date, international sanctions were imposed on South Africa and the country was effectively isolated from the rest of the world.
[28] http://www.studysa.co.za/studysa2.htm.

medical products and techniques have been created by local R&D institutions, few of these opportunities have been converted into commercial successes[29]. There are several reasons for the lack of success, one of which is a relatively low level of venture capital investment for both early and late-stage R&D in health biotechnology. There are a small number of venture capital firms that are beginning to invest in biotechnology, however the capital available remains minimal and their confidence to invest in an industry that tends to be either capital-intensive or volume-based is low. The inadequate levels of funding means that the medical industry is failing to develop to its full innovative potential and the benefits of research and inventions are mainly accrued to developed country companies.

Summary of Key Issues

An overview of South Africa's innovation structure which is supported by 5 pillars:

- Attractiveness of the environment for exploiting science and technology
- Intellectual property protection
- Government tax credits and subsidies for R&D
- R&D spending
- Procurement of advanced technologies

Biotechnology clusters are discussed within the context of the following critical impact areas:

- Production and process sophistication
- Product and process collaboration
- Local supplier quality
- Advancement of cluster formations

The quality linkages are important for creating a cohesive innovation system. Key issues in South Africa are:

- The absorptive capacity for new technologies
- Public-private partnerships and collaborations
- Access to and the availability of venture capital

[29] http://www.catalystii.net/news/news-medjour.html

III. An Overview of the Health Innovation System

In presenting the Health Sciences Innovation Survey results[30], Luce puts forward a model comprising 5 innovation pillars and identifies potential policies that could contribute the most to driving innovation and health outcomes. The policy actions identified that would most benefit health innovation are:

- Trade issues influencing access to health services and technologies
- Intellectual property
- Regulatory environment
- Government funding for R&D
- Business environment
- Human resources

This chapter reviews the above innovation policies in relation to the set of R&D, IP and economic development policies and strategies existing in South Africa.

3.1 Trade Issues

3.1.i Price Controls

In 1996 the Minister of Health presented the National Drug Policy of South Africa whose objectives were, among others:

- to offer a clear description of the approach by which pharmaceutical services in the country will be managed; and
- to follow a clear and logical system for reducing inefficiency and waste and improving efficiency and effectiveness through the development of an adequate pharmaceutical infrastructure[31].

One of the significant outcomes of the National Drug Policy is the establishment of a Pricing Committee whose principle responsibility is to monitor and regulate drug prices. The committee is an instrument of the Policy, which recommends rationalisation of the drug pricing structure through:

- introducing transparency in the pricing structure of health service providers;
- introducing a non-discriminatory pricing system;
- regulating price increases; and
- where deemed necessary, controlling the price of drugs that are essential to the well-being of any sector of the population.

The issue of price-control in the pharmaceutical sector came to a head in 2001 when 39 pharmaceutical companies in South Africa took the government to

[30] Luce CB, Total Value of Innovation: Choosing Metrics that Matter in Health Sciences, 2004
[31] National Drug Policy for South Africa, http://www.doh.gov.za/docs/policy/drugsjan1996.pdf.

task against policies that are critical for securing medicines at affordable rates and exercising control over them. Mechanisms such as parallel imports and compulsory licensing in the public interest were deemed an important instrument for ensuring access to essential medication and equipment in case of a national crisis. The concern for the industry was seemingly the absence of safeguards that would ensure that such clauses are not abused. An understanding was eventually reached that any action taken by the South African government will be compliant with TRIPS[32].

3.1.ii TRIPS

The TRIPS Agreement establishes minimum standards for intellectual property rights. South Africa was obligated to modify existing property rights legislation such that property rights protection is tightened and coverage of these rights extends to all areas including medicines and pharmaceuticals[33]. The public health issues of the TRIPS agreement have been debated at length. Those who oppose the TRIPS agreement argue that:

i. TRIPS restricts access to medicines and promotes high cost of essential drugs. To address this issue, South Africa introduced price controls to regulate the costs of essential medicines.

ii. There is lack of clarity and scope with respect to Article 6, which allows for parallel imports. Article 6 permits governments to parallel import pharmaceuticals manufactured under a patent in one country, but sold at lower prices in another country, to be imported from the second country without permission from the patent holder. According to South Africa's Medicines and Related Substances Control Act, it would be possible in certain instances for South Africa to obtain a patented drug more cheaply from a foreign supplier than from the local subsidiary of the same manufacturer - that is, the local patent holder - provided that the drug is in the market with the consent of the patent holder. Such purchasing is known as parallel importing and is addressed in Section 15 of the Medicines Act.

iii. There are a number of open questions regarding the mechanisms that governments can use to make use of compulsory licensing. Compulsory licensing allows governments to permit a person, other than the patent holder, to produce a product without the consent of the patent holder. Section 15 of the Medicines Act gives the government the power to prescribe or determine that a party may lawfully produce pharmaceuticals as if they held a compulsory licence.

[32] 2001 Country Reports on Economic Policy and Trade Practices, Bureau of Economic and Business Affairs, US Department of State, Feb 2002.
[33] Williams M, The TRIPS and Public Health Debate: An Overview, International Gender and Trade Network, 2001.

When it was introduced, the South African Medicines Control Act appeared to grant the Minister of Health broad powers with regard to patents on pharmaceuticals. In essence, South Africa put into legislation the exemptions that TRIPS allows, enabling it to take advantage of compulsory licensing and parallel imports with respect to pharmaceuticals only.

Pharmaceutical companies make investment decisions for the exploration and development of a new drug treatment on the basis of the scientific probability of success and their ability to recoup their investment and make a reasonable profit. The potential for a pharmaceutical company to recoup its investment is heavily driven by its confidence that a reasonable price can be charged for new health technologies introduced to the market. South Africa's pharmaceutical industry was caught between its obligation to its shareholders and the pressure to provide support to urgent medical needs. Given the public health sector crisis in developing countries, it is therefore critical that a workable solution is found that addresses both the urgent need for affordable treatment (including drugs) and the legitimate industry concerns on recouping investment.

3.2 Intellectual Property (IP)

South Africa has been complying with TRIPS regulations since 2000, meaning that it has in place the 20-year market exclusivity allowed by the TRIPS Agreement. At the time of signing up to TRIPS, South Africa's intellectual property rights laws were already well established and the country was a signatory to many of the international treaties that the TRIPS Agreement incorporates.

3.3 Regulatory Controls

All clinical trials are by law subject to review and approval by national statutory bodies, including the Medicines Control Council (MCC) and the Department of Health. In addition, many institutions that are able to conduct clinical trials have ethics committees that review clinical trial proposals. The Department of Health has published guidelines on the minimum standards that are acceptable for conducting clinical trials in South Africa. South Africa has a long history of being a clinical trial site of choice in the developing world and is therefore attractive to pharmaceuticals and researchers because of existing infrastructure, training resources and know-how.

MCC approval is required to conduct clinical trials of non-registered and registered drugs and ethical approval is required from the National Health Research Ethics Council. The MCC uses established expertise found at research institutions to assist it in a number of areas, including post-marketing surveillance.

According to the Medicines Act, manufacturers and distributors of pharmaceutical products are required to apply for a licence to distribute, import or export medicines. The Medicines Control Council is responsible for ensuring that applicants comply with legislation with respect to the registration of entities, quality assurance, manufacturing practices, and compliance with international registration requirements where applicable.

Harmonisation of regulations on a regional and global basis

Two approaches have been adopted by the MCC in this area to promote harmonisation at a regional and global level. First, new drug registration application procedures are aligned with the EU system of drug regulation and second, efforts are underway for drug regulation harmonisation within the Southern Africa Development Country group of countries. South Africa has a development responsibility to its neighbours and as a result has made attempts to use its expertise and strengths in health provision to bring about region-wide benefits. The increase in global trade in medicinal products has raised strong arguments for further harmonisation of drug regulatory procedures. In favour of this argument is the fact that country-based technical regulations related to drug safety, efficacy and quality have become more complex and the pharmaceutical industry is under pressure to bring new chemical entities to market faster, in a wider market, and at a reduced cost in order to achieve an acceptable return on R&D investments.

3.4 Government Funding for R&D

3.4.i Available Funding

Government support of health R&D and specifically health biotechnology has been growing. The Department of Science and Technology has been instrumental in identifying research priority areas, developing and implementing strategies, and providing incentives for the biotechnology sector. The government has supported research in the biosciences through a number of structures, the most significant of which is through the establishment of bio-clusters designed to act as nuclei for the development of biotechnology platforms. Other funding streams available to the bioscience industry include sponsorship from the Innovation Fund and Science Councils, namely the National Research Foundation, the Medical Research Foundation, and the Council for Scientific and Industrial Research.

3.4.ii R&D Infrastructure

Compared to other African countries, South Africa has a relatively strong scientific and technological infrastructure. Of the 22 institutions of higher education in South Africa, 8 are active in varying degrees in bioscience research. Due to the cross-cutting nature of the biosciences, most science councils are involved in health-related

research in one form or the other. Newer areas of science such as bio-prospecting are now benefiting from the research infrastructure developed during a time when South Africa was strongly focused on developing its own research capacity. R&D institutions continually try to upgrade or replace out-dated equipment and much of this expense is made possible by project grants and research partnerships that have supported capital expenditure for new instruments. Where it makes sense, institutions have collaborated to fund large equipment and research facilities, whose use and maintenance is shared.

3.4. iii Incentives for the Development of Treatment Targeting Priority Disease Areas

The National Drug Policy tries to encourage the national pharmaceutical industry to manufacture and market drugs that are listed in South Africa's Essential Drug list. Manufacturers are encouraged to promote national self-sustainability in the production of essential drugs. In this regard, the national pharmaceutical manufacturing industry receives a maximum of 15% price preference as recommended by the World Bank in the awarding of public sector drug tenders. The export of locally manufactured pharmaceuticals to neighbouring countries is also encouraged, thus ensuring that they too benefit from the access to health products that South Africa is able to provide.

3.5 Business Affairs

This section takes a brief look at the economic impact of the intellectual property system. It is acknowledged that patents are not the only drivers for economic development and that complimentary policy instruments are necessary to stimulate technological innovation. As discussed in the previous chapter, South Africa utilises a combination of policy instruments that use different mechanisms to encourage technological innovation. These include indirect support for R&D by enhancing incentives or direct support for innovation via subsidies, sponsored research, and procurement of technologies[34].

Unfortunately, small and medium enterprises in South Africa engage in very little novel research and as a result are poor in developing new products and processes that are patentable. The low level of innovation within this sector of the economy suggests that there is little use of supply and value chains and optimum use is not made of the existing science and technology infrastructure. There can be a number of reasons for this - including lack of access to new technologies - and therefore outdated technology is employed, poor technology support to small and medium industries, low entry rates into the manufacturing sector, high failure rate of new business start-

[34] Intellectual Property Rights in South Africa: An Economic Impact, The Edge Institute; http://www.the-edge.org.za/pdf/Intellectual%20property%20Rights.pdf

ups, a low risk-taking investment community, and poor access facilities to support and promote small and medium enterprise innovations. To stimulate an entrepreneurial culture around new technologies there is a need to provide a mechanism to optimise, commercialise and package newly-developed technologies for implementation in the small and medium enterprise sector in South Africa[35].

To move innovation forward, there needs to be coherence in the overall policy framework. Developing countries need to carefully examine the impact of various policies and regulations on the economy and public health, particularly pertaining to biotechnology and new business practices as these impact on the advancement of R&D systems, economic growth, employment creation, productivity and international competitiveness.

3.6 Human Resources

Despite a general skills shortage in the supply of scientists and qualified researcher managers, the Biotechnology Audit reveals that biotechnology companies in South Africa show a relatively even distribution of employee qualifications ranging from technical staff to post-graduates. As to be expected, research groups are dominated by employees with at least a degree qualification. The reason for this is that skills distribution between the private and public sector favours the former[36]. Most biotechnology groups in South Africa belong to the private sector and private R&D facilities typically offer more attractive salary packages, state of the art facilities and equipment, and better working conditions. South Africa's economy is growing at a faster rate than there are available skills to meet this growth. The bio-economy needs industry-relevant skills to create a competitive environment that is able to deliver appropriate biotechnology goods and services. To achieve this, South Africa has adopted a number of parallel strategies that include incentives for skills development that look at recruitment, training and capacity development; partnerships with industry; career guidance and youth mentorship; and funds for bursaries and scholarships. Such programmes set out to achieve:

- Faster transfer of skills to previously disadvantaged communities
- Address competency gaps caused by skills migration, brain drain and the HIV/AIDS pandemic
- A decrease in unemployment through job creation
- More even demographic representation
- More rapid skills development to fulfil the needs of a growing economy

Summary of Key Issues

[35] http://www.africabio.com/status/godisa.htm
[36] Mbanga S, Strategies for Addressing the Skills Gap in the South African Public Sector: A People's Development Tool, SDR, Vol 3, No 2, 2004.

The chapter identifies key policy interventions that impact on the innovative capacity in health R&D in South Africa. The key policy actions discussed are:

- Trade – issues that influence access to new health technologies and products
- The intellectual property system
- Regulatory controls and the harmonisation of the regulatory system to improve efficiency and effectiveness
- Government funding for R&D
- The status of the R&D system.

IV. Impact of Research Collaborations

R&D partnerships in South Africa are not new and vary in scale, scope and character. A great number of these partnerships are institutionally based and are governed by the skills, practices and commonalities that exist between partner organisations. Such partnerships are developed not only to strengthen learning networks and coalitions, but to build institutional capability through capacity development, knowledge and technology exchange[37]. Positive features that have attracted collaborators to South Africa include good institutional infrastructure, effective coordination, strong governance, sound policy to guide practice, and reasonable human and S&T capacity to generate, apply and build knowledge.

4.1 Regional Collaborations

Some of the best known examples of S&T partnerships in Africa are the S&T programme of the New Partnership for Africa's Development (NEPAD) and the University Science, Humanities and Engineering Partnerships in Africa (USHEPiA) collaborations that extend through Africa. Each is succeeding in creating a strong research network – one to support and promote collaboration between African R&D organisations, the other to build research capacity in Africa.

NEPAD's S&T programme focuses on four key areas:

- Monitoring continent-wide developments in science, technology and innovation
- Building efficient and effective R&D institutions and networks for Africa's sustainable development
- Promoting international cooperation in science and technology
- Building capacity in S&T

The USHEPiA partnership is an attempt to develop African research capacity using a network of institutions. Through the fellowship programme involving 8 African institutions, scientists are able to work for higher degrees and benefit from the resource strength of other institutions by spending part of their tenure at partner institutions. This programme is aimed at promoting collaboration amongst African researchers to build institutional and human capacity.

Regional partnerships, whether formal or informal, offer opportunities for sharing and pooling scarce resources. Such partnerships help to improve the effectiveness of research through improved coordination of research activities, resulting in less duplication of work and more efficient use of human and material resources[38].

[37] Oyelaran-Oyeyinka B, Partnerships for Building Science and Technology Capacity in Africa, Africa-Canada-UK Exploration, London, UK, 2005.
[38] Kameri-Mbote P, Wafula D and Clark N, Public/Private Partnerships for Biotechnology in Africa:

4.2 International Collaborations

A great number of collaborations exist between institutions and/or government units and international agencies. Such collaborations take different forms and use different models to achieve joint objectives. A number of partnerships have been established to address public health issues in South Africa by harnessing biotechnology innovations [Motari]. For example, the South African Aids Vaccine Initiative is taking a leading role in the developments of HIV/AIDS vaccines, while the Global Alliance for TB Drug Development programme is focused on researching TB treatment options that act over a shorter treatment period and are more effective against susceptible, drug resistant and latent tuberculosis. Similar programmes exist in the areas of malaria and cover a broad range of fields from genetics, to diagnostic testing, clinical trials, and health systems research. South African researchers make an important contribution to the generation of new scientific knowledge and bringing greater understanding to the study of parasitic diseases.

Some of the key concerns, and in some cases experiences, with international collaborations include:

- Key development takes place in developed country institutions
- Developed country institutions attract and in many cases retain the best African researchers
- Low benefits are realised for infrastructural development of local institutions
- Negative exploitation of local resources, for instance, in the areas of bioprospecting and indigenous knowledge

There have been many successful international collaborations where developing country institutions have experienced:

- Research and institutional capacity development
- Indirect benefit to other local structures, for example, in the case of clinical trials where the broader community can benefit
- Much needed funding for further research and development through grants and bursaries
- Stimulation of innovation and knowledge generation
- Addressing local imperatives
- Encouraging policy development

North-South collaborations are characterised by a set of unique dynamics. The partners are often unequal in terms of scientific resources, access to funding and networks of research resources. The partnerships are frequently driven by the potential to access specific opportunities whether it be a population group, unique facilities, indigenous knowledge or biological resources [Banji]. The impact of the partnerships on research development differs depending on the type and model of

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The future agenda, African Centre for Technology Studies, Nairobi, Kenya, 2001.

partnership involved. Examples of three different types of partnership are characterised below.

i. The principle partner controls resources, makes decisions, assigns tasks and assesses performance. In this case, the subordinate partner complies with decisions made and carries out assigned tasks.
ii. A consultative relationship is established to allow for joint decision making on tasks, resource use, and priorities and actions to be carried out.
iii. A coalition partnership which is facilitated by a partnership manager. In this case, the partners recognise that they have a shared agenda and interests, accept collective responsibility for the initiative, and are committed to joint ownership of processes and products.

South Africa has a good telecommunications infrastructure and therefore it is relatively fortunate in that problems of communication with partners are minimal. Due to the availability of modern forms of communication local institutions are able to gain access to relevant and necessary knowledge. However, the issue of mistrust between resource-rich and resource-poor partners cannot be ignored. This mismatch has raised concerns over exploitive habits and self-benefit, particularly in the areas of bioprospecting and traditional knowledge.

From a policy perspective, there needs to be greater attention to the interplay between policies and the practices of those whose behaviour is targeted by policy. South Africa has worked hard at ensuring policy coherence and relevance to make sure that research networks are supported through regulation, funding and capacity development. To fully benefit from regional or international partnerships, policy that directly encourages the forging of partnerships and provides guiding principles in the areas of intellectual property rights, business development and investment is required. These policies should help create the best possible climate for biotechnology investors and researchers.

Summary of Key Issues

The chapter provides an overview of regional and international collaborations, citing examples of such collaborations. Issues discussed include key concerns and strengths, partnership models, and policy.

V Conclusions and Recommendations

South Africa has worked systematically to address its social and economic challenges. While the economic status of the country is improving, the impact has not reached the large population that is poor. Poverty is increasing and the economic gap between the haves and have-nots is widening. South Africa has the advanced R&D infrastructure, policy environment, and stakeholder will to improve performance where social responsibility is concerned, but this still needs to bring benefits to the poor.

Policy Challenges

After 1994, South Africa embarked on an intense programme of transformation. This created a unique situation whereby almost every spectre of government and industry was under scrutiny for restructuring and reform. As a result, an unusual number of policies and strategies were introduced to bring equity and evenness to all spheres of economic and social function. While South Africa may offer interesting lessons to similar economies, it is important to acknowledge the unique circumstances that exist.

i. Addressing public health needs

Health issues are prominent in all science and technology policies and in particular the biotechnology strategy. The National R&D strategy acknowledges that new innovations are not readily used to address poverty and that there is a need to create an environment and technologies to reduce the effect of poverty on the spread of disease.

It takes many years for policy to bring about change to a system. In the meantime, the HIV/AIDS crisis is putting increasing pressure on the health system which urgently requires cheap and effective diagnostics, drugs and vaccines to provide for the millions of sufferers.

Recommendation: There needs to be prioritisation of scientific research and an earnest effort to develop and transfer crucial technologies to the market in the shortest time possible. Incentives for small enterprises to invest in new technologies for neglected diseases are needed and a technology assessment system to pick winning technologies is required. Building the capacity of local businesses to engage in the development and manufacturing of health technologies should be a priority.

ii. Policy appropriateness, relevance and compatibility

Policies need to be aligned with economic and social development strategies and the mandates of various stakeholders within the system need to be clearly defined. One of the challenges in policy development is ensuring that policies owned by a particular government department are compatible and complementary with those of other departments.

Recommendation: There needs to be closer relations and information sharing between government departments. Further, there needs to be clear allocation of responsibilities and accountability between different departments to make sure that duplication of effort is minimised and conflicts between policies is avoided.

iii. Fresh approaches – sustainable solutions?

a. South Africa has a highly regarded R&D competency and capacity to innovate. The impact of benefits from the innovation system is being seriously compromised by the decreasing numbers of scientists, technologists, and research professionals.

***Recommendation*:** Priority to skills development at all education levels is essential. It is important to identify areas in the education system where there is a high attrition of students, and programmes designed to attract students into science and engineering subjects are important. In addition, skills development programmes to enable workers to gain higher degrees are essential. Where possible, institutions should pool resources to provide regional training programmes and information sharing.

b. South Africa has a rich biodiversity which is a valuable source of new compounds with potential physiological activity. This resource, combined with local knowledge on the use of medicinal plants, holds great potential for science to add value and discover new drug leads.

Traditional healing plays a crucial role in supporting and strengthening the health system, especially in rural and poor areas where access to appropriate and affordable primary healthcare is a challenge.

Recommendation: While the new Biodiversity Bill regulates the management and conservation of biological diversity, it does not provide adequate guidance on issues concerning benefit sharing, intellectual property protection, and ethical practice when researching traditional knowledge systems. South Africa needs to speed up the introduction of the Indigenous Knowledge Systems Bill which, it is anticipated, will recognise and protect indigenous knowledge.

South Africans have an opportunity to exploit indigenous knowledge and science innovation in a manner that can deliver better health and provide economic gain [Motari]. Technology and knowledge-sharing needs to take place in a regulated manner and should be locally driven to ensure sustainability and that development benefits reach local

communities.

c. South Africa has a dependency on technologies developed by more advanced countries. As a result, there is an inward flow of technologies and an outward flow of revenue. Most technologies generated by the local R&D system are licensed early to outside companies and return to South Africa as high-value finished products.

Recommendation: The "innovation chasm" between the generation of local knowledge and the production of industrial products needs to be bridged. Development capacity needs to be strengthened by providing infrastructure, resources, venture capital and incentives for businesses to enter into technology development. Health needs that require basic solutions can and should be met by domestic production.

Recommendation There are many essential technologies required by the health system which are easy to manufacture. Some of these technologies are no longer under patent protection and are available for others to manufacture. A database of such technologies is recommended and assistance to countries like South Africa to manufacture such products for regional benefit is suggested.

An Enabling Environment for Health Innovation

While the above recommendations provide guidance to what actions are required to accomplish strategic and policy goals, how this can be achieved remains a challenge for all stakeholders. South Africa will need to exploit its strengths and remedy its weaknesses to meet health needs through building innovative capacity. Biotechnology, as a driver for sustainable socio-economic growth, needs to meet local health needs in a manner that benefits both investors and consumers alike.

DEVELOPING INNOVATIVE CAPACITY IN **CHINA** TO MEET HEALTH NEEDS

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Introduction[39]

Broadly speaking, innovative capacity can be interpreted as "the potential for innovation and technological creativity"[40]. Motivated by the swift development of technology and its profound impact on human life, innovative capacity, especially at the national level, has become a focal point for both academic and policy interests. In a recent study by Scott Stern, Michael Porter, and Jeffrey Furman, national innovative capacity is defined as "the ability of a country to produce and commercialize a flow of innovative technology over the long run" (Scott Stern etc, 2000). In the same article they also built an analytical framework for innovative capacity, which has been broadly used by many international organizations for the purpose of comparing national innovative capacity. This theoretical research, including its analytical framework, serves as a guideline for this paper as well.

The purpose of this paper is to present an empirical examination of the innovative capacity of the pharmaceutical industry in China, review its function in meeting local health needs, and draw some lessons from China's experience for the international community, especially developing countries. According to the analytical framework mentioned previously and the research guidelines, we divided the paper into six parts. The first is about the business environment, which includes three aspects: the disease burden, the health expenditure, and the market size. The second part is about China's regulatory environment, where we review the administration system, GMP practice, as well as the pricing policy. The third part focuses on IP management in China. The fourth part discusses the investment of innovation in China's pharmaceutical industry. We focus on government funding and other support to the industry. The emerging partnership between public and private sectors and China's promising bio-pharmaceutical and traditional medicine sectors are also reviewed here. The fifth part is on the human resources of the industry. The last section is on trade and trade-related issues. We examine the market structure in China, the joint ventures, China's international trade, and of course the medical access problem and the impact of WTO membership on China.

[39] This paper is commissioned by MIHR as a part of a series of research for the World Health Organization Commission on Intellectual Property Rights, Innovation and Public Health.
[40] For more on basic concepts, see www.innovativecapacity.com

I. Business Environment

1.1 China's Disease Burden

Infectious diseases are always major concerns for developing countries. It is the same case in China. In general, China has achieved much in combating major infectious diseases. Some serious infectious diseases, including cholera, plague, smallpox, typhus, and kala azar have been eliminated already. Smallpox was eliminated as early as 1977. Thanks to China's compulsory immunization programme, which has been financed by public money, China also eliminated (or almost so) poliomyelitis, diphtheria, kinkcough and measles. Most of the iodine-related diseases have also been well- controlled (Xinhuanet (1), 2004).

Table 1. Reported Incidence and Death Rate of 27 Infectious Diseases in 2003

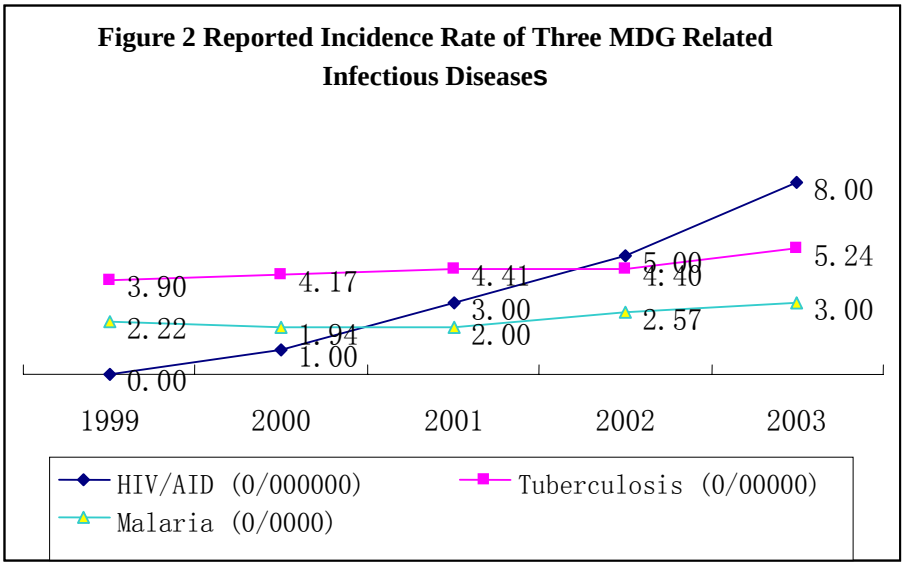
Diseases	Incidence Rate (1/100 000)	Death Rate (1/100 000)	Deaths per 100 patients
Pulmonary Tuberculosis	52.36	0.08	0.16
Gonorrhea	14.09	0	0
Measles	5.55	0.01	0.11
Syphilis	4.5	0	0.05
Malaria	3	0	0.14
Hemorrhage Fever	1.68	0.01	0.76
Scarlet Fever	0.75	0	0.01
Encephalitis B	0.58	0.03	4.66
Brucellosis	0.48	0	0
Pertussis	0.41	0	0.05
SARS	0.4	0.03	6.55
Typhus Fever	0.3	0	0.05
Encephalitis	0.19	0.01	5.48
Newborn Tetanus	0.18	0.03	14.51
Hydrophobia	0.15	0.15	97.2
Leptospirosis	0.13	0	3.33
HIV/AIDS	0.08	0.03	33.1
Anthrax	0.04	0	1.66
Kala Azar	0.01	0	0
Dengue Fever	0.01	0	0
Poliomyelitis	0	0	0
Diphtheria	0	0	33.33

Source: China Health Statistic Digest 2004, Ministry of Health (MOH), 2004

However, some concerns remain. The control of some infectious diseases, including encephalitis, encephalitis B, hydrophobia, and typhus fever, seems stagnant and shows no sign of further decline. At the beginning of 2005, encephalitis broke out

regionally. Some diseases are increasing, including sex-related diseases like gonorrhea and syphilis, tuberculosis, hepatitis, schistosomiasis and HIV/AIDS. Tuberculosis and schistosomiasis had been well controlled before, but seems resurgent in recent years. China has also seen an outbreak of SARS in 2003 though it has been controlled quickly by impressive government actions. Further, three diseases identified by the UN's Millennium Development Goals are somehow on the increase.

Figure 2 Reported Incidence Rate of Three MDG Related Infectious Diseases



Source: China Health Statistic Digest 2004, Ministry of Health, 2004

The steep increase of HIV/AIDS incidences in China has gained special attention from the international community. China identified its first HIV/AIDS case in 1985. Till the end of 2002, the Chinese government estimates that 840,000 persons are infected with HIV/AIDS. In recent years, HIV/AIDS incidence rates increased more than 30% annually. China might have 10 million people infected with AIDS by 2010 if no effective measures are applied. The government has set up a special committee on HIV/AIDS prevention and treatment, and has issued an ambitious plan that aims to control the number of infections to 1.5 million before 2010.

As a transitional economy, China is now experiencing fast economic growth, which is not only changing the map of its economy but the disease burden structure as well. The basic fact is that chronic diseases grow very fast and increasingly become a major threat to human health.. From the perspective of top ten morbidity rates, chronic diseases have outpaced infectious diseases in China. The increasing trend of chronic diseases is more obvious in China's urban areas than in rural areas. This shows that the development gap between urban and rural areas is reflected in disease structure. It is reasonable to project that as the fast trend of urbanization keeps going, China will see a rapid growth of chronic diseases.

Table 3 2003 Morbidity Rate of 10 Main Chronic Diseases (%)

Diseases	Urban	Rural	Total
Hypertension	54.7	16.4	26.2
Gastroenteritis	9.8	10.5	10.3
Rheumatoid Arthritis	8.4	8.7	8.6
COPD	8.2	7.3	7.5
Cerebrovascular Disease	13	4.4	6.6
Cholelith & Cholecystitis	8.5	4.7	5.7
Diabetes Mellitus	16.3	1.9	5.6
Intervertebral Disc Disorders	8.1	4	5
Ischaemic Heart Disease	12.4	2	4.6
Peptic Ulcer	3.4	3.8	3.7
Total (computed by patients)	177.3	104.3	123.3

Source: China Health Statistic Digest 2004, Ministry of Health, 2004

This tendency is also shown in China's changing therapy structure. According to IMS Health, in 2003 therapeutic classes for chronic diseases experienced very fast growth. Among the top ten fastest growing therapies, five were for treatment of diseases of cardio-vascular and central nervous system; three were respiratory, anti-inflammatory and anti-ulcer drugs; and only two were for infectious diseases, which might have been affected by the sudden impact of SARS.

Table 4 2003 Ten Fastest Growing Therapies in China (million $)

Therapeutic Classes	**Country Sales**	**Percentage Growth**
Polyvalent Immuno-Globulins-Intramuscular	2	269
Combinations of B2-Stimulants with Corticoids	2	260
Ophthalmic Nonsteroidal Anti-Inflammatories	1	182
Specific Immuno-Globulins-Antibacterial	2	177
Coronary Therapy Excluding Calcium Antagonists and Nitrites	8	172
Anti-Alzheimer Products	3	121
Vitamin B Complex	31	116
Antifibrinolytics	15	112
Other Haematologicals	5	108
All Other CNS Drugs	22	95

Source: IMS Health

1.2 Health Expenditure

In absolute numbers, China's health expenditure has seen a fast growth. From 1980 to 2002, total expenditure has increased almost 40 times. It is impressive even though the level will be less if the high inflation rate in the 1980s and early 1990s was taken into account. In per capita terms, health expenditure was US$53.39 (442.6 RMB) in 2002[41], which is much lower than developed countries and thus shows a huge potential for pharmaceuticalceutical market growth that we will discuss later. However, it is still high considering the low income level in China. The ratio of health expenditure to GDP has reached the baseline of 5% in 1999, and passed the global average level in 2002. The high health expenditure contributes to the development of public health. In contrast to 1990, by 2000 China's number of hospital beds increased 21.8% and healthcare professionals increased 15.2%. In 2001, health institutions increased more than 70% compared to 1995 (MOH).

Table 5 China's Long-Term Health Expenditure

	1980	1990	1995	2000	2001	2002
Total Health Expenditure (100 million RMB)	143.2	747.4	2155.1	4586.6	5025.9	5684.6
Government Health Expenditure	51.9	187.3	387.3	709.5	800.6	864.5
Social Health Expenditure	61.0	293.1	767.8	1171.9	1211.4	1503.6
Personal Health Expenditure	30.3	267.0	1000.0	2705.2	3013.9	3316.5
% of Health Expenditure	100.0	100.0	100.0	100.0	100.0	100.0
Government Health Expenditure	36.2	25.1	18.0	15.5	15.9	15.2
Social Health Expenditure	42.6	39.2	35.6	25.5	24.1	26.5
Personal Health Expenditure	21.2	35.7	46.4	59.0	60.0	58.3
% of GDP	3.17	4.03	3.69	5.13	5.16	5.42
Per Capita Health Expenditure	14.51	65.4	177.9	361.9	393.8	442.6

Note: The data in this table is calculated at current prices.
Source: China Health Statistic Digest 2003, Ministry of Health, 2003

However, there are several problems that we can identify from table 5. First, the share

[41] It is an absolute number transferred with the fixed foreign exchange rate of 8.28 and without the adjustment of PPP. The following numbers in this paper will be in the same calibre unless otherwise stated.

of government health expenditure has seen a continuing decrease. To make things worse, the social health expenditure, which mainly refers to the expenditure from employers, has also decreased since the 1980s, and only seen a little growth very recently. Meanwhile, personal expenditure has spiked from 21% in 1980 to 58% in 2002. The reason comes from China's economic transition. China had built a relatively complete co-operative healthcare net that covered 90% of the population in both urban and rural areas from the 1950s to 1978 (MOH, 1985). However, healthcare insurance was built upon the planned economy and it could not survive the elimination of the commune system. The reform and opening-up policy that followed greatly promoted China's economic growth, but the healthcare insurance system has been lagging behind. A new market-oriented system has yet to be set up. China is trying to build a new healthcare system, however it is moving forward with the speed of a turtle. Therefore, the burden of health expenditure falls more and more on the individual or family. In particular, the relative decrease of government expenditure has weakened access to medicines of the poor and people in poor regions much more.

The second problem is fairness, which partly relates to the first issue. China has a big development gap between urban and rural areas. Since the 1990s, government has begun to set up a new health insurance system in urban areas, which has been expedited in recent years. But in rural areas there is almost no progress. Considering the serious income gap between rural and urban areas, which is US$316.67 (2622 RMB) and US$1023.19 (8472 RMB) respectively in 2003 (SSB, 2004), rural people have a considerable medicine access problem. Recently, Zhu Qingsheng, the deputy minister of MOH, claimed that about half of the farmers in China do not have enough money to see doctors, especially in the poor western region. It shows us the seriousness of the problem (Xinhuanet (2), 2004).

1.3 Market Size

China has a total population of 1.3 billion, and its economy has grown by about 8% per annum for more than two decades, which contributes to an increasing market size for health and pharmaceuticals. China is already ranked in the top ten of the world's pharmaceuticals markets. According to research by Boston Consulting Group, China's ethical and OTC drugs market will keep enlarging, and is going to amount to US$24 billion by 2010, which will rank it as the fifth biggest market in the world (table 6).

Table 6 Estimated Market Size for Ethical and OTC Drugs (U.S. $ billions)

1996 Top 11	2000 Top 10	2005 Top 10	2010 Top 10
United States 91	United States 150	United States 262	United States 466
Japan 52	Japan 58	Japan 65	Japan 81
Germany 20	Germany 17	Germany 24	Germany 37
France 18	France 17	France 21	France 28
Italy 10	United Kingdom	United Kingdom	China 24

	11	16	
Brazil 8.4	Italy 11	Italy 15	United Kingdom 24
United Kingdom 8.2	China 6.8	China 14	Italy 23
Spain 6.0	Brazil 6.7	Brazil 10	Canada 17
South Korea 4.5	Canada 6.3	Canada 10	Spain 16
Canada 4.3	Spain 6.2	Spain 9.8	Brazil 15
China 4.3			

Source: Boston Consulting Group's Analysis: "China's Growing Drug Market, Will You Be a Contender?" 2002

There are three driving forces behind the market expansion. First is that the trend of economic growth will continue in the foreseeable future, which will increase the disposable income of residents and thus grow expenditure on health and pharmaceuticals. As discussed before, China's expenditure on health is still at a considerably low level. In 2000, per capita health expenditure was US$45, only about one tenth of the US's and even much less than South Africa's US$253 and Brazil's US$265. The percentage of health expenditure to GDP was a modest 5.5%, less than most of the other countries (table 7).

Table 7 Comparative Heath Expenditure in Selected Countries

	China		**India**		**Brazil**		**Cuba**		**South Africa**		**United States**	
	Per Capita	% GDP	Per Capita	% GDP	Per Capita	% GDP	Per Capita	% GDP	Per Capita	% GDP	Per Capita	% GDP
1997	33	4.6	23	5.3	362	7.4	137	6.6	315	9	3939	13
1998	36	4.8	22	5	348	7.4	143	6.6	270	8.7	4095	13
1999	40	5.1	23	5.2	246	7.8	163	7.1	264	8.8	4287	13
2000	45	5.3	23	5.1	265	7.6	175	7.1	253	8.7	4540	13.1
2001	49	5.5	24	5.1	222	7.6	185	7.2	222	8.6	4887	13.9

Note: Per Capita refers to the health expenditure per capita of the country in current US$; % GDP refers to the percentage of the total health expenditure to the country's GDP.
Sources: World Bank, WDI database

However, we can also find from table 7 that the growth rate of health expenditure in China outperforms other countries. The annual growth rate of per capita health expenditure in China is 12%, the United States is 6%, and the other four countries are almost stagnant. The percentage of health expenditure to GDP is also growing in

China. Together with the tendency of high growth rate of GDP, it is not difficult to project the expansion of the market.

The second driving force is demographic transition. China is now beginning to experience the senile society. According to the Ministry of Civil Affair, the population aged above 60 amounted to 134,000,000 in 2003, which is more than 10% of the total population. This amount consists of half of the aging population in Asia and one-fifth of the world. Furthermore, the aging population is growing at an increasing pace since 2000, and the estimated annual growth rate will be up to 3.2% in the future (Xinhuanet (3), 2003). The increase of the aging population will put growing demand on the pharmaceutical markets, broaden the market size, and promote market transformation from the cure of infectious diseases to the treatment of chronic diseases.

Thirdly is the enlargement of the health insurance system. As discussed before, China's health insurance system greatly lags behind economic development. But China has begun to launch several initiatives to promote the new healthcare system. In 1998, China implemented comprehensive health insurance reform in urban areas. By the end of 2003, altogether 106,470,000 people had been covered by the system, an improvement from 15,087,000 in 1998, with an annual growth rate of 120% (MOLSS, 2004). In 2002, China began its new co-operative health insurance system in rural areas. Though at present only about 13% of the rural population has been covered by different kinds of health insurance, China vows to meet the goal of 100% coverage by the year 2010 (MOH, 2004). The health insurance system can improve medicine accessibility and promote purchasing power for pharmaceuticals, especially for western pharmaceuticals.

II. Regulatory Environment

2.1 Administration System

China's administration system on pharmaceuticals used to be part of the Ministry of Health, and has experienced several reforms. So far it has developed a framework with two major administrators: State Food and Drug Administration (SFDA) and State Administration of Traditional Chinese Medicine (SATCM). SFDA was established in 2003 based on the former State Drug Administration and streamlined with some food monitoring tasks. The basic functions of SFDA include: 1) build up regulatory policies, law enforcement, and set up national standards; 2) monitor and inspect drug-related activities from registration to manufacturing to marketing; and 3) organize the investigation and management of influential drug-related events (SFDA, 2004). The SFDA is built upon the model of the US's Food and Drug Administration. Like the FDA, China set three stages for new drug pipeline, and the process is also considerably strict.

SATCM's function is focused on the field of Chinese traditional medicine. It is more like an organization for the purpose of industry promotion, though it does have some functions of policy implementation as well as monitoring. Furthermore, SATCM's administration covers the Chinese traditional hospital system but not new drug applications, which makes it different from SFDA (SATCM (1), 2004).

2.2 Good Manufacturing Practices (GMP)

GMP system was initiated by WHO in the 1960s. It is a quality control system that defines a set of standards for pharmaceutical manufacturing processes to guarantee the quality of products and eliminate the possibility of contamination errors. China adopted GMP in the beginning of the 1980s. In 1988, the Ministry of Health issued China's first GMP standards. It has been revised in 1992 and in 1999. The new standards incorporate some recent GMP developments in the WHO and some developed countries.

Because of the higher cost it would incur, the enforcement of GMP standards in China was not running smoothly in 1990s. There had been only 70 firms approved with GMP authentication in 1998. The government has enhanced enforcement since then. Now it requires that all pharmaceutical preparation and ingredients must be manufactured under GMP standards after July 1, 2004, otherwise the manufacturers must stop production and even be closed down. To enhance the enforcement, SFDA set up a weekly monitoring system for those firms compulsorily closed down. The policy has sped up the process of GMP. There were 3200 firms approved by GMP authentication by June 30, 2004.

China also issued other related standards, including Good Clinical Practices (GCL),

Good Supply Practices (GSP), Good Laboratory Practices (GLP), Good Use Practices (GUP), and Good Agricultural Practices (GAP, on Chinese traditional medicine planting).

2.3 Pricing Policy

In China, one of the most debated policies on pharmaceuticals is price control, which has been set for keeping the price of drugs affordable. The policy began in 1998, has been revised several times, and has formed three categories of pricing mechanism. First is the government-determined price, in which the central government (National Development and Reform Committee) sets the ceiling prices for certain products. The drugs that fit into this category include those on the "Drug List for National Basic Healthcare Insurance" and the products with market monopoly. The second category includes some special drugs like narcosis and first class pnuema drugs, drugs for the national immunization plan, and family planning drugs. For these, the government may recommend prices for guidance. The third category is other drugs that can have their prices decided by markets.

The policy has lowered the significantly. For example, from 1998 to 2000, the government lowered prices six times and saved an estimated of US$0.97 billion (8 billion RMB) for the consumer. In 2001, the government lowered prices for 69 antibiotics, 49 Chinese traditional medicines, and 383 chemical drugs, which is estimated to have saved consumers US$0.65 billion (5.4 billion RMB) annually. From 1997 to 2002, the growth rate of China's pharmaceutical retail price index has been decreasing: 4.4%, 2.8%, 1%, 0.3%, -1.5%, -3.5% (NDRC, 2004).

There are criticisms as well. First, the policy is accused of distorting the market mechanism. The price change on antibiotics in 2001 was said to have wiped off almost 50% profits of some big manufacturers. This might weaken their growth potential. Second, to promote innovation, those products that come from so-called "original R&D firms" can be exempted from price regulation. Because of the fact that most "original R&D firms" are Multi-National Companies (MNCs) from developed countries, the result is that many MNCs can take advantage of the policy and sell their products, even those off-patent already, at higher prices than local companies.

To lower prices, China is also trying to promote competitive bidding on drugs purchasing. The policy is aimed at pharmaceutical middlemen who account for 40% of the retail price.

III. Intellectual Property

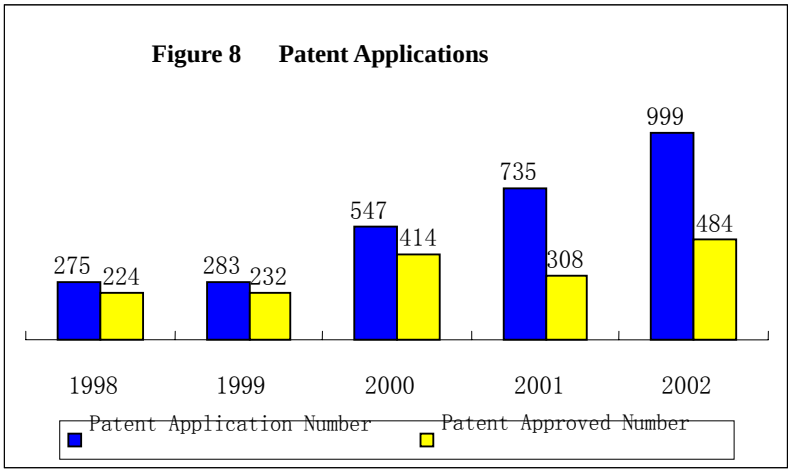
China has a relatively short but fast-developing history in intellectual property protection. In 1980, with the approval of State Council, the Patent Office of PRC (CPO) was founded to protect intellectual property, encouraging invention and creation. The office was renamed as the State Intellectual Property Office (SIPO) in 1998 (SIPO, 2004). China's first Patent Law was passed in March 1984 and came into force in April 1985. Before that, all inventions in China were free to use though the government might give some awards to the inventors.

However, the 1984 Patent Law excluded some categories from protection, which included pharmaceuticals, chemicals and agriculture products. Though the manufacturing method was under protection at that time, Chinese pharmaceutical firms could legitimately copy the existing products of foreign companies. At the beginning of the 1990s, China's practices on patent protection had been increasingly criticized by developed countries, especially by the US. In 1992, China revised the 1984 Patent Law (allowable since the beginning of 1993), to permit granting patent protection on new pharmaceutical compounds per se, new uses for known pharmaceutical compounds, pharmaceutical compositions, and agricultural compounds per se. Also, the revision extended the patent protection period from 15 years to 20 years. To meet the requirement of TRIPS, the Patent Law was amended a second time in August 2000, in which "offering for sale" has been taken as the exclusive rights of patents holders. The amendment also supplies the methods of compensation to patents holders when infringements happen.

Besides the Patent Law, China issued its Trade Mark Law in 1982, Copyright Law in 1990, and Unfair Competition Law in 1993. These laws and their revised versions, together with their implementation rules, are the basic building blocks for the legal framework of China's IP protection. The enforcement of IP protection has been improving, though it still draws criticism and complaints. A group of special courts that focus on IP protection has been built into China's judiciary system.

China also has a regulation system on IP protection, which is now being debated on its necessity. In 1985, China issued Regulation on Pharmaceutical Administrative Protection (RPAP). In the regulation and its later revisions in 1992 and 1998, China offers administrative protection on "new pharmaceuticals", defined as those pharmaceuticals being manufactured (NOT sale) first time in China. According to a classification, there are 5 categories of "new pharmaceuticals", and the protection periods are 12 years (first category), eight years (second and third) and six years (fourth and fifth). The regulation aims at promoting China's production capacity and controlling generic competition. However, MNCs actually can use it to extend the protection period for their patent-expired products in China. Furthermore, the regulation does not help reduce the price and thus also has a negative impact on medicine access.

Figure 8 Patent Applications



Source: National Science and Technology Committee (NSTC), *China S&T Statistics Year Book*, China S&T Publish House, 2003

Though me-too products dominate the production of Chinese pharmaceutical manufacturers, the awareness of the importance of patents in the industry has improved greatly especially as China's IP protection keeps improving. Patent applications have seen a fast increase. In 1998, patents approved to Chinese firms were 224, after four years the number more than doubled to 484. Partly due to the increasing awareness of the importance of patent protection, the number of patent applications grew more rapidly, with 275 filed in 1998, which tripled to 999 in 2002. Meanwhile, China's firms are starting to apply for international patents too, though it is still at an early stage.

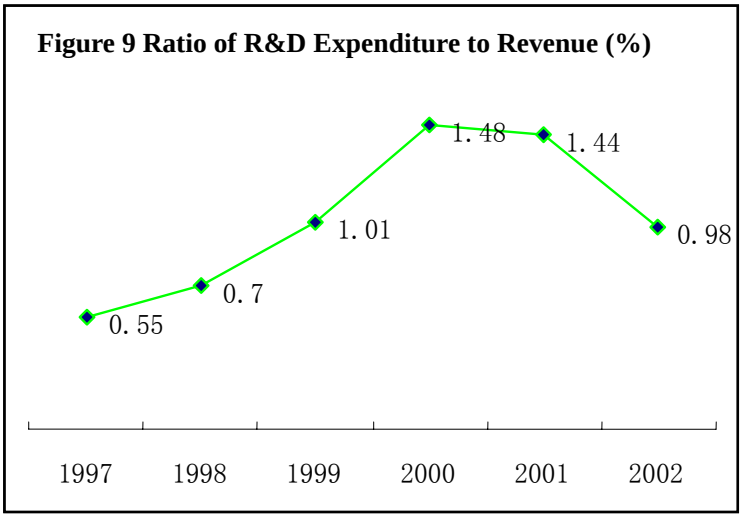
IV. Innovation Investment and Government Funding for R&D

Generally speaking, China's pharmaceutical industry is in a primary stage and positioned at the low end of the world value chain. The industry is still propelled ahead by generic production rather than innovative technology. While the picture is gloomy, there are some encouraging aspects. The innovative capacity in the industry is enhancing steadily; government supports innovation activities highly, which is very important to the innovation and development of the industry. Like some other developing countries, China has set up a relatively strong public research and innovation system financed by government. Recently, these public research institutions have re-gained their strength after a decade of difficult economic transition. The partnerships between public research institutions and pharmaceutical companies are emerging. Some sectors, especially bio-pharmaceuticals and the modernization of Chinese traditional drugs, are showing a promising future.

4.1 Innovation in Industry

Pharmaceutical innovation is a capital intensive activity that involves high risk. The features of China's pharmaceutical industry, fragmented and with small-size manufacturers as major players, shape its low capacity and risk-bearing ability in innovation. Two basic facts: almost 97% of products other than Chinese traditional pharmaceuticals manufactured by Chinese pharmaceutical firms are copycats of foreign products; and the ratio of R&D investments versus revenue of Chinese pharmaceutical firms are only between 0.5%-3%, far less than the average level of MNCs in developed countries (Qu Fenhong, 2002).

Figure 9 Ratio of R&D Expenditure to Revenue (%)

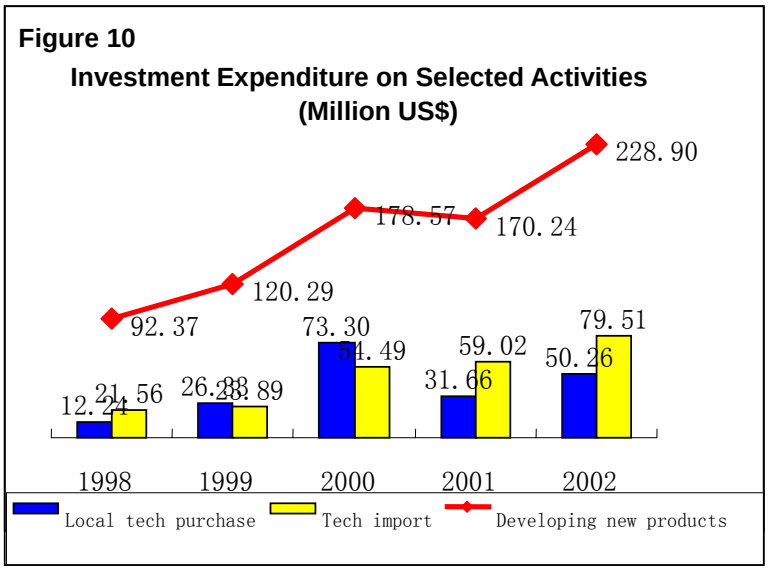


Source: National Science and Technology Committee (NSTC), *China S&T Statistics Year Book*, China S&T Publish House, 2003

From figure 9 we can see that the ratio of R&D expenditure to revenue is still increasing though the absolute level is always low. This is also the case in other innovation-related activities. For example, in new products development, the industry has seen the investment expenditure increased from US$92.37 million in 1998 to US$228.9 million (current price) with an annual increase rate of 37%. Meanwhile, the number of projects for new products increased from 2007 to 2663 (however, it is worthwhile to know that the total amount is still less than 1% of revenue annually). The expenditure on technology has improved rapidly. The investment for both domestic technology and imports increased more than three times from 1998 to 2002. The increase in innovation investment is more obvious in the bio-pharmaceutical sector, in which the expenditure on new products development increased from only US$5.33 million in 1998 to US$21.43 million in 2002.

Figure 10

Investment Expenditure on Selected Activities (Million US$)



Source: National Science and Technology Committee (NSTC), *China S&T Statistics Year Book*, China S&T Publish House, 2003

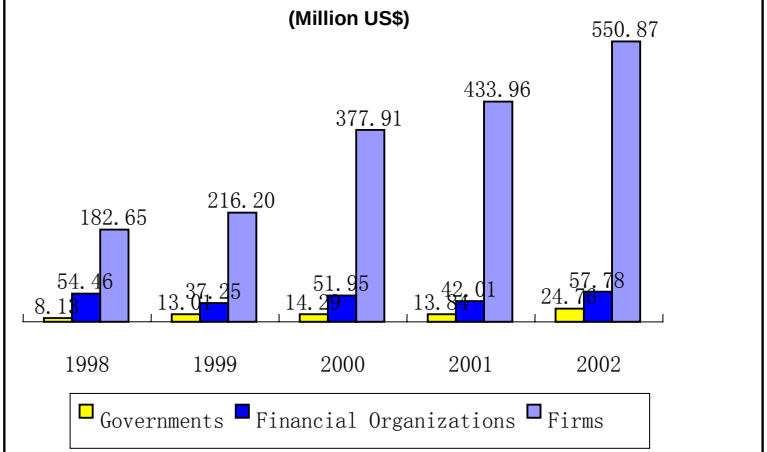
The investment is paying off. From figure 10 we can see that the revenue of the firms from the new products increased greatly from US$1255 million in 1998 to US$3005.5 million in 2002 with the same growth pace of investment.

4.2 Governmental Support

Since the 1980s, the Chinese government has taken pharmaceuticals as one of the nation's key industries and put it on the top of the development agenda. Government support was enhanced by the 21st century. Now the relative incentive policies mainly include: 1) "Tenth Five-Year Plan on National Economic and Social Development"; 2) "Tenth Five-Year Guideline on the Development of High-Tech Industries"; 3) "Tenth Five-Year Guideline for the Development of Pharmaceutical Industry"; 4)

"Tenth Five-Year Plan for Chinese Traditional Medicine"; and 5) "Chinese Traditional Medicine Modernization Development Programme". Most recently, China issued its first "Pharmaceutical Science and Technology Policy (2002-2010)" in 2002. The policy shows that the Chinese government is resolved to promoting the pharmaceutical industry on the track of innovative development, and bio-pharmaceuticals and modernization of Chinese traditional medicine have been the two fields with development priority.

Figure 11 Financial Sources for S&T Activities



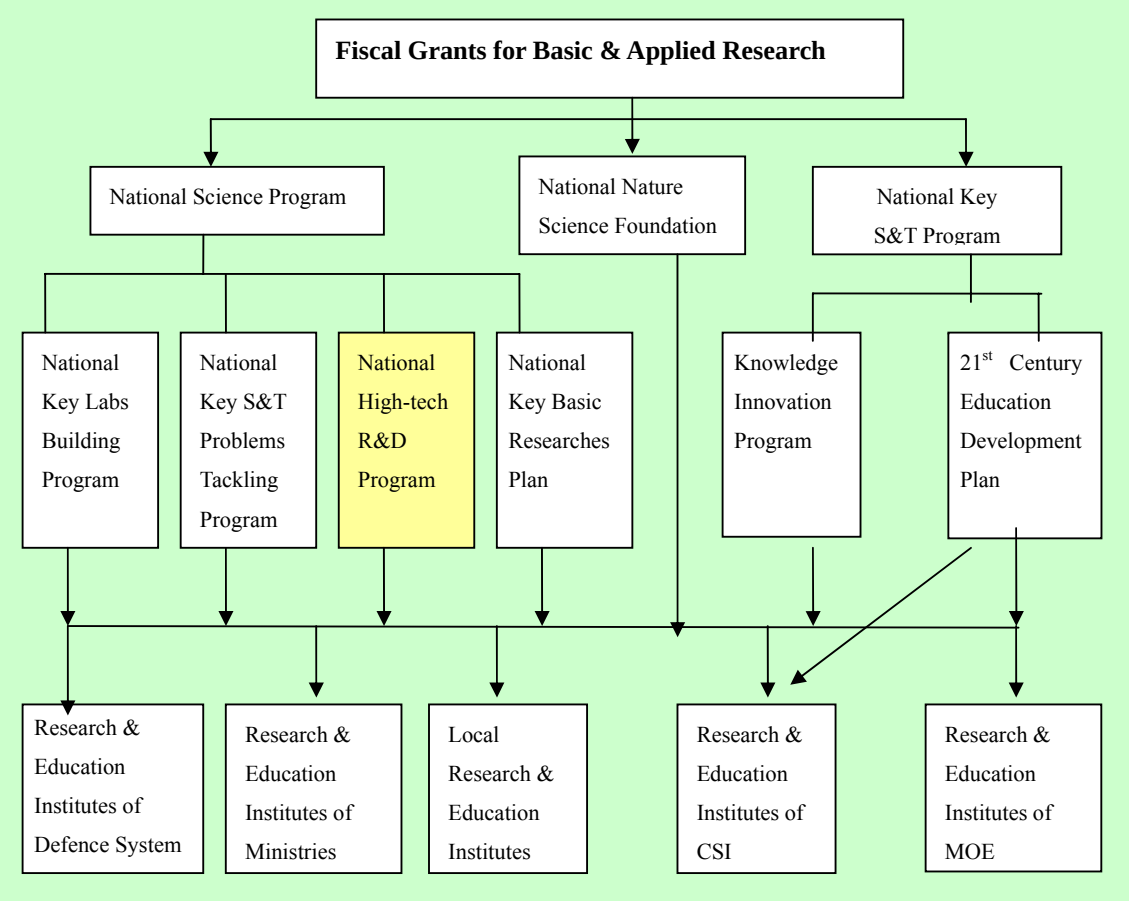
Source: National Science and Technology Committee (NSTC), *China S&T Statistics Year Book*, China S&T Publish House, 2003

In investment, the government plays a significant role as well. From 1998 to 2002, government finance for the S&T activities of the industry has tripled from US$8.13 million to US$24.76 million. This contrasts sharply with financial organizations, which are supposed to be one of the most important financial sources but seem stagnant during this time. Though in absolute terms government investment is relatively small among the three categories in figure 11, it has been invested in some key programmes and has the function of leveraging other sources into innovation.

China has built up a nation-wide research and education system where the most talented brains are concentrated. The system consisted of institutes that are financed by government, own relatively advanced facilities, and are the most important innovative sources for industries including pharmaceuticals. Understanding the importance of S&T to the future of China, and the fact that the country's capacity in S&T still lags far behind developed countries, China has since the 1980s organized these institutes collaboratively to undertake some national key research programmes and promote innovation. As a result, China has developed a unique national

innovation system with public research institutes as the locomotive. Because of the strategic role of the pharmaceutical industry, it has always been positioned as an important part of these innovative programmes. After nearly two decades, these national programmes have turned out to be very helpful to the building up of the industry's innovation capacity.

Figure 12 China's Public Science & Technology Innovative System



Among all of these innovation incentive programmes, one of the most important is National High-Tech Research and Development Programme, China's so-called Eureka Programme (pan-European network for industrial R&D). In March 1986, several renowned Chinese scientists wrote a letter to China's former leader Deng Xiaoping. They claimed that there was a science revolution happening in the world that would profoundly change humanity, and to catch up with the trend China needed to concentrate some government resources to develop several key programmes. The recommendation was quickly turned into the country's ambitious plan to promote high-tech R&D (it is also called 863 Programme because of when it was set up). From 1986 to 2000, the 863 Programme pooled the best brains of China together and invested 5.7 billion RMB in six high-tech fields, among which biotech was the top priority. The programme makes in-depth improvements and has far-reaching influences on China's S&T. During the 15 years, about 6500 scientists participated in the 863 Programme's biotech sector, and among them 90% were young scientists. They produced 455 patents and published 10,278 research papers (Xiping Jia, 2001). It has directly promoted the innovative capacity of bio-pharmaceutical, and has

developed and commercialized 18 new pharmaceuticals. Now the second term of the 863 Programme has been launched, from 2001 to 2005, with an investment of 15 billion RMB (Dongning Tang, 2001).

The Chinese government also tries to promote better collaboration between public institutes and pharmaceutical companies. One of the most common practices is the setting up of various high-tech parks and bio-parks, where the government invites companies and research agencies to work together to take advantage of the so-called "cluster effects". In the bio-park, the government supplies high-quality infrastructure and gives significant tax breaks to enterprises. Now China has 168 such "parks" with 64 specialized as "bio-pharmaceutical parks", and each province or major city has its own "parks" (S&T Yearbook, 2003). Some of these "parks" are very successful and become hotbeds of new technology.

Other forms of business and research partnership are also growing. For example, CSPC, one of the top ten local pharmaceutical manufacturers, has cooperated with the Institute of Materia Medica of Chinese Academy of Medical Sciences and successfully developed NBP (N-Buthlphthide) in 2002 – a state-level Category I new drug for ischemic stroke. The intellectual property of NBP is owned by CSPC. Some companies even try to acquire the research institutions through purchasing. In 2002, China's Lizhu Pharma Group acquired Hubei Province Pharma Engineering Institution; and Fuxing Industry acquired Chongqing City Pharma Engineering Institution (Ma Yu, 2003).

4.3 Future of Bio-Pharmaceuticals and Chinese Traditional Medicine (TM)

Though relatively young, China's bio-pharmaceutical has been experiencing a rapid growth since the 1980s, and become a boom industry with a dynamic innovative capacity. Now there are more than 400 biotech related colleges and research institutes in China. From 1998 to 2002, the number of bio-pharmaceutical companies increased from 240 to 335, revenue of the bio-pharmaceutical sector increased from 7.42 billion RMB to 17.06 billion RMB, and the grew from 0.87 billion RMB to 1.93 billion RMB, more rapidly than the average level of the pharmaceutical industry (SSB, 2003).

Since its first innovative bio-pharmaceutical product Recombinant Interferon<1b was developed in 1989, China has had 15 bio-pharmaceutical products approved for markets (Qi Hua, 2004). Though most of them are still imitations, innovation is definitely on the way and China begins to develop innovative products more than ever before. Now China has made some substantial progress in therapeutic antibodies, severe acquired respiratory syndrome (SARS) research, gene therapy, functional genomics, and stem cells. For example, China announced the world's first gene therapy in January 2004, and several research groups are pioneering research on adult stem cells and embryonic stem cells (Li Zhenzhen, 2004). Furthermore, there are 139

drugs currently in China's pipeline; 60 of these new candidates are biologics including 19 antibodies and 11 vaccines. There are an estimated 700 biologics in clinical development worldwide, 150 of which are in late clinical stage (Sabine Louët, 2004).

Table 13 Selected Examples of Chinese Health Biotechnology Products

Sector	Type	Application	Producer
Vaccines	Recombinant hepatitis B surface antigen	Hepatitis B	Shenzhen Kangtai Biological Products (Shenzhen,)
	Recombinant live oral vaccine, which expresses protective antigens of both Products *Shigella flexneri* 2a and *Shigella sonnei*	Shigella dysentery	Lanzhou Institute of Vaccines and Biological (Lanzhou)
Therapeutics	Recombinant interferon □1b	Ulcerative keratitis/ Hepatitis B and C	Changchun Research Institute of Biotechnology (Changchun) Shanghai Research Institute of Biotechnology
	Recombinant epidermal growth factor	Skin injuries	Shanghai Dajiang (Group) (Shanghai)
	Recombinant human interleukin-2	Many uses, including for cancer (e.g., renal cell carcinoma)	Shenzen Neptunus Interlong Biology Technique Holdings (Shenzen)
	Recombinant granulocyte colony-stimulating factor	Neutropenia	Amoytop Biotechnology (Fujian)
	Recombinant erythropoietin	Anemia	Shenyang Sunshine Pharmaceutical (Beijing)
	Recombinant human somatotropin	Dwarfism	Changchun Jinsai Pharmaceutical (Changchun)
	Recombinant Ad-*p53* gene therapy	Head and neck squamous cell carcinoma	Shenzhen SiBono GenTech (Shenzhen)
Diagnostics	Enzyme-linked immunosorbent assays	Hepatitis C and human immunodeficiency virus	Shanghai Huaguan Biochip (Shanghai)

Note: Some of these products have more than one producer in China.
Source: Li Zhenzhen et al, 2004

Several advantages contribute to the development of China's bio-pharmaceutical. First is that China has a relatively advanced biotech sector, which supplies a sound base for the development of bio-pharmaceutical. China is the only developing country to have joined the Human Genome Project and has successfully sequenced 1% of human genome with an accuracy of 99%. Second, China's large and multiethnic population is a natural advantage for clinical trials. Patients are easier to acquire in China than in western countries. Thirdly, China has a good reserve of cheap but highly-educated

doctors, scientists and engineers. It is estimated that the R&D cost in China is comparable only to about 30% of developed countries. Fourth, Chinese central and local governments give special support to bio-pharmaceutical. Several programmes have been set up for supporting the industry, including an important one that focuses directly on biotech in 1999 (table 14). Local governments also give special tax break arrangements in the bio-parks. Considering the fact that venture capital activity is very weak in China, governments also set up some foundations to nurture the early-stage projects.

Table 14 Health-Biotech Related Government Supporting Programmes

Programme	Starting Year	Ministries on Watch	Finance Structure	Beneficiaries
Torch Programme	1988	National and local S&T Committee	Special Loans and firm's own sources	High-Tech Product Development; High-Tech Park Building
National Key S&T Programme	1992	National Reform & Development Committee	Fiscal grant and others	High-Tech Industrial Programmes
Innovation Foundation for S&T Medium and Small Size Enterprises	1998	National S&T Committee	Fiscal grants from central and local gov; loans; firm's own source	Medium and Small Size Enterprises with S&T
"863" Programme	1986	National S&T Committee	Fiscal grant from central gov	Colleges & Universities; research institutes; enterprises; high-tech industrial bases
Special Programme on Bio-Tech	1999	National Reform & Development Committee	Fiscal grants from central and local gov; loans; firm's own source	Industrialization of biotech and products; Industrial bases building for biotech

Another promising field is the modernization of Chinese traditional medicine. China has developed a complete traditional medicine system including 2682 specialized Chinese traditional hospitals, 25 colleges and universities, and 94 research institutes (SATCM (2), 2003). But because of cultural differences, Chinese traditional medicine has some problems entering the mainstream markets of western countries, but it has enjoyed a considerate market share in East Asian countries, including Japan and Korea, and in some South East Asian countries for a long time. Most Chinese traditional medicines are synergistic drugs with multiple active components, and have experienced thousands of years of successful "clinical trials". As a kind of herbal therapy, Chinese traditional medicine has much less side-effects and drug-fast effects than chemical pharmaceuticals, and they do show considerable functions in the

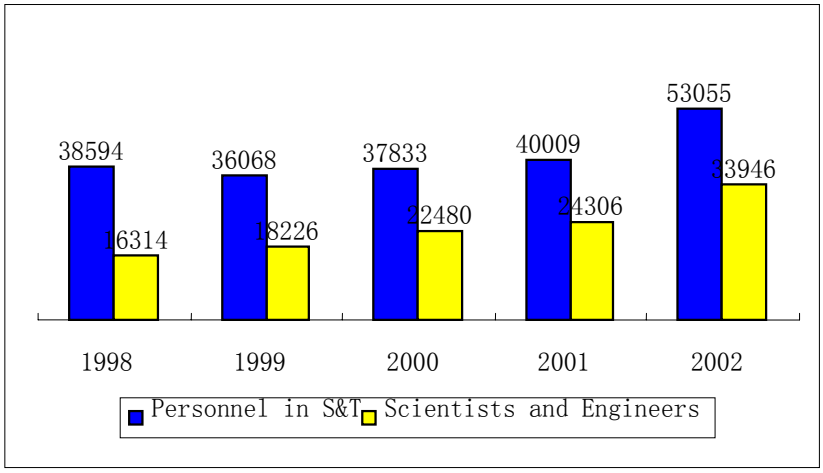
treatment of many modern diseases. From 2000 to the end of 2004, China has invested 8 billion RMB on education and S&T activities in traditional medicine (SATCM (2), 2005).

One of the success stories of modernization of Chinese traditional medicine is artemisinin. Artemisinin is a herbal derivative from the 'sweet wormwood' plant (Artemisia annua), which has for a long time been used for malaria treatment in China. It can be documented in a medical book of Mawangdui dating back the Han dynasty in 168 BC. In 1972, organized by the Chinese government, several groups of Chinese scientists successfully isolated its primitive active ingredients in a collective effort, and produced an effective new drug for malaria treatment. Now, with the cooperation between Chinese firms and MNCs, especially Novartis, artemisinin has paved the way to become a first-line treatment for malaria in the world. There are many other traditional medicines and therapies that have the potential to be developed into modern pharmaceuticals.

V. Human Resources

In general, consistent with the weak R&D activities in the industry, the human resource reserve in China's pharmaceutical industry is low. But we do see an increase across time. From 1998 to 2002, the total personnel in the industry decreased from 860,000 to 820,000, mainly because of industry consolidation. However, personnel involved with science and technology increased steadily from 38,594 to 53,055. The number of scientists and engineers in the industry, which are designated as technical posts in China, increased from 16,314 to 33,946. And thus the ratio of scientists and engineers versus total personnel increased from 1.9% to 4.1% during this time (NSTC, 2003).

Figure 15 Personnel Involved with S&T Activities



Source: National Science and Technology Committee (NSTC), *China S&T Statistics Year Book*, China S&T Publish House, 2003

The human resource in the biopharmaceutical sector has been increasing particularly fast. From 1998 to 2002, the personnel for S&T activities increased from 1,896 to 3,298, and the number of scientists and engineers increased from 1,038 to 2,425, which makes the ratio of top-end talent considerably high. The resource pool of the biopharmaceutical sector has also been enhanced by those who return from overseas with high education and research experience in developed countries, and bring back to China the industry know-how and even advanced technology (Qi Hua, 2004).

Furthermore, China is increasing the pool of talent through expanding higher education. China's higher education a rapidly expanded since the mid-1990s, benefiting the pharmaceutical industry as well. For example, the number of newly-enrolled students in chemical engineering and pharmaceuticals at university level was 3,1701 in 2000, but the number in 1999 was only 2,6197(MOE, 2001); since 1997, each year about 5000 students majoring in biotech graduated from colleges and

graduate schools. This is even more obvious in medicine. As shown in table 16, the number awarded a degree in medicine grew from 1,240 in 1998 to 3,073 in 2002, with an annual growth rate as high as 19.42% (SCEDMO, 2004).

Table 16 Doctor's Degree Education Majoring in Medicine

	Number Recruited	Number Enrolled	Number Graduated	Doctor's Degree Awarded
1998	1777	4918	1219	1240
1999	2407	5952	1436	1612
2000	3030	7527	1520	1758
2001	3965	9546	1774	2100
2002	4497	11687	2166	2444
2003				3073

Source: State Council Education Degree Management Office, 2004

VI. Trade Issues Influencing Access to Health Services and Technologies

6.1 Industry Structure

There are three basic features of China's pharmaceutical industry: fast growth in production volume, strength in generic production, and fragmented supply structure.

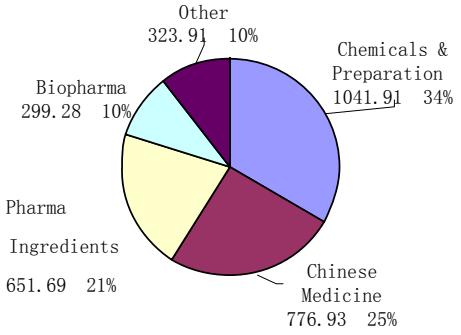
4) **Fast Growth in Production Volume**

China's pharmaceutical industry experienced a fast growth since the beginning of the 1980s, and now has developed a relatively complete manufacturing system with production capacity in pharmaceutical ingredients, chemical preparations, bio-pharmaceutical products, traditional medicine, and medical and pharmaceutical equipment. From 1995 to 2003, the annual growth rate of production and revenue was higher than 20%, and the profit growth was even higher than 40% (table 17). All of these indicators are higher than other industries, and put pharmaceuticals as one of the fastest growing sectors in China. Among different products, bio-pharmaceuticals have enjoyed the fastest growth. From 1995 to 2002, the production value of bio-pharmaceuticals increased from US$0.56 billion to US$2.34 billion; revenue increased from US$0.52 billion to US$2.06 billion; and the profit volume increased from US$0.082 billion to US$0.23 billion. The revenue proportion of bio-pharmaceuticals in the industry increased from 4.8% to 7.5% (SSB, 2003). The increase in production capacity has improved access to medicine in China. Furthermore, China becomes an important source of generic pharmaceuticals and API for the world market.

Table 17. Some Basic Data for China's Pharmaceutical Industry (billion

	Revenue	Profit
1995	10.90	0.62
1996	12.60	0.80
1997	14.22	0.88
1998	15.27	0.94
1999	16.65	1.23
2000	19.66	1.65
2001	23.24	2.03
2002	27.54	2.43
2003	33.22	3.09
Annual growth rate	25%	49%

Figure 18 2003 Profit Breakdown (Million US$)



Note: the value is in nominal terms with a fixed exchange rate at 8.28RMB/US$
Source: Combined State Statistic Bureau, *China Statistic Year Book 2003*, China Statistic Publish House, 2003; China Pharmaceutical Statistics Net. www.yytj.com

5) **Strength in Generic Products**

Cheap labour and cost-efficient production has strengthened China's generic production, and made it the world's second largest producer of pharmaceutical ingredients after the United States with an output of 800,000 tons in 2003, half of which is for export. Especially in chemical ingredients, China has an annual production capacity of 1500 categories, and enjoys 22% of the world market with a sale of US$3.7 billion (YYTJ, 2004). Chinese firms rank first in the world in the production of five pharmaceutical chemicals: penicillin (28,000 tons or 60% of world total), vitamin C (98,000 tons, of which 54,000 tons are sold abroad, or 50% of the world total), terramycin (10,000 tons, or 65% of the world total), doxycycline, hydrochloride and cephalosporins (Grace, 2004).

The production of generics still has a bright future considering that between 2000 and 2007 many pharmaceutical patents will be expiring, including 29 products with annual revenue above US$500 million. Globally, the production of generics and pharmaceutical ingredients is now transferring to Asia; China and India have a promising future to be the global hub of pharmaceutical ingredients. India seems somehow moving faster in this competition. Up to July 2003, EDQM has issued 1,398 Certificates of Suitability (COS) certificates. There are 18 Chinese companies with 30 products that have COS, meanwhile the number for Indian products is 141. By the end of 2003, 52 pharmaceutical ingredients firms from China passed FDA authentication, whilst the number of the Indian firms is 60[42].

However, the disadvantage is obvious due to the path-dependence on generic production. The bulk production of me-too pharmaceuticals put China on the lower end of the global pharmaceutical value-chain. As a result, the innovative capacity of China's pharmaceutical firms is weak - 97% of the drugs manufactured in China other than Chinese traditional medicine are copies of foreign products, and the market competition is concentrated on cost control and cheap prices. The average profit for China's generic products is between 5% and 10%, far less than the global average of 40% (Wang Yanzhong, 2001).

6) **Fragmented Supply Structure**

Like India and many other developing countries, China's pharmaceutical industry is considerable fragmented, especially in the 1990s. In 1996, the number of Chinese pharmaceutical firms peaked at 5,396. Even in 2002, after intense effort trying to improve the industry concentration rate initiated by the government, the number of firms was still as high as 3,681. In industry concentration rate, as shown in table 19, the CR10 in 2003 is 15.48%[43]. The rate is considerably low compared to Japan's CR8

[42] The number comes from a Chinese news report and waiting to be further confirmed
[43] CRn is concentration rate, refers to the percentage of summarized revenue amount of top n firms to

in 1996, which was 44%; the UK's CR4 in 1993 was 35%; and Germany's CR4 was 28% in 1991. Globally, as M&A became a trend in the industry since the 1990s, the concentration rate has improved greatly, and CR10 was 40% in 2000 globally (Cao Liquan, 2002).

the total revenue amount of the industry.

Table 19 Top Ten 2003 Revenue of Pharmaceutical Producers (Million US$)

	Company	Revenue	Profit
1	HPG (Harbin)	881.87	54.58
2	NCPC (Huabei)	845.41	71.26
3	Yangtze	731.33	81.57
4	CSPC (Shijiazhuang)	685.61	107.94
5	TJPC (Tianjin Jinyao)	412.85	42.27
6	Xinhua Pharm	407.97	10.21
7	Xi'an Janssen	332.90	75.71
8	Tianjin Zhongxin	294.07	12.18
9	Shenghua Group	280.23	17.09
10	Tasly	271.53	32.98
Compare	Sum	5143.77	505.79
	CR10	15.48%	16.37%
	Merck & Co (2002)	51790.3	20020.1

Note: Exchange rate taken as 8.28RMB/US$
Source: State Statistics Bureau, 2004, and www.merck.com

In recent years, especially since 2002, China's pharmaceutical industry is experiencing unprecedented M&A activity as well, which is now rapidly changing the map of the national industry. These M&A activities are involved with many of the bigger pharmaceutical firms that listed on stock markets. Chinese pharmaceutical giants are in development. For example, during the first three quarters of 2004, there have been 43 M&As, such that there were new M&As every week, and the total capital involved with M&A reached US$0.42 billion. Some of this M&A has gone cross-border . In 2003, China's 999 Group acquired 51% of shares in Japan's East Asia Pharmaceutical Co. Some optimistic analysts claim that there will be four to five Chinese pharmaceutical firms joining the world's top 50 companies within the next five years. Meanwhile the total number of Chinese pharmaceutical firms will decrease to about 2600 (Xia Jinbiao, 2004).

6.2 Joint Ventures in China

Since Japanese pharmaceutical firm Otsuka opened a joint venture (JV) in China's Tianjin in 1978, JVs in pharmaceutical have experienced fast development. The amount of FDI in the sector was hitting US$1.5 billion in 2000. Now, among the 500 biggest JVs in China, there are 15 in the pharmaceutical industry. And the total number of JVs in pharmaceutical was approaching 1,800 by the end of 2000. About 40% of domestic pharmaceutical firms currently have co-operative projects with foreign manufacturers. Among the 25 largest international manufacturers, 20 of them now have operations in China.

Table 20 Foreign Manufacturing Presence in China through Joint Ventures (2002)

Local Company	Foreign Owning Company	Domestic Owning Company/Partner
Bayer	95% Bayer	5% BETIDC
Beijing Fresenius	75% Fresenius-Kabi (Germany)	25% Beijing Frensenius Pharma Co.,
Boehringer Ingelheim Shanghai	90% Boehringer Ingelheim	10% Sine
China Otsuka	50% Otsuka, Japan	50% China National Pharma Corp.
Gruenenthal-Sanhuan	75% Gruenenthal, Germany	25% Sanhuan
Roche	70% Roche, Switzerland	30% Shanghai Sunve Co.
Sino-American Shanghai Squib	50% Bristol-Myers Squibb	50% Shanghai Trust Corp State Pharma Administration of China
SSPC	51% Pharmacia Corp, USA	49% China National Pharma Corp
Xi'an-Janssen	52% Janssen, Belgium (J&J, USA)	48% Shanxi Provincial Pharma Corp

Source: IMS Health Pharmaceutical Company Directory

The JVs have an impressive performance in China's markets so far. Forty of the 50 best selling brands in 2000 were produced by JVs. In 2003, they accounted for 22.2% of the industry's revenue, 28.5% of the profit, and 25% of the tax share. Meanwhile, the asset share of JVs is 18.6% (SSB, 2004).

JVs contribute greatly to the innovation capacity in China. They bring China's firms new products for in-licence manufacturing, new technologies, and even advanced management. China's firms benefit from them through learning-by-doing. Though JVs generally aim at China's market share, and MNCs are conservative in technology transfer, JVs still contribute to some innovation directly. For example, patent applications from JVs were 6, 28, 6, and 12 from 1999 to 2002, and the number of patents approved were 3, 23, 8, and 5 respectively (NSTC, 2003).

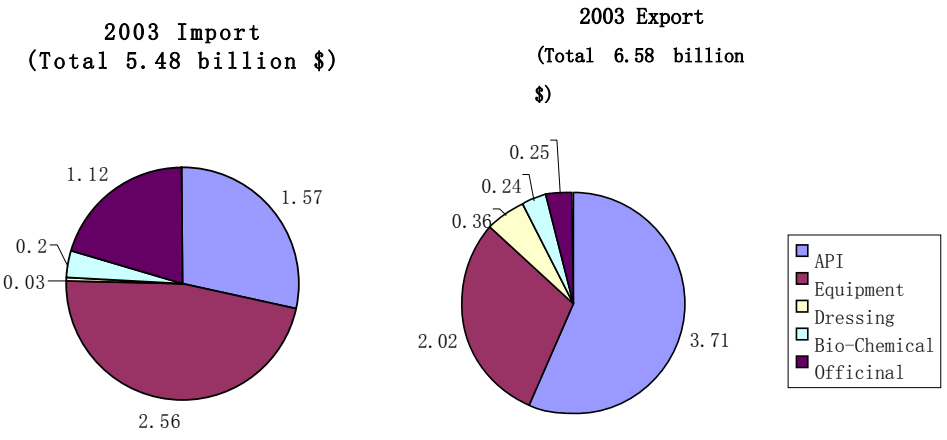
In recent years, MNCs have shown more interest in R&D investment in China. Several moves by MNCs have been made in 2003 and 2004: Roche established its fifth biggest R&D centre in China's Shanghai, which is also its only R&D centre in a developing country; GSK set up an OTC R&D centre in China's Tianjin; Eli Lilly built a testing centre in Shanghai; and Novo Nordisk doubled the size of its R&D centre in Beijing (Li Qin, 2004). The collaboration between MNCs and local research institutes is also enhanced. So far GSK, Roche, AZ, and Pfizer have cooperated in R&D with China's universities and research institutes.

This new trend is driven by low-cost R&D resources as well as improving IP protection in China. It is supposed to enhance the R&D capacity in China in long term. Meanwhile, it brings competition to China too, and now local firms feel pressure more and more.

6.3 International Trade

China has been an important player in the global pharmaceutical market for a long time, and both its imports and exports have grown significantly in the past decade. In 2003, total imports and exports of western pharmaceuticals and equipment reached US$12.89 billion, consisting of US$5.48 billion in imports and US$6.58 billion in exports, an increase of 25.54% from US$10.2 billion in 2002.

Figure 21 Breakdown of Import & Export of 2003



Source: YYTJ, 2004

China's international trade covers both developed and developing countries. Its three most important trade partners are the US, Japan and Germany. However, its exports to other regions keep growing. In 2003, its exports to Asia (excluding Japan) was US$2.11 billion, to South America US$0.46 billion, and to Africa US$0.28 billion, an increase from 2002 of 20.18%, 30.14% and 21.23% respectively.

Table 22 1998 Top Ten Exporters and Importers in Developing Countries (m $)

Top Ten Exporters	Amount to Industrialized Countries	Amount to Developing Countries		Top Ten Importers	Amount from Industrialized Countries	Amount from Developing Countries

China	1079	592	Brazil	1325	263
India	288	576	Mexico	955	109
Hong Kong	66	815	Hong Kong	761	294
Mexico	304	410	Argentina	638	139
Singapore	166	426	Chinese Taipei	676	26
Israel	347	33	Singapore	522	69
Argentina	25	277	Korea, Rep.	463	92
Korea, Rep.	85	204	China	423	103
Brazil	64	183	Israel	500	12
Colombia	10	173	Colombia	294	202

Source: Bale, 2001

6.4 Bulk Manufacturing and Problems of Access to Medicines

Chinese firms' capacity for bulk production on generics helps to cut production costs and helps to keep drug prices relatively low, which is of great assistance to low-income patients. Because of increasing exports, China's low-cost production also helps to lower the price of drugs in many other developing countries. China's emerging capacity in innovation, though still at a very low level, helps to cure the infectious diseases in China, which is important not only nationally but to the whole world as well. China can now manufacture 41 vaccines for the prevention of 26 viruses, amounting to one billion dosages annually, including 0.5 billion for the prevention of hepatitis B, poliomyelitis, measles, kinkcough, diphtheria, and tetanus. It is a very solid and important back-up for China's Free Compulsory Immune Plan (Yin Hongzhang, 2004).

On the other hand, the relatively low -level innovative capacity makes the patented drugs from abroad very expensive, which creates affordability problems. However, in some cases the bulk production capacity also helps to supply advanced drugs to the market with cheaper prices as long as the patents have expired. This happened in China's ARV market. In 2002, after GSK renounced its patent ahead of schedule on Zidovudine (AZT), a component of HAART for HIV/AIDS treatment, China's Northeast Pharma Company quickly obtained the licence for producing generic AZT on August 6, 2002. Several months later another three components, Didanosine(ddI), Stavudine(d4T) and Nevirapine(NVP) were also approved licence for production by Shanghai Desano[44]. Now China can manufacture two sets of HAART locally. The price for the therapy decreased dramatically from 3000 RMB monthly to 3000—5000 RMB annually (Chou Yong, 2004).

[44] There is a patent issue here. The three ARVs are patented by Bristol-Myers Squibb. But Shanghai Desano applied for approval before BMS applied for patents in China. Also, Shanghai Desano claimed its formulas are different from BMS's.

There are also many other patented ARV drugs that are either unavailable or too expensive in China, including: Zalcitabine (ddC), Lamivudine (3TC), Abacavir (ABC), Combivir (AZT+3TC), Trizivir (AZT+3TC+ABC), Delavirdine (DLV), Efavirenz (EFV), Saquinavir (SGC), Indinavie (IDV), Ritonavir (RTV), Nelfinavir (NFV), Amprenavir (APV), and Lopinavir/Ritonavir. Some drugs, including 3TC and EFV, are critical to fighting HIV/AIDS and are on the list of the WHO.

6.5 Impact of WTO Membership

Membership of the World Trade Organisation (WTO) is having a significant impact on China's pharmaceutical industry.

The first is with international trade. China is scheduled to decrease its tariff level from 20% to 6.5% within 10 years, which will increase the share of imported drugs and induce greater market competition. Meanwhile, the lowering of tariffs and other non-tariff barriers from other countries will help increase China's exports. In generics, China's global market share might increase.

The second impact is on service. China has announced it will open its pharmaceutical distribution system to the world at the end of 2004. The move helps bring to market China's wholesale and retail system. To prepare for the open market, the government has opened the distribution system to domestic private capital. The increasing market competition has lowered prices and improved drug accessibility. There has been a lot of "par value pharmacy" emerging in big and medium-sized cities in China in recent years. The supposed entry of global circulating giants might bring more competition to the market.

The third impact is on IP management. China's IP-related law is now compliant with TRIPS, and patent protection has also been greatly enforced. The positive side of the situation is obvious: enhanced IP protection will enhance innovative activities of Chinese firms, and also help MNCs expedite their R&D outsourcing to China.

However, because Chinese firms' innovative capacity is still nascent, there are several negative aspects:

1) With the decrease of copycats, innovative pharmaceuticals will be much higher priced and create affordability issues.
2) For innovative pharmaceuticals for infectious diseases HIV/AIDS, TB, hepatitis and schistosomiasis, the affordability issue can turn into public health problems. The lack of essential ARVs in China is an example.
3) Patent applications is a game of "All or None". China has invested a lot in biotech. Some of the research may be fruitless because foreign companies applied for patents one step ahead.

4) Because of the fact that there is almost no technology transfer arrangement in TRIPS, the prohibition in copying of innovative drugs, though very important to R&D investment, will possibly result in technology regression in China.

China therefore needs to take some initiative as well. The government and firms need to reform pharmacy purchasing systems. Enhance group bidding and negotiation with MNCs. If necessary, China should put TRIPS' flexibilities, like compulsory licensing and parallel imports, into use for the purpose of public health protection. Fourthly, at the time when more and more MNCs as well as domestic firms show interest in the modernization of Chinese traditional medicine, IP protection of traditional medicine should be put on the agenda as soon as possible.

Conclusions and Policy Implications

Pharmaceuticals is a special industry, it is not only about business but also about people's health. China's pharmaceutical industry has seen significant developments since the 1980s, however, its innovative capacity is still nascent and at a low level. There are several lessons one can draw from China.

Generic production is an important way to meet local health needs, as well as to improve manufacturing capacity and accumulate capital for future innovative investment. To achieve that an open and competitive market is helpful, meanwhile, forming a relatively high industrial concentration rate is also important for building competitive capacity, especially through voluntary M&A activities among firms. China has somehow benefited from its vast population and market scale. For smaller developing countries, a regional arrangement for market access may be achievable for the same purpose.

Innovative capacity is the solution for health needs in the long-run. However, because of the low revenue and limited profit, the innovative capacity of firms in developing countries is always weak. It is hard for them to invest too much in R&D, especially considering the high-risk of the R&D return in the pharmaceutical industry. Therefore market failure of innovation will exist. To solve the problem government should input significantly in capacity building, including investing in education, training, R&D facilities, tax breaks, and even a special nurturing fund arrangement. In developing countries, R&D capacity is always reserved in public research institutes rather than private firms; therefore, promoting the partnership between public and private is important. In China, the practice of setting up high-tech parks is a successful case study for that end. It is also important to build partnerships between local companies and MNCs. Learning-by-doing may help local firms grow faster.

To meet the needs of public health, local government as well as firms should enhance their price negotiation capacity with MNCs, both in technology and final products. TRIPS's flexibilities might be a help to protect public health. However, it is far from enough. TRIPS needs to make some arrangements on technology transfer from developed countries to developing countries, and finally to help build up the innovative capacity of developing countries. It is particularly true of those technologies for curing the "global public bads"—infectious diseases.

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DEVELOPING INNOVATIVE CAPACITY IN **BRAZIL** TO MEET HEALTH NEEDS

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Abbreviations

Associação Brasileira das Indústrias de Medicamentos Genéricos [Brazilian Association of Generic Medicine Industries]	Progenericos
Associação Brasileira das Indústrias de Química Fina, Biotecnologia e suas Especialidades [Brazilian Association of Fine Chemical, Biotechnology and Specialties Industries]	ABIFINA
Associação dos Laboratórios Farmacêuticos Oficiais do Brasil [Association of Official Brazilian Pharmaceutical Laboratories]	ALFOB
Agência Nacional de Saúde Suplementar [National Agency for Supplementary Health]	ANS
Agência Nacional de Vigilância Sanitária [National Health Surveillance Agency]	ANVISA
Agreement on Trade-Related Aspects of Intellectual Property Rights	TRIPS Agreement
Antiretroviral	ARV
Banco Nacional de Desenvolvimento Econômico e Social [Brazilian Development Bank]	BNDES
Câmara de Regulação do Mercado de Medicamentos [Regulation Board for the Medicine Market]	CMED
Centro de Desenvolvimento Tecnológico em Saúde [Centre for Technological Development in Health]	CDTS
Conselho Administrativo de Defesa Econômica [Administrative Council for Economic Defense]	CADE
Conselho Interministerial de Preços [Interministerial Price Council]	CIP
Conselho Nacional de Desenvolvimento Científico e Tecnológico [National Counsel of Technological and Scientific Development]	CNPq
Comissão Nacional de Ética em Pesquisa [National Commission for Ethics in Research]	CONEP
Comitês de Ética em Pesquisa [Committees for Ethics in Research]	CEP's
Conselho de Gestão do Patrimônio Genético [Management Council of Genetic Heritage]	CGEN
Contribuição de Intervenção no Domínio Econômico [Contribution for Intervention in the Economic Area]	CIDE
Coordenação de Aperfeiçoamento de Pessoal de Nível Superior [Coordination for the Improvement of Higher Education Personnel]	CAPES
Empresa Brasileira de Pesquisa Agropecuária [Brazilian Agricultural Research Corporation]	EMBRAPA
Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro [Foundation for the Support of Research in the State of Rio de Janeiro]	FAPERJ
Fundação de Amparo à Pesquisa do Estado de São Paulo [Foundation for the Support of Research in the State of São Paulo]	FAPESP

Financiadora de Estudos e Projetos [Research and Projects Financing]	FINEP
Fundação Oswaldo Cruz [Oswaldo Cruz Foundation]	FIOCRUZ
Gross Domestic Product	GDP
Índice Nacional de Preços ao Consumidor-Amplo [National Index for General Consumer Prices]	IPCA
Instituto Brasileiro de Geografia e Estatística [Brazilian Institute of Geography and Statistics]	IBGE
Instituto de Pesquisa Econômica Aplicada [Institute for Applied Economic Research]	IPEA
Instituto Nacional da Propriedade Industrial [National Institute of Industrial Property]	INPI
Instituto Oswaldo Cruz [Oswaldo Cruz Institute]	IOC
Instituto de Tecnologia do Paraná [Technology Institute of Paraná]	TECPAR
Ministério da Ciência e Tecnologia [Ministry of Science and Technology]	MCT
Ministério da Saúde [Ministry of Health]	MS
Política Industrial, Tecnológica e de Comércio Exterior [Industrial, Technological and Foreign Trade Policy]	PITCE
Política Nacional de Medicamentos [National Medicines Policy]	PNM
Programmea de Apoio do Desenvolvimento da Cadeia Produtiva Farmacêutica [Support Programme for the Development of the Pharmaceutical Productive Chain]	Profarma
Programmea Nacional de Biotecnologia [National Biotechnology Programme]	PRONAB
Programmea de Apoio ao Desenvolvimento Científico e Tecnológico [Scientific and Technological Development Support Project]	PADCT
Programmea para Inovações Tecnológicas em Pequenas Empresas [Programme for Technological Innovation in Small Companies]	PIPE
Relação Nacional de Medicamentos Essenciais [National List of Essential Medicines]	RENAME
Sistema Único de Saúde [Unified Health System]	SUS
Subprogrammea de Biotecnologia [Biotechnology Subprogramme]	SBIO
Universidade Estadual de Campinas [State University of Campinas]	UNICAMP
Universidade de São Paulo [University of São Paulo]	USP
World Health Organization	WHO
World Trade Organization	WTO

Introduction[45]

This work examines the policies, strategies and capabilities in the field of health innovation in Brazil. Brazil has a long tradition in biomedical oriented research, has developed policies for universal access to public health, has proved to be extremely active in international negotiations concerning intellectual property, offers excellent vaccinal coverage to its entire population, and has built a model of free antiretroviral therapy. Certain weaknesses curtail innovation in Brazil's health system; the most significant is its limited innovative capability which severely hinders fulfilling the population's requirements, especially those with low family incomes.

This work is composed of four parts, with the first providing an overall insight into the Brazilian health system, its capabilities in medicines, vaccines and biotechnology, as well as the main aspects of health research and innovation policies. The second part is from a commercial approach: the relationship between TRIPS and public health, pharmaceutical patents and Industrial Property Law, legal safeguards, the regulation of prices, and the Brazilian model of access to antiretroviral medicines. The third part studies regulations, funding for R&D, the business environment, and human resources. The final section advances recommendations for future policies.

This paper is part of a body of work under the title "Case Studies: developing innovative capacity in developing countries to meet their health needs", commissioned by the Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH) of the World Health Organization. The other participants are China, India and South Africa.

[45] Please note: this work does not necessarily reflect the opinion of the Brazilian government.

I. Brazilian Healthcare: General Overview

1.1 Human Health in Brazil: Main Aspects

Brazil has a population of approximately 183 million, predominantly still young. Due to economic modernization and increasing urbanization, fertility rates have dropped progressively. Its population has a rather complex composition resulting from intense miscegenation (indigenous population, African, European and Asian immigration, amongst others).

Brazil's nominal GDP is currently around US$500 billion. The present economic situation is the result of changes occurring mainly during the 1980s and 1990s. The 1980s were marked by major economic crisis and by the exhaustion of Brazil's "import substitution" model (a government policy that stimulated the local production of many manufactured goods, intended to avoid the entry of imported goods). The 1990s were prodigious in reforms (free market, deregulation, privatization) aiming to attract foreign investment. Brazil participated actively in the creation process of the WTO, adhered to the main international trade agreements (TRIPS Agreement, amongst others) and implemented a profound revision of its legal structure in the field of intellectual property rights. The persistent inflationary process was halted by the "Plano Real" – a monetary stabilization plan set up in 1994.

In the mid 1980s, Brazil initiated structural reforms in the field of health. The re-democratization of the country and the creation of SUS altered the health organizational structure. The constitutional right of universal access (both public and free) to healthcare began to be implemented through decentralized actions, either at state or municipal levels, through technical and financial cooperation with the federal government[46]. The activities of the federal government are based on annual plans that guide all the decisions made in the field of human health. Various regulatory and financial changes occurred providing many benefits and also challenges.

On the other hand, the state reforms, which occurred mainly in the 1990s, put great emphasis on devising public policies and the creation of regulatory agencies, notably ANVISA and the ANSS in the field of health. Both agencies are answerable to the Ministry of Health.

The National Health Surveillance Agency (ANVISA) has the purpose of safeguarding the health of the population by exercising control over the production and marketing of products and services subject to sanitary surveillance. Amongst its legal attributes is the right of "prior approval" for the grant of patents for pharmaceutical products and processes.

[46] Law n. 8,080 of September 19, 1990; Law n. 8,142 of December 28, 1990.

The National Agency for Supplementary Health (ANS) handles the regulation of the private healthcare sector, protecting the public interest in supplementary healthcare assistance, and regulating the sector operators, which also includes their relationship with professionals and consumers.

Developing countries such as Brazil have unique characteristics: a very attractive market for health products, a reasonably well-developed productive capacity, a well-structured research capacity, a still immature innovative capacity, low integration between scientific and industrial policies together with a lack of innovation in health policies, and limited negotiation capacity (especially in the public administration sector in negotiations involving technology transfers and intellectual property rights). There has been an increase in the introduction of new (mainly imported) technologies in health support (such as diagnostic methods, latest generation research equipment, etc.), however it still remains insufficient. Furthermore, it is fraught with serious geographical distribution inequities (with the more favoured regions of the country having easier access). Another important aspect concerns the diseases prevalent in Brazil. Apart from the various diseases typical to high poverty situations (malaria, schistosomiasis, Chagas' disease, etc.), there are emergent and resurgent diseases (HIV/AIDS, tuberculosis, etc.) of major importance to the health surveillance systems, as well as the diseases typical of developed countries (coronary disease, etc.).

The impact of the structural health reforms is apparent, for example, in the data for access by the population to basic sanitation services. The proportion of the population served by public collection of solid residues increased from 60% (1991) to 76% (2000), the proportion served by the public water supply went up from 52% (1980) to 76% (2000), with public sewerage expanding from 25% (1980) to 44% (2000). Despite significant advances, the goal of total availability has not yet been attained. A large amount of sewage is not treated and the destruction or disposal of solid residues is inadequate (Ministry of Health, 2004).

Between 1980 and 2001, the overall mortality rate for all diseases showed a decline of 11.1%, from 6.3% to 5.6% per 1,000. The improvements in the mortality rates are attributed to: the increase of basic sanitation services, especially the increase in the number of homes receiving water supply; higher investments in health research; an improvement of the health and basic care services offered; the implementation of programmes directed to women and child health (antepartum assistance, childbirth, breastfeeding, oral re-hydration therapy, amongst others); increase in vaccine coverage; increase in pharmaceutical assistance (including medicines having high costs and requiring prolonged use); and a drop in fecundity.

Despite being able to note a significant improvement in the epidemiological profile relating to infectious diseases in Brazil, its incidence still constitutes a serious public

health problem. While AIDS has now become the most notable communicable disease in Brazil, various illnesses cause enormous losses to the population. Due to precarious social, sanitary and environmental conditions, old diseases return with other characteristics and new diseases spread at a fast rate. The Ministry of Health classifies the situation of communicable diseases in Brazil in three broad tendencies: (i) communicable diseases having tendency to decline; (ii) communicable diseases having tendency to persist; and (iii) emergent or resurgent communicable diseases. The offensive on these diseases varies between control and eradication whenever possible. The intensification of vaccine coverage is intended in the cases of immunoprophylactic preventable diseases (for example diphtheria, German measles, whooping cough, and tetanus). Others, such as typhoid fever, require the improvement of sanitary conditions. Many endemic and epidemic diseases, however, require intense investigation to determine solutions (diagnostic, treatment, control, etc.) to combat each disease effectively[47].

1.2 Capability in Medicines

The Brazilian pharmaceutical market has an oligopolistic structure similar to the structures found in developed countries. Having suffered different forms of intervention in the course of its development after the Second World War, it is presently characterized by a lack of support for research and development activities in a continuous and intensive manner. The Brazilian pharmaceutical structure emphasizes productive learning, with incremental innovations.

In the 1980s there was a clear intention on behalf of the government to augment the production of pharmochemical products. The Edict n. 4 of 1984, jointly issued by the Ministry of Health and the Ministry of Industry and Commerce, was protectionist in character, with a major increase in import tariffs. In harmony with the patent policy[48], there was an incentive to produce substitutes for imports in the field of pharmaceutical raw materials, since the law then in force[49] stimulated the copy of existing molecules. In 1987, around 420 products were manufactured by more than 90 companies, corresponding to a production value of US$521 million and occupying something between 60% and 70% of the market. There was a real accumulation of productive and technological capability (directed at an improvement of the productive processes). On the other hand, the capability for discovering new drugs was incipient. Local companies were too fragile for high-cost and high-risk activities. For the multinational corporations, Brazil was not an attractive market for establishing R&D

[47] The technological solution ought to be accompanied by policies for urbanization, environment, migration process control, and the control of major infrastructure construction liable to modify ecosystems.

[48] Pharmaceutical products and processes were not eligible for protection.

[49] Industrial Property Code n. 5.772/71.

centres. Quite frequently, they forwarded the argument that the "loophole" (non-protection of pharmaceutical products and processes) in the patent protection legislation was one of the main hindrances to research activities. The few initiatives occurred in the field of adaptations, for example galenic research (Queiroz & Gonzalez, 2001).

In the 1990s, with policies for economic freedom, the former 1980s model was interpreted as being a barrier to international commercial relations. In 1996 new Brazilian legislation contemplated pharmaceuticals as patentable subject matter[50]. The process of economic freedom also brought an end to price control and an increase in medicine sales[51]. The import tariffs for inputs and medicines were reduced. Thus, the turnover of the pharmaceutical sector went from US$3.6 billion in 1992 to US$10 billion in 1998. At the end of the decade a declining trend in unit sales was observed (Frenkel, 2001; Queiroz & Gonzalez, 2001; Gadelha, 2002). One of the effects of opening up the economy was the increase in imports and the generation of commercial deficits. The sector became heavily dependant on imports: the import of pharmaceutical products (the majority then without patent protection) rose from US$170 million in 1981, to approximately US$2 billion in 2002. Countries such as China and India significantly increased their participation in the Brazilian market through the sale of pharmochemicals, from 0.2% in 1990 to 9.2% in 1997.

The local production of pharmochemicals did not disappear but certainly diminished during the 1990s, falling to about only 20% of the market. The activities of the multinational corporations were heavily concentrated on the completion of the products[52] and their commercialization. The large scale of imports brought about problems beyond the balance of payments.

The PNM instituted in 1998, and which is part of the National Health Policy, defined the guidelines and priorities of the Ministry of Health for the sector. The adoption and permanent update of RENAME[53], together with the decentralization of distribution through a redefinition of the roles of the federal, state, and municipal management systems, are the main measures implemented by the Ministry of Health in the field of pharmaceutical assistance. Generic medicines, advancement of quality, safety and efficiency, promotion of R&D, and development of human resources are also subject to attention by the National Medicines Policy.

Brazil stands out on the world medicine market. Today, according to data from Intercontinental Medical Statistics, Brazil possesses 551 companies in the pharmaceutical area (laboratories, distributors and exporters) and holds 11th place in

[50] Industrial Property Law n. 9.279/96

[51] Accompanied by a successful monetary stabilization plan.

[52] Formulation, filling/finishing and packaging. A large part of the active principles and synthesis intermediates were imported from country of origin.

[53] List of medicines that the Unified Health System (SUS) follows in its purchases.

the ranking of the pharmaceutical world market. However, amongst the 12 biggest companies of the pharmaceutical industry, which combined represent around 45% of the Brazilian market, there is only one company, Aché, built with local capital. Between 70% and 80% of sales on the internal market are credited to multinational corporations (around 20 companies).

Law n. 9.787 was passed in 1999 and established a policy for the adoption of generic medicines in Brazil[54]. This law defines the characteristics of a generic medicine and conditions for safety, efficiency and quality[55], as well as the norms for their approval and commercialization in Brazil. Government acquisition of medicines began to give priority to the purchase of generics. The basic purpose of this policy is to guarantee access to medicines and promote a reduction in prices, chiefly for medicines required for chronic diseases. In 2000 the first six generic medicines were registered; by 2004 there had been 1,033 registrations.

According to Progenericos, in Brazil generic medicines are available in 3,580 dosages, 56 therapeutic categories, 249 active principles, and 944 registries. They account for more than 60% of all prescribed medicines, and cover the pathologies most frequently afflicting the Brazilian population and a large majority of the chronic diseases. Generic medicines represent 8.37% of unit sales in the overall pharmaceutical market. The generic medicine industry has invested close to US$1 billion in the construction and modernization of industrial plants in Brazil, providing direct employment for more than 10,000 people. During this period, 35 new laboratories for bioequivalency assays were built. Today, the top four manufacturers are established from local capital. Approximately 80% of the generic units commercialized in Brazil are produced locally. By source of capital, 74.6% of sales in the Brazilian generic market are made by local companies. Indian capital is the second most represented, with 10.3% participation, followed by companies of German (4.7%), Swiss (4.6%), US (3.8%), and Canadian (2%) origin.

The Brazilian pharmaceutical market also includes a network of public laboratories (at federal, state and municipal levels) united by ALFOB. With a production capacity estimated at 11 billion pharmaceutical units per year, the 18 laboratories supply around 10% of the purchases made by the Ministry of Health. They are important players in the government's health policy, both as public medicine providers and price regulators. Farmanguinhos[56] alone increased its turnover from US$5 million to US$50 million during the 1990s. The build-up of official productive capability (frequently in partnership with the private sector) provided the necessary support for the Brazilian antiretroviral access policy (Gadelha, 2002).

[54] Initially, there was severe criticism of this policy on the part of the multinational laboratories.

[55] The technical criteria for registering these medicines are similar to those adopted in countries such as Canada and the US.

[56] The laboratory of the Oswaldo Cruz Foundation, Ministry of Health.

The R&D activity of the Brazilian pharmaceutical industry reinforces the profound dependence of the country in this field of knowledge. Neither the multinational corporations nor local ones undertake any significant efforts, with the average R&D expenditure in 1998 being in the order of 0.59% of turnover, of which more than 70% is for development, 24% for applied research, and a mere 3.4% for basic research (Hasenclever et al., 2000).

It is interesting to note the increase of clinical research in Brazil towards the end of the 1990s. GlaxoSmithKline dedicates around US$2 million annually to this purpose (15 studies in 60 centres, involving 1,200 patients). Novartis invests approximately US$3 million per annum. These figures are not to be treated lightly considering Brazil's history for learning in the pharmaceutical area (Queiroz & Gonzalez, 2001).

An as-yet poorly exploited field is that of research in biodiversity with the purpose of detecting new molecules. There are many university projects with this aim, but few projects for the development of phytopharmaceuticals with any corporate backing, and patents requested from projects of this type are rare. One of the few examples is the US$3.2 million agreement reached in 1999 between GlaxoSmithKline and Extracta[57], a company founded in 1998 at the Fundação Pólo Bio-Rio (Bio-Rio Pool Foundation), which is the biotechnology business incubator under the auspices of the Federal University of Rio de Janeiro. In view of Brazil's vast biodiversity, the experience of the scientists (around 70 research and chemistry groups for natural product pharmacology), and the moderate costs of the research activities, this may well be a niche interest to local companies (Queiroz & Gonzalez, 2001).

In March 2004, the Brazilian government initiated the PITCE. The pharmaceuticals and medicines sector was selected as being one of the four strategic areas for the policy. The main aims are: to increase the national production of vaccines and medicines considered as priorities by the National Health Policy (with emphasis on generic medicines and those intended for the treatment of Sexually Transmitted Diseases, including AIDS); increase access by the population to medicines; and avoid the continued increase in the trade deficit. Investments will be applied to modernize public laboratories and the purchasing power of the state will be harnessed.

One form of funding for the sector will be Profarma, backed by the BNDES[58]. This programme will have three main courses of action: investment in production; investment in R&D; and the consolidation of locally-controlled companies. A specific management, Chemical Engineers for Health, was formed to implement the Profarma.

[57] Extracta Moléculas Naturais S.A. was the first company to obtain a licence to undertake the collection of genetic material from the Brazilian biodiversity for commercial ends, granted by the CGEN.

[58] The concept was created at a seminar to define what would be the part played by the Development Bank in the health sector, in March 2003.

1.3 Capability in Vaccines

Moacyr Scliar[59] refers to the campaign for the eradication of smallpox instigated by Oswaldo Cruz[60] at the beginning of the 20th century as the first mass vaccination campaign in Brazil.

The production of vaccines dates back to the beginning of the 20th century, starting with the founding of the Butantan Institute and the Instituto Soroterápico Federal (now Oswaldo Cruz Foundation). Since 1973, the government has implemented vaccination strategies (chiefly through national vaccination days) that reach all Brazilian municipalities. Up until the end of the 1970s vaccines were supplied by the private sector or through imports. With the closure of Sintex do Brasil in the 1980s, the Ministry of Health decided to strengthen this area through a programme that would stimulate local capability, since not all could be imported[61]. Currently, the production of vaccines in Brazil is concentrated in the public domain. Since 1986, more than US$150 million has been invested in the modernization of the installations and equipment of public laboratories producing serums and vaccines, enabled by the National Programme for Self-Sufficiency in Immunobiologicals (PASNI) of the Ministry of Health. PASNI was created in 1985 with the specific purpose of strengthening the industry and establishing a policy of national production.

Brazil is one of the biggest markets in the world for vaccines and relies on a far-reaching immunization programme. Brazil has attained self-sufficiency in the production of antiophidic serums, antivenins, antitoxics for therapeutic use, and eight vaccines: BCG; poliomyelitis, recombinant-hepatitis B; diphtheria; tetanus; whooping cough (DTP); yellow fever; *Haemophilus influenzae* type b (Hib), dispensed jointly with DTP; and influenza for the elderly (Homma et al, 2003). Two local manufacturers, Biomanguinhos/Fiocruz and Instituto Butantan, concentrate 89% of all sales to the Ministry of Health. The other manufacturers are Tecpar and the Fundação Ataulpho de Paiva. Sanitation control in the field of vaccines is the responsibility of the ANVISA.

A more recent approach emphasizes the formation of strategic alliances for the production of vaccines in Brazil. This is the case of the tetravalent DTP+Hib vaccine, whereby the DTP is produced by the Instituto Butantan and is dispensed jointly with the Hib vaccine from the BioManguinhos (Unidade de Produção de Imunobiológicos da Fiocruz)(Immunobiological Production Unit of Fiocruz)[62].

[59] Famous Brazilian doctor and writer.

[60] Brazilian scientist (1872 - 1917).

[61] Certain antiophidic serums, for example, due to the specificity of the venoms.

[62] Biomanguinhos is also starting to invest in the development and production of biopharmaceuticals.

The vaccine against the bacillus Haemophilus influenzae type b (Hib) was obtained through cooperation between BioManguinhos/Fiocruz and GlaxoSmithKline. With the national production of this formally imported vaccine, 100% of the Ministry of Health requirements for the basic vaccination calendar will be met, representing direct savings of US$3.7 million per annum for Brazil. The import of vaccines rose from the level of US$70 million (1997/1998) to US$125 million (1999/2001) (Gadelha, 2002).

Investments in technological research and development are on a small scale. There are, however, research initiatives in universities and research institutes such as the Oswaldo Cruz Foundation (Fiocruz).

There is an urgent need for investment in innovation for the development of vaccines in Brazil. The technological content in the new vaccines is very high; the dependency of Brazil with respect to foreign suppliers is also increasing. There are other elements to consider: state purchasing power, the negotiation of patent rights, and the negotiation of technology transfers.

Nationwide vaccinal coverage, beyond the basic vaccines, includes a vaccine for hepatitis B, a vaccine against Haemophilus influenza type B, a tetravalent vaccine (DTP+Hib), triple viral vaccine (measles, mumps and rubella) administered at 12 months, and the vaccine for the elderly against flu, tetanus and pneumococcal pneumonia. In 2001 and 2002, women of fertile age were the targets of a campaign to control congenital rubella, which reached 95.68% coverage of this target group. This same population group received vaccination against tetanus, with the aim of eliminating neonatal tetanus. In 1999 the vaccination against flu for the elderly attained 87.3% vaccinal coverage, making it one of the largest in the world, reaching 7.5 million people over 65 years of age. As of 2000 the age range was lowered to 60 years, providing vaccines to 1.8 million more people than the year before and reaching a total of 9.3 million. In 2001 the vaccination coverage increased to 10.8 million people over 60 years of age. The rise continued through 2002 with 11 million vaccinations and totalled 12.3 million in 2003. Due to these results, the National Immunization Programme has become a reference for other countries including East Timor, Palestine (Cisjordan and the Gaza Strip), Surinam, Angola, Senegal and Algeria (data from the Ministry of Health, Bureau of Health Surveillance, 2004).

From 1995 to 2003, the Ministry of Health made available around 2.4 billion doses of vaccine, rising from 214 million doses in 1995 to 295.4 million doses in 2003, which represents a growth of 38%. The investment in the purchase of immunobiologicals also rose, from US$19 million in 1995 to US$147 million in 2003, with a budget

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So as to render this new activity viable, a technology transfer agreement was signed between Brazil and Cuba in August 2004, enabling the production of recombinant human alpha 2b Interferon and recombinant human alpha Erythropoietin.

increase of US$127 million for the programme. Imports jumped from US$70 million (1997/1998) to US$125 million (1999/2001). Exports only became significant in 2001 (Gadelha, 2003). In 2003, local laboratories produced 71% of the total immunobiologicals employed in Brazil.

Amongst the challenges for the National Immunisation Programme is an attempt to attain homogeneity in vaccinal coverage to all municipalities across Brazil, to create incentives to discover new drugs, to ensure the non-resurgence of already eradicated diseases, and to consolidate the elimination of measles. In negotiating access to future technology, the challenge is in the capability to link the use of state purchasing power with the already accumulated capability and any eventual associated intellectual property rights.

1.4 Capability in Health Biotechnology

The competency accumulated in Brazil in the field of health biotechnology dates back to the beginning of the 20th century with the creation of institutions such as the Oswaldo Cruz Foundation and the Butantan Institute.

Brazilian health biotechnology began to receive greater investment in the 1970s. The CNPq – the government agency for incentivizing research –identified serious faults in the academic state of the basic biological sciences. There were few productive groups, little multidisciplinary training, few doctors managing research projects, and low levels of scientific interchange, either national or international. Other analyses also noted the increasing global importance of genetic engineering. There were obstacles in developing this area at a business level, with little interest on the part of the companies to internalise the R&D, as well as at the academic level, with few researchers dedicated to the biochemical field. The response to these structural problems included the creation of Integrated Biotechnology Centres and technological pools and parks.

After the 1990s, the promotion of biotechnologies consolidated, creating numerous opportunities for funding in all agencies at federal[63], state and municipal levels. The funds were in the form of regular payments or for special projects geared towards specific themes. Brazilian research in biotechnology has made great advances in important areas such as genomics, proteomics, bioinformatics, nanobiotechnology, and stem cells.

Certain institutions developed a broad capacity to manipulate the various disciplines related to biotechnology in health. This is the case of Fiocruz, the Butantan Institute, the Ludwig Institute for Cancer Research, and various university departments. Fiocruz is a prolific knowledge generator in the biomedical area. In 2003, the IOC – one of the Fiocruz technical units with 218 researchers – published 351 papers in peer-reviewed indexed journals.

In the area of business, one of the most prominent examples is the Biobras biopharmaceutical company. In the 1990s this company was one of four in the world to develop recombinant human insulin and managed to patent its invention in the US. At the end of 2001 the company was acquired by Nova Nordisk for US$31 million. Another example is FK Biotecnologia, a successful start-up biotech company. Its main area of interest is the commercialization of immunodiagnostic kits. In the field of technological pools, the best examples are BioRio, in Rio de Janeiro, and Biominas, in Belo Horizonte.

1.5 Research and Innovation in Health

[63] Finep, CNPq, CAPES, etc.

The country's National System for Innovation in Health is composed of a complex network that includes universities, research institutes, pharmaceutical companies, medical-hospital equipment manufacturers and suppliers, government agencies and controlling bodies, and hospitals. It possesses similarities but also peculiarities compared with the equivalent systems found in developed and developing countries. A scientific infrastructure turned to biomedical research with relatively regular government investment is, quite possibly, the more privileged aspect of the Brazilian system. Barriers hindering the full potential of the system have previously been identified as large deficiencies in the education system, with low school attendance rates and a high rate of illiteracy, and little involvement on the part of the corporations (both multinational and local) in activities for innovation in health (Gadelha, 2003a; Cassiolato & Albuquerque, 2000). The convergence of scientific, innovation and business strategies around a policy for science, technology and production in health remains a field to be better exploited.

One of the challenges for government policy is encouraging the incorporation of researchers into the business environment. Data from Capes and the IBGE attest that in 2000, private companies in Brazil employed 4,000 employees with a Master's degree or Doctorate[64]. Universities and research institutes, state-owned laboratories and Non-Government Organizations (NGOs) employed 42,000 researchers.

Advances in the fields of information technology, new materials, nanotechnologies and other areas cause the frontiers of health research to expand rapidly, which makes closing the existing gap in the scientific and innovative capability between Brazil and developed countries more difficult and costly each year, with severe consequences for the country's population.

In 2007 the CDTS will be established at Fiocruz on a 9,000 square metre site. The Centre will offer Brazilian scientists the possibility of transforming promising results from basic research with vaccines, medicines and diagnostic kits into products for the country’s health sector. It will allow Fiocruz to enter actively in the areas of genomics, proteomics, transgenesis and genic therapy.

The promotion of health research in Brazil is further reinforced by the diversified ecosystems encountered across the country. Various institutions invest in the structuring of biological collections (Embrapa, Fiocruz, Rio de Janeiro Botanical Gardens, Unicamp, USP, etc.).

The policies and activities instigating science and technology in health have been increasingly debated under the sponsorship of the Ministry of Health. The national research and development policy for health is coordinated by the Bureau of Science, Technology and Strategic Inputs, under the auspices of the Ministry of Health in

[64] For all fields of knowledge.

accordance with its responsibilities under Law n. 9,636/98, modified by the Provisional Measure n. 2,143/2001. The National Conference for Science and Technology in Health, held in 1994 and 2994, were of special relevance for the construction of the National Policy for Science, Technology and Innovation in Health. Other initiatives contributing to this area include the award of the Prize for Incentive in Science and Technology for the SUS (2002, 2003, 2004); and the National Agenda for Priorities for Technological Research and Development in Health (2004).

The most relevant indicators of the evolution of health research in Brazil at the moment are the volume of publications. Medical research produced 7,365 articles from 1997-2001 (0.9% in this area worldwide), which ranks 23rd in the world and third internally, representing 16.9% of the total articles indexed for the country on the basis of the ISI Standard. The biomedical area showed slightly higher output than the medical area, with 8,366 articles for this period (0.9% in this area worldwide),securing Brazil 21st place in the world ranking and second place internally, representing 19.0% of all the country's articles indexed on the basis of the ISI Deluxe (Guimaraes, 2003).

However, Brazilian participation in world patent grants remains very low (0.2%) and reinforces the necessity of developing specific incentive programmes for technological research. In Brazil, the assessment of projects undertaken by agencies still judges researchers chiefly by their results in terms of publications. The matter of Intellectual Property is beginning to be incorporated in the analyses of researcher productivity, but this is not yet an established routine in the academic community.

The data from the Directory for Research Groups of the CNPq indicates that the groups that undertake health research produce a considerable amount of work with predominantly bibliographic-academic characteristics. For every 10 works published only one represents research of a technical nature that results in some kind of protection with the purpose of eventually obtaining intellectual property rights. Not all institutions have the adequate support for providing protection to intellectual property or for the identification of patentable subject matter.

II. Trade Issues Influencing Access to Health Services Technologies

2.1 Brazil, TRIPS and Public Health

In Brazil, the agreements of the Uruguay Round that included the TRIPS Agreement and the creation of the World Trade Organization came into force on the January 1, 1995, subsequent to Presidential Decree n. 1,355, of December 30, 1994[65]. Brazil thus recognized again the importance of a multilateral system under constant improvement. In a polemic move, it also relinquished the non-requirement of the immediate application of the provisions in Article 65 of TRIPS.

The Law n. 9,279 of May 14, 1996, considered pharmaceutical products and processes as privileged. Furthermore, a "pipeline" mechanism[66] was established for the retroactive protection of inventions in Brazil. A patent application covering pharmaceutical products and processes could be filed by a national or by a person domiciled in the country, to whom was assured the publication date, provided that its object at the time of pipeline entry was not introduced in any market by the direct initiative of its owner or by a consented third-party, neither had been carried out serious and effective arrangements towards the exploitation in Brazil of the object of the application by third parties. According to the interpretation of various jurists, the principle of novelty was thus violated. This aspect of the legislation was later altered with the publication of the Provisional Measure n. 2,014 of December 30, 2000, which became the Law n. 10,196 of February 14, 2001.

The Provisional Measure n. 2,014, and then the Law n. 10,196, amongst other measures, initiated the requirement of "prior approval" for Brazilian patents. Patent applications that involve pharmaceutical products and processes have to undergo prior analysis by the ANVISA. This is actually a complementary analysis system that examines patent eligibility of the INPI. The "prior approval" in the scope of the ANVISA does not infringe any of the provisions in TRIPS and is totally compatible with Brazilian legislation, bringing constant legal improvements towards advancing the welfare of the population. The ANVISA provides technical support to the INPI in the task of verifying if the pharmaceutical product or process complies with the requirements laid out in the TRIPS Agreement and found in Brazilian law - novelty, inventive activity, and industrial application.

The debate over intellectual property goes far beyond the sphere of WIPO. Since the

[65] The process for the approval of the TRIPS measures underwent heavy criticism from various sectors of Brazilian society. The main argument was that the TRIPS Agreement established levels of protection far more compatible with the standards of technological build-up found in developed countries and not favouring developing nations.

[66] In spite of the fact that the Law n. 9,279 was in force only as of May 15, 1997, two articles, 230 and 231, had been put into force by the time of its publication on May 15, 1996, being applicable up to May 15, 1997.

instruments of intellectual property have received great relevance in trade relations, organizations such as WTO began to play key roles in the international strategies related to intellectual property rights. Other organizations such as WHO were also called upon to participate, due to occurrences such as the AIDS epidemic and the pressure applied by developing countries. The participation of Brazil in the negotiations of the international agreements and in the dialogue with these organizations is quite active, with a strong leadership among developing countries. This capacity stems from its long experience with intellectual property rights. It is worth remembering that Brazil passed its first patent law in 1830 and was one of the first signatory members of the Paris Convention for the Protection of Industrial Property.

The evolution of the TRIPS Agreement culminated in the approval process of the Declaration on the TRIPS Agreement and Public Health[67] in Doha, which allowed certain flexibility. The concern of having a TRIPS Agreement that could be interpreted in a more flexible manner arose because of certain conflicts of interest and divergent interpretations of some of its provisions. The call for the use of flexibility with the Agreement was in the name of the general welfare of humanity.

Due to the pressure exerted by developing countries, with strong leadership from Brazil, the Declaration included the importance of the implementation and interpretation of the TRIPS Agreement in consonance with the public health interests of each country concerning access to new medicines. The Council for TRIPS was convinced that the TRIPS Agreement cannot impede the members of the Agreement from taking the necessary measures to have access to medicines. Amongst the measures, the mechanism for compulsory licences for patents may contribute to reduce the costs of treatment for serious endemic diseases (such as AIDS, malaria or tuberculosis).

Brazil has evolved with its active role in the development of intellectual property rights and the relationship between intellectual property and public health. In August 2004, Brazil and Argentina forwarded the “Proposal by Argentina and Brazil for the Establishment of a Development Agenda for WIPO”. The proposal merited the immediate incorporation of a development agenda within the sphere of WIPO. It also highlighted the fact that certain standards of protection currently under debate (Substantive Patent Law Treaty, for example) involve a superior standard than that which can be supported by less-developed countries. It reminds of the still-costly adaptation process to the TRIPS provisions. Amongst other topics to be considered are effective transfer of technology to developing countries, and the preservation of public interest flexibilities and policies in member countries. The Proposal received the support of countries such as Cuba, Bolivia, Iran, Venezuela, Egypt and South Africa.

[67] Adopted on November 14, 2001.

2.2 The New Law for Industrial Property and Pharmaceutical Patents

After much heated debate, the revision of the Industrial Property Code (Law n. 5,772, of December 21, 1971) ended in 1996 with the promulgation of the Industrial Property Law (Law n. 9,279, of May 14, 1996). The main discussions were around the question of the protection of pharmaceutical patents and the conflicts between Brazil and the US. The new Brazilian law completely fulfilled the TRIPS Agreement, and indeed went beyond - it did not consider the grandfather clause offered by TRIPS and established the "pipeline" mechanism, as outlined above.

In the pharmaceutical field, the main change was the elimination of the restrictions present in Article 9 of Law n. 5,772, which did not deem pharmaceutical products and processes as privileged. The old provision allowed for the development of a pharmaceutical industry in Brazil, which remained in full swing until the early 1990s. With free trade, and later with the new industrial property law, the imports of the active principles and intermediates were given priority. The Law n. 9,279 also included another national legal innovation: transgenic micro-organisms became patentable subject matter.

The effect of the law in the pharmaceutical area was a general increase in the filing of patent applications at the INPI[68], especially from foreign applicants. A study undertaken using the INPI database demonstrated this growth (Oliveira et al, 2004). Table I below shows the number of patent applications filed in Brazil relating to pharmaceuticals by country of origin for the period August 1992 to December 1995, and January 1996 to December 2002. The participation of Brazilian applicants in the patent filing process is very small, demonstrating a condition of technological frailty. The chief reason resides in the country's limited technological capability. This number could be slightly higher (although not much above the present figure) if there was more attempt to protect inventions on the part of the universities and research institutes. However, due to the extremely low corporate efforts in R&D there is no expectation of significant growth in these numbers.

[68] The official Institution with the incumbency of granting patents in Brazil.

Table I. Pharmaceutical Patent Applications in Brazil by Country of Origin

Country	August 1992 to December 1995	January 1996 to December 2002
United States	40	2,854
Germany	24	854
France	14	627
Great Britain	10	535
Switzerland	37	384
Japan	14	352
Sweden	2	283
Brazil	0	221
Italy	4	136
Belgium	0	158
Netherlands	2	132
Denmark	0	127
Canada	2	127
Spain	0	69
Australia	2	45
Hungary	3	24
Monaco	3	4

Source: Oliveira et al (2004)

The data relating to technology transfer contracts in the pharmaceutical area is shown in Table II. It refers to the period from 1992 to 2001. In compliance with Law n. 9.279, the INPI must register all contracts that involve the transfer of technology, franchise agreements and the like that effect third parties. Total contracts registered dropped progressively over the course of the given period. Contracts involving technology supply or cost-sharing R&D are almost irrelevant. The effective transfer of technology has been a real difficulty for Brazil.

Table 2: Technology Transfer Contracts in the Pharmaceutical Industry Brazil, 1992-2001

Year	License for Brand Name Use	Franchising	Technology Supply	Patent Exploitation	Research and Development	Technical Assistance Services	Other	Total
1992	104	-	-	-	-	2	4	110
1993	90	-	-	1	-	7	-	98
1994	66	-	4	-	-	8	1	79
1995	50	-	-	1	-	8	3	62
1996	49	-	3	1	2	11	1	67
1997	39	-	1	-	3	9	-	52
1998	14	3	5	-	-	11	-	33
1999	34	3	7	2	-	10	-	56
2000	22	2	6	1	-	15	-	46
2001	16	-	2	2	-	14	-	34

Source: Oliveira et al (2004)

The very poor operational conditions and the lack of qualified personnel at the INPI also contribute to the limited use of the industrial property system in Brazil. The Institute is currently undergoing a process for restructuring the organization, which has demonstrated great difficulty in analysing and granting patents in any reasonable time.

2.3 Safeguards

The Law n. 9,279 regulates the practice of compulsory licences, which can be invoked in the following cases: (a) the abuse of economic power; (b) the abuse of rights; (c) the dependency of a patent on another, without agreement between the bearers; (d) national emergencies; and (e) public interest. The provisions of Law n. 9,279 require the grant of compulsory licences to be restricted to "persons with a legitimate interest and having the technical and economic capacity to efficiently exploit the object of the patent".

Decree n. 3,201 of October 6, 1999, regulates the conditions of the compulsory licence in the cases of national emergency and public interest, foreseeing local production or import. Certain aspects of the Decree n. 3,201 were altered under the Decree n. 4,830 of September 4, 2003.

Compulsory licences are much more an exception rather than a rule, demanding an evaluation and prior negotiation. The evaluation assesses the costs, the benefits and the impacts of the decision, which may be far from trivial depending on the motives for which the licence was requested. The negotiation seeks to obtain, for example,

significant cost reductions of the active principles in special situations as an alternative to the grant of a compulsory licence. However, should negotiations come to nothing, the safeguards remain. Practice has shown that the option for a compulsory licence is only justified after complete exhaustion of all possibilities of agreements through voluntary licences.

There is no doubt that the Brazilian antiretroviral access policy constitutes a special situation. The sustainability of this policy guides government actions, and all pertinent strategies are built around it.

Brazilian law does not permit "parallel imports", which is the practice that allows a country to purchase a drug from another importer country that has obtained lower prices from the manufacturer. A draft law is in the Chamber of Deputies that intends to authorize this mechanism in Brazil (PL 139 of March 2, 1999).

2.4 Price Control

In Brazil, as in various countries, price regulatory mechanisms are favoured in complex environments, such as the pharmaceutical field, that involve the conciliation of private interests and social necessities. In recent Brazilian economic history, the government has exercised some degree of intervention to limit and/or restrain practices that were not in accordance with what could be considered reasonable, in view of the standards of national technological build-up in the health area, the income levels of the population, and the channels for pharmaceutical assistance, amongst other factors.

Up to the end of the 1980s, the economic context favoured mechanisms of intense protectionism for local industry and the direct control of prices[69]. In the early 1990s, together with the free economy, came a reorganization of the level of government intervention and business conduct. Instruments favouring consumer rights and for restricting the abuse of market power, including prevention, began to progressively appear (Romano & Bernardo, 2001).

In 1991, a schedule for the deregulation of products was drafted and divided in three pharmaceutical classes: (i) free sale, (ii) medical prescription, and (iii) chronic diseases. The first classes to be released were those with greater number of products and companies. After the progressive deregulation of prices[70], only products for chronic diseases were subjected to price control (ibid).

The direct control of prices ended in 1992. Edict n. 13 of February 27, 1992, initiates

[69] Through the CIP, instituted by Decree n. 63.196 of August 29, 1968. Only homeopathic, phytotherapic and officinal medicines were not submitted to any control.
[70] Authorised by Edicts n. 940 of October 8, 1991; n. 275 of November 7, 1991; n. 309 of November 26, 1991, and n. 363 of December 20, 1991.

the process for deregulation of prices for medicines for chronic diseases, and in May 1992 the process was concluded. Up until 1994 prices remained unregulated.

With the implementation of the "Plano Real", which brought monetary stability in 1994, the government began to negotiate price readjustments every six months with the companies on a reasonable basis. Cases of possible abuse led to investigation under the Law of Competition (Law n. 8,884, 1994)[71]. This method of semi control remained in force until 1996, when the prices were again deregulated. It is worth remembering that between 1994 and 1997 the turnover of the pharmaceutical industry increased by more than 60%. The rise in the medicine sector went far beyond other products.

In 1998, due to the rather high readjustments, a new system for price surveillance was implemented. The laboratories were called upon to justify to the government the price increases in medicines requiring medical prescriptions.

In 1999, the main argument by the laboratories to justify price increases was the devaluation of the real (local currency) in relation to the dollar. As a large part of the raw material for the production of medicines is imported, a more expensive dollar was claimed to have increased production costs which ended up being paid by the consumer. Another aspect of the question should also be considered: Barbosa (2001)'s work alerts us to the problem of transfer pricing. The regulation of foreign trade is notoriously fragile concerning intra-firm trade between branches of the same company. The transparency of the remittances of foreign exchange credits should be a priority concern for governments. Fiscal measures may be developed to correct distortions of this nature.

Provisional Measure n. 2,063 of December 15, 2000 was published to create new control conditions. This was substituted by Provisional Measure n. 2,138-2 on December 28, 2000 which gave origin to Law n. 10,213 of March 27, 2001 which instituted the Parameter Formula for Readjustment of Medicine Prices and created the Board of Medicine, responsible for judging requests for extraordinary readjustments of medicine prices.

June 2003 saw the publication of Provisional Measure n. 123 that substituted the protocol agreement of December 31, 2002 between government representatives and the pharmaceutical industry. This Measure, still currently in force, establishes the annual readjustment of medicine prices and created the CMED. The CMED,

[71] It is worth mentioning here a problem related by Romano & Bernardo (2001) and by Mello (2001). There are divergences in relation to the question of interpretation of price abuse as an anticompetitive practice. Certain jurists defend a less interventionist position; others affirm that the abuse of market power is characterized by the increase of prices. Due to the specificity of the pharmaceutical sector, Mello proposes developing an explicit system combining characteristic antitrust elements with an evaluation of the social benefits, seeking to avoid excessive control practices and a cost increase for the economic system overall.

composed of representatives from the Ministries of Health, Justice, Finance and Chief of Staff's Office, has amongst its main incumbencies the regulation of the market and the establishment of criteria for defining and adjusting prices, including for any new medicine dosages. According to the new rules, the adjustment of prices can only occur every 12 months. The readjustments are limited to a maximum price that can be defined taking into consideration the IPCA, calculated by the IBGE; a productivity factor; and an adjustment factor for the relative prices both intra-sector and inter-sectors, all expressed in percentages. The Ministry of Health chairs the CMED, which was formerly the prerogative of the Ministry of Justice, and the ANVISA assumes the role of Executive-Secretary.

Another move, which may be considered complementary to the process for the regulation of prices, is the approval of the Law of Generic Medicines (Law n. 9,787, 1999), which places low-cost medicines on the market thus making them accessible to a larger segment of the population. The strategy for the adoption of generics is still in the expansion phase.

The regulatory strategy can then be achieved by means of a direct limitation of prices, central purchasing, flexible negotiation mechanisms between the government and medicine manufacturers, the construction of the local productive and technological capability, and the offer of generic medicines. Furthermore, the Lei de Defesa da Concorrência (Competition Protection Law) establishes, in Article 21, that the conditions to evaluate price abuse are the imposition of excessive prices or their unjustified increase. However, interpretation of this point in the sphere of the CADE has been no easy task.

2.5 Intellectual Property (IP) and the Antiretroviral Access Policy

Since the end of the 1980s the Ministry of Health has supported policies for providing antiretroviral medicines and other drugs for opportunistic infections. In 1991, *Zidovudine* was already provided to seropositive patients with the support of the government, although the supply suffered certain discontinuities. The Decree n. 9,313 of November 13, 1996 assured all patients infected by HIV free access to all medication necessary to their treatment. The distribution of medicines for triplex therapy with protease inhibitors was started in December 1996.

Currently 15 antiretrovirals[72] (ARVs) are made available by the Ministry of Health, with eight of them already produced locally. Some are not protected by patents, having being commercialized before Law n. 9,279. Those having patent protection increase therapy costs considerably. There is a natural tendency for the intensive use of products having more recently entered the market, due to the resistance developed by certain patients to some compositions. Access to medicines has since become increasingly expensive.

[72] In 2005, Enfuvirtide T-20 will be included in the Brazilian AIDS drug assistance programmeme.

The strategy for maintaining the antiretroviral access policy has various dimensions: systematic follow-up of patents in force, as well as in the public domain, in this field of knowledge; negotiations with the suppliers; use of the safeguards; local production and import of generic medicines[73]; intensification of local R&D activities to try to close the technological gap; and adjustments in the legal procedures to facilitate access measures. Five companies in Brazil possess industrial and technological capability for the production of generic ARVs. The national access policy also includes the intense participation of various public laboratories, especially for the manipulation of imported active principles.

Government expenditure with this access policy has been around US$34 million in 1996, US$ 224 million in 1997, US$305 million in 1998, US$335 million in 1999, and US$332 million in 2000. In 2004, government expenditure with acquisition of ARVs has been around US$238 million[74] (80% with imports; 20% with local production). The increase in expenditure is mainly due to the increase in the number of patients under treatment, the increase in the proportion of patients having more complex therapies, and the updating of therapy recommendations.

The threat of compulsory licensing, a government recourse, forced the drop in price of three medicines in 2001 – *Indinavir*, produced by Merck, by 64.8%; *Efavirenz*, also from Merck, by 59%; and also *Nelfinavir*, from Roche, by 40%.

Apart from the direct benefits for that part of the Brazilian population infected by the HIV virus, the reduction in the mortality rate[75] and of opportunistic infections has seen the Brazilian programme serve as model for various countries. Angola, Nigeria, Venezuela, Guiana and Mozambique are in cooperation with the Brazilian government to develop production capability for antiretrovirals.

Furthermore, the Brazilian example has provoked changes in the manner of interpreting international agreements and in the attitudes of other governments. Although successful, the programme is still vulnerable. The main threat lies in the full adoption of the TRIPS provisions by countries supplying generic ARVs, such as India.

III. Regulatory Environment

Brazil has constantly attempted to update its legal system in line with world trends and adapting the concepts to the country's specific needs. In the field of regulating research and innovation in health, the following aspects should be noted: biosafety, clinical tests, sanitation surveillance, and genetic resources.

[73] Thirty-one private companies have registered generic antiretrovirals in the ANVISA system.
[74] 1.97% of the total budget of the Ministry of Health.
[75] It was 9.56% in 1996 and 6.35% in 2001.

Biosafety began to be regulated in Brazil with Law n. 8,794 of January 6, 1995. The Biosafety Law regulates all the aspects concerning the manipulation and use of GMOs in Brazil. Presently, a new biosafety draft law is in the National Congress, which includes research with stem cells.

Resolution n. 196 of 1996 deals with the regulation of clinical tests and created the CONEP, tasked with implementing the regulatory norms and guidelines for research involving human beings. CONEP acts through a network of CEPs organized within the institutions where research takes place. The institutional CEP must revise all the research protocols involving human beings and has the primary responsibility for decisions concerning the ethics of the research to be performed at the institution, in a manner so as to guarantee and protect the integrity and rights of the voluntary participants in this research.

The registration of medicines and vaccines are regulated by various edicts with their enforcement being coordinated by ANVISA.

With the publication of Provisional Measure n. 2,186-16 of August 23, 2001, the legislation concerning genetic assets was altered with respect to conservation of biological diversity, integrity of genetic assets, and associated traditional knowledge. Since this Provisional Measure n. 2,186-16 and Decree n. 3,945 of 2001, all access to and dispatch of genetic assets existing in the country depends on decisions reached by the CGEN, with the distribution of the benefits being subject to the legally established terms and conditions. Also, the exchange and diffusion of a component of a genetic asset and the associated traditional knowledge practised within indigenous and among local communities is preserved, provided it is to their benefit and based in their usual practice.

IV. Government Funding for R&D

Official data shows public and private expenditure of 1.1% of the GDP in science and technology activities for 2000[76]. The private sector spent approximately US$2.1billion; the federal public sector approximately R$2.3 billion; and the states R$0.9 billion[77]. Research incentive at federal government level occurs mainly through the Ministry of Science and Technology, with its agencies to this purpose (CNPq and FINEP); the Ministry of Health, through the Secretaria de Ciência e Tecnologia (Bureau for Science and Technology), Fiocruz, National Cancer Institute and the Evandro Chagas Institute; and the Ministry of Education, with emphasis on the formation of human resources (federal universities) and through the specific agency CAPES. It is important to point out that access to incentives occurs on a competitive basis established in accordance with international practices.

The investments in R&D in health receive encouragement from the government sector. Due to economic crisis, the regularity of the financial disbursements is sometimes compromised, affecting the management of long-term projects[78]. In accordance with the Ministry of Health, in 2001 health research in Brazil received around US$167 million in investments. It is estimated that at least 25% of the investments from the federal agencies for incentivizing research are intended for health research. The Ministry of Health participates with around 20% of the total public outlay in health research. There is a scarcity of data concerning the investments in health research from the private sector.

It is worth highlighting the creation of the Health Sector Fund in 2001[79], whose objective is technological capability in the areas of interest to the SUS (public health, drugs, biotechnology, etc.), the encouragement for the increase of private investment in related research and development, and the technological update of the Brazilian industry for medical-hospital equipment as well as the diffusion of new technologies that expand population access to health-related goods and services. The source of funds corresponds to 17.5% of the CIDE, raised through the 10% tax rate on the remittance of resources abroad for the payment of technical assistance, royalties and specialized or professional technical services, instituted by Law n. 10.168 of December 29, 2000. The budget for the Health Sector Fund in 2004 was US$5 million.

[76] For all fields of knowledge.
[77] Data from the PINTEC-IBGE Survey, 2002.
[78] A difficulty exists for obtaining precise data concerning Brazilian human health investments. A large part of the investments are provided by the government, fragmented in federal and state incentive institutions and eventually also municipal ones. The resources for research in health are concentrated in two large basic areas: biological sciences and health sciences. Some other applications may arise from the fields of engineering (biomedical engineering, for example) or economics (health economics, for example).
[79] Law n. 10.332, December 19, 2001.

At state level, there are various research institutes linked to state health bureaus and state incentive agencies. One of the more successful agencies is the FAPESP, which has been developing programmes in support of strategic research of high international and national relevance in health. Under the auspices of FAPERJ a programme in support of research in health was recently initiated.

V. Business Environment

The business incentive in biotechnology in health is still incipient in Brazil. The most prominent biotech examples in the country are concentrated in agribusiness. One of the best initiatives was the creation of the Projeto Inovar in May 2000. Coordinated by FINEP, an agency of the Ministry of Science and Technology, it has the purpose of promoting the development of small and medium Brazilian technological companies through the development of funding instruments, especially venture capital.

In the field of venture capital, one of the most promising funds is Votorantim Ventures, which administers a capital of US$300 million and favours the sectors of life sciences and information technology. The support of this fund gave rise to the company Scylla Bioinformática, the manufacturer of software that allows management, via the internet, of data for the sequencing of genomes.

The model of company incubators, linked or not to the university environment, is very widespread in Brazil. The Biominas Foundation was created in 1990 to stimulate entrepreneurship. It promotes the generation and development of new business focused towards biotechnology, fine chemistry and data processing. It helps more than 50 companies and works in partnership with the Ministry of Science and Technology and the Interamerican Development Bank, amongst others.

One action that may have great repercussion in the field of research in health is the promulgation of the Law of Innovation[80]. An increase in the partnerships between companies, universities and scientific and technological institutes is expected. The possibility of attracting university researchers to start companies dedicated to innovation is another strong point. It serves as a stimulus to the creation of technologically-based companies, capable of marketing the results of research undertaken in universities and research institutes. The participation of these researchers in the management or administration of private companies is now allowed, underlining the entrepreneurial potential of these professionals. It also allows sharing space and infrastructure of public research with private companies. The law promotes elimination of various bureaucratic hindrances, such as the requirement of a bidding process for the licensing of patents when these belong to a public agency. It also contains a series of imprecisions (see comments by Barbosa & Simões, 2004, that should be treated by later regulation or possible alterations.

[80] Law n.10.973, December 2, 2004.

VI. Human Resources

The formation of human resources in Brazil today is basically accomplished within the country. Bachelor, Master and Doctorate degrees can be achieved throughout the country. There is a government system for post-graduate support in the various fields of health, providing scholarships and support for international cooperation based on an assessment of academic merit. It is also possible to obtain backing for achieving a doctorate, either entirely in Brazil or partly abroad. The existing support is insufficient for the country's requirements. Another concern is that there are many doctorates oriented to the academic career, but universities cannot always absorb them all due to bureaucratic government structure. On the other hand, there lacks orientation to entrepreneurship and technological research.

Broadly speaking, there are four main components for health research in the country. There are the bio-scientists - physiologists, biophysicists, biochemists. Others are the clinical researchers, the collective health personnel, and the personnel in research and development at the productive – or industrial – health installations. Of the approximately 20,000 active research groups in Brazil, 25% to 30% are linked to the field of human health, with more than 18,000 researchers. However, relatively few researchers focus their research priorities based on the priorities established by health policies, which means that health research policy and health policy are out of step. We are attempting to make them work together (Guimarães). There are approximately 18,000 scientists active in the field of health, and 11,000 of them have doctorates.

VII. Policy Recommendations

The positive results of the policies for mass vaccination and free supply of ARVs are the result of various factors: (i) qualified human resources in the field of human health; (ii) continuous investment in post-graduate programmes (both master and doctorate degrees); (iii) academic research programmes specifically oriented to population needs; (iv) negotiating capability for the intellectual property agreements; and (v) capability of developing strategies for the reduction of prices; amongst others.

Notwithstanding having attained positive and innovative results, the weaknesses are evident and need to be overcome. The limited innovative capability of the Brazilian health system constitutes an obstacle to government policies for universal access to health. The dependency on imports for the maintenance of the strategic programmes is a vulnerability that may be potentially aggravated by variations in international financial markets. In view of the weak technological and industrial policies, the trend is for an increase in the difference between Brazil and countries with an intense production of knowledge and products with high aggregate value.

Due to the approval in November 2003 of the new Industrial, Technological and Foreign Trade Policy, this is an opportune political moment for building a favourable environment for research, technology and high risk business. The Policy sees biotechnology and the pharmaceutical industry as priorities. Amongst the strategies that may be adopted, we can cite: (i) better liaison between the investment policies and those for research and innovation in health; (ii) development of the capital market with attention to the technologically-based companies; (iii) an objective regulatory legal goal, with the definition of simple and facilitating rules that allow the integration of research, production and market; (iv) incentive for local business cultural changes, with emphasis on long-term investment in technology; (v) emphasis on the diffusion of entrepreneurship; (vi) better coordination of commercial, technological and health policies together with state purchasing power; (vii) modernization and expansion of the public and private laboratories, (viii) development of strategies for increasing corporate R&D; (ix) selection of niches for investment (vaccines, biopharmaceuticals, phytopharmaceuticals, pharmochemicals, generic medicines, neglected diseases, etc.); and (x) improvement of conditions for long-term funding.

Intellectual property rights are strategic and fundamental assets for the maintenance and expansion of health policies. As can be noted from the Brazilian experience, the wisdom of developing strategies in the field of international diplomacy associated with strategies for access to medicines and the reduction of prices is capable of making a difference. As IP rights are in constant evolution on the international scene and the Brazilian legal system, certain recommendations are valid. Amongst them are: (i) increase general understanding as to the specificity of public health questions in the negotiations for intellectual property; (ii) seek to increase the negotiation capacity

(including as a strategy for price reduction); (iii) take full advantage of opportunities and flexibility contained in international agreements; (iv) study the feasibility of incorporating all forms of safeguards (compulsory licences, parallel imports, Bolar provisions, etc.) into national law; (v) promote the overall consolidation of the National Institute of Industrial Property, especially concerning the technical examination of patent applications; (vi) systematically monitor the grant of patents in the areas of interest (so as to verify, for example, what is or is not of public domain, which are the most active companies, what is about to expire, etc.); (vii) after establishing a determined level of protection, verify the impact on local industry; and (viii) strengthen the management of intellectual property and technology transfers in research institutions and innovation systems for health.

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DEVELOPING INNOVATIVE CAPACITY IN **INDIA** TO MEET HEALTH NEEDS

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Abbreviations

AIIMS	All India Institute of Medical Sciences, New Delhi
ANDA	Abbreviated New Drug Application
API	Active Pharmaceutical Ingredient
AYUSH	Ayurveda, Yoga & Naturopathy, Unani, Siddha & Homeopathy
CAGR	Compounded Annual Growth Rate
CCMB	Centre for Cellular & Molecular Biology, Hyderabad
CDRI	Central Drug Research Institute, Lucknow
CIPIH	WHO Commission on Intellectual Property Rights, Innovation and Public Health
CSIR	Council of Scientific & Industrial Research, New Delhi
DBT	Department of Biotechnology, GoI
DC&F	Department of Chemicals & Fertilisers, GoI
DGCI&S	Directorate General of Commercial Intelligence & Statistics, GoI
DPCO	Drugs Price Control Order
DSIR	Department of Scientific & Industrial Research, GoI
DST	Department of Science and Technology, GoI
EMR	Exclusive Marketing Rights
FDI	Foreign Direct Investment
FMCG	Fast Moving Consumer Goods
GMP	Good Manufacturing Practices
ICMR	Indian Council of Medical Research, New Delhi
GoI	Government of India
ICS-UNIDO	International Centre for Science & High Technology, Trieste, Italy
IDMA	Indian Drug Manufacturers' Association, Mumbai
IGIB	Institute of Genomics and Integrative Biology, New Delhi
IICT	Indian Institute of Chemical Technology, Hyderabad
IISc	Indian Institute of Science, Bangalore
IMT	Institute of Microbial Technology, Chandigarh
IPA	Indian Patents Act (1970)
ISM&H	Indian Systems of Medicine and Homeopathy, Department of GoI
LC-MS	Liquid Chromatograph & Mass Spectrometer
MAPE	Maximum Allowable Post-manufacturing Expenses
MDF	Master Drug File
MIHR	Centre for the Management of Intellectual Property in Health Research and Development, UK
MNCs	Multinational Corporations
MoH&FW	Ministry of Health & Family Welfare, GoI
MTS / HTS	Medium Throughput / High Throughput Screening
NACO	National Aids Control Organisation, Pune
NDA	New Drug Application
NGOs	Non-Governmental Organisations
NHP	National Health Policy
NIH	National Institutes of Health, USA

NIMHANS	National Institute of Mental Health and Neurosciences, Bangalore
NISTADS	National Institute of Science, Technology and Development Studies, New Delhi
NPPA	National Pharmaceutical Pricing Authority, New Delhi
OPPI	Organisation of Pharmaceutical Producers of India, New Delhi
OTC	Over the counter
PSU	Public Sector Undertaking
R&D	Research & Development
Rs	Indian Rupees
S&T	Science and Technology
TKDL	Traditional Knowledge Digital Library
TM	Traditional Medicine
UAS	University of Agriculture Sciences, Bangalore
UNIDO	United Nations Industrial Development Organisation, Vienna
URDIP	Unit for Research & Development of Information Products, Pune
USFDA	United States Food & Drug Administration
USPTO	US Patent & Trademark Office
WTO	World Trade Organisation

I. Healthcare in India

1.1 Backdrop

India, a functioning democracy, is sustaining around 16.7% of the world's population afflicted with 21% of the global burden of disease. Catering to the health needs of such a large section of humanity is an awesome task. After independence in 1947, India took up a massive programme of public healthcare based on establishing primary, secondary and tertiary institutions linked through appropriate referral systems to generate human resources needed by way of medical, dental, nursing, paramedical, and complementary services personnel and pharmacists. Today, a vast health infrastructure and manpower at all levels in government, voluntary and private sectors has been built up. The statistics on the allopathic healthcare facilities are noteworthy – 15,000 hospitals with 875,000 beds, 500,000 doctors (growing at 4% per year), 737,000 nurses (growing at 3% per year), 350,000 retail chemists, and nearly 200 medical colleges throughout the country. The improvement in coverage and quality of healthcare and the implementation of national programmes for combating specific diseases have resulted in a steep decline in death rates by a factor of three, doubling of life expectancy, elimination of small pox and other diseases, near absence of polio, and significant reduction in incidence of most infectious diseases. The current doctor-population ratio is around 1:1800 for allopathic medicine. However, taking into account doctors of other systems of medicine, the ratio is 1:800 (that compares favourably with most developed countries as well). The vast reservoir of skilled medical and paramedical human resources developed over the years has helped to supplement the personnel needs of the Middle East, Africa, USA and UK.

1.2 Healthcare Providers

The government has been both a provider and financier of public healthcare facilities. It has established a vast network of healthcare institutions that are the sole source of healthcare in rural areas. It has accorded high priority to providing universal immunization not only in childhood but also when useful in later life, and periodically mounts national programmes to address specific diseases. The central government spends around 70% of its health expenditure on preventive and promotive activities whereas the state governments spend around 80% of the expenditure on curative aspects.

The private sector has played a significant role in health service delivery especially in the curative and hospital care areas. The contribution of the private sector has been increasing over the years and witnessed an explosive growth after 1991 with the globalisation of the Indian economy and fiscal incentives provided to the healthcare sector. The burgeoning middle class, presently 300 million strong, is driving the demand for quality healthcare with the result that private investment and private sector facilities are mainly located around cities, towns and neighbouring areas.

Private sector healthcare facilities comprise large specialized hospitals (comparable to the best in the world), corporate hospitals, smaller hospitals (nursing homes), and clinics and dispensaries. A majority (85%) of these institutions have a capacity of less than 10 beds and the specialized hospitals account for only around 2% of total hospitals.

In addition, around 7000 voluntary agencies are involved in health-related activities ranging from implementing government programmes to providing specialized healthcare. Currently, the private sector accounts for well over 80% of all outpatient visits and over 50% of inpatient hospitalization. The majority of people, irrespective of their income levels, still prefer to avail of public sector facilities for immunization and antenatal care.

1.3 Government Expenditure on Health

India has yet to develop a national health accounting system. Expenditure on health in India is reported to be around 5.1% of the GDP in 2001 and expected to rise to 8.5% of GDP by 2011. Although the per capita expenditure on health is modest by global standards, it has to be viewed in the national context of low cost of pharmaceuticals, the use of traditional medicine by over 60% of the population, the development of an extensive basic public health infrastructure and hospital system, and the cost of diagnosis, physician consultation, surgery and hospitalization, which are amongst the lowest in the world.

Table 1. Selected Advanced Surgery Costs*

(in US $)

	India	**Thailand**	**USA**
Bone Marrow Transplant	30,000	62,500	250,000
Open Heart Surgery (CABG)	5,000 – 7,000	14,250	30,000
Hip Replacement	4,500	6,900	-
Knee Surgery	4,500	6,900	20,000
Hysterectomy	500	2,000	-
Gall Bladder Removal	555	1,755	-

* Cost of surgery in specialized hospitals
Source: IBEF (Healthcare), www.ibef.org

Government expenditure on health is reported to be around 0.8 to 0.9% of GDP; this is the direct expenditure by the Ministry of Health & Family Welfare and does not include the indirect expenditure incurred by other government departments, bodies, agencies and enterprises. Public expenditure has been growing at around 15% CAGR .

1.4 National Health Policy (NHP) 2002

The Government, recognizing the changing demographics, the altered disease patterns, the health needs of the diverse sections of the people, and the intensification of technology interventions in delivering healthcare, announced the NHP 2002 which seeks to:

- expand and improve the primary healthcare facilities;
- meet the health needs of the disadvantaged sections (women, children, elderly & tribal groups) through special programmes; and
- mount programmes with specified timeframes for the eradication of polio, yaws, leprosy, kala azar & filiarasis, and control of diseases like HIV/AIDS, TB and malaria.

In May 2004 the new government committed to raise public spending on health to 2-3% of GDP to achieve the objectives of NHP 2002.

1.5 Health & Biomedical Services R&D

Health R&D encompasses: (a) health and biomedical services R&D; (b) pharmaceutical (including biotechnology and diagnostics) R&D (see Chapters 2 & 3); and (c) biomedical diagnostic instrumentation and equipment R&D. The objective of health and biomedical services R&D has been to evolve appropriate policies, strategies and delivery systems to mount effective programmes for improving public health. The publicly funded biomedical R&D network comprises 21 research institutes and six regional ICMR centres, six CSIR laboratories, four DBT institutions, two Atomic Energy Commission centres, around half-a-dozen autonomous institutes that carry out significant medical research, and some 25 medical colleges. There is also around 180 non-commercial voluntary scientific research organizations registered with the government for medical sciences and about a score of private sector healthcare providers that have significant biomedical R&D activities. The public sector R&D effort has been mainly directed towards applied research on three important aspects: (i) to improve the quality and efficiency of existing system of interventions; (ii) to reduce the cost of existing system of interventions; and (iii) to identify and develop new and more effective interventions.

Despite the emphasis on applied R&D, the basic research output of biomedical research and clinical medicine as measured by the papers in SCI journals, and taken as a percentage of all Indian papers in SCI journals, has been significant. A study done by Science-Metrix of Canada for the period 1990-2001 shows papers in biomedical research numbered 16,512, or 13.1% of all Indian papers, with an average relative impact factor of 0.6. The corresponding figures for clinical medicine were 17,280, 13.8% and 0.6. Together, the two fields account for around 27% of all Indian contributions. Considering that investments in basic research in this field have been low, the output is noteworthy.

1.6 Health & Biomedical Services R&D Expenditure

No estimates are available on expenditure on health and biomedical services R&D. Sporadic estimates have been made in the past on the basis of funding sources. Estimates have been made by the author based on the expenditure incurred on R&D by the 'performers' for 2001-02: ICMR, Rs1.50 billion; CSIR, Rs.0.90 billion; DST, Rs.0.10 billion; DBT, Rs.0.30 billion; autonomous medical institutions and other medical colleges, Rs.1.0 billion; private sector & NGOs, Rs.0.5 billion; and non-commercial scientific research organizations, Rs.0.50 billion. This totals to around Rs.4.8 billion, which is around 2.5% of estimated direct government expenditure on health.

II. Pharmaceutical Business Environment

2.1 The Origins of Indian Pharmaceutical Industry

The foundation of modern pharmaceutical industry was laid at the beginning of the twentieth century with the setting up of the Bengal Chemical and Pharmaceutical Works in 1901. This was followed by MNCs Parke Davis (1907) and Burroughs Welcome (1912) commencing trading operations for formulations. However, the end of the First World War saw the four global pharma majors ─ Glaxo, Boots, May & Baker, and Ciba Geigy ─ establishing their presence in India. After the Second World War practically all the global pharmaceutical MNCs had entered into India. Even then, in 1950 the total sale of pharmaceuticals was a mere Rs.100 million, of which more than 90% was of imported products. The prices of pharmaceutical products in India were then among the highest in the world and the reach of modern medicines did not extend to even 20% of the population. The MNCs continued to import finished pharmaceuticals and only in the late 1950s repackaged imported bulk formulation in merchandisable sizes.

Pre-independence, India had suffered from several devastating epidemics. Recognising the inadequacy of the pharmaceutical industry in India to respond to such potential eventualities and the lack of technology base for antibiotics in the country, the government set up the Hindustan Antibiotics Ltd. (HAL) in 1954, with the assistance of WHO and UNICEF, to manufacture penicillin, tetracycline and streptomycin. By around 1955 the sales of pharmaceutical products had risen five-fold to some Rs.540 million. Enthused by the performance of HAL in the antibiotics domain, the government sought to achieve still greater self-sufficiency in the production of other life saving drugs and with Russian technology established the Indian Drugs and Pharmaceuticals Ltd. (IDPL) in 1961. Around the same time, Glaxo & Roche set up plants to manufacture Vitamin A. Soon, the two PSUs emerged as major producers of critical bulk drugs, which were otherwise being imported. The success of the two large PSUs encouraged many Indian entrepreneurs to venture into the pharmaceutical industry sector.

2.2 The Present Scenario

The Indian pharmaceutical industry today ranks amongst the largest and the most diversified in the world. It is recognized as knowledge-driven and globally competitive that has contributed to the wide availability of quality pharmaceuticals to the Indian population at prices that are amongst the lowest in the world.

In 2003, the annual turnover of the industry was estimated at around Rs.300 billion with Rs.141 billion worth of exports to over 90 countries and imports of only around Rs.40 billion. The industry produced over 400 bulk drugs valued at around Rs.80 billion and over 60,000 formulations in 60 therapeutic categories valued at around Rs.220 billion. The overall capital investment in the industry was estimated at around Rs.45 billion, with direct employment provided to around half a million people and indirect employment to around 2.4 million people.

Presently, there are about 10,000 operating units (although official figures put the number of units over 20,000); of these, around 300 are in the primary sector and the rest are in the medium/small-scale sectors. Today nearly all the operating units are in the private sector. The two major public sector units, HAL and IDPL (and their subsidiaries and associates, which fuelled the growth of the pharmaceutical industry in the 1970s), have lost their relevance in the prevailing competitive globalized economy. Many of the small-scale formulators who depended on the supplies from these PSUs have also suffered or closed.

Table 2. Indian Pharmaceutical Industry: Decadal Progress

	1950-51	**1960-61**	**1970-71**	**1980-81**	**1990-91**	**2000-2001**
Manufacturers (No.)	200		2,300	6,400	16,000	20,000
Investment (Rs. Million)	50	560	2,250	6,000	9,500	30,000
R&D Expenditure (Rs. Million)	-	-	100	290	800	4,000
Production (Rs. Million)	100	1130	4,000	14,400	45,700	228,870
- Bulk Drug	20	130		2,400	7,300	45,330
- Formulation	80	1000		12,000	38,400	183,540
Export (Rs. Million)	-	16	85	463	7,848	87,300
- Bulk Drug	-	-	-	112	4,134	39,300
- Formulation	-	-	-	351	3,714	48,000
Import (Rs. Million)	-	176	243	968	4,075	29,800
- Bulk Drug	NA	-	-	872	3,226	22,650
- Formulation	NA	-	-	96	849	7,150

Source: Compiled from diverse IDMA & OPPI Publications

2.3 The Pharmaceutical Market

Pharmaceuticals presently reach only around 40% of the total population mostly in urban and surrounding areas (accounting for over 75% of pharmaceutical consumption). The pharmaceutical market in India is mainly a prescription-driven branded generic market. The prescription market is around 80% while the rest of the market is covered by OTC products and customized dispensing.

The pharmaceutical market is highly fragmented with no company (presently) controlling more than 6% of the total retail formulation market (very similar to global trends). The top 10 companies (of which three are global MNCs) command around one-third of the market. However, the share of the top ten has been gradually increasing from around 31% in 1998 to around 37% in 2004 (estimated) and is likely to increase still further on conformance to TRIPS. In terms of market segmentation based on therapeutic end use, the antibiotics sector still dominates with a share of 15.7%, but its share is going down as lifestyle-related diseases increase. The top 10 therapeutic sectors account for around 60% of the market.

Table 3. Major therapeutic segments (2003)

Therapeutic Segments	**Market Size/Share** **Rs. bln** (%)
Antibiotics	33.0 (15.7)
Cardiac Therapy	10.2 (6.9)
CNS & Psychiatric Therapy	9.6 (6.5)
Vitamins	8.9 (6.1)
NSAIDS & Anti Rheumatism	8.8 (6.0)
Respiratory Ailments	7.8 (5.3)
Antacids & Anti-Ulcerants	6.2 (4.3)
Anti Anaemic	3.7 (2.8)
Anti Diabetic	3.7 (2.7)
Anti TB	3.6 (2.5)
Total (10)	**95.5 (58.8)**

The market is highly competitive and there are several tens of manufacturers for a single bulk drug, as indicated in the figure below.

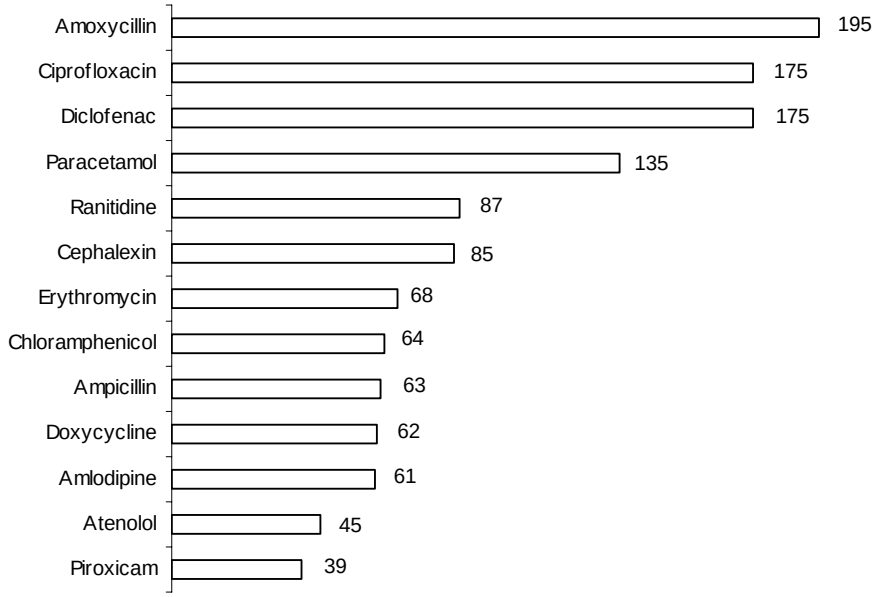

Fig.1. Bulk drug competition

(Brands available from 265 companies)

Source: ORG-IMS special study for OPPI & IDMA, September 2004

2.4 Pricing of Pharmaceuticals

Owing to the judicious application of pricing policy measures (DPCO), the prices of pharmaceuticals are generally several-fold lower than those prevailing internationally (even after adjusting for purchasing power parity).

Table 4. Pharmaceutical prices in selected countries circa 2002

(All prices converted to Indian Rupees)

	Drug Strength & Dosage for	India	Pakistan	Indonesia	USA	UK
I	**Anti-Infectives**					
1	Ciprofloxacin HCL 500 r tabs	**29.00**	423.86	393.00	2352.35	1185.70
2	Norfloxacin 400 mg tabs	**20.70**	168.71	130.63	1843.66	304.78
3	Ofloxacin 200 mg tabs	**40.00**	249.30	204.34	1973.79	818.30
4	Cefodoxime Proxetil 200 mg tabs	**114.00**	357.32	264.00	1576.58	773.21
II	**NSAIDS**					
1	Diclofenac Sodium 50 r tabs	**3.50**	84.71	59.75	674.77	60.96
III	**Anti-Ulcerants**					
1	Ranitidine	**7.02**	74.09	178.35	863.59	247.16

	150 mg tabs					
2	Omeprazole 30 mg caps	**22.50**	578.00	290.75	2047.50	870.91
3	Lansoprazole 30 mg caps	**39.00**	684.90	226.15	1909.64	708.08

Note: Price for pack of 10s

Source: Pharmaceuticals Pricing in India, Organization of Pharmaceutical Producers of India, Nov. 2004

The price increase of pharmaceuticals has on the average been (4-5%) lower than the increase in wholesale price index in India. The price growth of price-controlled drugs on the average has been around 1% a year and of the non-controlled drugs around 3%; in recent times, both these categories have shown a negative price growth.

The industry is highly competitive such that the market price of even controlled drugs is often times lower than the ceiling price fixed by the government (NPPA).

Table 5. Market Price of Selected Controlled Drugs (2003)

Drug Strength & Dosage form	Therapeutic Group	Govt. Ceiling Price Rs.	Market Price Rs.	% Price Reduction to control price
Rifampicin 150 mg 4 caps	Anti-TB	7.22	4.98	-31.0
Tetracyline 250 mg 10 caps	Antibacterial	8.16	7.94	-2.7
Chloroquine Phosphate 250 mg 10 tabs	Anti-Malarial	6.32	4.36	-31.0
Ciprofloxacin 250 mg 10 tabs	Antibacterial	30.66	21.00	-31.5
Carbamazepine 200 mg 10 tabs	Anticonvulsant	15.00	8.75	-41.7

Source: CIMS, India, Quoted in Pharmaceutical Pricing in India, OPPI, Nov.2004

The major cost components of the Indian pharmaceutical industry are material costs (estimated 50%) and employee costs (estimated 10%), unlike MNCs whose major cost components are for selling, manufacturing and R&D.

2.5 Trade in Pharmaceuticals

The exports of pharmaceutical products presently account for about 40% of the industry's production and in the past three years have shown a CAGR of around 30%. The export of formulations is placed at around Rs.100 billion and bulk drugs at Rs.40 billion. Exports to regulated markets in the US and Europe constitute over 25% of the total exports and have shown an increasing trend in recent times. The top export destinations are the US, China, Russia, Germany, Brazil and Nigeria. The top ten destinations account for around half of the total exports. The top ten pharmaceutical exporters account for 40% of all exports.

Table 6. Trend in Exports ($ Million)

Sl. No	Country	2000-01	2001-02	2002-03
1.	USA	56	136	251
2.	Russia	101	93	99
3.	Nigeria	74	74	71
4.	UK	23	29	52
5.	Germany	37	37	45
6.	Brazil	19	37	41
7.	Sri Lanka	34	28	40
8.	China	18	22	36
9.	Vietnam	34	34	35
10.	Nepal	28	30	33
	Total	424	520	703

Source: DGCI&S

Table 7. Top 10 Exporters(Rs. Million)

Company	Exports (FOB basis)		Imports (CIF basis)		Exports as % of sales	
	2003-04	2002-03	2003-04	2002-03	2003-04	2002-03
Ranbaxy Laboratories	23.46	17.75	5.32	5.08	69.0	65.8
Dr. Reddy Laboratories	9.82	9.19	2.19	1.63	58.9	60.1
Cipla Ltd	8.12	5.66	2.84	2.80	44.1	39.4
Aurobindo Pharma	6.42	5.64	5.40	4.93	51.0	50.6
Lupin Ltd.	5.58	4.01	2.75	2.22	47.4	42.0
Orchid Chem. Pharma	5.31	4.48	2.58	3.81	78.1	85.8
IPCA Laboratories	3.40	2.66	0.85	0.59	56.9	57.4
Biocon	3.00	1.08	2.11	0.74	59.8	42.6
Wockhard Ltd.	2.80	2.27	0.88	0.77	38.5	32.5
Strides Arcolab	2.48	1.73	0.55	0.42	90.0	75.1

2.6 R&D in Industry

Up to the beginning of the 1970s, very little R&D was carried out in-house by industry. R&D inputs and the human resources needed were mainly derived from publicly-funded R&D institutions. There have been exceptions - the two large PSUs, a few Indian companies and, surprisingly, two MNCs (Hoechst and CIBA) had established in-house R&D units. The real impetus to R&D came in the 1980s. The R&D was then largely focused on novel organic synthesis routes for known bulk drugs, substitutes for expensive imported intermediates and raw materials, and process development for enhancing the productivity and efficiency of the processes followed by research on formulations and known drug delivery systems. Later in the 1990s the attention of a few leading companies shifted to novel drug delivery systems, and later in mid-nineties, as the turnovers and exports increased, around a dozen of the leading Indian companies embarked on new drug discovery. There is now a three-fold increase in US patents granted for drugs and pharmaceuticals to India from 1999-2003, accentuated by publicly-funded R&D organizations like CSIR making forays in the international patent domain.

The past four years have witnessed another phenomenon; the emergence of technologically competent small and mid-sized firms that manufacture API and intermediates to global standards for MNCs and Indian generic companies. Several of these companies are undertaking custom synthesis and contract manufacturing for patented molecules for international clients.

At the same time, a few of the leading Indian pharmaceutical companies are shifting their R&D strategy from business-driven research to research-driven business aimed at developing innovative, non-infringing processes, novel drug delivery systems (NDDS), new chemical entities (NCE), and biopharmaceuticals. As a result, in 2003 India accounted for the highest Drug Master Files (DMF) applications (126) with the US FDA, more than China, Italy, Spain and Israel put together, and has the largest number of US FDA approved manufacturing facilities (over 60) outside of the USA.

2.7 New Drug Discovery

Indian companies till recently had sought to out-license any lead molecules to major global players at the pre-clinical stage due to the heavy investments and risks involved. But the scene has now changed. They are now conducting clinical trials of lead molecules on their own. New drugs in the pipeline by the 10 leading Indian companies exceed 20 and the rate of new developments is accelerating, as mid-sized companies graduate to bigger size and enhance their R&D spends for new drug discovery. See Table 8.

Table 8. New Drugs in the Pipeline

Company	Product	Status	Focus
Ranbaxy	Parvosin RBx 2258 alpha1-adrenoceptor antagonist	Ph II	Benign prostatic hyperplasia
	Clafrinast RBx 7796 VLA 4 antagonist	Ph II	Allergic rhinitis, asthma
	Ranbezolid RBx 7644 oxazolidinone	Ph I	Bacterial infections
	RBx 9901	IND filed	BPH
	RBx 7643	IND filed	Incontinence
	RBx 4638	Preclinical	Respiratory
	RBx 4467	Preclinical	Antifungal
	RBx 6198 a1A	Preclinical	BPH
	Unidentified	Preclinical	Malaria
Dr. Reddy's	DRF 10945 selective PPAR alpha agonist	Ph I	Dyslipidemia
	DRF 10945 PPAR alpha agonist	Ph I	Dyslipidemia
	RUS 3108 perlecan inducer	Preclinical	Cardiovascular disorders
	DRF 4158 selective PPAR alpha and gamma agonist	Preclinical	Type II diabetes
	DRF 11057 oxazolidinone molecule	Preclinical	Bacterial infections
	RUS 3108 perlecan inducer	Preclinical	Cardiovascular disorders
	DRL 11605	Preclinical	Metabolic disorders
	DRL 13792 oxazolidinone molecule	Preclinical	Bacterial infections
	DRF 5265	Preclinical	Cancer
	DRL 13792	Preclinical	Bacterial infections
Cadila Healthcare	ZYH1 Compound	Preclinical	Dyslipidemia, IND filed
	ZYH2 Compound	Preclinical	Type 2 diabetes
	ZYH3 Compound	Preclinical	Dyslipidemia and diabetes
	ZY1400 Compound	Preclinical	Inflammation and pain
	Several NME's	Biological Testir	Treatment of arthritis, obesity and bacterial infections.
Wockhardt	WCK 771 broad spectrum antibacterial	Ph Ib	Methicillin & vancomycin-resistant & sepsis
	WCK 1152 broad spectrum antibacterial	IND filed	Hospital & community acquired respiratory tract infections
	WCK 1457 broad spectrum antibacterial	Preclinical	Vancomycin-resistant bacteria
Nicholas Piramal	Flavopiridol	Ph II	
Sun Pharma	One molecule	Ph I	Allergy, asthma and anti-inflammation

Torrent	TRC-4XXX AGE	Preclinical	Heart disease
	TRC-303 isomer of solalol	Preclinical	Arrhthymia
	TRC-282 nitric acid enabler	Preclinical	Angina
	TRC-6XXX heat shock protein	Preclinical	Stroke
	TRC-8XXX DPP-IV dipeptidyl peptidase inhibitor	Preclinical	Diabetes
	TRC-9XXX vasopeptidase inhibitor	Preclinical	Hypertension
	TRC-5XXX stress protein upregulator	Preclinical	NA
Dabur	DRF-7295	Ph II	Anti-cancer molecule
	Second oncology molecule	Ph I	Activity against melanomas & leukaem
Glenmark	One molecule	Ph I	Diabetes
	2 molecules	Preclinical	Anti-diabetes/anti-obesity & anti-asthma
Lupin	An anti-TB molecule A molecule for intra-nasal administration Herbal based scientific formulation 2 compounds 2 compounds	IND IND Ph I Preclinical Preclinical	TB Anti-migraine Anti-psoriasis Anti-psoriasis Anti-inflammatory
Biocon	h-R3 anti-EGFr MAb Ph I	I. Ph II	Head & neck, brain and lung cancer
	h-T1 humanized anti-CD6 MAb	Ph II	T cell lymphoma, rheumatoid arthritis (RA), psoriasis
	q-T3 chimeric anti-CD3 MAb	Ph II	Organ transplant
	EGF cancer vaccine	Ph II	Cancer
	TGFalpha	Ph II	Cancer
	HER 1 cancer vaccine	Ph II	Cancer

Source: Dinesh Abrol (2004), " Post-TRIPS Development Strategies of Indian Pharmaceutical Industry", NISTADS, New Delhi

2.8 R&D Spending

Pharmaceutical R&D is carried out in-house by industry, publicly funded R&D such as the laboratories of the CSIR, ICMR, DBT, and a few of the other government institutions such as National Institute of Pharmaceutical Education & Research (NIPER), around 25 universities, and about a dozen pharmacy colleges. However, the figures of R&D expenditure generally quoted are those expended only by the industry. Here too there are significant discrepancies. The figures for R&D expenditure by industry put out by OPPI and the government departments do not tally. For example, the OPPI figure for 1998-99 is Rs.2.6 billion as compared to DST's figure of Rs.3.77 billion, and the figures for 2002-03 are Rs.6.6 billion by OPPI, over Rs.8 billion by the DSIR, and the author's own estimates are of Rs.9 billion.

This is corroborated by a study carried out by a business daily (Economic Times, Mumbai, Dec.15, 2004) that R&D expenditure for 2003–04 of the top 10 pharmaceutical companies was Rs.9.7 billion, which was 6.3%% of their turnover, and the total for all the pharmaceutical companies was around Rs.13.2 billion or 3.8% of their turnover – the highest for any industry sector in India.

Considering the vast diversity in size, range and segmentation of the firms and the low cost of human resources, the average R&D expenditure for the industry as a whole at 3.8%, with top 20 companies averaging to over 5.5%, is notable. In the past three years, the growth rate of R&D expenditure of the top 20 companies has far exceeded the growth rate of their turnover; the trend is likely to accelerate further.

This is only the direct R&D expenditure by industry itself; it has to be supplemented by the expenditure incurred by the publicly-funded R&D for pharmaceutical R&D, including biopharmaceuticals. It is estimated by the author that publicly-funded R&D expenditure for pharmaceutical R&D in 2003-04 was of the order of Rs.2 billion (CSIR: Rs.1 billion; ICMR: Rs. 0.20 billion; DBT: Rs.0.35 billion; DST: Rs.0.15 billion; DC&F: Rs.0.15 billion; and all others: Rs. 0.15 billion). Combining the R&D expenditures of industry and the publicly-funded R&D, the total expenditure comes to over Rs.15 billion for an industry turnover of around Rs.350 billion.

2.9 Consolidation & Foreign Collaborations

One hundred percent FDI and automatic approval for Foreign Technology Agreements is permitted for the pharmaceutical industry. As most of the global MNCs already have their operations or subsidiaries in India, there has been no significant increase in the FDI due to these measures, but due to the excellent valuations that the leading Indian pharmaceutical companies command, foreign institutional investment in these companies has been on an upswing.

Leading Indian companies have themselves been consolidating by acquisition of domestic units and brands to enhance their therapeutic coverage, develop economies of scale, and ease in accessing the medical fraternity. Most of the leading companies have acquired units abroad to gain access to technology and the regulated markets. Owing to the number of blockbuster drugs going off-patent in the US and Europe, the past four years have seen further upsurge in foreign collaboration arrangements of the leading Indian firms with foreign companies for out-licensing, contract manufacturing, and marketing arrangements.

Table 9. Recent Foreign Collaborations of Indian Companies

Indian Company	Foreign Company	Type of Collaboration	Specifics
Ranbaxy	Schwarz Pharma, Germany	Out-licensing	BPH Molecule
	GSK, UK	R & D	Drug Discovery & development
	KS Biomedix, UK	Marketing	Biomedix's Biopharma products
	Atrix Labs, USA	In-licensing	Lenoprobide acetate injection
Dr. Reddy's	Novartis, Switzerland	Out-licensing	
	Novo Nordisk, Denmark	Out-licensing	Antidiabetis molecule
	Pliva, Croatia	Dev. & Marketing	Oncology Products
Zydus Cadilla	Onconora, USA	Marketing	Special cancer products
	Fermenta Biotech, UK	In-licensing	Cbiral & Process technology for Lisinoprise Benzepail
	Mayne, Australia	Joint Venture	Generics
	Boehringer Ingelheim, Germany	Marketing & Contract Mfg.	Boehringer's new products in India
	Schering, Germany	Marketing & Contract Mfg.	Schering's patented products in India
	Berna Biotech, Switzerland	Marketing	Berna's Anti-rabies vaccine
Wockhardt	Ivax, USA	Contract Mfg.	Nizatidine (Anti-ulcerant)
Torrent	Novartis, Switzerland	Out-licensing	Advanced Glycosylation end
Glenmark	Forest Laboratories, USA	Out-licensing	Anti-asthmatic molecule
Nicholas Piramal	Biogen Idec, USA	Marketing	Biogen's Avonex-n (multiple sclerosis)
	Allergan, USA	Contract Mfg.	Bulk & Formulations
	Genzyme, USA	In-licensing	Sybvisc Viscose marketing in India
Lupin	Baxter Healthcare, USA	Marketing	Lupin's Ceftriaxone in USA
	Allergan, USA	Marketing	Lupin's Gatofloxacin ophthalmic
	Fujisawa, Japan	Contract Mfg.	Cefixime
	Apotex, Canada	Contract Mfg.	Lisinopril & Cofuroxime Axetil
Biocon	Bristol Myers Squibb, USA	Contract Mfg.	Bulk Drugs
	Nobex, USA	Codevelopment	Oral insulin
	Vaccines, USA	Codevelopment	Antibodies
Sun Pharma	Eli Lily, USA	Contract Mfg.	Anti-infectives, CVS products & Insulin
Cipla	Mortin Grove, USA	Collaboration	Manufacture & formulate generics

Source: Compiled from company and media reports

2.10 Summing Up

The competence profile of today's Indian pharmaceuticals industry is shown in the figure.

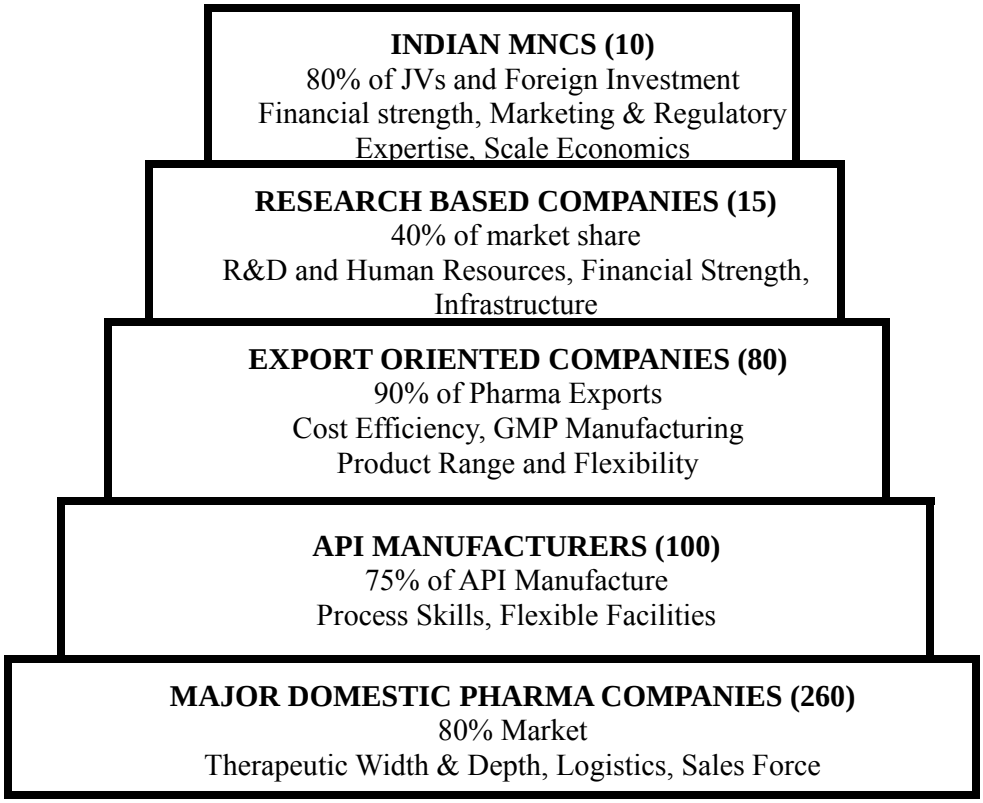

Fig.2. Competence Profile of Indian Pharmaceutical Industry

Domestic drug production is not only a viable option but a logical imperative for countries of the size of India with a large internal market, a viable manufacturing industry, and a high level of intellectual infrastructure for biomedical and pharmaceutical R&D.

III. Health Biotechnology Sector

3.1 Overview

Modern biotechnology has been assiduously nurtured by the Indian government for the past quarter of a century. In the mid-1970s, the three overarching Science Councils ─ ICAR, ICMR and CSIR ─ initiated R&D programmes in biotechnology in their areas of interests. In 1982, the government created a National Biotechnology Board to evolve a long-term plan for the development of the sector. The Board initiated programmes to develop human resources and to create the infrastructure for R&D for the emerging sector. Later, in 1986, the Board was converted to the Department of Biotechnology (DBT) under the Ministry of Science & Technology, charged with the responsibility to coordinate all the aspects pertaining to biotechnology in the country.

Since then, the DBT has played a pivotal role to catalyse the growing postgraduate and postdoctoral education programmes in biotechnology; set up a vast Biotechnology Information System Network; create centres of excellence in diverse specialized areas; set up six specialized R&D institutions and one public sector enterprise; stimulate and supported basic and applied R&D programmes; and nurture and support a budding industry.

The overall aggregate government investments in biotechnology over the 25-year period are estimated (by the author) at around Rs.25 billion, of which around one-third could be for the health biotech sector. These investments have resulted in the creation of an impressive biotech infrastructure, a competent human resource base, a balance in the R&D activities, and the development of a workable regulatory and legal framework that has stimulated the emergence of a viable industry sector.

3.2 Knowledge Capacity

Indian academic and publicly-funded R&D institutions have developed R&D capabilities over a wide range of modern biotechnology. As a result, there has been a near doubling of scientific papers contributed to international peer-reviewed journals (from 125 to 240), and also a doubling of biotech patent filing in India from 172 to 395 over the period 1995–2002. CSIR was the major patent filer accounting for 10% of the total patent applications, followed by five MNCs together accounting for 15% of the patent applications.

Table 10. Biotechnology patents filed in India

Year	Vaccines	Proteins	Total Biotech
1995	9	68	172
1996	8	64	193
1997	18	88	279
1998	13	69	287
1999	3	54	162
2000	13	69	265
2001	33	135	451
2002	17	94	395
Total	**114**	**641**	**2204**

Source: www.indiapatents.org

3.3 Biotech Clusters

The state governments in India were quick to recognize the economic potential of the emerging sector. Several states have taken steps to develop biotech promotional policies and to establish parks and clusters around strong academic and publicly-funded R&D institutions, and sometimes in the proximity of leading pharmaceutical/IT firms. The leading three states are: Andhra Pradesh, which has designated a 600 sq. km area around Hyderabad, home to India's bulk drug manufacturing industry, as Genome Valley, with around 75 biotech firms located there; Karnataka, which has spawned a Bangalore-based bio-cluster hosting around 90 biotech companies, including many start-ups; and Maharashtra, which has set up a biopharmaceutical-based cluster around Pune.

3.4 Health Biotech Industry

Assessing the size of the biotech industry is difficult as it includes pharmaceutical companies that have diversified into biopharmaceutical products and IT companies that have taken up bioinformatics. A recent survey carried out by the Association of Biotechnology Led Entrepreneurs (ABLE) in association with a publication, BioSpectrum, indicates the output of the sector as around Rs.28 billion in 2003–04, with a growth rate of 40% and exports of 60%. The vaccines sector accounts for about 40% of the output. The turnover of the vaccines and therapeutics is also included in the output of the pharmaceutical industry, covered in Chapter 2.

Table 11. Health Biotech Sector
(Rs. Billion)

	2003 – 03	2003 - 04	
Segment	**Production**	**Production**	**Exports**
Biopharma	**17.90**	**24.80**	**13.90**
• Vaccines	9.13	11.70	
• Therapeutics	3.37	4.15	
• Diagnostics	1.78	2.60	
• Others	3.62	6.35	

Bioinformatics	**0.75**	**0.80**	**0.69**
Bioservices	**1.35**	**2.75**	**2.50**
Total	**20.00**	**28.35**	**17.09**

Source: www.biospectrumindia.com

3.5 Vaccines

The manufacture of vaccines was initiated in several public sector units in the early 1900s. However, the real thrust for Indian vaccine manufacturing came in 1977 when India became signatory to the Alma Ata declaration for expanded programme of immunization, which gave rise to a huge market for vaccines against polio, measles, TB, pertussis, diphtheria and tetanus. This gave an opportunity to Indian entrepreneurs to venture into this arena. Today, except for the oral polio vaccine, India is not only self-sufficient in production of all vaccines but also exports a sizeable portion of the production through a judicious mix of around 20 public and private sector units.

Table 12. Export of Vaccines (2002 – 03)
(Rs. Million)

Vaccine for humans	Export
Cholera	150
Diphtheria	313
Tetanus	428
DPT	250
MMR	1,016
Anti-rabies	65
Hepatitis-B	20
All other	951
Total	**3,193**

Source: 42nd Annual Publication of IDMA

The vaccine sector is characterized by high volume purchases by government and NGOs for public health programmes. Thus, despite the absence of price control, the prices are low and competition between the few firms is severe. The presence of the public sector units has prevented cartels.

India has mounted a massive R&D programme on vaccines development. Some of the vaccines in the pipeline are:

Table 13. Vaccines in the Pipeline

Vaccine	Stakeholders/Partner	Collaborators & Stage of Development
HIV/AIDS Subtype C	IAVI	ICMR, AIIMS, DBT etc.; Phase I clinical trials
Rotavirus	Bharat Biotech	R&D effort with AIIMS, IISc., NIH a Stanford University; Phase I
Influenza	Biological E	In final stages of development; R&D with NIV, Netherlands
Combination Vaccine of DP Hepatitis B+ Typhoid	Shantha Biotechnics	
DNA Rabies Vaccine	Indian Immunologicals	R&D in progress with IISc.
Malaria	Bharat Biotech	Bill & Melinda Gates Foundation
Japanese Encephalitis	Bharat Biotech	
Leprosy	Cadila Healthcare	National Institute of Immunology; In final stages of development
Edible cholera vaccine (in Tomato)	DBT	Delhi University, IMT; R&D in progres
Edible rabies vaccine (in cantaloupes)	DBT	UAS, Bangalore; animal trials

Source: Compiled from company and DBT Annual Reports

3.6 Bio-therapeutics

The biopharmaceutical sector of the industry is compact, with the top 10 companies accounting for over 60% of the output, the next 10 companies having a 15% share, and about 100 companies sharing the rest. This augurs well as there is concentration of capacity, infrastructure and expertise amongst a few specialized players. Around 25 rDNA products have been granted marketing licences, and of these insulin, streptokinase and erythropoietin are already in the marketplace.

3.7 Diagnostics

The diagnostics market in 2003-04 was around 9% of the health biotech sector. The market is served by around 40 small diagnostic companies each with a turnover of less than Rs.50 million, and another 20 or so diversified companies, including MNCs, with a diagnostics turnover of Rs.100 million and more. The major market share is for diagnostics for Hepatitis A, B, C, HIV, TB, Typhoid, Malaria, Dengue, and for pregnancy and thyroid hormones. Almost half of the diagnostic kits are imported. Some new kits in advanced stage of development are for HIV subtype C, Hepatitis C, Malaria, TB, Leukemia & Aspergillosis.

3.8 Bioinformatics

The bioinformatics market is placed at around one billion rupees and is dominated by

leading Indian IT companies in alliance with specialized publicly-funded modern biology institutions. A few small pure bioinformatics companies have also emerged. The quality of their products and services are of global standards in keeping with India's high reputation in the international IT field. The advantage offered by India of a vast and competent IT workforce and expertise in modern biology has attracted several foreign IT MNCs to set up their bioinformatics R&D/ development centres in the country.

3.9 Positioning of Biopharmaceutical Companies

The comparative advantage of Indian biopharmaceutical companies is derived from the following factors:

- Highly qualified and competent human resource base in modern biology, IT and chemical sciences
- Access to a large brain bank of highly qualified NRI scientists/technologists and managers
- Well-established network of publicly-funded R&D laboratories amenable to public-private partnership
- World class USFDA / WHO approved manufacturing facilities
- Cost-competitiveness in R&D and manufacturing
- TRIPS compliant IPR regime
- Multiethnic, genetically diverse large patient base for all known diseases
- Heritage of well-established traditional knowledge medicinal systems
- Rich human, flora and fauna biodiversity
- Increased government empathy, support and investments in biotechnology

The handicap of the Indian biopharmaceutical companies as compared to MNCs arises from:

- Fragmentation and small-scale operations (the largest biopharmaceutical company has a turnover of around $120 million),
- Multiplicity of authorities for regulatory approvals and consequential delays in product introductions, and
- Inadequate GLP qualified *in vivo* animal testing facilities.

Considering the balance of positives and negatives, a few of the Indian biopharmaceutical companies have the potential to emerge as formidable players not only nationally but also internationally.

IV. Regulatory Environment

4.1 Drug Price Control Order (DPCO): Making Drugs Affordable

Several policy measures and instruments were evolved in the 1970s to develop the domestic industry's self-reliance. In the pharmaceutical sector, the DPCO (1970) was one such instrument devised to control the domestic prices of major bulk drugs and their formulations. In 1970, DPCO was applied to merely control the overall profitability of a pharmaceutical firm by stipulating a ceiling of 15% pre-tax profit of pharmaceutical sales (net of taxes). The MNCs who then controlled over 75% of the market were not significantly affected by this mild form of control and continued operating in the Indian market. The outcome was the stabilization of prices and the availability of pharmaceuticals at reasonable cost.

In 1979, the DPCO was revised to stimulate cost savings. It specified a ceiling on the return or net worth of capital employed for the manufacture of bulk drugs and for formulations. The retail prices were decided by applying the concept of MAPE (Maximum Allowable Post-manufacturing Expenses), akin to a mark-up on ex-factory costs to cover all selling and distribution costs including trade margins. A graded MAPE was prescribed: 40% for critical life-saving drugs and 100% on less critical formulations such as vitamins and supplements. The DPCO then covered 370 bulk drugs and around 80-90% of production. To stimulate indigenous innovation, it provided that production of bulk drugs based on 'indigenous technology' be exempt from price controls for a period of 5 years. The MNCs were severely hit as their profitability levels fell steeply, and several discontinued sale of many products in the Indian market. The Indian companies, with their small size and scientific and technical talents derived from the local chemical industry, were able to speedily develop alternative, locally appropriate and cost-effective process routes for bulk drugs that were imported or high-priced, as it gave them price advantage in the domestic market. An intense era of chemical process innovation in industry followed, often with assistance from the publicly -funded R&D system (mainly the CSIR).

By the mid-eighties, the industry had greatly matured technologically; Indian pharmaceutical products were then among the cheapest in the world, and imports balanced exports. A further shift in the strategy was called for to stimulate the industry to export. The DPCO was thus modified in 1987 to enable higher margins, a MAPE of 75% (enhanced from the levels of 40 and 55%) was allowed on more critical drugs, and the 100% MAPE continued. The number of drugs under price control was reduced from 370 to 143 and covered around 60-70% of the industry production. Concurrently, government provided incentives for exports by upgrading their facilities and undertaking R&D. These measures encouraged many Indian companies to venture into exports. As a result, exports increased ten-fold over the period 1986-87 to 1994-95 to Rs.22.7 billion (as

compared to imports of less than Rs.10 billion).

With the establishment of the WTO in 1995, the DPCO was revised to enable the industry to compete globally. Accordingly, the number of drugs under price control was nearly halved from 143 to 76 (less than 40% of the industry production was now covered). The revised DPCO also provided for a framework to prevent monopolistic pricing by specifying the benchmark for inclusion of drugs under its auspices. A uniform 100% MAPE was now allowed for all formulations, and in determining the ceiling price of bulk drugs a 14% post-tax return on net worth, or 22% return on capital, was permitted. To give a further boost to R&D, a new drug produced based on indigenous technology was exempted from price control for 10 years; bulk drugs produced from basic stage based on indigenous R&D, and formulations manufactured by using Novel Drug Delivery Systems, were exempt from DPCO for five years. The results were heartening - the industry invested heavily in R&D and exports further expanded, this time even to the regulated markets like the US and Europe. The industry grew at a quick pace and in 2002 a new Pharmaceutical Policy was announced, that, inter alia:

- reduced the number of drugs under price control to only 28; and
- extended the benefits of exemption from price control to 15 years for indigenously developed drugs.

The reduction in the number of drugs under price control has been challenged by an NGO in the Supreme Court of India, petitioning that it was the responsibility of the government to ensure that essential and life-saving drugs are available at reasonable prices.

DPCO has thus been a dynamic policy instrument applied innovatively to strike a balance between the ‘needs of an industry to adequate profit margins’ with social obligations of the government to provide access to drugs at reasonable costs.

V. Intellectual Property (IP) Regime

5.1 Indian Patent Act, 1970 (IPA): An Instrument to Fuel Innovation

At the time of India's independence, the Indian Patent and Designs Act of 1911 (IPDA) was in force. It was more liberal than even similar acts in Europe; 'it allowed even those inventions related to food, medicines, agrochemicals to be patented and provided for a patent term of 16 years with provisions for extension of the term by five years and in exceptional cases by even ten years'. There was widespread national discussion and debate on the appropriateness of the IPDA at that stage of India's development. A comprehensive and consolidated Indian Patents Act of 1970 (IPA) was subsequently enacted which, together with the rules, came in to force in 1972.

The IPA introduced significant changes related to inventions in the areas of food, pharmaceuticals and agrochemicals. Only methods or processes of manufacture were patentable for such inventions, and the patent term was restricted to seven years from the date of filing or five years from the date of sealing, whichever was shorter. Conditions for compulsory licensing were liberalized and, more importantly, such patents were liable for 'license of right' if these were not worked within three years from the date of grant. Working was defined as domestic manufacture. There was thus a deliberate tilting of the 'balance of advantage' in favour of the 'community' rather than the 'patentee'. Around that time, several other nations in Asia and Africa had gained independence from colonial rule and were struggling with pressing national development issues. The IPA came to be regarded as a paradigm that was pro-development and certain aspects of it were adopted by such countries in their patents framework.

Human Resources Development

The absence of product patents for pharmaceuticals provided an opportunity for entrepreneurs to manufacture these in India. It prodded the Indian S&T community to enter the fray. The R&D orientation of the CSIR from the seventies and even in the eighties was thus directed to developing novel processes for known essential drugs. This helped to build a formidable human resources base, capacity, and infrastructure for pharmaceutical R&D in the publicly- funded R&D system. Industry was also not far behind. The Indian chemical industry was then well developed and had a sizeable experienced technical human resources base, many of whom migrated to the promising nascent pharmaceutical sector. A strong technological capacity was thus built up in organic synthesis, process development, and in design, manufacture and operation of small capacity plants with flexibility to quickly diversify to new products. The number of manufacturers of bulk drugs proliferated. Concurrently, Indian companies developed expertise in devising generic formulations and known dosage forms assisted by the horizontal flow of human resources from the PSUs to mushrooming small-scale firms.

The expansive growth and investment in the bulk and formulations sector gave rise to a demand for appropriate processing, testing, packaging equipment, and quality assurance and environment control systems. Local skills, designs and manufacturing capacity were built up as well. Today, this ancillary industry has a turnover of over Rs.7 billion. In short, the IPA had a cascading impact on helping to build a strong human resource base for R&D, design, manufacturing, and quality assurance in management and marketing of pharmaceutical products. It also led to the expansion of pharmacy education to generate pharmacists needed in the industry and to man the burgeoning retail chemist outlets.

Thus, by striking a judicious balance between the rights of the community and a patentee, the IPA has resulted in the formation of immeasurable public and social goods aside from the tangible private goods.

5.2 Compliance with TRIPS

India joined the WTO, which has the mandate of administering TRIPS, as a founding member in April 1994. As a developing country, India had 10 years transitional time, up to December 2004, to comply fully with TRIPS. It has sought to do so by amending the IPA. The first amendment was in 1999 to fulfil the TRIPS obligation of having a product patent during the transitional period. The amendment mainly provided for:

- A 'Mail Box' facility, applicable retrospectively from 1.1.1995, to receive product patent applications in the field of pharmaceuticals and agro-chemicals.
- Exclusive Marketing Rights (EMR), under specified conditions, in respect of patent applications for products in the 'Mail Box'.

The second amendment, implemented in May 2003, made significant changes in the IPA:

- The term of all patents, whether product or process, was made 20 years from the date of filing.
- The 'license of right' was abolished.
- The burden of proof was reversed from the patentee to the alleged infringer.
- Publication of all patent applications after 18 months of filing.
- Compulsory licence was to be available in conformity with Article 31 of the TRIPS, under the following situations:
    - If the reasonable requirement of public was not satisfied or that the product was not available to the public at a reasonable price or that the patent invention was not worked in India.
    - In circumstances of national emergency or extreme urgency.

  The conditions provided for the compulsory license were:

  - the patentee to be paid adequate royalty, and
  - the licence to be predominantly for supplying in the Indian market.
- Three other modifications included in the amendment impacting the pharmaceutical sector were:
  - Disclosure of the source of biological material as a condition of patentability.
  - A provision akin to 'Bolar exemption' as in US Patent Law.
  - Importation of a patented product by a duly authorized person.

As a result of this, in the short period of six years since 1995 patent filing in the drugs sector had nearly quadrupled.

The third amendment to the IPA was made in December 2004 to meet the January 1 2005 deadline. It provides for:

- Product patent in all fields of technology
- Granting of compulsory licence for export of medicines to countries that have insufficient or no manufacturing capacity to meet emergent public health situations (in accordance with the Doha Declaration on TRIPS and Public Health)
- Both Pre-grant and Post-grant opposition in the Patent Office
- Circumscribing the rights in respect of mailbox applications from the date of grant of patent, and not retrospectively from the date of publication

On the whole, as a result of the three amendments the IPA is now fully TRIPS compliant and even incorporates a few of the concerns expressed in the Doha declaration.

<u>Concerns</u>

In the two months since the third amendment, there has been widespread national debate. The major concerns expressed are with respect to:

- Broad (and vague) criteria for patentability permitting 'greening' of patents, especially in pharmaceutical sector; and
- Cumbersome compulsory licensing provision making these inoperable.
-

The suggestions put forth are to:

- Establish formal mechanism for coordination between different organs of the Government, that is, Ministry of Health, Department of Chemicals & Fertilisers, the Drug Controller General of India & Patent Office, in implementation of IPA in regard to pharmaceutical products; and

- Permit civil society (NGOs, voluntary agencies) to intervene in EMR and pre-grant proceedings.

5.3 Impact of TRIPS

Impact of EMRs

The Indian Patent Office had received around 12,000 Mail Box applications by December 2004, of which around 7,000 are believed to be for pharmaceutical products. The Patent Office had considered only around a score of applications for the grant of EMRs. Three pharmaceutical products granted EMR are Glivec (imatinib mesylate) of Novartis, Nadoxin (nadifloxacin) of Wockhardt, and Cialis of Lily Icos. By the time Glivec was granted EMR, copies of it were being marketed by a few Indian companies. The Indian companies went to Court pleading for invalidation of the EMR granted (claiming that patents were filed prior to 1995), the non-affordability of the drug at patentee's prices ($27,000 versus $2,700 for a year's supply of the copies), the loss incurred by the companies due to wasted investments, and the failure of the Patent Office to invite opposition before the grant of the EMR. Novartis in turn filed a petition for implementation of the EMR and a stay order for stopping the marketing of the product by the Indian companies.

On the question of law, the Madras High Court held the Indian companies' petition untenable and ordered the parties to stop marketing the product. The result was that imatinib mesylate was unavailable to patients in India suffering from myeloid leukemia. A public interest litigation was filed in the same court. As an interim measure the Court, in a remarkable social activist mode, directed Novartis to supply Glivec free of charge to patients with income below Rs.0.336 million per month. Recent media reports indicate that the government is seeking information from Novartis on compliance with the Court orders.

Both Wockhardt's Nadoxin and Lily's Cialis have local copies and the competitors are challenging the grant of EMRs in courts. A beneficial fall-out of these cases has been that loopholes in the law and the process of granting EMR have been identified.

Post-January 2005, the Indian Patent Office has started processing the Mail Box applications, which should take about six months to open and another year or so to process them. The initial impact of EMRs will thus be modest, as the Indian government will do its best to demonstrate that prices are not significantly affected and MNCs will strategically keep the prices of drugs granted EMRs at the lowest end of the global scale.

Impact on the Consumers (Patients)

The prices of drugs protected by product patents would be definitely higher compared to what they would have been under the erstwhile IPA; as demonstrated by cases such as Glivec and Cialis and the comparatively higher prices of patented drugs in Pakistan & Indonesia as compared to India, where these are not patented.. How much higher the prices would be is anyone's guess, but they would be high enough to maximize global profits for the patent holder.

However, the Indian DPCO has been a dynamic instrument for price control and now includes drugs under its purview due to monopoly position/price rises. It is here that the NPPA, which administers the DPCO, has to play a proactive and vigilant role. With this type of safeguard, price rises can be kept within manageable, but not necessarily affordable, limits by a vigilant pricing authority working in tandem with the government drug regulatory authority to keep the list of essential drugs dynamically updated and under price surveillance.

Impact on Indian Companies

As the original pharmaceutical product patent holders now have no fear of copies of their product being made and sold in India, pharmaceutical MNCs may seek to have the products manufactured in India due to low costs and availability of FDA-approved manufacturing plants. The bigger Indian companies with GMP facilities can now maintain their position by taking up such contract manufacturing. This is already becoming evident since full compliance with TRIPS.

Indian manufacturers of generic drugs are expected to maintain their position, particularly since $45 billion or so worth of drugs worldwide will come off-patent in the next five years. Generic companies have the opportunity to seize a sizeable share of this market either through their own marketing arms or through collaborations with domestic companies.

R&D in the leading Indian pharmaceutical companies is currently not dictated by seeking local market share but by the race to access the more lucrative developed country markets as evidenced by over 50% of their production being exported. The impact of TRIPS compliance on their R&D will be minimal, as can be seen from the increased ANDA filings over the past four years by the top ten Indian companies.

On the whole, the impact of a TRIPS-compliant patent regime on the Indian pharmaceutical industry will be further specialization, differentiation, segmentation and consolidation. The output and growth of the Indian pharmaceutical industry may not slow down except that it will now be the survival of the biggest and the fittest (technologically & financially).

Impact on the operation of MNCs in India

The product patents regime safeguards the interests of MNCs to introduce new (patented) drugs in India without fear of reverse engineering. Most pharmaceutical MNCs have their operations in India and have now embarked on enlarging their own marketing/distribution system or by takeover/mergers. The share of MNCs in the domestic market is thus expected to expand. In 2003-04, only three MNCs figured among the top ten pharmaceutical companies and all MNCs together accounted for only around 22% of the Indian market share., This share is expected to double in the coming five years as more MNCs expand their operations.

Recognising the opportunity for undertaking cost-effective quality R&D and clinical trials in India, it is anticipated that more MNCs will set-up their R&D centers/facilities and undertake clinical R&D locally along the lines of the global IT industry setting up their R&D/technical centres in India. A few MNCs are already forging strategic alliances with Indian companies.

6. Role of Traditional Medicines (TM)

6.1 Backdrop

The role of TM in public healthcare was formally recognized as early as 1983 in the National Health Policy of that year, which referred to India's rich, centuries-old heritage of medical and health science and the vast decentralized infrastructure available in the Indian Systems of Medicine and Homeopathy (ISM&H) comprising of Ayurveda, Unani, Siddha and Homeopathy, for addressing the healthcare needs of the people. The Policy suggested that planned efforts were needed to integrate ISM&H in the overall healthcare delivery systems, especially in regard to the preventive, promotive and public health objectives. But not much was done for a decade.

In 1995, the Government set up a Department of ISM&H to ensure that TM had a significant involvement in public health programmes. In 1999, the overarching Central Council for Health and Family Welfare of the Union Government recommended, inter alia, that at least one physician from the ISM&H should be available in every primary healthcare centre (PHC) throughout the country, specialist ISM&H treatment centres should be introduced in rural hospitals, and an ISM&H wing should be created in existing state and district hospitals. Despite these pronouncements and initiatives, ISM&H still received only 2% of the total public health budget till the end of the 2001. However, in 2002 the government specifically announced a National Policy on ISM&H to fully realize its potential and contribute more meaningfully and extensively to the public health service.

6.2 National Policy on ISM&H 2002

The Policy recognized the inadequacies of the prevailing situation and sought to address these through diverse means, mechanisms and measures. Specifically it sought to:

- Reform education in ISM&H to improve the quality of teachers and clinicians;
- Ensure the availability of quality raw materials for therapeutics;
- Specify and set drug standards and Good Manufacturing Practices;
- Reorient, prioritize and enhance research in ISM&H;
- Strengthen the Intellectual Property protection regime for TM;
- Integrate the ISM&H with the public healthcare delivery system and National Health Programmes and campaigns; and
- Raise the financial allocation for ISM&H in the Tenth Five Year Plan (2002–07) to 10% of the outlay on public health and by a further 5% every Five Year Plan period.

These policy pronouncements led to the establishment of a National Medicinal Plants Board and 30 similar State Boards to provide quality material for herbal drugs; 21 state and several private drug testing laboratories set up to facilitate conformance to specified quality assurance standards; and accelerated preparation of pharmacopoeial standards and formularies.

Today a vast infrastructure exists for ISM&H comprising 0.6 practitioners/1000 population (more than the allopathic doctors) and around 10,000 pharmacies or units producing, most often locally, the required therapeutics. ISM&H is thus poised to play an increasingly important and integral role in public healthcare programmes.

6.3 Innovations in TM

It must be recognized that TMs are best suited for lifestyle, degenerative and age related ailments rather than infectious diseases, which were not prevalent at the time of their development. Ayurveda accounts for more than 80% of the coverage of TM in India and is more than 3000 years old with a sound doctrinaire and experiential base. It was developed in an era when healthcare was administered by the physician preparing his own medications, customized to a patient's individual needs, or preparation of medicines at the household level. Original Ayurvedic formulations are thus in the form of teas, decoctions, ash residues, etc. to be dispensed as fresh as possible to provide maximum efficacy. The manufacture, distribution and storage at mass level and thus standardization were not envisioned then.

Innovations have thus been made by the industry to bring the TM formulations to contemporary dosage forms by concentration of the liquids, modifications in the physical form, developing appropriate delivery formats, increasing shelf life, ensuring stability in storage, enhancing sensorial acceptance, undertaking limited clinical trials for validating drug safety resulting from new forms and procedures for preparations, standardizing the formulations based on active markers and finger print profiles, and last, but not less importantly, adapting, modifying, and designing the processing equipment to handle the botanical materials at appropriate conditions. This has been a dynamic and continuing process, spearheaded by about a dozen of the large and leading companies and a few of the publicly-funded R&D and academic institutions. As an example, a recent innovation by CSIR provides quantitative scientific representations of various Ayurvedic concepts using three-dimensional HPLC techniques. This invention has been patented in the US and other countries as well.

6.4 Market for TM

The merchandising of Ayurvedic and Unani therapeutics dates back to the period around 1890 to 1920, when around ten Indian private sector companies were active in this area.

The current market for traditional medicines in India is estimated at around Rs.45 billion, but this does not include the dispensing of medicines prepared by the physicians for the patients. There are around 9,800 licensed pharmacies but the market is dominated by some 20 leading companies that command about 50% of the market share. Also, due to the low cost of such medicaments, the size of the market expressed in monetary terms is not an appropriate metric for deriving the volume of TMs.

6.5 TKDL – An Innovation to facilitate Intellectual Property Protection

In 1999, CSIR had successfully challenged the US patent granted for turmeric powder as a wound-healing agent, used in Ayurveda for centuries. This highlighted the need for systematic documenting, classifying and creating databases on traditional knowledge (TK) generally, and more particularly on the Indian system of medicines. The Third Plenary Session of the Standing Committee on Information Technology (SCIT) of WIPO, held in June 1999, also expressed similar concerns.

Accordingly, India (CSIR) took up the challenge to systematically document and classify its TK, initially targeting Ayurveda. The International Patent Classification (IPC) system was adopted as a model with information/data to be classified under the concerned section, class, subclass, group and subgroup to assist with patent searches. The IPC group AK61K35/78 relating to medicinal plants was expanded into about 5000 subgroups for greater definition of TK of medicinal plants. This classification system was named Traditional Knowledge Resource Classification (TKRC).

Using the TKRC, converting the knowledge available in fourteen Ayurvedic texts was taken up through a trans-disciplinary taskforce set up by the government in 2001. Linkages were also established with IPC Union of WIPO for assessment and adoption of the TKRC for inclusion in the IPC. WIPO established a multi-national taskforce to examine the issue, which recommended detailed level classification of medicinal parts, under IPC 1A61K36/00, by adding a sub-class and including 200 sub-groups in it. The Intergovernmental Committee of WIPO considered and accepted the changes proposed in the IPC. Around 36,000 ancient Ayurvedic formulations have been translated to modern day scientific and medical terminology classified as per the modified IPC subclass and put in digital format. More importantly, the system has now made it possible for all TK to be brought under IPC.

VII. International Cooperation in stimulating Capacity Building

India had and is continuing to greatly benefit from technical, financial, material, managerial and human resource inputs and assistance from international agencies, developed countries, and in more recent times, international not-for-profit organizations for capacity building in the healthcare sector. In the early years, the assistance was mainly for human resources development through training abroad and domestically, infrastructural development, and financial and material assistance. As India has advanced in the healthcare sector, the nature of the recent programmes has shifted towards capacity-building in the community for health delivery and networking, policy framework, etc. The on-going initiatives encompass a large number of programmes/projects; for example, there are more than 30 on-going programmes with more than 700 activities being implemented in collaboration with WHO.

VIII. Recommendations

Sub-regional pharmaceutical price control mechanism

Pharmaceuticals affect the very life and well-being of the people and cannot be priced as purely private goods. Thus the market, however perfect, may not be the right instrument for pricing of pharmaceutical products as the consumer (patient) does not have choice of the product. A social balance thus needs to be struck between the profitability of pharmaceutical companies and the equitable price for their products. Diverse social forms of price control are in vogue the world over. TRIPS does not debar such price controls. However for small nations, with limited bargaining or technological capacity, this may be difficult to do at the national level. It may be feasible to do so collectively by a few neighbouring countries on a sub-regional basis, for example Laos, Cambodia, Myanmar and Vietnam. It is thus suggested that a viable option for smaller and similarly placed sub-regional countries is to have a common social price control system. WHO could perhaps help stimulate and catalyze such sub-regional cooperation.

Public-Private Partnership for Enhancing Pharmaceutical Accessibility

Even in India, despite a flourishing pharmaceutical industry, allopathic products do not reach a majority of the population. Similar conditions prevail in many other developing countries. However, a few FMCG MNCs have established distribution channels for their products to the remotest locations in such countries (e.g. Hindustan Lever Ltd. in India). In order to extend the reach of pharmaceutical products to such locations, public-private partnerships could be solicited to make available OTC and infectious disease therapeutics to the rural areas.

Creating clarity and competence for compulsory licensing

The only instrument that TRIPS provides the least-developed and developing countries to mitigate the monopolistic, albeit differential or even preferential, pricing by the patent holders is through compulsory licensing. It is an unused tool even for those countries like India that have had the tool in their patent kit for some time. Initiatives at WHO level need to be taken to develop capacity and skills among countries with low technological capacity to apply and use the tool judiciously, perhaps through the preparation of a manual and organizing applicable training programmes.

Healthcare Affordability Index

The present study has shown that the cost of pharmaceuticals, drugs, vaccines and healthcare delivery services like doctors' consultation, in-patient and out-patient costs are several-fold lower in India, Bangladesh, Thailand, etc. as compared to most other

countries, even after applying the purchasing power parity factor. In order to have a more equitable and fair comparison of healthcare affordability by people in different countries, and thereby tacitly facilitate the MNCs to establish differential pricing of pharmaceutical products, a healthcare affordability index could be devised.

Innovative Capacity for Diagnostic Services

The emphasis in the present study is mainly to assess the innovative capacity developed in drugs, pharmaceuticals and biopharmaceutical sectors, which form an important aspect of curative and preventive healthcare. High-tech diagnostic services have come to play an equally important part in healthcare. The cost of these services is quite high, especially in developing countries. It may thus be useful to assess the innovative capacity developed for diagnostic kits, instruments, equipments and associated facilities as well.

Transcending Technological Capacity

The term 'innovative capacity' is being interpreted as 'the potential for innovation and technological capacity' along the lines of studies by Suarez-Villa, *inter alia*, on economic development, technology and patents. Thus, for the social sector of healthcare, the Suarez-Villa approach may not fully capture the spirit and the benefits of the new and effective (thus innovative) means, managerial systems, processes of delivery, and social and institutional mechanisms devised to reach healthcare to the disadvantaged sections of the people. Defining innovative capacity for the healthcare sector may thus need to transcend mere technological capacity to encompass other relevant aspects as well.

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