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## **Opportunities for UK Companies in Biopharmaceuticals and Biotechnology in Brazil**

Brazil as a strategic partner for Generics and Vaccines

**MAXIME RICHÉ**

MPhil in Bioscience Enterprise  
University of Cambridge

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## **Abstract**

Although Brazil is still sometimes categorized as an emerging market, especially in the field of Health biotechnology, pharmaceuticals and vaccines, it is to be considered with interest. Brazil's strengths lie in its scientific capabilities and the quality of the research being carried out in the biotechnology clusters and universities. In addition to this, the country has numerous assets, whether purely scientific or based on the great biodiversity of its territory. This is why opportunities exist for the UK to invest in Brazil, whether directly or through partnerships with local Brazilian companies.

Brazil has become one of the major interests of the UK Government, as the UK is lagging behind in terms of investments in this country. UKTI wanted to assess the opportunities in the biotechnology and pharmaceutical sectors in Brazil, and emphasize the benefits of collaborations with Brazilian firms in this area.

What are Brazil's strengths in the generics and vaccines area? Can they be translated into commercial value? This dissertation considers the trade opportunities for the generics pharmaceuticals and vaccines sectors. How is Brazil placed in these domains and does it represent a partner of choice or only an outsourcing opportunity? What are the prospects in a global market? How could UK Trade and Investment support UK investments in Brazil?

## Acknowledgments

I would like to thank Dr. Iain Cloughley, Danielle Duran, Belinda Clarke and Ian Bunker from the UKTI Biotechnology team. My great thanks to William Bains for his availability and advice, and to Eduardo Flores for support and opinions on this topic.

## About this report

This report was written for the **UKTI** department (UK Trade & Investment, a department of the Government of the United Kingdom and Northern Ireland, part of the Department of Trade & Industry – **DTI**) by Maxime Riché, and does not represent the views and opinions of the UKTI, DTI or any other government department. For queries about how this report was written, please contact the author at [maxime.riche@gmail.com](mailto:maxime.riche@gmail.com).

The author was educated as a Generalist Engineer at École Centrale de Lyon, France, and also holds a MS in Biomedical Engineering from Columbia University, New York. Since then, he has studied on the MPhil in Bioscience Enterprise Programme at the University of Cambridge and has had several experiences as a consultant in France and the UK throughout his training. The author speaks and reads Brazilian Portuguese.

## Methodology

In researching the current report, the author has interviewed 12 people who have experience in either the Brazilian biotechnology industry directly, biotech-related research, or who have an interest in Brazilian technology. These individuals were drawn from the UKTI's contacts in the UK and Brazilian industry and governments, contacts at the University of Cambridge and personal contacts.

Additionally, people based in the UK and who were working in relationship with Brazil, or had an interest in biotechnology in the UK were contacted in order to assess the particular needs of UK biotechnology and pharmaceutical companies, and their expectations of partnership opportunities in Brazil. Literature on the subject was researched both in Brazilian Portuguese and English.

## Limitations

This report was produced by a single person using UKTI contacts. Meaningful statistics are scarce and telephone interviews of senior executives and companies in Brazil could only provide some degree of information due to the limited time available to conduct each interview.

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## Abbreviations and acronyms

ANVISA	Agência Nacional de Vigilância Sanitária – National Agency for Health Supervision
API	active pharmaceutical ingredient
ARV	anti-retroviral
CAGR	compound annual growth rate
CRO	contract research organization
GCP	good clinical practices
GDP	gross domestic product
GMP	good manufacturing practices
NCE	new chemical entity
SME	small and medium enterprise

## Executive Summary

Brazil has a fast-growing economy attracting a great amount of foreign investment, even if corruption, regulatory problems, a very high level of government intervention and a constraining trade policy remain a concern. Brazil's research level is impressive, but technology transfer is much less active than in the UK. The pharmaceutical market has a current value of US\$ 8.3 billion and a 12% CAGR forecast to 2010. The vaccines market of US\$221 million in 2005 is still mainly publicly owned and has tremendous expertise and production capabilities. The potential for new vaccines is evidenced by the increasing involvement of multinationals. The generics segment, worth US\$717 billion in 2005, is much more consolidated, with only 5 local companies accounting for 75% of the market, and numerous foreign players trying to get their share.

The regulatory framework has considerably improved and makes Brazil a preferred gateway to other Latin American markets.

- The 1996 Intellectual Property law now recognizes the patentability of pharmaceutical products.
- The 2005 Innovation law supports public-private partnerships in research.
- The 2005 Tax law will give more dynamism to private investments.
- The 2005 Biosafety law regulates biotech activities.
- Drug approval requirements are of the highest standard.

These new laws will support local and foreign investments and enhance Brazil's business environment.

The best opportunities for partnerships are:

- **In Vaccines:** R&D collaborations in new vaccines formulation, and building on the Brazilian expertise for expansion of manufacturing capabilities for lower margin vaccines for exportation, supported by UK Private investments.
- **In Generics:** bringing primary manufacturing and APIs capabilities to Brazil to tackle a huge and growing market. Increase of manufacturing capabilities for exportation.

Additionally, collaborations for clinical trials and new drug discovery for high quality products, based on biodiversity, are of great interest. Products with higher value can be achieved by investing in R&D and not only production.

To make these collaborations happen, on the Brazilian side, there is a call for:

- Increased communication about Brazilian research.
- Programs to identify the best university research programs and to organize technology visits in the UK, to make contacts with local firms.
- Communicating about the local market requirements and its potential.
- Developing private research
- Identifying win-win mechanisms for partnerships between public and private companies in higher margin products that do not fit the Ministry of Health requirements.

On the UK side, there is a need to:

- Communicate to UK industrial players the changes in Brazil.
- Send representatives of some UK SMEs to Brazil to realize the potentialities of the country to improve their perception. Forging contacts in Brazil is of prime importance as a local partner is required to give transparency to the collaborative process.
- Engage as much as possible with the Brazilian government to help market requirements and regulations move in the right direction, as well as suggest the most necessary improvements.

The UK can bring its culture of business and risk capital.

## Preface

### 1. Presentation of UKTI<sup>1</sup>

UKTI is the British Government organization supporting companies in the UK trading internationally, and overseas enterprises seeking to invest in the UK.<sup>2</sup> Funded partly by the Foreign Office (FCO) and the Department of Trade and Industry (DTI), UKTI acts as a support to help British companies succeed in global business.

UKTI is divided into Trade and Investment sections. The Trade Section incorporates sector groups, one of which is biotechnology, and regional market (geographical) desks. Within the UK it operates via regional International Trade Teams (ITTs) and sector specialists; overseas, teams of Commercial Officers are based in British Embassies and Consulates. UKTI works closely with both the FCO and DTI, which also play a role promoting British science and innovation (see Appendix 1).

The biotechnology sector team was established in 2003, based in Cambridge, to provide mentoring, networking, partnering and development support for biotech companies. The team gives independent advice to companies wanting to expand overseas, helps with information gathering (particularly commissioning market research overseas), offers grants and support for companies to travel abroad, and encourages publicity at key conferences.

### 2. Scope of the project

Brazil has become a major interest of the UK Government, as the UK investments are lagging behind in this country. UKTI wanted to assess the opportunities in the biotechnology and pharmaceutical sectors in Brazil, and emphasize the benefits of collaborations with Brazilian firms in this area.

This dissertation is based on the research conducted as part of an internship with UKTI in April-June 2006. Primary sources included interviews with UK and Brazilian Industry members or researchers, UK companies, regional networks and UKTI and international trade advisers. This was backed up by a literature search, including scientific journals, relevant company and association websites and market reports. Previous work done within UKTI included a Biotech Scoping Mission to Brazil conducted by Dr J. B Cloughley, Dr R. New and Dr. B Clarke in September 2005.

The dissertation begins by giving an overview of the Brazilian pharmaceutical, generics and vaccines markets, as well as the regulatory framework regarding patents and innovation. Chapter Three brings in a critical analysis of some scenarios for collaboration between UK and Brazilian companies, before to introduce potential hurdles that may have impeded them in the past. Conclusions and methods to form partnerships are considered in Chapter Four.

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<sup>1</sup> From Nicola M R Perrin, The Global Commercialisation of UK Stem Cell Research, June 2005

<sup>2</sup> [www.uktradeinvest.gov.uk/ukti](http://www.uktradeinvest.gov.uk/ukti)

## Chapter 1

### **Brazil – Country Statistics and Introduction to the Biotechnology, Generics and Vaccines Markets**

#### ***Abstract***

*Brazil is a rapidly growing economy attracting a great amount of foreign investment, with strong growth in health and biotechnology and substantial capabilities in vaccines and generics, but it is still hindered by some regulatory heaviness and corruption.*

# 1. Country statistics<sup>3</sup>



Figure 1: Map of Brazil

Brazil is the largest country of Latin America, covering an area of 8,511,965 square kilometers. It is divided into 26 states and a Federal District and had a population of 186.1 million people in 2005, predominantly still young, with a growth rate of 1.15% over the past 5 years. Growth forecasts can be seen in Figure 2. The country has the largest economy in Latin America, with a GDP of US\$619.9 billion and a GDP per capita of US\$ 3,510 in 2005, but exhibits one of the most profound social inequalities in the world with 63.4% degree of income inequality, as seen in Figure 3. Net foreign direct investments accounted for US\$ 9.3 billion in 2005<sup>4</sup>.

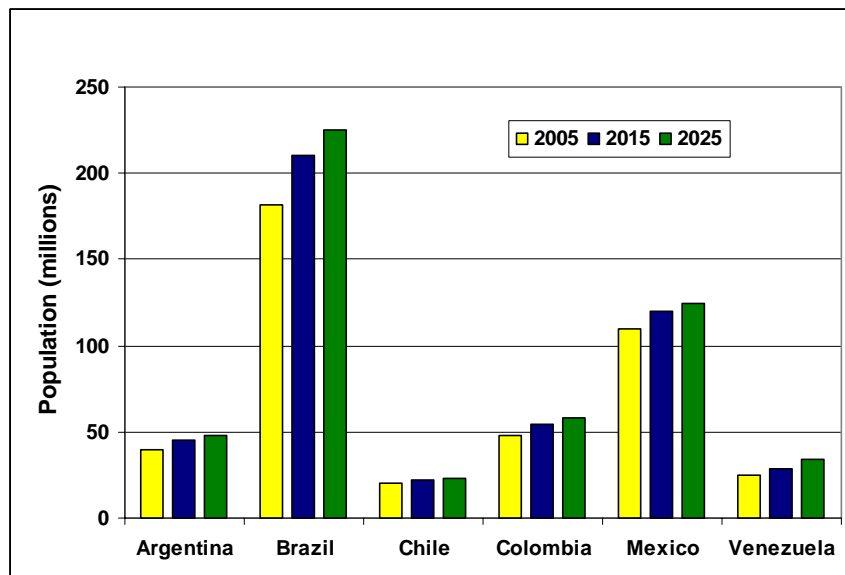
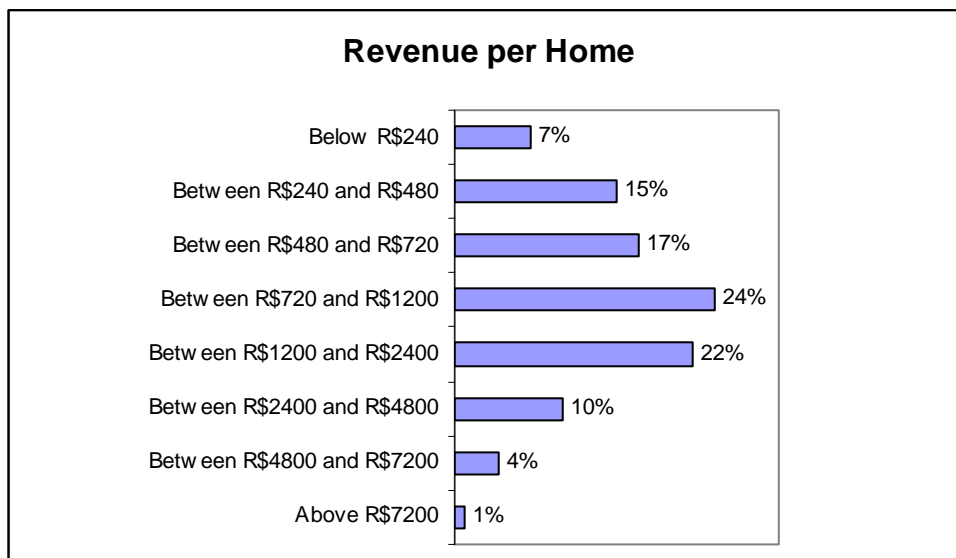


Figure 2: Population growth forecast in Latin America

Source: United Nations Population Division

<sup>3</sup> This part is based on the Index of Economic Freedom data from the Heritage Foundation, [www.heritage.org](http://www.heritage.org)

<sup>4</sup> Source: The Heritage Foundation



**Figure 3: Revenue profile of Brazilian homes**

Source: Grupo Pro Genericos, Consumer Profile and study of buying decision criteria for generic drugs in Brazil. 1R\$ = about 2.25 - 2.5US\$ in 2005

The exports of goods and services accounted for US\$ 87.9 billion in 2005, Brazil's major export trading partners being the USA (22.9%), Argentina (6.2%), China (6.2%), The Netherlands (5.8 %) and Germany (4.3%). Brazil's imports of goods and services accounted for US\$ 63.8 billion this year, with major import trading partners being the USA (20.1%), Argentina (9.6%), Germany (8.7%) and Japan (5.2%).

### Foreign Investment

Foreign capital may enter Brazil freely. The Ministry of Development has tried to simplify the process of setting up new companies, currently still relatively complex. Restrictions remain on foreign investment in nuclear energy, health services, media, rural property, fishing, mail and telegraph, aviation and aerospace.

### Monetary Policy

From 1995 to 2004, Brazil's average annual rate of inflation was 8.65%. Below is a table showing Brazil's Inflation rates over the past years.

Year	Inflation Rate (%)	% Growth
2001	7.7	
2002	12.5	63.30%
2003	9.3	-25.80%
2004	6.0	-35.50%
2005	4.8	-20.60%

**Table 1: Brazil inflation, 2001-2005**

Source: Datamonitor

Brazil's top income tax rate is 27.5%. The top corporate tax rate is 25%.

## Regulation

Brazil's administrative structure is still heavy and not entirely transparent. Legal requirements to start a business still call for about 100 different documents according to a study by Brazil's small-business association, with the result that 70% of entrepreneurs who try to open a business legally never conclude the process. The labor market is still quite rigid.

## Corruption

Brazil's Corruption index is 3.7 out of 10 (1 being the most corrupt)<sup>5</sup>. Therefore, corruption is still a problem in business in Brazil, but varies greatly depending on the region and is not always openly perceptible.

## Trade Policy

Brazil is a member of the Southern Cone Common Market (MERCOSUR), and adheres to a common external tariff that ranges from zero to 25 percent. The government places controls on certain imports, and the custom clearance was qualified by the U.S. Department of Commerce as one of the slowest in the Western Hemisphere.

**The 2006 Index of economic freedom ranks Brazil at the 81<sup>st</sup> position.** This index gives a documented indicator for the degree of economic dynamism of the country' and its freedom from economic, governmental, or informal and corruption-related actuators. The factors studied are given a mark on a scale of 5 (5 being the worst score)<sup>6</sup>, by 0.5 increments and are given in the Table below.

<b>Global score</b>	<b>3.08</b>
Trade Policy	3.5
Fiscal Burden	2.8
Government Intervention	4.0
Monetary Policy	3.0
Foreign Investment	3.0
Banking and Finance	3.0
Wages and Prices	2.0
Property Rights	3.0
Regulation	3.0
Informal Market	3.5

**Table 2: Brazil indicators for 2006**

Source: Index of Economic Freedom, The Heritage Foundation

Below are tables giving the general score of selected Latin American countries for the past years. Average score in 2006 is 3.02 and median score is 3.03. Brazil's scores have slightly worsened since 2003, but remain within the norm of most advanced countries in Latin America.

<sup>5</sup> Index of Economic Freedom score, Heritage Foundation, [www.heritage.org](http://www.heritage.org)

<sup>6</sup> Characteristics for each score can be found at:

[http://www.heritage.org/research/features/index/chapters/htm/Index2006\\_Chap5.cfm](http://www.heritage.org/research/features/index/chapters/htm/Index2006_Chap5.cfm)

Country	2006 Economic freedom score	Corruption index*	GDP/capita in \$
Argentina	3.30	2.8	7,165
Belize	2.78	3.7	3,635
Bolivia	2.96	2.5	1,017
Brazil	3.08	3.7	3,510
Chile	1.88	7.3	5,872
Colombia	3.16	4.0	2,017
Costa Rica	2.69	4.2	4,410
Cuba	4.10	3.8	2,516
Mexico	2.83	3.5	5,877
Paraguay	3.31	2.1	1,407
Peru	2.86	3.5	2,131
Uruguay	2.69	5.9	5,235
Venezuela	4.16	2.3	4,009
United Kingdom	1.74	8.6	26,391
United States	1.84	7.6	36,067

\* The Corruption index ranks countries on a scale of 1 to 10, with 1 being the most corrupt.

Note: Shading indicates two or more instability risk factors such as high poverty, low educational attainment, unfree political system, or unfree economy.

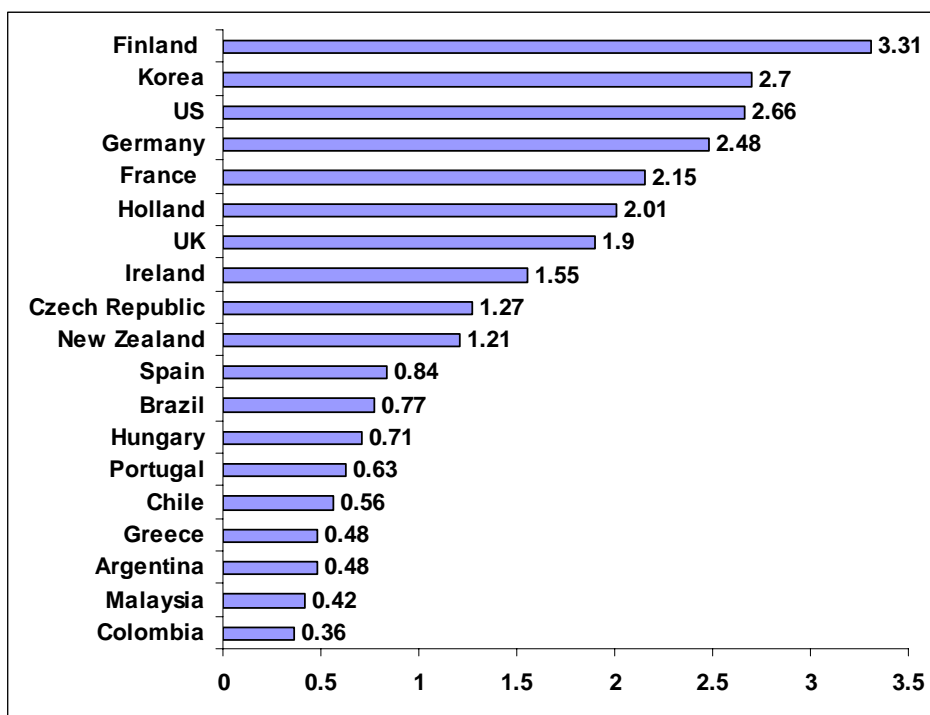
**Table 3: Selected Country indicators in Latin America**

Source: 2006 Index of economic freedom, Heritage Foundation, 2006, [www.heritage.org](http://www.heritage.org)<sup>7</sup>

<sup>7</sup> For a description of the methodology used to compute these scores, as well as further information on rankings and sources, see <http://www.heritage.org/research/features/index/index.cfm> and [http://www.heritage.org/research/features/index/chapters/htm/Index2006\\_Chap5.cfm](http://www.heritage.org/research/features/index/chapters/htm/Index2006_Chap5.cfm)

## 2. General characteristics of academic research and technology transfer

Latin America in general is characterized by lower investments in R&D as a % of GDP than in European or North American countries. In Brazil, 0.77% of GDP was invested in R&D in 2003. Most R&D is financed directly by the Brazilian Government (18.4%) or through Universities (43.6%), with a lower role for the private sector (37.4%), which is reflected in a lower rate of patenting (0.081 patents/GDP/capita, compared to 2.66 for the USA and 0.19 for the UK)<sup>8</sup>.



**Figure 4: Investment in R&D as a percentage of GDP for selected countries**

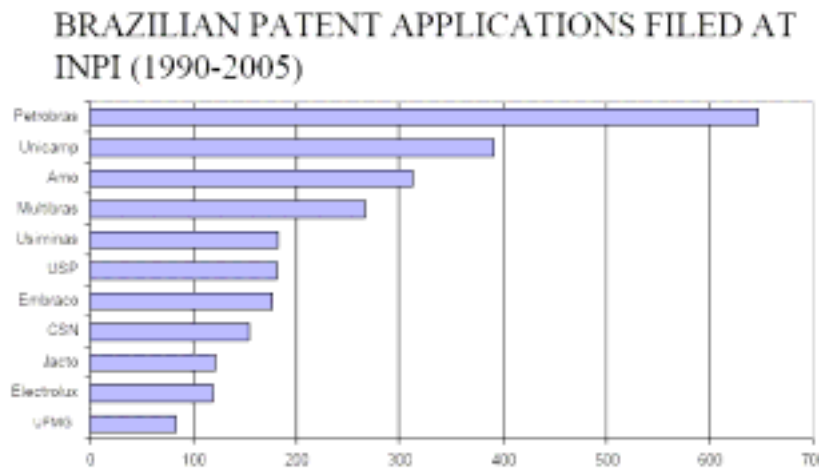
Source: The Global Competitiveness report, 2002-2003. From Rosana Ceron DI Giorgio.

Additional data from [www.nsf.gov](http://www.nsf.gov) and DTI

The characteristics of technology transfer in Brazil therefore follow a pattern consistent with the overall characteristics of the R&D. If a university research program is funded by the government, the resulting IP belongs to the university, and a national patent application may be funded by the university or the government, or in some cases by the inventor. An international application will not generally be pursued without financing from a licensee.

The Technology Licensing Offices, if existing, usually are only nascent, university-operated business incubators are commonplace in Brazil. Below is a figure showing some of the most active patenting bodies in Brazil between 1990 and 2005. It is noticeable that Unicamp, USP and UFMG are universities.

<sup>8</sup> Source: OECD (2003) and RICyT (2001) indicators, [www.nsf.gov](http://www.nsf.gov) and DTI



**Figure 5: Brazilian patent applications filed at INPI (National Institute for Intellectual Property) (1990-2005)**

Source: Rosana Ceron Di Giorgio, Unicamp, University Technology Transfer Practices in Latin America, LES International Conference 2005

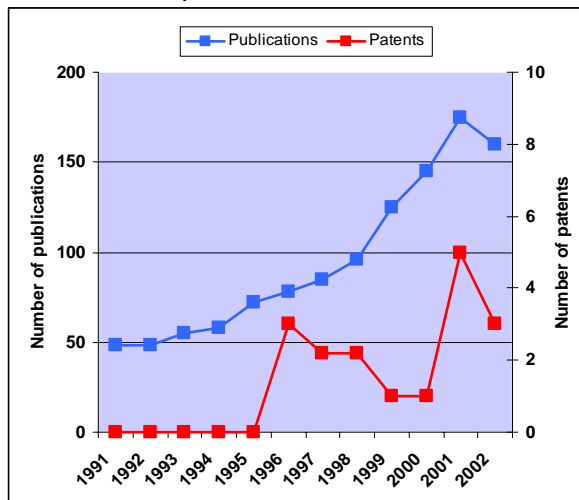
The academic sector in Brazil is highly dynamic. Major state universities possess a very strong research base and a large pool of graduate PhD and Master’s students in all disciplines.

### 3. The biotechnology sector

#### The academic participation

The Brazilian biotechnology sector is characterized by a high number of publications in health biotechnology. The government has been encouraging biotechnology developments since the 1970s, by launching the Integrated Program on Genetics (PID) and the Integrated Program on Tropical diseases (PIDE) and later, the National Biotechnology Program (PRONAB) in 1981.

In the last fifteen years, Brazil’s participation in International scientific publications increased from 0.5 to 1.5%. Presently, the Brazilian scientific output in the sector accounts for nearly half of what that is produced in Latin America. Below is a graph of Brazil’s number of publications and patents.



**Figure 6: Brazilian publications and USPTO patents in health biotechnology (1991-2002)**

Source: Nature Biotechnology, 2004

Brazil is carrying out cutting-edge research in tissue engineering and stem cells and has launched one of the world's largest treatment trials for patients with heart disorders, backed by 1,200 patents. Phase I and phase II studies with stem cells have also been initiated in cardiac, neurological and hepatic diseases.

Brazil has a major strength in genome sequencing (GENOMA project). Sequencing projects have been successfully completed for 5 plant pathogens, and several programs are under work for eucalyptus (GENOLYPTUS), rice (ORYGENS), banana (MUSA Genome) and the whole sequencing for *Bos indicus* has been completed.

Brazil was one of the first countries to develop the cloning of cattle on the commercial scale, and the technique is now well established<sup>9</sup>.

The biotechnology sector is in frank expansion in Brazil, backed by a governmental policy, the Forum of Competitiveness in Biotechnology, set in September 2004 to define strategies to implement biotechnology in Brazil. The government is to vote on it in July/August 2006. Identified niches of opportunities are:

- Human Health
- Vaccines
- Biomaterials
- Industrial Enzymes
- Biopolymers
- Diagnostic kits
- Natural pharmaceuticals
- Phytotherapies
- Agribusiness
- Biomass, biofuels

### **The industry**

Brazil is promoting the biotechnology sector to stimulate industrial development. The Federal Government continuously improves its policy concerning foreign capital investment, simplifying its regulations for goods and services, and facilitating imports of equipment. US\$5 million were invested in a biotechnology center in the Amazon region, the Amazon Biotechnology Center, with 20 laboratories, established in 2002 to promote research of profitable pharmacological drugs and to boost the sector in the region<sup>10</sup>.

### **Venture Capital in biotechnology**

This sustained interest for biotechnology is attracting Venture Capitalists at a fast growing rate. Votorantim Ventures, FIR Capital and Rio Bravo had resources representing US\$300 million, US\$45 million, and US\$10 million respectively in 2003. The Votorantim Group, the largest Brazilian industrial conglomerate, has agreements to develop biotechnology research with most of the important Brazilian Universities<sup>11</sup>.

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<sup>9</sup> J.B. Cloughley, R. New, B. Clarke, UKTI Biotech Scoping Mission to Brazil, November 2005

<sup>10</sup> Vania Resende, The Biotechnology Market in Brazil, International Market Insight, Dec. 2003

<sup>11</sup> *ibid*

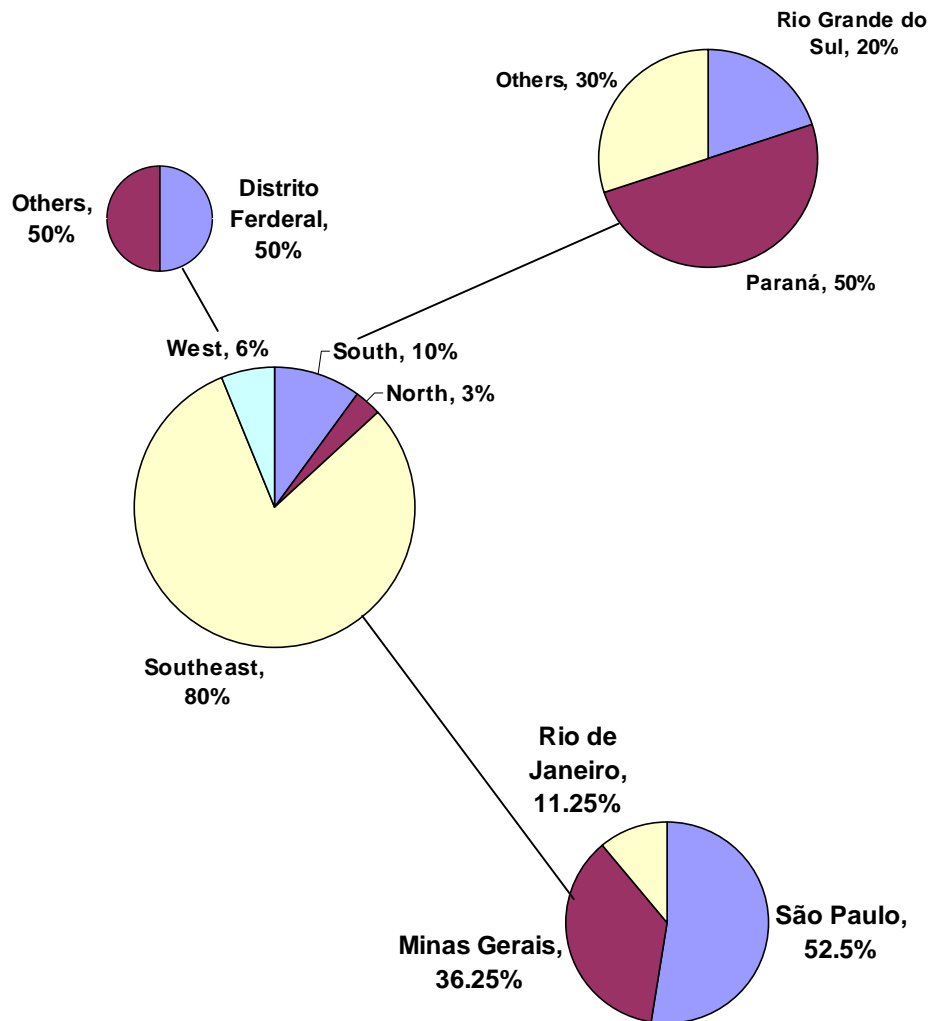
### 3.1 The main Brazilian biotechnology clusters

This information is from Vania Resende, *The Biotechnology Market in Brazil, International Market Insight*, December 2003.

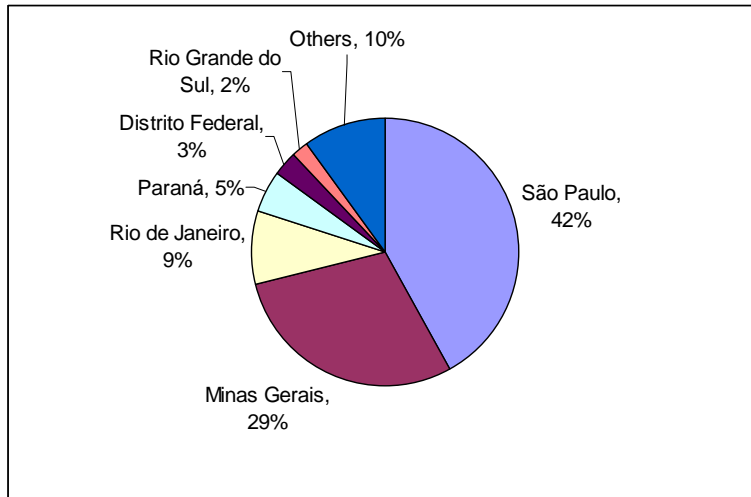
There are three main biotechnology clusters in Brazil:

- The Minas Gerais cluster centered around Belo Horizonte
- The Bio-Rio cluster in Rio de Janeiro
- The São Paulo cluster

Apart from these established biotechnology centers, additional centers are emerging in the states of Paraná, Santa Catarina, Rio Grande do Sul, Distrito Federal, Goiás, Mato Grosso do Sul, Pernambuco, Paraíba and Pará.



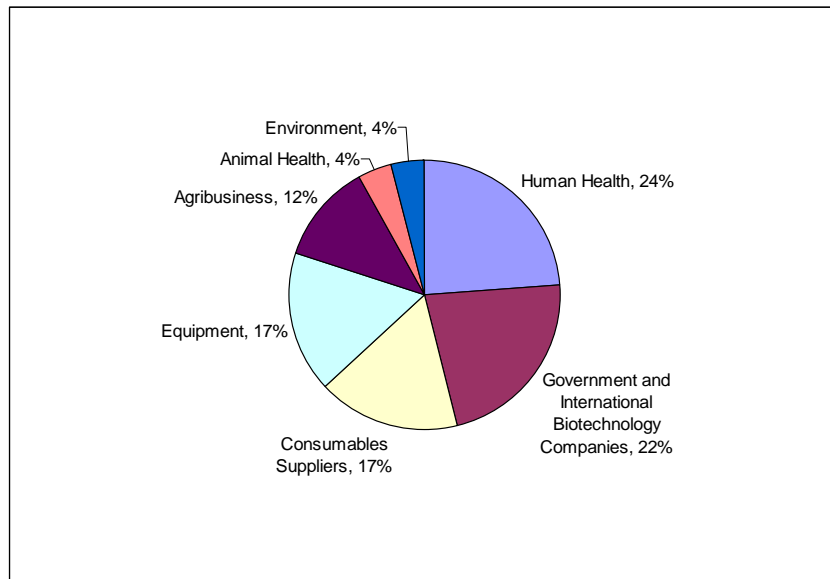
**Figure 7: Breakdown of Brazilian biotechnology companies per region and state**  
 Data from: *The Biotechnology Market in Brazil* <http://www.stat-usa.gov> and Biominas Foundation.  
**Note: percentages indicated as contribution to a region's contribution**



**Figure 8: Breakdown of Brazilian biotechnology companies per state**

Data from: Vania Resende, The Biotechnology Market in Brazil <http://www.stat-usa.gov> and Biominas Foundation. **Note: percentages indicated as contribution to total value and not as percentage of a region’s contribution**

The breakdown by segments is shown in the Figure 21 and the largest pharmaceutical and biotechnology companies conducting research, investment, and production are indicated in Table 25.



**Figure 9: Breakdown of Brazilian biotechnology companies per segment**

Source: The Biotechnology Market in Brazil <http://www.stat-usa.gov> and Biominas Foundation

Region	Company
Northeast	Biogene, TMED
Southeast	Genesearch, Biominas, Biobrás, FAPESP, Biosoft, Fiocruz, Interbiotech, In vitro, Hormogen, Microbiológica, Nichols, Instituto Butantan
South	SIMBIOS, Nano Endolumial, FK Biotec

**Table 4: Major pharmaceutical and biotechnology companies per region in Brazil**

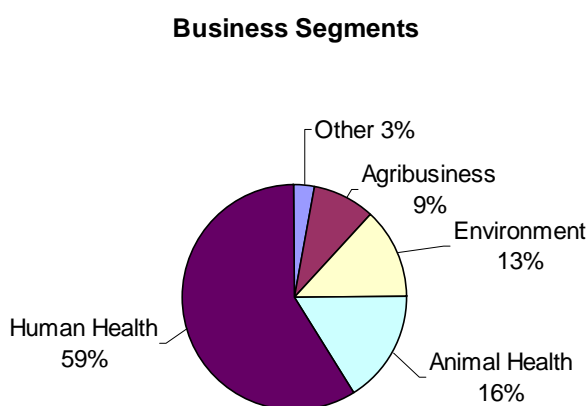
Source: The Biotechnology Market in Brazil <http://www.stat-usa.gov> and Biominas Foundation

### 3.1.1 The Minas Gerais Cluster

The most important biotechnology center in Latin America is centered around Belo Horizonte, the capital city of the southeastern state of Minas Gerais, with about 60 companies located in and around Belo Horizonte itself<sup>12</sup>.

#### Company segments in the Cluster

The main companies present in the Minas Gerais cluster can be broken down by activity as shown below.



**Figure 10: Business segments in the Minas Gerais Cluster**

Source: Foundation Biominas

Sector	Companies
Human diagnostics	Diamed, CEPA, In Vitro, Biobrás Diagnósticos, Labtest, Hereditas, Microbiológica, Bionn, Biocod, Biokits, Diagon, Katal, Micra, Analisa Diagnóstica, Bioeasy, Gene, Quibasa
Pharmaceuticals	Biofar, Bravir, Biobrás Div. Farmacêutica, Belfar, CIFARMA, Hipolabor, FUNED, Laboratório Globo, Hypofarma, Osório de Moraes, Quiral
Support services	Biobrás Software, Biotech Agency, Cetec, EMLAB, Fundação Biominas, LM Laboratório de Biotecnologia, René Rachou, Santa Casa de Misericórdia, and Theriaga
Biomaterials	Einco Biomaterial, Ferrara Ophthalmics, JHS, Labcor, Tri-Technologies
Veterinary	Vallée, Hertape, Tecsa, Phoneutria, and Lema Biologic
Phytotherapeutics	Belém Jardim, Catedral, and Caiçara
Environment	LM and Biológica
Equipment manufacturers	R.Chapman and Spectrolab
Industrial firms	CONAP and Biocarbo
Agro-biotechnology	Santa Helena Sementes

**Table 5: Main companies in the Minas Gerais cluster by segment**

Source: The Biotechnology Market in Brazil <http://www.stat-usa.gov> and Biominas Foundation

<sup>12</sup> Inter-American Development Bank (IDB)

The **Fundação Biominas** is a business incubator, and was granted the Anprotec Award for the best incubator in Brazil in 2004. It has incubated 12 companies that have been spun out since 1997 and have generated cumulative sales of R\$49million in 2004. The Foundation is currently incubating an equal number of companies and works in relation at the State and Federal level with the Bioindustry Development program and the Forum of Competitiveness in Biotechnology, as part of the Federal program of Industrial, Technological and External Trade Policy (Politica Industrial, Tecnológica e de Comercio Exterior – PITCE).

The foundation reports that the Minas Gerais cluster is still in its early stage of development, with young companies of 50 employees per company on average and a third of companies of three years or less, and a third between 3 and 7 years of maturity<sup>13</sup>.

### 3.1.2 The Rio de Janeiro cluster – Bio-Rio

The Biotechnology cluster in the State of Rio de Janeiro is called Bio-Rio. Besides being an incubator, it is an industrial park regrouping companies in various sectors as shown in the table below.

Sector	Companies
Stations to Treat Effluents and Equipment for the Purification of Water	AMBIO
Diagnostic Kits, Culture Media and Quality Control Analysis	Baktron
Pharmaceutical Products	Brasco
Cosmetics	Dalmatia
Production through Biodegradation of Organic Materials used to Treat Effluents	Ecobac
Research and Development of Natural Molecules	Extracta
Pharmaceutical Products	M & N
Enteral and Parenteral Nutrition and Chemotherapy	Nutriente
Software to Control Processes and for Practice	Q-Controll
Labs of Medicines and Antiseptics	Silvestre
Advisory in the Elaboration of Protocols and Analysis of Data in the area of Health	Trianel
Diagnostic Kits	Vectron
Micro-propagated Sprouts	Vitrogen

**Table 6: Companies by segment in the Bio-Rio cluster**

Source: Vania Resende, The Biotechnology Market in Brazil, STAT-USA: <http://www.stat-usa.gov>

<sup>13</sup> Data from Foundation Biominas

### 3.1.3 The São Paulo Cluster

The research carried out in the state of São Paulo is of great importance for the overall Brazilian Biotechnology landscape, as the top four Bio-Science Research Universities in Brazil are located in the State of São Paulo as indicated below.

University	Location	Patents
University of São Paulo	São Paulo, SP	Biodiversity, Genoma Project, Animal Toxines
University of Campinas	Campinas, SP	Biodiversity, Genoma Project, Animal Toxines
Paulista State University	São Paulo	Biodiversity, Genoma Project, Animal Toxines
Federal University of São Paulo	São Paulo	Health, Medicine

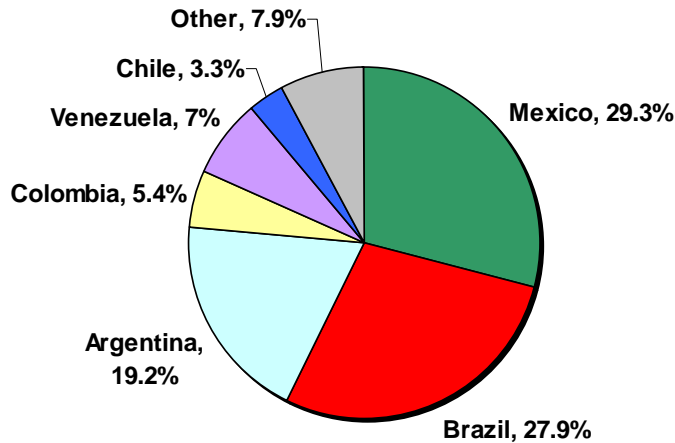
**Table 7: São Paulo State universities contributing to research in Brazil and patents held**

Source: Vania Resende, The Biotechnology Market in Brazil, STAT-USA: <http://www.stat-usa.gov>

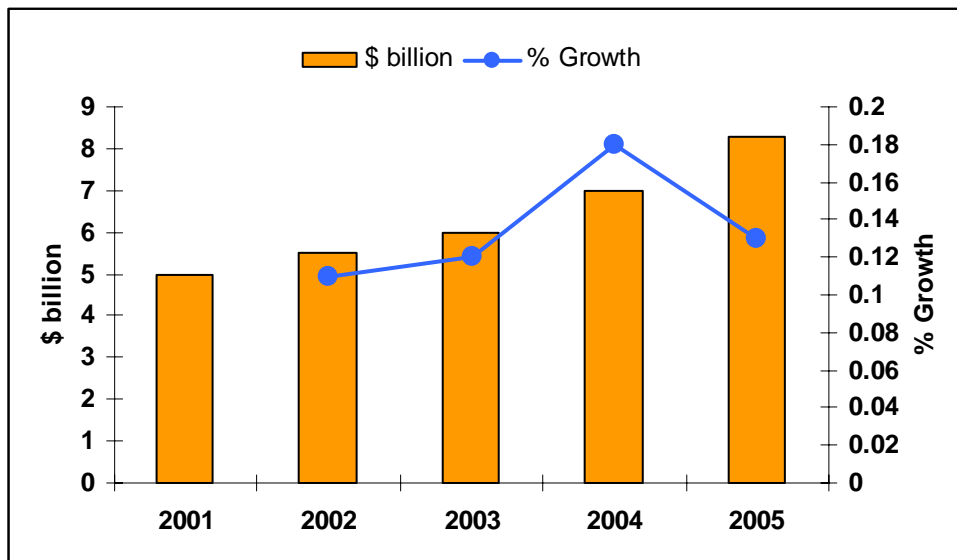
## 4. The pharmaceutical sector

### 4.1. Characteristics

Brazil's pharmaceutical market is the 11<sup>th</sup> largest in the world and second in Latin America after Mexico since the devaluation of 2001. It had a value of **US\$8.3bn in 2005**<sup>14</sup> and should continue to grow at a 12% CAGR to reach US\$ 14.6bn in 2010. In comparison, the Canadian pharmaceuticals market was worth \$11.3 billion in 2005.



**Figure 11: The Latin American pharmaceutical market in 2004**  
Source: La Federación Latinoamericana de la Industria Farmacéutica



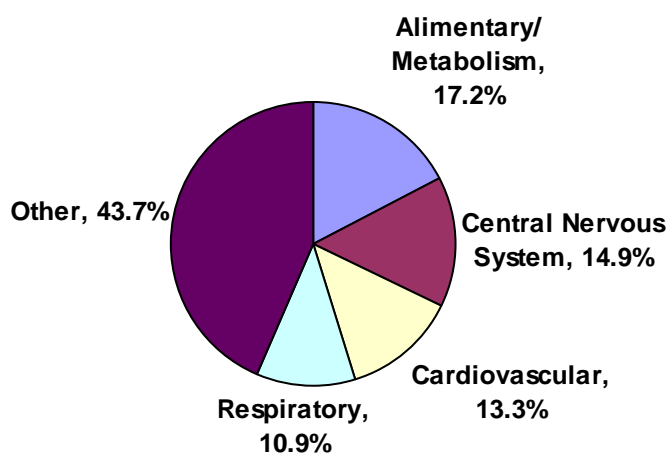
**Figure 12: Brazil pharmaceutical market value in US\$ billion, 2001-2005**  
Source: Datamonitor, December 2005

Brazil possesses a large consumer base, as the population is ageing and growing rapidly. There are no medicine reimbursement schemes, but the Government provides medicine

<sup>14</sup> Datamonitor, Pharmaceuticals in Brazil, Industry Profile, December 2005

for enrolled patients for specific diseases, e.g. diabetes, HIV, and hemophilia. New legislations should require private health insurers to partially reimburse the costs of medicines, which could make the pharmaceutical market grow considerably.

Skincare products, vitamins and minerals represent the top segment and it is estimated that the whole natural medicine market will increase up to 20% per year<sup>15</sup>.



**Figure 13: Segmentation of the pharmaceutical market. Share by value**

Source: Datamonitor, December 2005

The leading therapeutic classes and products as compared to other markets are introduced in Tables 8 and 9.

	<b>USA</b>	<b>Europe</b>	<b>Japan</b>	<b>Latin America</b>
<b>1</b>	Cholesterol Reducers	Cytostatics	Cytostatics	<b>Anti-rheumatic, non-steroid</b>
<b>2</b>	Anti-depressants	Cholesterol Reducers	Anti-ulcerants	<b>Non-narcotic Analgesic</b>
<b>3</b>	Anti-ulcerants	Anti-ulcerants	Calcium Antagonist, Plain	<b>Hormonal Contraceptive</b>
<b>4</b>	Cytostatics	Anti-depressants	Cholesterol Reducers	<b>Anti-ulcerants</b>
<b>5</b>	Anti-psychotics	Angiotensin-II Antagonists	Angiotensin-II Antagonists	<b>Broad Spectrum Penicillins</b>
<b>6</b>	Anti-epileptics	Non-narcotic Analgesics	Cephalosporins & Combs	<b>Anti-depressants</b>
<b>7</b>	Erythropoietins	Anti-rheumatics, Non-steroid	Anti-rheumatics, Topical	<b>Cholesterol Reducers</b>
<b>8</b>	Anti-rheumatics, Non-steroid	Anti-psychotics	Platelet Aggregation Inhibitors	<b>Infant Formula</b>
<b>9</b>	Narcotic Analgesics	Calcium Antagonists, Plain	Anti-histamines, Systemic	<b>Anti-epileptics</b>
<b>10</b>	Anti-diabetics, Oral	Ace Inhibitors, Plain	Anti-diabetics, Oral	<b>Cephalosporins &amp; Combs</b>

**Table 8: Leading therapies by region**

Source: IMS Health, Dec 2004, From Jorge Raimundo, Global vision of the pharmaceutical industry, August 2005

<sup>15</sup> Danielle Duran, Sonia Guida, UKTI Market Summary, Pharmaceuticals & Biotechnology, Brazil, July 2005

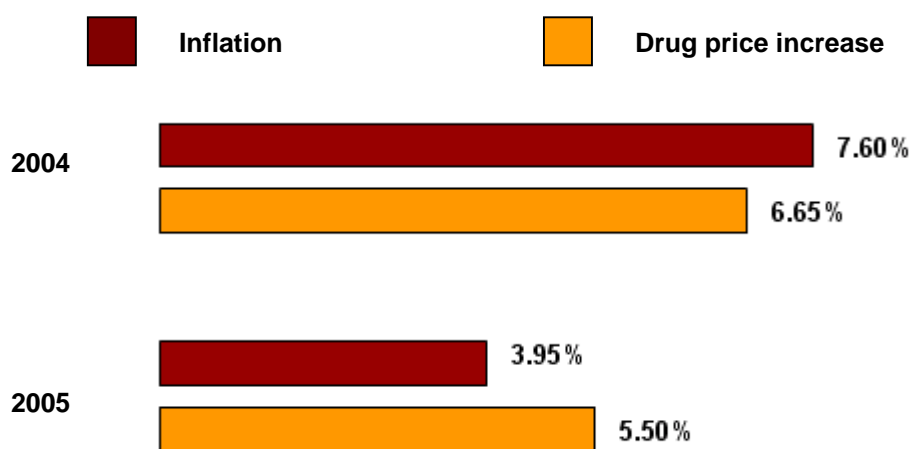
Rank	Product	Rank	Product
1	Voltaren	6	Xenical
2	Viagra	7	Nan
3	Asprin Bayer	8	Novalgine
4	Lipitor	9	Cialis
5	Celestone	10	Plavix

**Table 9: Leading products in Latin America**

Source: IMS Health, Dec 2004, From Jorge Raimundo, Global vision of the pharmaceutical industry, August 2005

**Future Trends**

The average drug price increase as compared to the inflation in 2004 and 2005 shows the Brazilian market is evolving toward a mature market stage and away from an emerging pharmaceutical market stage.

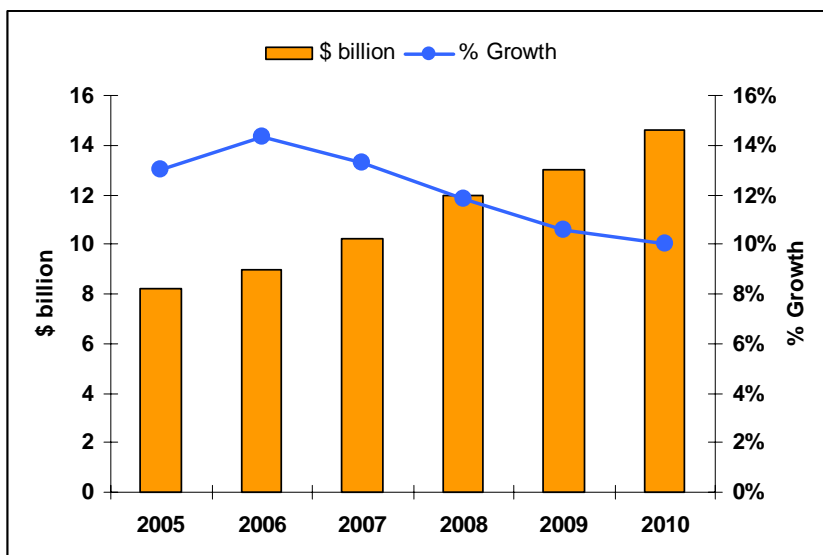


**Figure 14: Average drug price increase 2004-2005 as compared to inflation**

Source: [www.info4.com](http://www.info4.com)

In coming years, the Brazilian market is forecast to decelerate its current performance, with 12% CAGR until 2010, which should drive its value to \$14.6 billion. In comparison, the Canadian market is also expected to decelerate its current performance, with a forecast market value of \$15.5 billion in 2010<sup>16</sup>.

<sup>16</sup> Datamonitor, Pharmaceuticals in Brazil, Industry Profile, December 2005



**Figure 15: Brazil pharmaceutical market value forecast in US\$ billion, 2005-2010**  
Source: Datamonitor

Brazil’s market is clearly a key market to drive the global development of any pharmaceutical company with international ambitions, and many have located regional headquarters in the country.

## 4.2 Major players

Brazil has over 350 pharmaceutical companies – 25% multinationals, 70% local private laboratories and 5% state-owned. Foreign companies account for approximately 60% of the domestic market, and most leading world pharmaceutical companies have operations in Brazil, as shown below.

	USA	Europe	Japan	Latin America
1	Pfizer	Sanofi-Aventis	Takeda	Pfizer
2	GlaxoSmithKline	Pfizer	Pfizer	Sanofi-Aventis
3	Johnson & Johnson	GlaxoSmithKline	Roche	Roche
4	Merck & Co.	Novartis	Otsuka	Novartis
5	AstraZeneca	AstraZeneca	Sankyo	GlaxoSmithKline

**Table 10: Leading corporations by region**

Source: IMS Health, Dec 2004, From Jorge Raimundo, Global vision of the pharmaceutical industry, August 2005

### State-owned pharmaceutical manufacturers

The network of 18 public laboratories listed in Table 11 is established in different entities such as the Ministry of Health, the Armed Forces, state governments and universities, and produce medicines and biologicals to supply the public health system. The existing production capacity is estimated at 11 billion pharmaceutical units per year as shown in Table 12.

<b>Northeast Region</b>	State Pharmaceutical Laboratory of Pernambuco –L AFEPE Pharmaceutical Laboratory of Alagoas – LIFAL State Pharmaceutical Laboratory of Paraíba – LIFESA Center for Research on Food and Medicines (RN)– NUPLAN College of Pharmacy, Dentistry and Nursing – UFC – FFOE Pharmaceutical Technology Laboratory – UFPB – LTF
<b>Southeast Region</b>	Institute of Technology in Medicines – FARMANGUINHOS Ezequiel Dias Foundation – FUNED Foundation for Popular Medicines – FURP Vital Brazil Institute – IVB Air Force Chemical and Pharmaceutical Laboratory – LAQFA Navy Pharmaceutical Laboratory – LFM Army Chemical and Pharmaceutical Laboratory – LQFE
<b>Southern Region</b>	Pharmaceutical Laboratory of Rio Grande do Sul – LAFERGS Pharmaceutical Laboratory of Sta. Catarina – LAFESC Laboratory of Teaching and Research in Medicines and Cosmetics – LEPEMC Medicines Production Laboratory – LPM
<b>West-Central Region</b>	State Chemical Company of Goiás – IQUEGO

**Table 11: Distribution of public laboratories by region**

Source: Jorge A. Z. Bermudez, M.A. Oliveira, Intellectual Property in the Context of the WTO TRIPS Agreement: challenges for public health, Sept 2004

The production of these public laboratories represents close to 3% of national production in monetary value and 10% in unit numbers, corresponding to almost 10% of total medicine purchases by the Ministry of Health<sup>17</sup>.

<b>LABORATORY</b>	<b>PRODUCTION VOLUME</b>
FURP	3,903,840,000
LIFAL	1,728,144,000
LAFEPE	1,345,680,000
FARMANGUINHOS	1,289,067,280
FUNED	692,340,000
IQUEGO	618,000,000
LAFERGS	375,800,000
LAQFA	242,352,000
LQFE	209,419,590
LTF	193,080,000
LFM	120,800,000
LPM	96,000,000
LIFESA	80,000,000
LAFESC	38,400,000
LEPEMC	21,000,000
IVB	10,680,000
FFOE	7,200,000
NUPLAM	876,320
<b>TOTAL</b>	<b>10,972,679,190</b>

**Table 12: Public laboratory production in pharmaceutical units, 2003**

Source: Jorge A. Z. Bermudez, M.A. Oliveira, Sept 2004, Data from ALFOB, 2003

<sup>17</sup> Jorge A. Z. Bermudez, Maria Auxiliadora Oliveira, Sergio Arouca, Intellectual Property in the Context of the WTO TRIPS Agreement: challenges for public health, September 2004

## 5. The generics segment

### 5.1. Characteristics

The Brazilian pharmaceutical market is changing structure. Generic drugs are eroding branded products market share and although copy drugs have maintained a constant share of the market in both volume and value terms during the last three years, their share will erode in the future from the combined impact of patent enforcement and generics<sup>18</sup>. Generics are outperforming the pharmaceutical market as a whole – the pharmaceutical sector in Brazil had a 20% growth between 2003 and 2004, compared to 42% for generics<sup>19</sup> – driving this segment to a value of **US\$717 million and 157 million units in 2005**. Its evolution in 2003-2004 can be seen below.

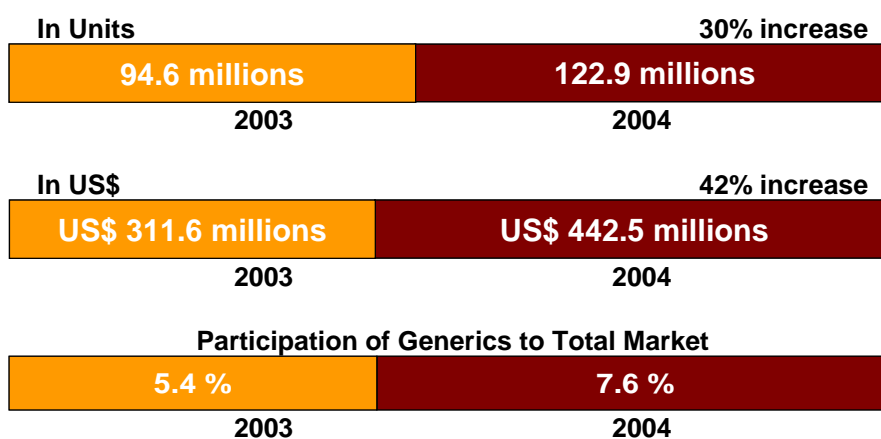


Figure 16: Evolution of the generics segment in 2003-2004 and participation to the total market. Source: [www.info4.com.br](http://www.info4.com.br)

Grupo Pro Genericos expects the Generics segment to reach 30% of the total sales in units by 2007, and eventually sales of US\$ 1 billion by 2008.

ANVISA gave priority to processing generic application in line with government policy since 2000, and the number of marketing authorizations has risen exponentially to reach about 4,500 this year, mostly in the antibiotic, anti-hypertensive and anti-ulcerant categories. Most of these products are manufactured by local companies. There are today 288 active principles registered<sup>20</sup>.

Sales of generic drugs should also be further boosted by the Brazilian Government campaigns to encourage the population to request generics during visits to physicians, complemented by pharmacy promotion. These combined factors let assume that Brazil will ultimately become an exporter of generic drugs, and Indian companies have chosen to set up operations and production plants in Brazil.

#### Downward pressure on prices

Competition from copy products and generics has eroded the price of original brands since 1999, leading to price cuts as high as 50% for Merck's Renitec (enalapril) and Bristol-Myers Squibb's Capoten (captopril), corporate decisions in an attempt to compete

<sup>18</sup> IMS Health 2003, Generics take off in Brazil

<sup>19</sup> Grupo Pro Genéricos (the Brazilian Generic Drug Association)

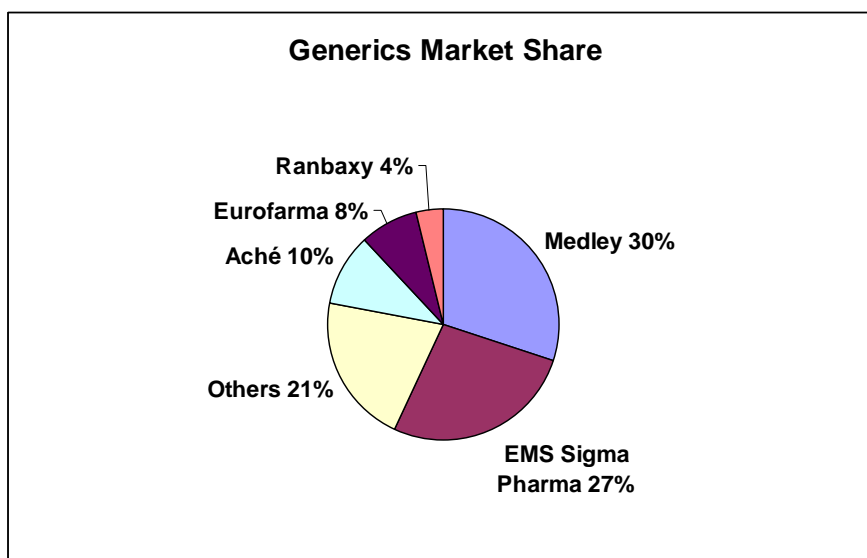
<sup>20</sup> Exame magazine, June 2005, Danielle Duran, UKTI Market Summary, Pharmaceuticals & Biotechnology, Brazil, July 2005

with generics. As more manufacturers enter the market, it is likely that price will be the only competitive advantage of products. Eventually, the number of competing products will be limited by economic viability<sup>21</sup>.

## 5.2 Major players

### National companies

Local companies are building new production facilities to increase their output. They currently dominate over 80% of the Brazilian generic market, as shown below.



**Figure 17: Generics market share in Brazil.**

Source: IMS Health, Exame Journal, April 2006. Note: only Ranbaxy is foreign-owned.

### International companies

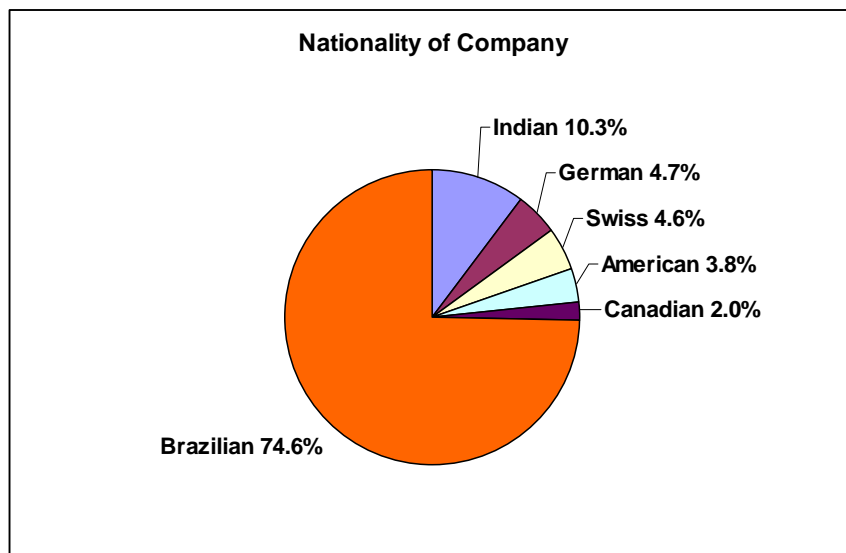
Attracted by financial incentives, major international generics companies are setting up local production facilities in Brazil to reduce their dependence on imports, but over 80% of the raw materials used in the production of generic drugs in Brazil are still imported<sup>22</sup>. These local production facilities could be used for exports to Mercosur countries in the future. Multinational suppliers are not absent, with Novartis and Abbott, for example, already present. Multinationals inactive in the generics market may have to rethink their strategy and enter the generic area for fear of facing erosion of their profits in Brazil as the demand for generics increases<sup>23</sup>.

The market breaks down by company origin as follows:

<sup>21</sup> IMS Health, Generics take off in Brazil, 2003

<sup>22</sup> Jefferson Oliveira, Market overview of drugs and pharmaceuticals, July 2003

<sup>23</sup> *ibid*



**Figure 18: Generics produced in Brazil by nationality of company**

Source: Grupo Pro Genéricos, 2005

The 4500 generics currently registered at the ANVISA were manufactured in 2004 by 53 pharmaceutical companies, of which 25 were national and 28 were international, as described in Table 13.

Pharmaceutical Laboratory	Origin of Capital	Number of Registered Medicines	Pharmaceutical Laboratory	Origin of Capital	Number of Registered Medicines
EMS	National	166	Ranbaxy	Foreign	89
Eurofarma	National	121	Apotex	Foreign	44
Medley	National	108	Novartis	Foreign	37
Prati-Donaduzzi	National	66	Mepha	Foreign	35
Teuto	National	61	Brainfarma	Foreign	33
Biosintética	National	48	Hexal	Foreign	33
Neoquímica	National	36	Abbott	Foreign	32
Cristália	National	34	Merck	Foreign	21
Natures´S Plus Ftca	National	28	Ativus	Foreign	11
União Química	National	17	Abfarmo	Foreign	10
Green Pharma	National	10	Cinfa	Foreign	10
Ducto	National	06	Alcon	Foreign	09
Hipolabor	National	06	Prodotti	Foreign	08
Hypofarma	National	05	Asta Medica	Foreign	07
Halex Istar	National	05	Arrow	Foreign	05
Theodoro F Sobral	National	03	Bristol	Foreign	04
Bunker	National	01	Ipca	Foreign	04
Equiplex	National	01	Sanval	Foreign	04
Esterlina	National	01	Kinder	Foreign	03
Genon	National	01	Allergan	Foreign	02
Jp	National	01	Biolab Sanus	Foreign	02
Lafepe	National	01	Luper	Foreign	02
Novafarma	National	01	Altana Farma	Foreign	01
Vitapan	National	01	Biobras	Foreign	01
Rioquímica	National	01	Cellofarm	Foreign	01
			Knoll	Foreign	01
			Libbs	Foreign	01
			Zambon	Foreign	01

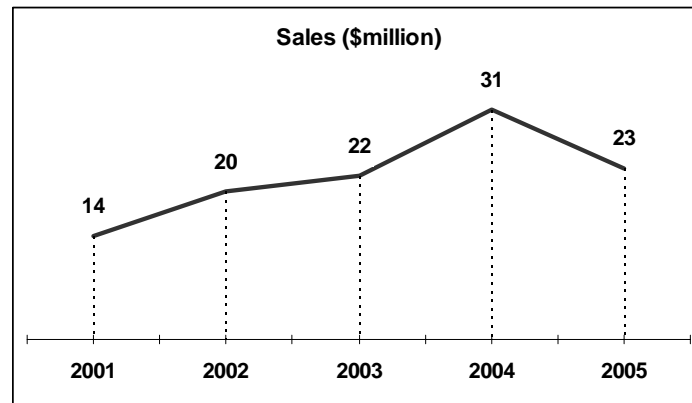
**Table 13: Major generic producer companies, by origin of capital and number of generic medicine registered by ANVISA in Brazil, 2004**

Source: ANVISA, 2004

The Brazilian market is harsh, and international players can make mistakes, as did Ranbaxy of India. The company entered the Brazilian market in 2000 and was supposed to start operations at a US\$10 million plant located in Rio de Janeiro by the end of 2005. Ranbaxy was expected to increase its product offering with its new plant and was already standing third in the generics market in Brazil in 2002.

After five years, failing to start its plant, results are poor and sales dropped by 26% in 2005. Since 2003, Ranbaxy has been losing shares for several national laboratories that increased their production capabilities exponentially and started producing generics against AIDS. Today, the company has a production line equal to half of that of its major competitors and its market share fell from 14% to 4% in about three years<sup>24</sup>.

<sup>24</sup> Daniel Hessel Teich, *Indianos em Crise*, Exame Journal, April 26, 2006



**Figure 19: Sales per year for Ranbaxy in Brazil**  
 Source: Ranbaxy. From Exame Journal, April 2006

National laboratories were better armed with a largest product portfolio and carried out an aggressive pricing policy in retail stores. When Ranbaxy entered the Brazilian market, the profitability was high and the regulation was low, but this trend reversed very quickly within the past years, and Ranbaxy has been unable to adapt to this rapidly changing market, as the company strategy is being designed at an international level<sup>25</sup>. It is therefore crucial to enter this market with a real understanding of its requirements and watch out for rapid changes.

<sup>25</sup> Daniel Hessel Teich, *Indianos em Crise*, Exame Journal, April 26, 2006

## 6. The vaccines segment

### 6.1. Characteristics

In **2004**, the vaccines market in Brazil reached **US\$ 221 million**, 43% of which was destined to the private sector, mainly with the Hepatitis B vaccine. The general profile and needs of the market in 2000 is shown in the table below.

Vaccine	Public segment		Private segment		Total
	R\$ M	%	R\$M	%	R\$M
Influenza	47.732	46,9	54.143	53,1	101.875
HiB	66.471	89,1	8.108	10,9	74.579
MMR	25.316	85,3	4.366	14,7	29.683
Hepatitis A/B		0,0	22.686	100,0	22.686
Hepatitis A	0.88	0,4	21.063	99,6	21.151
Smallpox	4.858	23,5	15.810	76,5	20.669
Hepatitis B	10.067	57,0	7.589	43,0	17.656
Anti-Rabies	14.941	100,0	N/A	0,0	14.941
Measles, Rubella	12.096	100,0	N/A	0,0	12.096
Poliomyelitis	10.488	98,5	0.157	1,5	10.646
Pneumococcus	7.979	80,5	1.934	19,5	9.914
Yellow Fever	9.200	100,0	N/A	0,0	9.200
DTP acellular+ Polio+Hib		0,0	7.311	100,0	7.311
MMR/DtaP	0.211	2,9	7.129	97,1	7.341
BCG	4.270	59,5	2.907	40,5	7.178
Meningitis A/C	0.992	18,9	4.269	81,1	5.261
Meningitis B/C		0,0	4.896	100,0	4.896
MMR bacterial/DTP	3.622	76,8	1.093	23,2	4.715
Measles, Rubella bacterial	3.344	91,8	0.298	8,2	3.642
Measles	2.250	71,4	0.900	28,6	3.151
Rabies	2.243	81,0	0.527	19,0	2.770
Tetanus	N/A	N/A	2.400	100,0	2.400
DTP+Hib		0,0	1.266	100,0	1.267
Pneumococcus conjugated		0,0	1.020	100,0	1.020
Rubella		0,0	0.170	100,0	0.170
Mumps		0,0	0.84	100,0	0.85
<b>Total</b>	<b>226.168</b>	<b>57,0</b>	<b>170.135</b>	<b>43,0</b>	<b>396.304</b>

**Table 14: National vaccines market in Brazil, 2000**

Source: J. Gomes Temporao, The private vaccines market in Brazil: privatization of public health

Brazil's public policy in the 1980s was aimed at self-sufficiency in vaccines and immunobiologicals, which explains the high level of development of the research carried out in these domains. Being a state resolution and not a government resolution, this action was implemented regardless of changes in governments.

The Brazilian **Immunization Program** is now one of the best world immunization programs and has an increasing offering of vaccines. The government coordinates the acquisition and distribution of vaccines, at no cost, according to an established schedule<sup>26</sup>.

<sup>26</sup> Rosiceli Barreto Gonçalves Baetas, Vaccines in Brazil: a new pattern of research, development and production articulation is necessary to innovation

## 6.2. Major players

There are few Brazilian vaccine manufacturers. The majority of private companies offering vaccines buys them in bulk and re-labels them for sale.

### Public sector

The Butantan Institute and Bio-Manguinhos – part of the Foundation Oswaldo Cruz, Fiocruz – are the two leading public producers of vaccines, focused on the internal public market. Bio-Manguinhos is the major world supplier of Yellow Fever vaccine, through UNICEF and WHO purchase systems.

These firms dominate the public market, and comply with strict criteria in order to assure high quality and competitive price, referring to UNICEF or Pan-American Health Organization (PAHO) guidelines. Both firms have received important investments from the Brazilian Government to build new facilities with Good Manufacturing Practice certifications.

These firms have been active in research and vaccine production for over a century and have accumulated important expertise. While their estimated production capacity is approximately 300 million doses per year, they currently produce only around 200 million doses yearly, 80% of which is provided by the Butantan Institute to the Ministry of Health, at set prices<sup>27</sup>.

Twenty years after the implementation of the self-sufficiency policy in vaccines, the Butantan Institute is now creating its first innovative products that will impact public health in Brazil and potentially other countries. These products include a new pulmonary surfactant for use in newborns, a new cellular pertussis vaccine with very low reactogenicity, and a new adjuvant based on monophosphoryl lipid A<sup>28</sup>.

### Private sector

Some private companies still import vaccines destined for the Brazilian private health sector. Their contribution to the importations of the private sector in 2001 is shown below.

Private producers	Total (US\$)	%
Aventis Pasteur	9.452.717	48,55
Smithkline Beecham	5.958.999	30,61
Novartis	1.614.052	8,29
Merck Sharp & Dohme	1.083.531	5,57
Wyeth	893.037	4,59
Others	467.876	2,40
Enila	0	0,00
Total	19.470.212	100,00

**Table 15: Private vaccine producers in 2001**

Source: J. Temporão, The private vaccines market in Brazil: privatization of public health

Brazil has a unique position as compared to other South American and African countries, as a result of a high degree of maturity in the vaccine and anti-sera areas, comparable to some Asian countries. However, the total amount of researchers and PhDs is much lower in Brazil than in the US or India. Furthermore, most of the research carried out at Brazilian universities is not transferred to the industry sector, as the universities are not prepared to fill patents and in many cases are reluctant to do so.

<sup>27</sup> For instance, the Hepatitis B vaccine is provided at US\$ 0.23 per dose

<sup>28</sup> For more information about the offerings of the Butantan Institute and Fiocruz, see Appendix 5.

## Chapter 2

### The Regulatory Framework

#### **Abstract**

*The regulatory framework has tremendously improved in the past decade. The Brazilian Intellectual Property law (1996) now recognizes the patentability of pharmaceutical products. The new Innovation and Tax laws (2005) will support public-private partnerships in research and give more dynamism to private investments.*

## 1. The Patent law and the TRIPS agreement

### Origins of the Intellectual property in Brazil<sup>29</sup>

According to Barbosa<sup>30</sup>, Brazil was the first developing country to establish a patent law, in 1830. In 1883, Brazil signed the Paris Convention, which defined the international system of Intellectual Property, through three basic principles: independence of patents and trademarks, similar treatment for nationals and foreigners and priority rights.

The Brazilian legislation on industrial property protected pharmaceutical products and processes until 1945, when were excluded the inventions that covered food products or substances, pharmaceuticals and materials or substances obtained by chemical processes. In 1969, a change in the Brazilian Industrial Property Code completely abolished the patentability in the pharmaceutical area, until the new patent law of 1996 was enacted.

Historically, as the Brazilian Intellectual property law did not recognize the patentability of pharmaceutical products, the Brazilian government exploited a time lag until international patent rules applied in Brazil to produce generic versions of antiretroviral drugs at lower cost<sup>31</sup>. This decision created tensions and the US complained to the WTO, leading to an Agreement on Trade-Related Aspects of Intellectual Property rights (TRIPS), negotiated in the 1986-94 Uruguay Round. The TRIPS resolutions were enforced in January 1995, leaving an 11 year period for Brazil to implement them.

The TRIPS still allows Brazil to use the “compulsory licensing” argument in case the local production of a drug is required in a public health emergency. In August 2001, there was controversy when Brazil’s health minister threatened to breach Roche’s pharmaceutical patent on the anti-AIDS drug Nelfinavir after six months of negotiations failed to lower the price. By manufacturing the drug locally, the minister estimated that the price could be reduced by 40%<sup>32</sup>.

### The new Patent law

The Brazilian Patent law of 1996 recognizes patents for pharmaceuticals and chemical products to the level of the TRIPS agreement and differentiates non patentable items, for the reason of not being inventive, in addition to some absolute statutory exclusions, in accordance with European standards.

### Pipeline provision

According to Velasquez and Boulet<sup>33</sup>:

“Pipeline protection is a (...) retroactive protection, to the effect that pharmaceuticals already patented in other countries but not yet patented nor marketed in the “pipeline” country (...) may be claimed for protection as soon as the Agreement comes into force.”

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<sup>29</sup> Translated from J. A. Bermudez, R. Epsztejn, M.A. Oliveira, L. Hasenclever, The WHO TRIPS agreement and Patent protection in Brazil: Recent changes and implications for the local production and access of population to medicines, 2000

<sup>30</sup> Barbosa, Patents: Critic of the rationality, 1983

<sup>31</sup> \$3,000 per year for a cocktail sold between \$10,000 and \$15,000 in the US, Faiz Kermani, Regional Roundup: Brazil, Contract pharma, 2005

<sup>32</sup> *ibid*

<sup>33</sup> VELÁSQUEZ G., BOULET P., Globalization and Access to Drugs – Perspectives on the WTO/TRIPS Agreement. Geneva:WHO, 1999.

On enforcement of the 1996 patent law, the chemical products, food and pharmaceutical inventions were granted special filing rights in Brazil, to be requested from 1997 to 1998. During this period, applications regarding such inventions previously filed abroad were accepted and patents were granted for the remaining term of the original patent, limited to the maximum Brazilian term (20 years). However, no patents were issued for inventions that were already commercialized in any market by the holder or with his consent or that were already worked by third parties in Brazil<sup>34</sup>.

The main alterations to the original law and their comparison with the TRIPS requirements are introduced below.

TRIPS agreement	Law 9.279/96	Law 5.772/71
<b>Patentability requisites</b>		
Article 27.1 specifies that any invention, in all technological sectors, will be patentable, so long as it is new, involves an inventive activity and is subject of industrial use. In this form, the pharmaceutical sector is privileged	Article 8 agrees with the TRIPS, and requires the same 3 patentability requisites, but does not specify that the inventions from all technological sector are patentable	Article 6 asserts that the invention is privileged so long as it fulfills two requirements: novelty and susceptibility of industrial use. The requisite on inventive activity was included later through the Normative Act 17
<b>Material not patentable</b>		
To the aim of protecting human health and life, the environment and national interests, Articles 27.2, 27.3 and 73 define the exceptions to patentability. They allow the Member to consider non patentable: methods, therapeutic and surgical diagnostics for the treatment of human beings or animals. The subparagraph 27.3(b) addresses the question of the non-privileged patentability of biological material, this paragraph only being subject to revision in four years. This demonstrates the difficulty of the Members to reach a consensus on this topic	Articles 18 and 10 deal with the material not patentable, aligning the national legislation with the minimum models set in the international legislation. It did not exclude the pharmaceutical sector from patentability. In the subparagraph 18 III, it allows to patent genetically modified microorganisms so long as they fulfill the three patentability requirements and have not merely been discovered	Article 9 deals with the non privileged material, including in its subparagraph 9c a negation of the privilege of substances, materials, mixtures or food products, chemical pharmaceuticals and drugs of all types as well as the respective manufacturing or modification processes
<b>Validity</b>		
Sets the validity of patents to a minimum of 20 years since the filing (Art. 33). To the contrary of other articles, this article specifies the duration of the protection	The patent will be valid for 20 years starting at the filing date. The duration of validity cannot be less than 7 years starting on the granting date (Art. 40)	The privilege of the invention is valid for 15 years starting on the filing date (Art. 24). The law does not specifies a minimum validity period
<b>Shift of the Burden of Proof</b>		
Article 34 asserts that the owner of a patent on processes can require through court action the proof that the derivation of a specific product is not made through the patented process. This guarantees to the defendant the secret of the result, in the event of a contrary proof	Article 42 paragraph 2 asserts that the owner of a patent on processes can require, via judiciary process, the identification of the derivation process of a product. The law does not mention the confidentiality of the judiciary process	The law is inexplicit on this point

<sup>34</sup> Denis Borges Barbosa, The New Brazilian Patent Law

<b>Pipeline</b>		
Independently of the enforcement date of the Agreement in the Member state, it will have to possess an adequate structure to receive all patent applications for pharmaceutical products and chemical products for the agriculture (Art. 70.8)	Through Articles 229, 230 and 231, the law allows that patent applications be filled for processes or substances, materials or chemical and pharmaceutical products as well as drugs that have a protection granted outside the country or on-going application for Brazil, so long as they have been released on any existing market	The law is inexplicit on the Pipeline
<b>Compulsory license</b>		
The Agreement allows other uses of the object of the patent without authorization of the patent holder, according to the disposition of Article 31	The laws allows the compulsory licensing, according to the specifications of Article 68, completed by Article 73 paragraph 6	The law allows compulsory licensing, according to the specifications of Articles 33 and 34
<b>Parallel Import</b>		
The Agreement deals with the exceptions limited to the exclusive rights of the patent in the Article 30, without being specific on the motives on which Member States can base these exceptions	Articles 68 paragraph 3, 4 and 74 allow the import through third parties of products manufactured in agreement with process- or product-related patents	The law is inexplicit regarding the parallel import

**Table 16: Comparison of the new Brazilian Patent law with the TRIPS requirements**

Source: Translated from J. A. Bermudez, L. Hasenclever, The WHO TRIPS agreement and Patent protection in Brazil: Recent changes and implications for the local production and access of population to medicines

## 2. The Generics law

The 1999 law (9.787/99) and the ANVISA (Agência Nacional de Vigilância Sanitária – National Agency for Health Supervision) regulate the implementation of the generic pharmaceuticals policy in Brazil, establish the technical standards and define the concepts of bioavailability, bioequivalent drugs, innovators, reference drugs and similars.

This created a new category of copies of medicines commercialized in Brazil, called similars, thus creating three categories of medicines:

- The innovator, or reference drug product, with brand names, patented or not. An Innovator is “a drug presenting in its composition at least one active drug that has already been covered by a patent (even if that patent has expired) that was taken out by the company responsible for its development and innovation in the market of its country of origin. If the innovator drug product is available on the national market, it is generally considered to be the drug product of reference”<sup>35</sup>.
- Similar medicines, also with brand names and similar to the reference drug, but not submitted to bioequivalence tests. A similar product is “a drug containing the same or more active principles, presenting the same concentration, dosage, means of administration, posology and therapeutic indication. Moreover, it has to be equivalent to the drug product registered at the ANVISA. It may only differ with regard to its size and shape, period of validity, packaging, labeling, excipients and vehicles”.
- Generic versions, interchangeable with their respective reference medicines. Generics are “similar to a product of reference or to an innovator drug, and are meant to be interchangeable with this product. They are generally produced after the patent’s expiration or after a rejection of the patent protection or of any other rights of exclusiveness”. Unlike similar drug products, registering generic drugs requires bioequivalence and bioavailability testing.

Until May 2003, similar drugs were registered only using the criteria of similarity. On this date, the ANVISA established new requirements to obtain market approval for similar medicines, which include “relative bioequivalence” tests requirements to compare the similar with the reference drug. During the next five years all similar medicines commercialized in Brazil will therefore have to be submitted to bioequivalence testing<sup>36</sup>.

The Brazilian generic policy is aimed at promoting competition between medicines, in their relevant markets, to reduce prices, especially for medicines for chronic conditions. The current 4500 products (i.e. with a variation of one of the following: drug, dosage, formulation, packaging) registered as generics in Brazil in agreement with the legislation mentioned above were submitted to the bioavailability and bioequivalence tests required by the ANVISA, by quality control laboratories licensed by ANVISA.

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<sup>35</sup> Anvisa, 10 Resolution on generic drugs, RDC n°10, January 2, 2001

<sup>36</sup> That is the demonstration of pharmaceutical equivalence between products presented in the same dosage form, containing identical composition of drug(s), and that have comparable bioavailability when studied under the same experimental design. Source: Bermudez, Oliveira, Intellectual Property in the Context of the WTO TRIPS Agreement, Sept 2004

### 3. Registration of pharmaceutical products in Brazil: ANVISA

To have the right to commercialize drug products in Brazil, it is necessary to register with the National Agency for Health Monitoring (Agência Nacional de Vigilância Sanitária - ANVISA). ANVISA is the Government agency responsible for the regulation and approval for the sale of all medical and pharmaceutical products in Brazil. It was established in 1999 and is modeled on the structure of the American FDA, although operating on a budget of about one tenth of that of the FDA. This registration, however, does not require the applicant firms to be engaged in local production.

**The Ministry of Health in Brazil does not accept international approval certificates issued in other countries** – e.g. FDA, CE Mark, etc...Therefore all imported products require approval and registration by the ANVISA before importation and distribution in Brazil. This is an expensive and quite bureaucratic process and must be carried out by a company established locally, an agent, a representative or a local subsidiary of the foreign supplier. It usually requires 4 to 6 months and can take up to one year<sup>37</sup>.

For medicines, the fees are:

New	\$26,667
Similar	\$7,000
Generic	\$2,000

**Table 17: Registration fees with ANVISA in 2004**

Source: Danielle Duran, Registration of Medical Devices and Pharmaceutical Products in Brazil, Aug. 2004

Registration is valid for 5 years and must then be renewed, with a fee reduced by 10%. There is a scale of fees depending on company size:

Registration fees are reduced by:

- 15% for companies with an annual turnover between R\$20 million and R\$50 million.
- 30% for companies with an annual turnover between R\$ 6 million and R\$ 20 million
- 60% for companies with an annual turnover of less than R\$ 6 million
- 90% for small enterprises
- 95% in the case of micro enterprises, except for pharmaceutical products (90% fee reduction for micro enterprises in this case)

There is a specific regulation in Brazil that classifies companies in small and micro enterprises, with specific tax regimens. The above conditions are calculated based on the turnover of the company established in Brazil that carries out the registration process. It is vital to seek the assistance of a local attorney to complete these procedures<sup>38</sup>.

Drug registration criteria and conditions obviously vary depending on whether an innovator product, a similar drug product or a generic drug is involved (see chapter on the Generics law). Despite the 1996 Brazilian Generics law, generic ARVs, as such, are almost non-existent on the local market. In fact, most off-patent ARVs are not registered as “generics” but as “similar”.

<sup>37</sup> UKTI Market Summary template, Healthcare market in Brazil, Sept. 2005

<sup>38</sup> Danielle Duran, Registration of medical devices and pharmaceutical products in Brazil

The Brazilian standards for bioequivalence tests are similar to the FDA's. Nevertheless, the difficulties in obtaining the required availability levels established by the Brazilian standards do not mean that the medicine is not good or safe. According to Orsi, Hasenclever et al., it is believed that ANVISA has adopted such high generics standards so as to be able to guarantee the effective implementation of this segment, seeing that physicians were once very skeptical about prescribing generics, doubting their efficiency in comparison with reference medicines<sup>39</sup>.

#### 4. The Innovation law

This law, implemented in April 2005, allows public funds to be spent on industrial projects. It encourages public and private sectors to share staff, funding and facilities thus increasing technology transfers between universities and the industry. Until then public sector researchers had to ask permission to work on privately funded projects, even when this did not interfere with their university positions, and they could not accept any pay for this work. With this law, scientists expect a boom in the sector in the next few years<sup>40</sup>.

Intellectual property held by universities may now be licensed out, allowing the commercial utilization of publicly sponsored inventions by private companies. Universities will also be able to grant their own researchers 3-year renewable licenses to establish businesses to develop promising innovations. A government initiative for technology transfer from overseas also allows a period of five years access to the Brazilian market before the transfer of production techniques for local manufacture.

The Innovation law contains clear provisions for joint ownership of patents, which will allow academic institutions to incubate both joint ventures and private companies. This new law is extremely important, and is somewhat similar to the Bay-Dohle Act in 1980 in the US, that had a huge impact on spin-out and technology transfer activities in public universities. This gives positive expectations about how technology transfer agreements could grow in coming years in Brazil. Additionally, this means UK's experience in this area can now be exported successfully to Brazil.

#### 5. The Tax law

Implemented in April 2005, this law provides tax breaks and grants to stimulate innovative companies and foreign investments. In 2006, the Brazilian tax authority will lower the tax rate to 15% (from 22%) on capital gains to non-exempt local investors, and will issue a new exemption to foreign investors that are not based in tax free jurisdictions<sup>41</sup>.

This will support investment from the private sector, an area where Brazil has been very weak and which has hindered the development of the biotech industry. The tax nevertheless remains very high – 15 to 20 % – and is often cited as a deterrent for investment, as all imported goods are subject to this tax.

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<sup>39</sup> Fabienne Orsi, Lia Hasenclever, Beatriz Fialho, Paulo Tigre, Benjamin Coriat, Intellectual Property Rights, Anti-AIDS Policy and Generic Drugs. Lessons from the Brazilian Public Health Program, 2003

<sup>40</sup> Danielle Duran UKTI Market Summary, Pharmaceuticals & Biotechnology, Brazil

<sup>41</sup> Álvaro L. Gonçalves, ABVCAP The Brazilian Association of Private Equity and Venture Capital, Belo Horizonte, April 2006, 4th Annual VC Summit

## 6. Is the regulatory framework competitive?

The regulatory framework in Brazil has considerably improved, and now brings a greater protection for pharmaceutical products, as well as mechanisms to revitalize joint projects between public and private actors.

Additionally, the 2005 **Biosafety law** regulates biotech activities and allows the production of genetically modified organisms. It sets a framework for the use of embryonic stem cells in research, permitting the use of blastocytes, which have been surplus to requirements for *in-vitro* fertilization procedures and frozen for three years.

The **ANVISA** has very high standards for approval of novel drugs, generics or biologics, which make the regulatory validation on the Brazilian market a flagship for entry to any other market in Latin America, and by 2010 all three product categories will have the same stringent requirements. It is noteworthy that because Brazil is in a tropical zone, bioequivalence and stability tests required by the ANVISA are more demanding than tests carried out in Europe or the US and must satisfy stability criteria of a zone 4-humidity category.

This regulatory control therefore makes Brazil competitive with Ireland, Turkey, Greece, and maybe even India<sup>42</sup>. Most companies starting on the Brazilian Market are prepared to enter European markets because of these high standards. For instance, EMS is already established in Portugal, and exporting to Italy, Spain and the Netherlands. Medley also has access to the European market. However, Brazil still crucially lacks an efficient framework to speed up the clinical trials approval. The approval of a phase I protocol can currently take up to 6 months for lack of trained personnel at the ANVISA to process applications.

Improvement of this framework is a dynamic process and the Brazilian government is aware of the efforts that will be required to increase Brazil's competitiveness and attractiveness to foreign investments. This should allow Brazil to benefit from an enhanced business environment in coming years.

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<sup>42</sup> For instance, the Brazilian firm LIBBS pharmaceutical obtained a GMP certification from German authorities in April 2006

## Chapter 3

### Critical Analysis of Opportunities

#### **Abstract**

*The best opportunities for partnerships are:*

- *Collaborations in new vaccines formulation and expansion of manufacturing capabilities for lower margin vaccines for exportation*
- *In generics: building of primary manufacturing capabilities and APIs expertise; increase of manufacturing capabilities for exportation*
- *Collaborations for clinical trials*
- *New drug discovery collaborations for high quality products, based on biodiversity*

#### **Method**

The opportunities analyzed were identified according to a systematic literature analysis, complemented by interviews with professionals based in Brazil and in the UK. Each point was thoroughly analyzed according to its interest, achievability and viability. For each opportunity, a scenario was drawn for collaboration, outlining what complementary skills were present and could be brought from the Brazilian and UK side.

#### **Assessment of complementary skills**

Scenarios are summarized in tables with ticks where the country was deemed as having a competitive advantage to bring to a partnership. The absence of tick does not indicate that this skill is non-existing in the country, but that the other partner may have superior skills or resources in this domain. All criteria are evaluated from the perception and opinion of several contacts interviewed when information was available and may not reflect accurately the state of the art in the country.

Relative scores of these scenarios can be found in Appendix 2.

## 1. Opportunities in generic pharmaceuticals

This segment has a clear potential for expansion and Brazil's strengths have been demonstrated in the past in this area with reverse engineering successes. Generic drugs for neglected diseases, hemoderivatives, biopharmaceuticals and antibiotics present the main interest.

Far-Manguinhos/FIOCRUZ already has negotiations and partnerships in progress with RPG LS (India), Cristalia (Brazil), Aventis (France), Roche (Switzerland), Torrent (India), Hetero (India), GSK (UK), Médecins sans Frontières, Merck Sharp & Dohme and Chron Epigen Ltda. They take the form of technology transfer agreements, cooperation agreements, technical and scientific agreements, or licensing deals for exportation or raw material supply<sup>43</sup>.

The major strengths and potential in pharmaceuticals are summarized in the table below.

Critical competitive factors	Sources of advantages in Brazil	Technological niches and market niches	Main policies of competitiveness
<ul style="list-style-type: none"> <li>- Innovation potential in Biotechnology and fine chemistry</li> <li>- Technological impact and market impact</li> <li>- Development and permanent launch of new products on the market</li> </ul>	<ul style="list-style-type: none"> <li>- Size of Domestic market</li> <li>- Important presence of the State in the purchases in various specific programs</li> <li>- Existing capability in pharmaceuticals, including multinationals</li> <li>- Potential for growth of the production capability</li> <li>- Biodiversity</li> <li>- National scientific base</li> </ul>	<ul style="list-style-type: none"> <li>- Drugs for neglected diseases</li> <li>- Phytopharmaceuticals</li> <li>- Hemoderivatives</li> <li>- Biopharmaceuticals</li> <li>- Products of Renome (Relação Nacional de Medicamentos Essenciais, National Essential Medicine Relation)</li> <li>- Generics</li> </ul>	<ul style="list-style-type: none"> <li>- Articulation of public programs for pharmaceutical assistance (strategic drugs, generics, ..) with economic and technological reinforcement of national products</li> <li>- Negotiation with world leaders for investment in technology, internalization of drugs production and achievement of commercial balance</li> <li>- Consolidation of R&amp;D public structures and articulation with private sector</li> <li>- Expansion of service structures and certification structures</li> <li>- Political commercial action to lower the technical and sanitary barriers to promote exportation</li> </ul>

**Table 18: Industrial pharmaceutical complex: policies and factors of competitiveness**

Source: Buss, Temporão, da Rocha Carneiro, Vaccines, Sera and Immunization in Brazil

### 1.1 How realistic is the need?

The Brazilian pharmaceutical market can grow substantially as only 25-30% of the population currently has access to medicine. As most of the market is driven by the Brazilian Ministry of Health buying drugs to provide them at lower cost to the population, this ensures an initial customer base.

The sale and/or manufacture of pharmaceuticals for the Brazilian market is certainly of interest as manufacturing costs are about 20% of those in the UK. Even Indian Companies Ranbaxy and Zydus have recently established manufacturing plants in Brazil.

Brazil is also a gateway to other Latin American markets, and its regulatory framework set at a standard equivalent to that of most western countries gives any company producing for the Brazilian market the validation to gain regulatory approval on over 50% of other Latin American markets. The combined Brazilian and Mexican markets represent a value of US\$15bn in 2005.

<sup>43</sup> P.M.Buss, J. Temporão, J. da Rocha Carneiro, Vaccines, Sera and Immunization in Brazil, Chap 3, Fiocruz2005

Strengths	Weaknesses
<ul style="list-style-type: none"> <li>• Good expertise and capabilities in secondary manufacturing of private national firms, with strong production park</li> <li>• Far-Manguinhos used strategically to copy patented and off-patent AIDS products. Used to oblige multinationals to lower their selling price to the Brazilian Government<sup>44</sup></li> <li>• Important spare production capability. Potential to increase output in many firms</li> </ul>	<ul style="list-style-type: none"> <li>• Lack of primary manufacturing facilities for raw materials and chemical synthesis</li> <li>• Low annual healthcare expenditure per capita<sup>45</sup></li> <li>• Most Brazilian health insurance companies do not reimburse patients for prescription drugs. Yet, the 25% of population that is able to access drugs through out-of-pocket expenses represent about 47 million people (equal to the UK population able to afford their own drugs)</li> <li>• Access to remainder of market is necessarily through the government</li> <li>• Approval for registration of new products is only granted to companies implanted in the country, and local production may also be necessary.</li> </ul>
Opportunities	Threats
<ul style="list-style-type: none"> <li>• Highly attractive domestic market, and strategic gateway to other markets</li> <li>• Production of fixed-doses generics for cardiology, diabetes, and other high prevalence diseases</li> <li>• Brazil to produce NCEs with UK platform technologies in the longer term</li> <li>• Need for Active Pharmaceutical Ingredients (APIs). Only a couple of laboratories are currently doing formulation development</li> <li>• Developing the biogenerics segment<sup>46</sup></li> <li>• UK to ensure a quality production in Brazil with high standards for exportation</li> <li>• UK may be able to bring creative financing solutions to domestically manufacture or import drugs at low prices</li> </ul>	<ul style="list-style-type: none"> <li>• Private national firms dominate the market</li> <li>• Brazil attracts companies who see in the Generics law an opportunity to tackle a huge market. Even Indian companies have set up manufacturing operations in Brazil.</li> <li>• The market is already saturated by local and multinational players.</li> <li>• The health market in Brazil is constrained by the government and local players. Pricing and distribution to the 50,000 pharmacies throughout the country is a vital component of the Brazilian public health policy, which has widely been acclaimed as a model in fighting HIV.</li> </ul>

**Table 19: SWOT analysis for the generics segment**

<sup>44</sup> **Roche** for the Antiretroviral drug **Nelfinavir** in August 2001 and **Abbott** for the **Lopinavir/Ritonavir** combination (**Kaletra**) in June 2005

<sup>45</sup> Approximately of \$31.8 per year according to IMS Health 2005 data, far below the \$500 recommended by the WHO

<sup>46</sup> As compared to India, Brazil does not currently produce any biogenerics, apart from a recombinant Insulin formerly produced by Biobras, later sold to NovoNordisk.

Therefore, investing capabilities, time and money in the Brazilian market requires a long term commitment as well as finding a local partner in order to access sales in that market.

## 1.2 Scenario for collaboration

The major success of the healthcare anti-AIDS policy in Brazil was based upon providing **low-cost generics** to the broadest base of HIV patients.

Brazil still lacks infrastructures for chemical synthesis and raw chemical material supply as well as APIs production capabilities and is highly dependent on imports. The UK could provide investment or expertise for a local production capability in the country.

In the longer term, increasing the number of high quality products requires the development of local manufacturing capacity. The UK could bring expertise in this area.

### Proposed scenario for collaboration

***“Bring UK investment or expertise for a local production capability of raw materials for generics, for domestic or export use”***

Expertise and Capability	UK	Brazil
○ Domestic Market size and growth		✓
○ Private investments, creative financing	✓	
○ Primary manufacturing (raw chemicals and APIs)	✓	
○ Secondary manufacturing		✓
○ Low manufacturing costs		✓
○ Scale up in Generics manufacture		✓
○ Distribution network		✓
○ Potential for access to other markets		✓

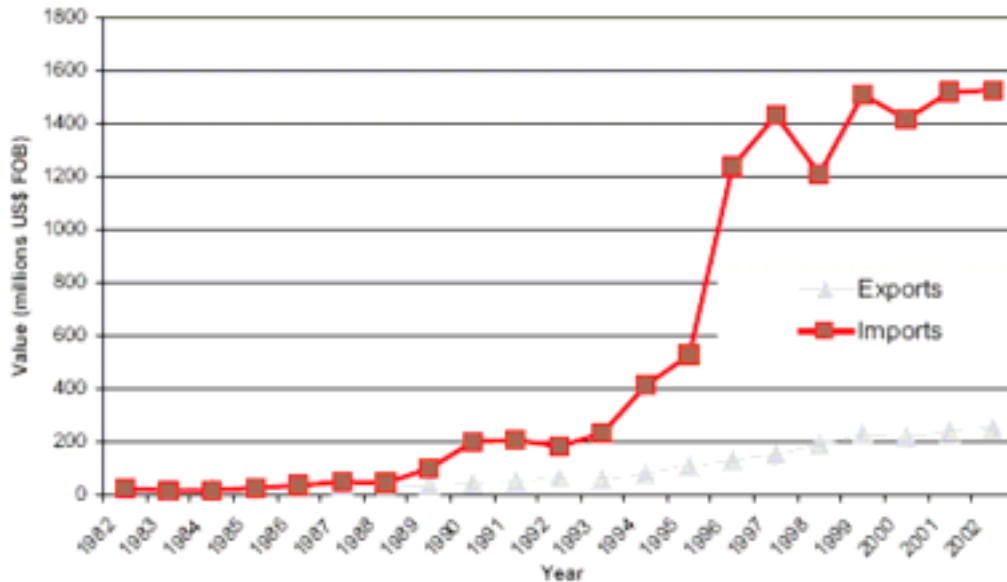
**Table 20: Scenario for generics collaboration**

### ***Feasibility***

If low margin drugs may not be the major interest of major pharmaceutical companies, financing this production may on the other hand be attractive. In addition, the UK possesses strengths in the chemical processing area, so providing cheaper production technologies would certainly be of great interest, with the promise to tackle new and extremely fast-growing markets which access would be gained through the Brazilian market.

The major need in Brazil is for companies providing equipment and bringing production capabilities for reagents and raw chemicals in the country. There is a great lack of API facilities in Brazil, as many were closed in the 1990s and raw material has to be imported

from India and China among others. Since then, there has been a considerable increase in importation by the pharmaceutical industry, and Brazil tends to be increasingly dependent technologically on these imports. There is therefore a real will from local firms to build up a manufacturing substitute to these imports (see Figure below).



**Figure 20: Brazil's balance of trade in the pharmaceutical industry, from 1982 to 2002**

Source: Brazilian Statistical Directory, in Bermudez, Intellectual Property in the Context of the WTO TRIPS Agreement

However, it is noteworthy that the ANVISA requires additional bio-equivalence tests carried out by an ANVISA-Certified CRO<sup>47</sup>. It will be necessary in every case to do these bioequivalence tests again, whether for innovator or generics products, as Brazil is located in a zone 4 humidity and stability area, and tests carried out in another zone cannot guarantee the stability of the compound. It is expected that by 2014, the ANVISA will have the same requirements than European regulatory bodies.

<sup>47</sup> e.g. Anafarm in Canada, AAI in the US and Germany

## 2. Opportunities in vaccines

This area has great potential in Brazil. In the scientific domain, it is witnessed that projects are rather driven by curiosity, as a self-legitimacy to the eyes of the scientific community, with publication as the main objective. There is still a blatant gap between the research and production, because the National Immunization Program (Programa Nacional de Imunização, PNI) in 1973 and the public health policy did not manage to stimulate the research and development of new vaccines, for lack of funding for the basic applied research in this area.

The two best cases that represent a national breakthrough in this area are the production of the Hepatitis B (Hep B) vaccine by the Butantan Institute and the production of the *Haemophilus influenza* type B (Hib) vaccine by Bio-Manguinhos/FIOCRUZ. They evidenced a dynamic interaction between an internal R&D base and an industrial base for technological development<sup>48</sup>.

Below is a table emphasizing the factors of competitiveness of Brazil in vaccines:

Critical competitive factors	Sources of advantages in Brazil	Technological niches and market niches	Main policies of competitiveness
<ul style="list-style-type: none"> <li>- Innovative potential in Biotechnology</li> <li>- Technological impact</li> <li>- Entry in the category of higher value products</li> </ul>	<ul style="list-style-type: none"> <li>- Size of National market and consolidation in the National Immunization Program (PNI)</li> <li>- Production capacity and technological potential of the major producers</li> <li>- Infrastructure for control and quality</li> <li>- National Scientific base</li> </ul>	<ul style="list-style-type: none"> <li>- New vaccines used in the PNI: Hep B, Hib</li> <li>- New combined vaccines (e.g. DTP+Hib+HepB)</li> <li>- Development of new vaccines on the base of the national epidemiologic profile</li> </ul>	<ul style="list-style-type: none"> <li>- Joining of the PNI purchases with the development of the innovative capacities of the producers</li> <li>- Modernization of the management model of public producers</li> <li>- Consolidation of the R&amp;D structures of Fiocruz and Butantan</li> <li>- Elimination of the legal restrictions to the exportations of the public producers</li> </ul>

**Table 21: Industrial vaccines complex: policies and factors of competitiveness**

Source: P.M. Buss, J. Temporão, J. da Rocha Carvalheiro, Vaccines, Sera and Immunization in Brazil

<sup>48</sup> P.M.Buss, J. Temporão, J. da Rocha Carvalheiro, Vaccines, Sera and Immunization in Brazil, Chap 3, Fiocruz2005

## 2.1 How realistic is the need?

Barreto identifies two areas of competition for a firm willing to contribute to the vaccine segment<sup>49</sup>:

- **New Vaccines:** with a greater profitability, they benefit from more recent scientific developments<sup>50</sup>. Barriers to entry are high because of economies of scale in R&D and marketing, intellectual property and complex regulation. In this category there are few competitors, products are differentiated, prices are higher, and the bargaining power of the customer is low. Actors in this segment form a cartel and can take joint action to deal with the threat from substitute products, or pressure medical associations, in order to use them as influential allies in increasing the volume and price of the new vaccines<sup>51</sup>. This arena is dominated by multinationals, and the large number of alliances between smaller biotechnology companies and the multinational pharmaceutical leaders evidences the difficulty for the former to become vaccine producers, and not only suppliers of R&D services.
- **Traditional vaccines:** with a lesser profitability such vaccines are for example: oral polio vaccine, anti-DTP (diphtheria, tetanus and whooping cough) vaccine, and measles vaccine, produced by a large number of competitors, with low differentiation, usually bought by governments or international health organizations willing to pay the lowest possible price. In general, companies that fit the profile of being a follower mainly participate in this category. Multinationals also participate, but with the aim of collecting the income resulting from the end of the life cycle of their products. Barriers to entry are lower than in the first case, but remain high for potential market entrants.

The Brazilian vaccine producers have developed competencies and have entered the second market and act as technological followers. These companies are now facing a growing pressure to innovate and develop new vaccines for illnesses predominant in Brazil in which multinationals have no interest. In order to innovate and launch new vaccines, they have to acquire new competencies, access new sources of technology as well as different financing sources.

As a characteristic of the second case the Brazilian vaccine market has been strongly oriented toward public health concerns. In this context, the Brazilian government has just approved a public policy for vaccines, the National Competitiveness Program, focused on 4 main themes:

- Innovation
- Modernization and suitability of structures
- Industrial development
- Regulation

This program allows potential interactions and interfaces with private firms, in order to increase the relations with the private sector.

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<sup>49</sup> Rosiceli Barreto Gonçalves Baetas, Vaccines in Brazil: a new pattern of research, development and production articulation is necessary to innovation

<sup>50</sup> For example, combined vaccines with the new version of the anti-pertussis component (aP), or conjugate vaccines (against *S. Pneumoniae* hepta valente and *Meningitis C*)

<sup>51</sup> There is little chance an anti-monopoly legislation is passed presently in Brazil as many firms are publicly-owned. The government will therefore have to deal with this dilemma before to enact a law.

<b>Strengths</b>	<b>Weaknesses</b>
<ul style="list-style-type: none"> <li>• Strong “pro-vaccine” national culture</li> <li>• Highly efficient public infrastructure: 125,000 vaccination clinics allow vaccination of 100% of children – 30million – over a weekend</li> <li>• Important national R&amp;D and production capacity (Bio-Manguinhos and Butantan)</li> <li>• Centenary expertise, and experience in high volume fermentation and purification, high-scale culture and logistic</li> <li>• Expertise in vaccines adjuvant</li> <li>• Experience in strategic alliances with multinationals (GSK, Novartis, Institut Pasteur)</li> <li>• Long term stability forecast and sustainable growth of Brazil’s economy</li> </ul>	<ul style="list-style-type: none"> <li>• Investments from public and private sectors do not cover the current needs</li> <li>• No significant local biotech companies to fill the gap between research and production</li> <li>• The new regulatory framework allows private firms to do technology transfer and be the only supplier to the Government Immunization program for 5 years before to fully transfer the technology to the public institution. This mechanism is not satisfactory for new and more expensive vaccines with a high strategic content<sup>52</sup>. Companies would prefer to sell these products directly</li> </ul>
<b>Opportunities</b>	<b>Threats</b>
<ul style="list-style-type: none"> <li>• R&amp;D partnerships with national firms for new vaccines to speed up their current projects or license patented products</li> <li>• Opportunity for UK companies that cannot license products to large UK pharmaceutical firms for lack of interest</li> <li>• Governmental control over the Brazilian market ensures a captive market for 5 years and a steady sales stream</li> <li>• Urgent demand for new products from the public health programs to increase access to WHO essential medicines for reimbursement</li> <li>• Public firms are looking for technology transfer<sup>53</sup> partnerships for the Latin America Market and Africa</li> <li>• Bio-Manguinhos has a portfolio of 25 WHO-designated essentials vaccines, planning to add 10 more to this list</li> </ul>	<ul style="list-style-type: none"> <li>• The bulk of the market is public and under Government control for pricing</li> <li>• Butantan Institute and Bio-Manguinhos dominate the market and are already well settled, producing enough traditional vaccines for the domestic market</li> <li>• Common barriers in the vaccine sector are the long production cycles and the high costs of good manufacturing practices and quality control</li> </ul>

**Table 22: SWOT analysis for the vaccines segment**

<sup>52</sup> Such as vaccines for cervical cancer, Dengue fever, malaria or HIV

<sup>53</sup> Recent agreements signed pharmaceutical companies such as Aventis or GSK for a Rotavirus vaccine and a cervical cancer vaccine demonstrate that collaboration to speed up current projects or even to bring new technologies and products is welcome and allows an earlier market entry.

There is still a great need in vaccines in Brazil. If the average cost for a mature vaccine is still low, the new vaccines will be expensive to develop. If private companies are to make significant investments for new vaccines, the Brazilian Government must give them a market access to the Brazilian purchasers. The current model allows getting access to a large population through the Public Immunization program, but the transfer mechanisms have to change for future innovative products.

It currently seems necessary to partner with a public laboratory. In addition to the two main public institutions mentioned, Butantan or Fiocruz, FUNED is also looking for such partnerships and is a key institution in the vaccines area. However, the product has to answer the needs of the local market, as set by the government.

A positive point is that the Brazilian government is open-minded and realized its broad reimbursement schemes were cannibalizing the private market. The paradigm shift is occurring and it is now realized that people who can afford it should pay for healthcare so that the Government could pay for those who get access to healthcare.

## 2.2 Scenario for collaboration

Beyond the provision of **low-cost vaccines** to the broadest base of patients, public laboratories are eager to develop new vaccines. There is a great expertise in the vaccine domain in Brazil, but many opportunities exist to build on this expertise to scale up the production of traditional vaccines for exportation and develop new market opportunities. Opportunities in new vaccines are also of great interest.

***Proposed scenario for collaboration***

***“Bring UK expertise and investments in production with Brazilian expertise and capabilities for TB, Malaria vaccines to tackle new markets through Brazil”***

<b>Expertise and Capability</b>	<b>UK</b>	<b>Brazil</b>
○ Expertise in Vaccine Development	✓	✓
○ Expertise in Vaccine Production		✓
○ High volume vaccines fermentation		✓
○ High volume vaccine purification		✓
○ Scale up in Vaccines		✓
○ New Vaccines and R&D	✓	
○ Large domestic market		✓
○ Access to other markets		✓
○ Private investments	✓	

**Table 23: Scenario for vaccine collaboration**

## ***Feasibility***

### **Is investing in R&D for tropical and neglected diseases a priority for the UK?**

Beyond the sole Brazilian Market, there is a world-wide need for vaccines against tropical and neglected diseases. Although treatments for these diseases do not seem as attractive as the next blockbuster drugs, the very high volume potential outstandingly compensates for the lower prices of these cures. UK companies such as Acambis and DiagnoVis are highly interested in developing Yellow fever, Dengue, Tuberculosis, Malaria, West Nile and Typhoid vaccines.

In Brazil, GSK is actively developing its Vaccines pipeline, mainly through the creation of new products such as the Meningitis C or cervical cancer vaccines, but lower-value vaccines are also considered as a way to amortize R&D costs for products at the end of their life-cycle.

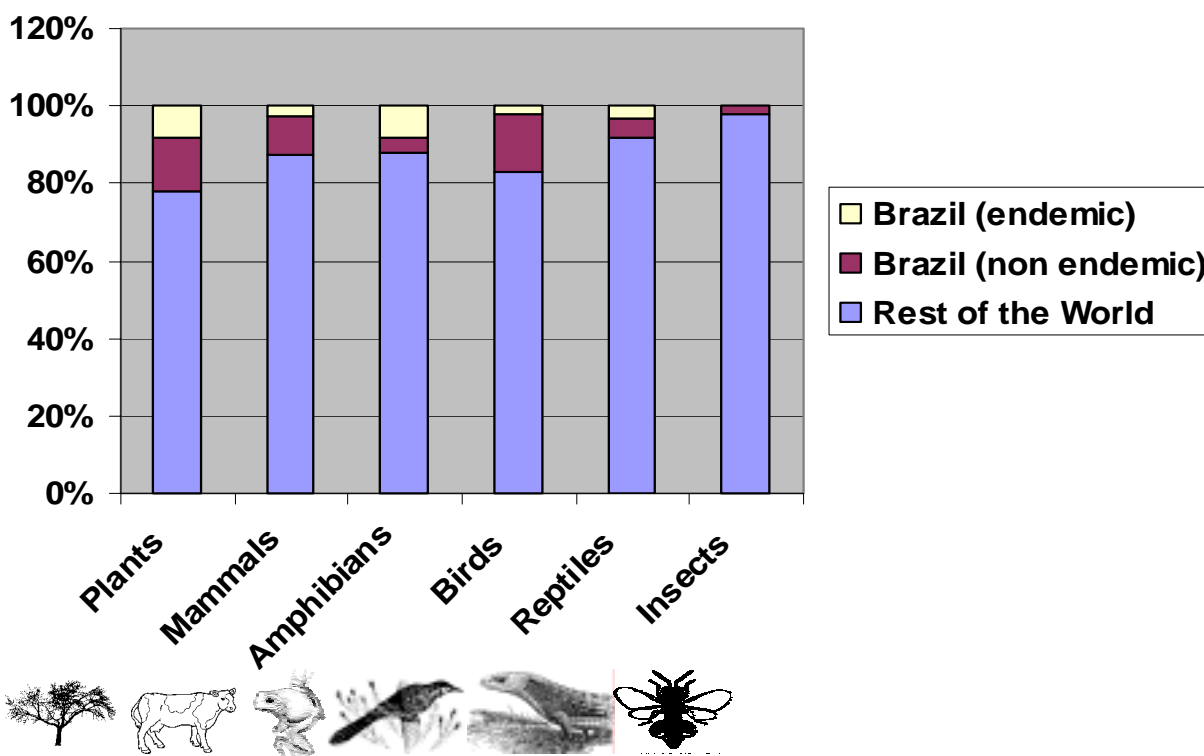
### 3. Related scenarios of interest for generics and vaccines

#### 3.1 Biodiversity-based drug discovery

Brazil has the world's greatest biological diversity, and the Amazon region alone represents 26% of the world's remaining tropical forests. Along with 15 other countries, including India, Brazil accounts for 70% of the world's animal and plant species<sup>54</sup>.

	Number of species in Brazil	Number endemic
<b>Plants</b>	55,000	N/A
<b>Mammals</b>	578	131
<b>Amphibians</b>	695	454
<b>Birds</b>	1712	207
<b>Reptiles</b>	651	258
<b>Freshwater fish</b>	3,000	N/A
<b>Insects</b>	15,000	N/A

**Table 24: Brazilian species diversity and endemic species**  
 Source: World Resources institute, Earth Trends<sup>55</sup>



**Figure 21: Percentage of World species found in Brazil, and endemic to Brazil**  
 Data from: World Resources institute, Earth Trends

The great diversity of the Cerrado, Amazon rainforest, Pantanal wetlands, Caatinga region, Araucaria and Atlantic forests makes Brazil the partner of choice to find novel molecules, whether for drug discovery or cosmetics and natural products.

<sup>54</sup> Senator Marina Silva, Biodiversity: Opportunities And Dilemmas, National Congress of Brazil, April 2002

<sup>55</sup> [http://earthtrends.wri.org/searchable\\_db/index.php?theme=7](http://earthtrends.wri.org/searchable_db/index.php?theme=7).

The 1995 Convention on Biological Diversity (CBD) and the Bonn Guidelines on Access and Benefit-Sharing provide the basis for building partnerships that enable countries like Brazil to use the potential of their biodiversity for research to meet domestic needs. The Foundation Oswaldo Cruz has selected some compounds of interest for its research programs on tuberculosis, malaria and T-cell immunological diseases<sup>56</sup> and has identified biodiversity as a source of NCEs against defined molecular targets for these diseases.

However, past highly controversial agreements with pharmaceutical companies make this subject very sensitive in Brazil and collaborations can be envisioned only within clear and transparent frameworks<sup>57</sup>.

**Proposed scenario for collaboration**

***"Setting up a collaborative 'active agent' discovery Joint Venture using Brazilian biodiversity and UK systems biology knowledge and platform technologies"***

<b>Expertise and Capability</b>	<b>UK</b>	<b>Brazil</b>
○ Biodiversity		✓
○ Extraction expertise and facilities		✓
○ Private investment (VC and Angel)	✓	
○ Analytical/Combinatorial chemistry	✓	
○ Investments in innovative research	✓	
○ Lower R&D costs		✓
○ Platform technologies	✓	
○ Cellular/Molecular assays	✓	✓
○ Systems biology	✓	
○ Drug Development	✓	
○ Pre-clinical studies	✓	
○ Clinical studies		✓

**Table 25: Scenario for biodiversity-based collaboration**

<sup>56</sup> Luiz A. Basso et al., The use of biodiversity as a source of new chemical entities against defined molecular targets for treatment of malaria, tuberculosis and T-cell mediated diseases – A review, Mem Inst Oswaldo Cruz, Vol 100, 2005

<sup>57</sup> A description of the sensitivity of this subject is proposed in part 4 of Chapter 3

## Feasibility

There certainly exists an interest in benefiting from Brazilian expertise in extracting natural molecules. Even some generic antibiotics, or topical steroids are produced by fermentation and extraction of natural entities, as their entire synthetic manufacturing is too complex.

Far-Manguinhos runs a biodiversity program and has identified and patented 20 molecules. Brazilian CROs could find interest in collaborations with UK companies that would bring financial resources and platform technology expertise to take forward the molecules extracted by a Brazilian partner<sup>58</sup>. The sensitivity of the biodiversity and the Amazonian forest makes necessary the creation of a joint venture with a local partner.

### 3.2 Collaboration for clinical trials

Brazil is from many points of view a good environment to carry out clinical trials. The lower costs – 30% of the costs for clinical trials carried out in Europe and the USA – as well as qualified professionals and CROs are some of its strengths.

Brazil's **large and varied population** allows finding of all types of diseases, from tropical and neglected diseases to diseases most prevalent in western countries as the population is moving toward a more urbanized life-style. For companies working in niche areas, this situation increases the chances of finding individuals with rare diseases.

Brazil's population is highly **multiethnic**. Brazil is the host country of the largest Japanese community outside Japan (about 1.4 million Japanese, compared to 800,000 in the United States). This is a real benefit because of the difference in genetic profile of the subjects of the Japanese branch. Finding descendants of many ethnic groups allows building more relevant patient samples, which is important to validate the significance of a clinical trial.

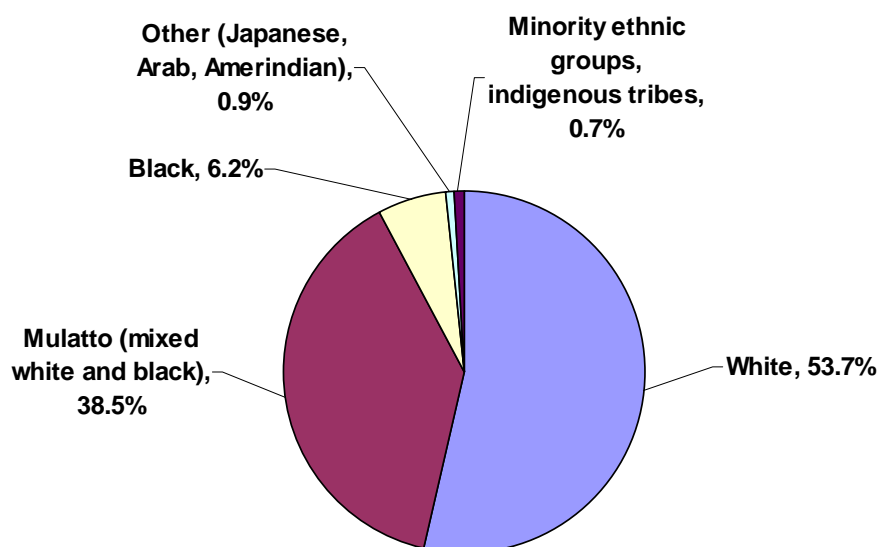


Figure 22: Population breakdown by ethnic group, 2000 census

<sup>58</sup> The firm Extracta is doing biodiversity screening with GSK and is contracted to find molecules that target a specific receptor for treatments against specific diseases. It uses GPS technology to record the collection site and delivers the molecules to the contractor firm, which will carry out the development and pay milestones to Extracta, as well as royalties if the product is commercialized.

**Proposed scenario for collaboration**

**“Bringing together the UK innovative pipeline and Pre-clinical studies with Clinical trial opportunities for Phase II and III in Brazil”**

Expertise and Capability	UK	Brazil
○ Novel molecules	✓	
○ Regulatory expertise	✓	
○ Qualified physicians and professionals	✓	✓
○ Large and varied population		✓
○ Lower cost		✓
○ Pre-clinical	✓	
○ Clinical Phase I	✓	
○ Clinical Phase II		✓
○ Clinical Phase III		✓

**Table 26: Scenario for clinical trials collaboration**

**Feasibility**

As a lower proportion of the population has had access to complex drugs, many patients could still be considered “**drug-naïve**” and would be of interest for clinical trials. Finding drug-naïve patients for studies is a major problem in developed markets.

Brazil has about 205 physicians per 100,000 of the population, which represents a potentially large pool of investigators for clinical studies. Many of these physicians have followed post-grad training in the US and Europe and so clinical practice in reference hospitals is aligned with international clinical guidelines. At major universities, physicians have already been trained in GCP and are experienced in multi-center international clinical trials in conformity with US-IND or EU guidelines<sup>59</sup>.

There is also a great interest in Brazil for pre-clinical studies and clinical phase I studies, but this has not historically been a strength of the Brazilian clinical research, rather focused on human studies and immunization programs. Brazil’s strengths rather lie in phase II, III and post-launch studies, where the assets of the population characteristics can best be employed. However, there is no doubt that over the years, phase I capabilities will develop in Brazil. A good opportunity for Brazil is to build a service industry in pre-clinical and clinical drug development along with the clinical trials to increasing the credibility of clinical research teams<sup>60</sup>.

However, the current regulatory environment for clinical trials is complex and the approval of a clinical trial can take between four and six months. Work must be done jointly with

<sup>59</sup> Faiz Kermani, Regional roundup: Brazil, Contract Pharma, October 2005

<sup>60</sup> The Center of the Federal University of Ceara, has specific projects to develop drugs with various companies already and is carrying out bioequivalence studies.

the industry to try to accelerate this time frame, because this clearly makes Brazil less competitive than the US or European countries.

### 3.2 R&D collaboration for new medicines

Public and private research centers of very high standard have great expertise in extraction of formulae from natural products, vaccines manufacturing, or Clinical trials design among others. Academic research carried out in major Universities, concentrated in the States of São Paulo (UFSP, Unicamp), Rio de Janeiro (UFRJ, PUC), Rio Grande do Sul (Porto Alegre), Ceara and Minas Gerais (UFMG), as well as success in the genome project (GENOMA Network) gave Brazil the ability to sequence a genome faster than any other country. Research in stem cells and other biotechnology key areas further demonstrate the capabilities of the scientific teams. Several private hospitals in São Paulo and Rio de Janeiro are well positioned in the field of cancer and cardiovascular research.

Expertise and Capability	UK	Brazil
○ Combinatorial chemistry	✓	
○ Platform technologies	✓	
○ Drug discovery	✓	
○ Novel drug delivery	✓	
○ Stem cells	✓	✓
○ Systems Biology	✓	
○ Biology		✓
○ Agribiotech		✓
○ bioinformatics		✓
○ Genomics	✓	✓
○ Clinical research	✓	✓

Table 27: Research complementarities

**Proposed scenario for collaboration**

**“A UK company provides expertise to a Brazilian company to do drug discovery and/or cosmetic/agrochemical discovery”**

Expertise and Capability	UK	Brazil
○ Innovative research and expertise	✓	
○ Lower R&D cost		✓
○ Private investment (VC and Angel)	✓	
○ Platform technologies	✓	
○ Drug development	✓	
○ Professional services, CROs	✓	
○ Regulatory and compliance	✓	
○ Pre clinical	✓	
○ Clinical trials organization	✓	✓

**Table 28: Scenario for new medicines collaboration**

**Feasibility**

In licensing novel compounds, techniques or technologies from Brazil’s impressive and world-class R&D output is of interest for the UK. Brazilian research centers have stunning scientific capabilities that indicate a strong and easy future in collaborative research ventures. As the UK is moving toward systems biology, it will need to bring in multidisciplinary teams with expertise in chemistry, biology, bioinformatics and many other areas.

Beyond the need for traditional vaccines and ARV drugs, the Brazilian market is developing the characteristics of most advanced western markets, and will need the same innovative drugs. Brazilian companies such as LIBBS are looking for **innovative products with a good patent protection**, as they mainly operate in the Ethical pharmaceutical segment<sup>61</sup>. The UK could bring R&D efforts in this area to carry out co-development of vaccines, pharmaceuticals, biologicals, and immunologicals in Brazil, where R&D costs are about 25% of those in the UK.

**Licensing** a product from a UK company would also be of interest. Brazilian companies have been too focused on similars and are now are facing a gap in R&D. Shifting from Marketing to R&D focus is long and difficult, and in the meanwhile, UK companies could license-out their new compounds for production and distribution in Brazil. However, for real co-development deals with research carried out in Brazil in the area of innovative drugs, the Brazilian local infrastructures may not be ready yet, especially if involving APIs in the production. Contacts interviewed estimate that the context would be more favorable in two years for such opportunities.

<sup>61</sup> That is, the pharmaceutical segment that requires prescriptions

## **Conclusion**

The major asset of UK companies in all cases studied above is bringing the culture, the knowledge of transformation of innovative ideas into products, highly qualified personnel and practices, as well as a high level R&D. The strong culture of risk capital, and venture capitalists present in the UK barely exist in Brazil. This, coupled to the monetary capabilities of the UK would be beneficial for the development of the private sector in Brazil.

The Brazilian contribution is highly valuable, ranging from a huge potential for new markets, to very rigorous regulatory frameworks and state-of-the-art research and development capabilities in domains where the UK may not be as good historically.

### **The best opportunities are:**

- Research collaborations between UK and Brazilian R&D teams for new drugs and products, building on the Brazilian universities and research centers high level, backed by UK capital.
- Developing clinical trials for phase II and III with the assets of the Brazilian expertise and diversity of the population is also of interest
- ***In Vaccines:***  
Discovery of new products, R&D collaborations for novel vaccines, building on the Brazilian expertise in the vaccines field, supported by UK private investments.
- ***In Generics:***  
The UK would bring chemical synthesis and APIs capabilities to Brazil to tackle a huge and growing market.

## 4. Barriers to partnerships

### 4.1 *Bias and perception*

The cultural difference between Brazil and Europe as well as distance and language can overwhelm UK companies. It is very important to speak the local language to do business in Brazil, and there is some reluctance in some milieus to partner with foreign firms.

However, universities and private hospitals will seize the opportunity to build international collaborations. It is not in the local culture to do R&D for a foreign firm, go outside Brazil and there is a lot of ignorance on IP in the academic universe, whereas there is a lot of sophistication and understanding in the UK in this domain.

In some areas related to biodiversity, a foreign firm exploiting local resources is a concern. The cooperation agreement signed between the Brazilian Association for the Sustainable Use of Biodiversity in the Amazon (BioAmazônia) and Novartis in 2000 raised a public outcry about multinationals coming to Brazil and exploiting the rainforest. This agreement provided for the large-scale transfer of extracts derived from the Amazon's biodiversity, allowing Novartis exclusive rights to patent and control the products developed. It was severely criticized and the government eventually considered it harmful to the country's interests and recommended it be suspended, particularly because Brazil had no legislation in force with which to guarantee its sovereignty over its own genetic resources<sup>62</sup>. The concept of **biopiracy**<sup>63</sup> emerged with this problem, and is creating a quandary, as the potential of the Brazilian Biodiversity is now starting to be realized but there is no consensus on how to best use it.

Collaborations involving a Brazilian company extracting the molecule and active principles, and the UK player screening them with its platform technology, in Brazil, could solve this problem. The Brazilian Government has identified opportunities for a foreign company to produce on site, but it would be preferable to partner with a local player to avoid repeating the case above. More and more educated people are more visionary, as they know Brazil needs to move forward to become competitive as a country on the global stage.

### 4.2 *Regulatory issues and government intervention*

#### **Regulation**

Even if Brazil has the most transparent administration in Latin America, regulation is still a concern. The approval process at ANVISA is expensive, long and stringent, and the bureaucratic burden makes this process very unsatisfactory. Brazil lacks people trained to write patents, and the National Institute for Intellectual Property (INPI) lacks trained examiners, this is why patent applications can be frustratingly long (up to 7 years).

In clinical trials, physically importing a foreign product for clinical trials in Brazil requires going through 3 committees, a very lengthy process, whereas if the molecule is produced in Brazil, only one committee is required.

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<sup>62</sup> Senator Marina Silva, Biodiversity: Opportunities And Dilemmas, National Congress of Brazil, April 2002

<sup>63</sup> Access and Benefit sharing (ABS) in Brazil: the new legal formula for legitimizing biopiracy, [www.socionambiental.org](http://www.socionambiental.org),

### Government intervention

Federal bureaucracy is still high, as the government in Brasilia has important delays, as well as the state administration in Rio de Janeiro. The São Paulo region is more focused financial returns and therefore has faster procedures. Porto Alegre is also more dynamic.

Twenty pharmaceutical laboratories were fined in 2005 for having boycotted the entry of generics in the country. They were denounced by the Pharmaceutical Regional Council of the Federal District and the Administrative and Economic Defense Council (CADE) considered they had violated the anti-trust law by forming a cartel in 1999. Janssen Cilag had to pay a fine of 2% of its 1998 turnover, and nineteen other laboratories paid a fine of 1% of their 1998 turnover in Brazil<sup>64</sup>:

Abbott	Akzo Nobel
Eli Lilly do Brasil	Glaxo Wellcome
Roche	Merck Sharpe Dohme
Pharmacia Brasil	Astra Zeneca do Brasil
Biosintética	Boeringher Ingelheim do Brasil
Schering Plough	Aventis Behring
Bristol Myers Squibb Brasil	Sanofi-Synthelabo
Aventis Pharma	Wyeth-Whitehall
Bayer	Janssen-Cilag
Eurofarma	Byk Quimica Farmaceutica

**Table 29: Laboratories fined to 1% of their 1998 turnover by the CADE**

Source: Terra Espana, 14/10/2005, Network Médica

### Tax

Tax is between 15 and 20% due to the action of the government to control inflation and encourage economic growth. Import Tax on scientific equipment discourages shipments of technical equipment to Brazil and reducing these taxes on pharmaceutical production is slow and will take many years to adjust the taxes on pharmaceuticals in Brazil to a reasonable level, regardless of which party is in control in Brasilia<sup>65</sup>.

Finally, as the Brazilian government controls prices in the Healthcare sector, this policy deters some private investments. The combined problems of tax, a tough market, and price control makes Brazil a difficult place to operate and some companies prefer to choose easier environments.

## 4.3 Market characteristics

The Brazilian market requires a long term market commitment. The overall context, the lesser attractiveness of the exchange rate<sup>66</sup> and the risk of reverse engineering also discouraged investors in the past. This is why most initiatives and businesses are still publicly financed.

<sup>64</sup> Terra Espana, 14/10/2005, Network Médica at <http://www.cbgnetwork.org/1208.html>

<sup>65</sup> Jefferson Oliveira, Market overview of drugs and pharmaceuticals, International Market Insight , July 2003

<sup>66</sup> May 2004: 1£=5.6 R\$; May 2005: 1£=4.5R\$; May 2006: 1£=4.12R\$

### 4.3.1 Lack of private investment

There is the relatively small proportion of private investment and risk capital. The venture capital activity is developing slowly, but is currently qualified of very immature, as there are extremely few venture capital investors, and few business angels.

The price of money being so high – 15.75% interest rate – it is very difficult to borrow money to increase production capacities, or simply create a business. This high cost calls for higher profitability margins to recoup expenses. There is therefore a tremendous need for foreign private investment, which is not dependent on these interest rates.

Reflected in the biodiversity issue, there certainly exists technical expertise to harness the rainforest but no private investment, and therefore no automated business methods: the company Natura has built a massive business based on rainforest material but its suppliers are local gatherers who collect material from the forest, and a shortage in supply could cause concerns to a shareholder.

### 4.3.2 Other factors

Foreign firms do invest in Brazil, as testified by important Net foreign direct investments of US\$ 9.3 billion. However, these investments are often made in production capacity but not in R&D. **This strategy is not visionary**, as the greatest need of the Brazilian market today is precisely R&D investments, and most valuable Brazilian partners are looking for added value to their current expertise.

Brazil is careful about not giving the same image as India when it opened itself to foreign investments a few years ago, or to solely propose to produce generic drugs at low cost. If the government is starting to lower barriers to entry like India, it remains careful to attract partners that care first about the needs of the country.

Corruption can also be worrying but it is believed that a UK company seeing a potential in Brazil would not be stopped because of this factor, as the potential of doing business in Brazil would be much higher.

#### **Brazil Cost**

There is a general recognized cost of doing business in Brazil, commonly identified as the “Brazil cost” that can be assimilated to an opportunity cost, barriers to action and delays in business. Brazil can be highly bureaucratic and at the same time rules are not always clear and can be subject to interpretation. Doing business there can take time and be frustrating. A contact interviewed explains: “We had to send cells in dry ice to Brazil. As the time to clear customs was growing, we were getting extremely nervous that the content of the shipping be completely lost in case the ice thawed. The shipment cleared the customs at the very limit to salvage its content. Some rules are overly protectionist, and importing is expensive. Labor law is complicated and there are over 50 different taxes in Brazil, at various Municipal, State and Federal levels, and they vary from state to state, which does not make things easier. The pharmaceutical sector is still under price control by the government, and the ANVISA registration process is still extremely tough: rules are not very clear and are often changing. The ANVISA is modeled on the FDA but operates with a budget of one tenth of that of the FDA”.

## Chapter 4

### Conclusion

Brazil can no longer be classified as an emerging market. It requires a sophisticated strategy, as well as patience and a long-term strategy. This market can be very challenging, but the rewards are equally important.

Brazil is deliberately creating a business environment and sending the message that the country is open for business. It fulfills the key variables considered for investment decisions<sup>67</sup>:

- A pricing policy that recognizes the relevance of innovation
- A Patent law that ensures intellectual property rights
- A stable and well defined regulatory policy geared toward innovation
- An industrial policy for long term investment and innovation

Coupled with the richness of the Brazilian research and innovative capabilities, this attracts investors from abroad, competitors of the UK in the biotech sector: France, Germany, Japan and Korea are particularly active and developing commercial and technical links.

Additionally, since the Brazilian biotech industry is still relatively new, the expertise of UK companies across a wide range of disciplines such as regulatory compliance, management, best clinical practice, Intellectual property and Good Manufacturing Practices would have great marketing opportunities. The UK could also serve as a platform for Brazilian companies to set up operations to sell their products as a gateway to Europe<sup>68</sup>.

#### 1. Key methods of doing business

The business environment in Brazil is very similar to the USA and European countries. It takes understanding of the culture and market needs to hone a strategy. It is especially important to Brazilians to have personal contact, and UK companies must be ready for frequent in-country visits and phone calls in addition to written contact.

The official language is Brazilian Portuguese, somewhat different from European Portuguese, which should be avoided. English and Spanish are increasingly used in business, but, some senior professionals still mainly speak Portuguese, so it is important to be able to communicate in the local language.

Association with a local partner is the best way forward, as it enables a combination of the local market knowledge with the foreign expertise. Furthermore, in the public sector, products must be purchased through tenders, and only companies established in the country and approved by the Ministry of Health can import equipment. However, licensing a product to a local partner does not necessarily mean this must be from a Brazilian company. There are indeed many multinationals companies implanted in Brazil.

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<sup>67</sup> Jorge Raimundo, Global Vision of the Pharmaceutical Industry, 3<sup>rd</sup> International Convention for Technical Directors of the Pharmaceutical industry, August 2005

<sup>68</sup> Iain Cloughley, R. New, B. Clarke, Market Summary, UKTI Biotech Scoping Mission To Brazil, Sept 2005

## **2. Way forward to forge partnerships**

### **2.1 What can Brazil do?**

It is not a tradition among Brazilian manufacturers and researchers to engage internationally. The most urgent action would be for Brazilian researchers and industries to communicate more about research projects and needs. This could be achieved through travel grants to Brazilian scientists to increase the presence at international conferences and solve this lack of publicity.

In the medium term, identifying best universities research programs and organizing technology visits in the UK – for instance at the Cambridge Science Park or the Cambridge biocluster in general – would allow making contacts with UK firms.

It is surprising to see some Brazilian Graduates and physicians' capabilities being questioned when they go back. The Brazilian Medical Council understandably protects the medical profession, but those people trained abroad are the very ones with international contacts and links, and better incentives should be given to them to come back.

In the longer term, it is important to bridge the communication gap to let foreign players be aware of the market requirements and potential. The government drive to develop private research is very encouraging, but more efforts must be done to further improve public-private partnerships. Currently, the market exclusivity access mechanism granted by the Brazilian Government cannot attract firms with higher margin products that do not fit the Ministry of Health requirements. However, the Brazilian government is realizing this mechanism is cannibalizing Brazil's private market – people who can afford it should pay for healthcare so that the government can pay for those who cannot afford it – and an encouraging paradigm shift is occurring.

### **2.2 What can UKTI do?**

On the UK side, a similar communication action can be envisioned in the short term. It would be beneficial to make UK industrial players realize that things are changing in Brazil, and send representatives of some UK SMEs to Brazil to improve their perception of the country's potential.

In the medium term, forging contacts in Brazil is of prime importance. It is vital to find a local partner to give transparency to the collaborative process, and it is possible to get grants in the biotech and human health areas and incentives from local city halls in case of a partnership with a local company. It is worth stressing that it is not necessary for a UK-based research team to move out of the UK to relocate in Brazil, as it can find a local team in Brazil to lead the project jointly.

In the longer term, the UK should engage as much as possible with the Brazilian government to help market requirements and regulations move in the right direction, as well as suggest the most necessary improvements. By proposing more some scientific interactions, the UK could help Brazil to become self-sufficient in the domain of technology and become a partner of choice for Research collaborations.

Finally, Brazilians sometimes describe themselves as good scientists and technicians, but not good businessmen. From its culture of business and risk capital, this is precisely what the UK can bring to Brazil.



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- Dr Paulo Lee Ho, Instituto Butantan (São Paulo)
- Dr Roger New, Executive Director and Do-Founder, Proxima Concepts
- Dr. Paulo Wrobel, Advisor on Trade Promotion at the Embassy of Brazil in the UK
- Jeff Chapkmans, BioProcess UK
- John Anderson, Exellion (Petropolis, RJ)
- Jorge Raimundo, President of Advisory Board, INTERFARMA
- Mr. Dianary Oliveira, Business Development LIBBS Farmacêutica Ltda
- Rogerio Ribeiro, President of GSK Brasil Ltda (Jacarepagua, RJ)

## Appendices

### Appendix 1: Relationship between UKTI, DTI and Foreign Office<sup>69</sup>

#### 1. Department of Trade and Industry (DTI)

[www.dti.gov.uk](http://www.dti.gov.uk)

The mission of the DTI is 'to create the best environment for business success in the UK'. The Department helps people and companies become more productive by promoting enterprise, innovation and creativity. This includes supporting successful business, ensuring fair markets, and promoting science and innovation.

As part of the remit to promote the UK's science, engineering and technology, the DTI is responsible for:

- UK Science Policy, through the Office of Science and Technology (OST)
- Public engagement with science, through the Science and Society programme
- Promoting the development and use of technology by industry
- Helping organizations understand the importance of innovation
- Providing collaborative grants.

There is also an international focus to this work:

- OST International Directorate:  
Develops and manages UK involvement in the EU's science and technology activities. Maintains strong links with major science partners across the world.
- Global Watch service:  
Enables UK companies to improve their competitiveness by identifying and accessing innovative technologies and practices from overseas. The service includes: international secondments, group missions overseas, a network of International Technology Promoters providing consultations and hands-on assistance to UK firms interested in improving their technological capability, and international information via the Global Watch website ([www.globalwatchonline.com](http://www.globalwatchonline.com)). This service is currently outsourced to the consultancy firm Pera.<sup>70</sup>

#### 2. Foreign and Commonwealth Office (FCO)

[www.fco.gov.uk](http://www.fco.gov.uk)

The purpose of the FCO is 'to work for UK interests in a safe, just and prosperous world'. The overseas network includes over 200 diplomatic offices, and the objectives include:

- To lead and co-ordinate the UK's European and international policies
- To promote UK policies and values around the world
- To provide important direct services abroad to UK citizens and businesses
- To provide expert foreign policy advice to Ministers and the Prime Minister
- To pursue UK interests on the ground in crisis regions
- To negotiate for the UK in international organizations
- To gather, analyze and target information for the Government and others
- To organize senior level international contacts.

<sup>69</sup> From Nicola M R Perrin, The Global Commercialisation of UK Stem Cell Research, June 2005

<sup>70</sup> <http://www.pera.com/website/innovationthroughaglobalperspective.aspx>

In order to deliver these objectives, the FCO has established a Science and Innovation Network which fulfils the following functions:

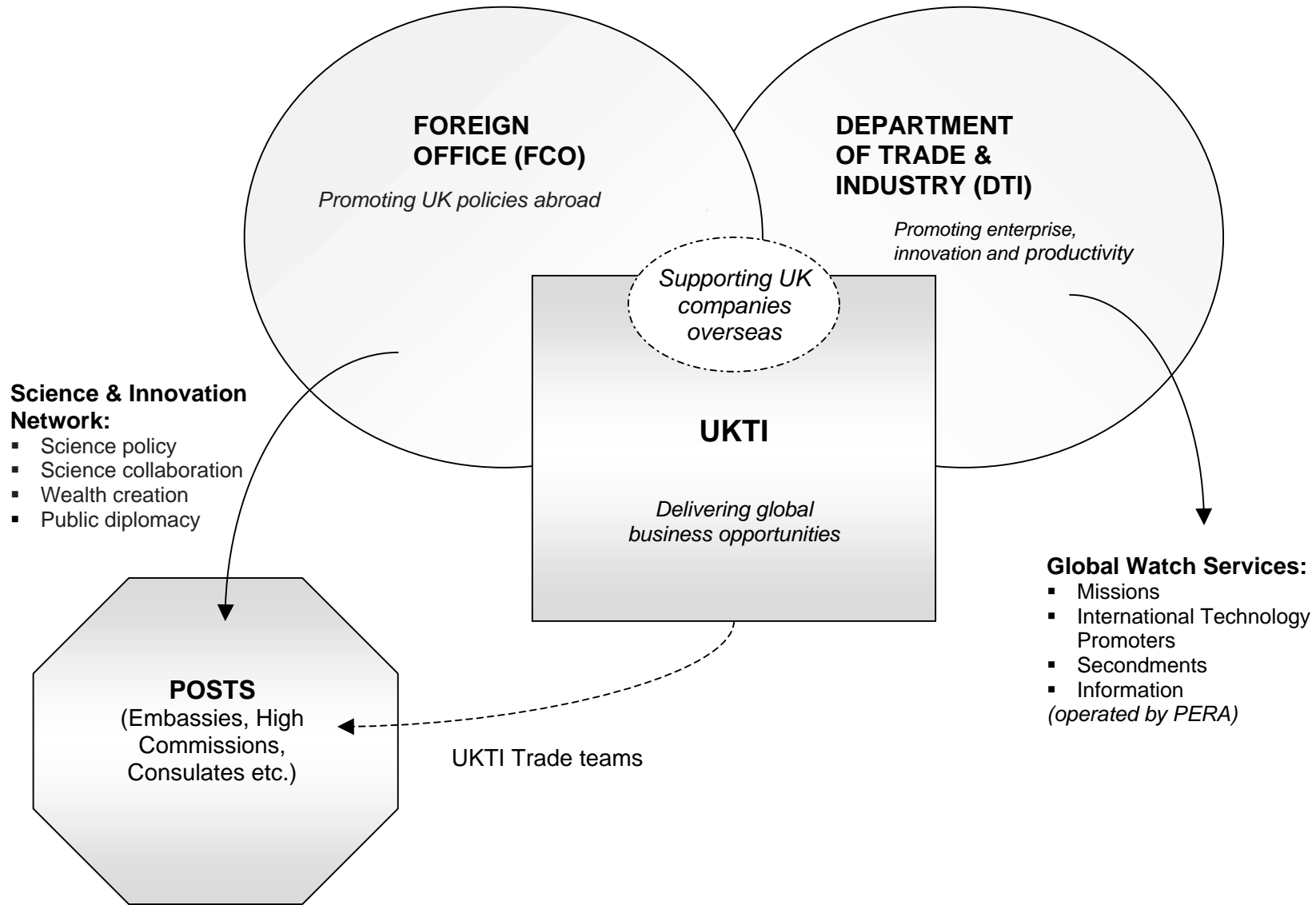
- Analysis of, and reporting on, policy and S&T developments in the host country
- Identifying key contacts and bringing together opinion formers and experts
- Helping to arrange missions and visits to study particular sectors
- Lobbying and influencing international negotiations
- Raising awareness in country of UK S&T policy and achievements
- Developing links for the UK science base
- Promoting exchange of ideas.

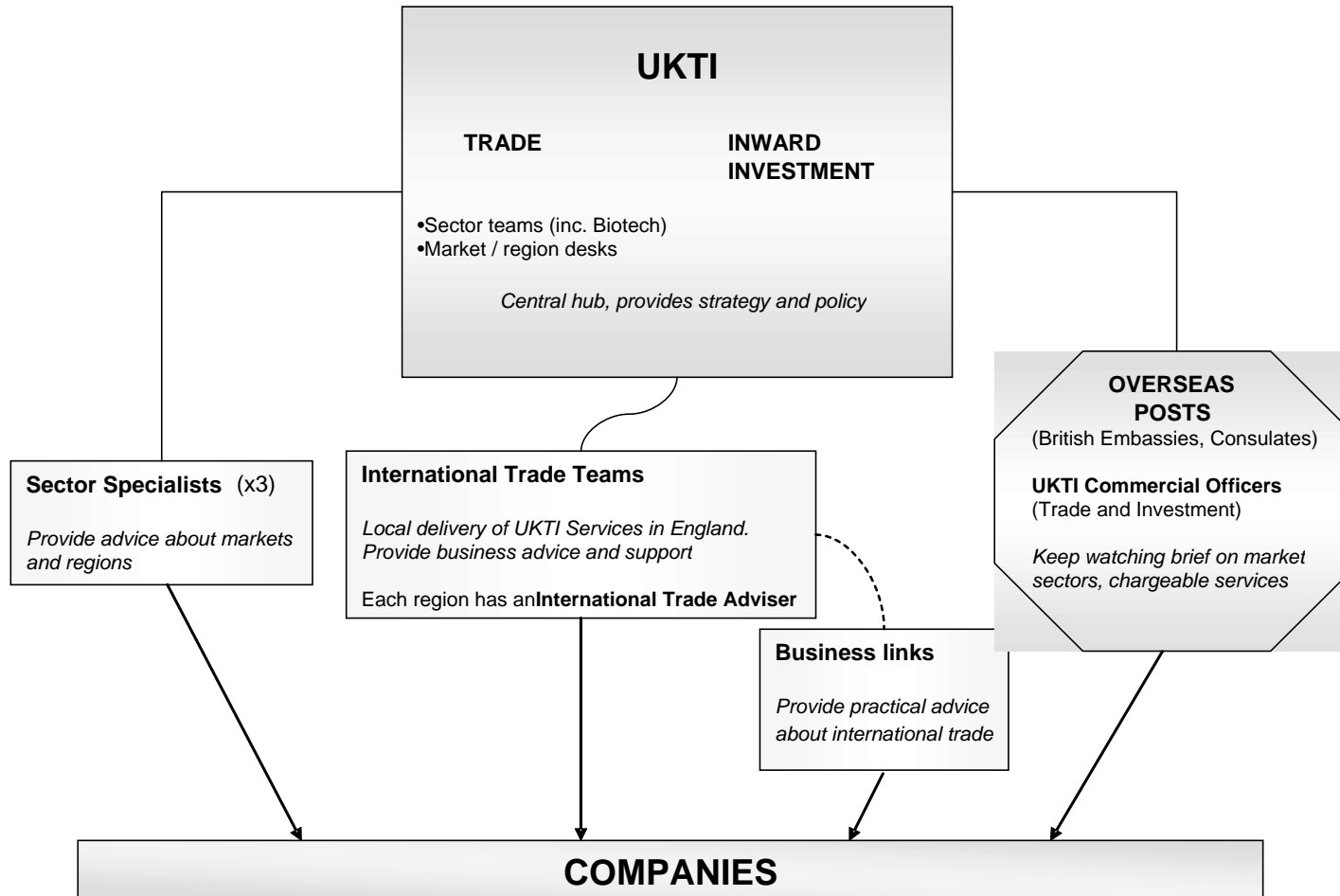
### **3. UK Trade and Investment (UKTI)**

[www.uktradeinvest.gov.uk/ukti](http://www.uktradeinvest.gov.uk/ukti)

UKTI is funded by the DTI and the FCO, and helps to deliver global opportunities to UK businesses. UKTI supports companies in the UK which aim to trade internationally, and overseas enterprises seeking to invest in the UK. The organization provides practical advice about exporting, information on specific opportunities in markets and sectors, and a network to promote UK business overseas.

UKTI works closely with both the DTI, with regional advisors to support local businesses, and the FCO, with trade teams in major foreign embassies and consulates. The relationship between the different organizations is illustrated in the Figures below.





## Appendix 2: Scores on proposed scenarios

### Method

The opportunities analyzed were identified according to a systematic literature analysis, complemented by interviews with professionals based in Brazil and in the UK. Each point was thoroughly analyzed according to its interest, achievability and viability. For each opportunity, a scenario was drawn for collaboration, outlining what complementary skills were present and could be brought from the Brazilian and UK side.

### Assessment of complementary skills

Scenarios are summarized in tables with ticks where the country was deemed as having a competitive advantage to bring to a partnership. The absence of tick does not indicate that this skill is non-existing in the country, but that the other partner may have superior skills or resources in this domain. All criteria are evaluated from the perception and opinion of several contacts interviewed when information was available and may not reflect accurately the state of the art in the country. It was not possible to assess the political or social context of each scenario; scores therefore do not take this into account.

### Method for scoring

Where skills are complimentary, each item is assigned a score of 1. When skills exist in both countries, the item is valued at 0. Values are added up and normalized by the number of factors considered, thus giving a score on a scale from 0 to 1, the worst case – 0 – being if both countries already possess all they need and do not see any benefit in collaborating. This score can also reflect the probability that such a partnership could take place according to the interest both parties would find in doing this collaboration. It allows a relative ranking of opportunities, but should not in any case represent an absolute value of attractiveness.

## 1. Collaboration in generics

***“Bring UK investment or expertise for a local production capability of raw materials for generics, for domestic or export use”***

Expertise and Capability	UK	Brazil
o Domestic Market size and growth		✓
o Private investments, creative financing	✓	
o Primary manufacturing (raw chemicals and APIs)	✓	
o Secondary manufacturing		✓
o Low manufacturing costs		✓
o Scale up in Generics manufacture		✓
o Distribution network		✓
o Potential for access to other markets		✓

**SCORE = 1**

## 2. Collaboration in vaccines

***“Bring UK expertise and investments in production with Brazilian expertise and capabilities for TB, Malaria vaccines to tackle new markets through Brazil”***

Expertise and Capability	UK	Brazil
○ Expertise in Vaccine Development	✓	✓
○ Expertise in Vaccine Production		✓
○ High volume vaccines fermentation		✓
○ High volume vaccine purification		✓
○ Scale up in Vaccines		✓
○ New Vaccines and R&D	✓	
○ Large domestic market		✓
○ Access to other markets		✓
○ Private investments	✓	

**SCORE = 0.889**

## 3. Biodiversity-based drug discovery

***“Setting up a collaborative 'active agent' discovery Joint Venture using Brazilian biodiversity and UK systems biology knowledge and platform technologies”***

Expertise and Capability	UK	Brazil
○ Biodiversity		✓
○ Extraction expertise and facilities		✓
○ Private investment (VC and Angel)	✓	
○ Analytical/Combinatorial chemistry	✓	
○ Investments in innovative research	✓	
○ Lower R&D costs		✓
○ Platform technologies	✓	
○ Cellular/Molecular assays	✓	✓
○ Systems biology	✓	
○ Drug Development	✓	
○ Pre-clinical studies	✓	
○ Clinical studies		✓

**SCORE = 0.917**

#### 4. Collaboration for clinical trials

*“Bringing together the UK innovative pipeline and Pre-clinical studies with Clinical trial opportunities for Phase II and III in Brazil”*

Expertise and Capability	UK	Brazil
○ Novel molecules	✓	
○ Regulatory expertise	✓	
○ Qualified physicians and professionals	✓	✓
○ Large and varied population		✓
○ Lower cost		✓
○ Pre-clinical	✓	
○ Clinical Phase I	✓	
○ Clinical Phase II		✓
○ Clinical Phase III		✓

**SCORE = 0.889**

#### 5. R&D collaboration for new medicines

*“A UK company provides expertise to a Brazilian company to do drug discovery and/or cosmetic/agrochemical discovery”*

Expertise and Capability	UK	Brazil
○ Innovative research and expertise	✓	
○ Lower R&D cost		✓
○ Private investment (VC and Angel)	✓	
○ Platform technologies	✓	
○ Drug development	✓	
○ Professional services, CROs	✓	
○ Regulatory and compliance	✓	
○ Pre clinical	✓	
○ Clinical trials organization	✓	✓

**SCORE = 0.889**

### Appendix 3: Some Brazilian biotechnology and pharmaceutical companies

This list is from UKTI Biotech Scoping Mission to Brazil, Sept 2005

#### **PP&D/Recepta Biotech (Sao Paulo, SP)**

[www.ppdbiotec.com.br](http://www.ppdbiotec.com.br)

JOSE FERNANDO PEREZ, Co-founder & MD.

Tel: +55 11 3709 2140

Fax: +55 11 3709 2143

E-mail: [fernando.perez@ppdbiotec.com.br](mailto:fernando.perez@ppdbiotec.com.br)

PP&D is in the process of being set up to exploit four anticancer monoclonals developed by the Ludwig Institute in Brazil specific for epithelial malignancies, targeting antigens such as Lewis Y. A clinical trial is shortly to be initiated under the auspices of Biocancer (q.v.) with the indication to be confirmed, but probably ovarian cancer. The first antibodies will be produced under contract, but future manufacture in new cell lines may well take place in Butantan (q.v.). The CEO, Prof Perez, a physicist, was formerly research director of FAPESP (q.v.)

#### **Cryopraxis (Rio de Janeiro, RJ)**

[www.cryopraxis.com.br](http://www.cryopraxis.com.br)

Eduardo Cruz, CEO

Phone: +55 21 2209-0686

Phone/fax: +55 21 3867 5568

E-mail: [dirplan@cryopraxis.com.br](mailto:dirplan@cryopraxis.com.br)

Cryopraxis, located in the Bio-Rio Technology Park, works in the areas of wound healing and stem cells. The company first set up their Criobiologia operation, which set up a bank of umbilical cord blood samples, processed and frozen in such a way, as to allow the recovery of stem cells for future prospective therapeutic purposes. Now most of the company's researchers, either within the company itself, or sponsored via grants and studentships etc, are heavily involved in the various studies currently in progress throughout Brazil in therapies using autologous bone marrow stem cells for treatment of cardiac and liver disorders. The company also markets Extragraft XG3, a bone generation matrix combining hydroxy apatite and collagen, which encourages extensive growth of new bone. Successful application has already been demonstrated in cases of maxillo-facial and cranial reconstruction.

Another two interesting life sciences companies located at Bio-Rio and described to the Mission Team were:

**Extracta Moleculas Naturais S.A.** ([www.extracta.com.br](http://www.extracta.com.br)) a company specialising in rapid screening, identifying and preparing new bio-active molecules from Brazil's vast plant biodiversity, and **Silvestre Labs Ltda.** ([www.silvestrelabs.com.br](http://www.silvestrelabs.com.br)), which is developing and marketing products in wound management including antibacterial (effective against MRSA), burn and diabetic ulcers.

#### **Exellion (Petropolis, RJ)**

[conselhogestor@petropolis-tecnopolis.com.br](mailto:conselhogestor@petropolis-tecnopolis.com.br)

John Anderson (job title)

Tel: +55 24 2243 4802

Mob: +55 24 9964 0133

E-mail: [john@oriundo.biz](mailto:john@oriundo.biz)

Exellion is a spin-out from the Federal University of Rio de Janeiro (UFRJ), where a group has been leading the field in use of bone marrow stem cells to treat heart disease patients with myocardial infarction, acute & chronic cardiomyopathy and Chagas disease. After a successful Phase I trial (reported in Circulation vol 107), an efficacy study is underway in 1200 patients at 33 centres in Brazil. A large number of the UFRJ team will be moving to work in Exellion, and will be processing bone marrow samples both on-site and off-site. A state-of-the art facility was under construction in the Petropolis Tecnopolo at the time of the Mission, and first products are expected in November 2005.]

### **GlaxoSmithKline Brasil Ltda (Jacarepagua, RJ)**

[www.gsk.com.br](http://www.gsk.com.br)

Rogério Ribeiro, President

Tel: +55 21 2141 6201

Fax: +55 21 2141 6039

E-mail: [rogerio.r.ribeiro@gsk.com](mailto:rogerio.r.ribeiro@gsk.com)

GSK has a state of the art (1998) filling and tableting plant in the southern outskirts of Rio de Janeiro, its other site, belonging originally to SKB before the merger, having now been sold to FIOCRUZ (q.v.) and called Pharmangeiras. No chemical synthesis is performed in Brazil, and vaccines are shipped in from outside untouched, although a partnership with **FIOCRUZ** on Hib & MMR has recently been set up under similar terms to the Aventis/Butantan (q.v.) relationship. GSK supplies 50% of the private vaccine market in Brazil, with the private market constituting 20% of the total. GSK conducts many Phase III clinical trials in the country (currently 9 in pharma, 9 in biologicals) and vaccination standards in Brazil are considered "best practice" according to WHO standards. The GSK plant just outside Rio has excess production capability and the company is keen to consider toll manufacturing and packaging operations representing a good opportunity for UK companies to enter the Brazilian market.

### **Biommm Technology (Belo Horizonte, MG)**

[www.biomm.com](http://www.biomm.com)

Paulo Guatimosim Vidigal, Business Development Director

Tel: + 55 31 3292-5003

Fax: + 55 31 3291-9212

E-mail: [pgvidigal@biomm.com](mailto:pgvidigal@biomm.com)

Biommm holds valuable intellectual property and know-how originally developed by Biobras (prior to its takeover by Novo) relating to recombinant synthesis of insulin and other peptides, enabling production of these peptides without infringement of other patents in the field. The company has a research laboratory conducting work on a pilot scale, and is looking for companies to licence the technology. Biommm is in the Biominas Cluster as are the following two companies

### **Ferrara Ophthalmics Ltd (Belo Horizonte, MG)**

[www.ferrararing.com.br](http://www.ferrararing.com.br)

Carlos Eduardo Mendes Guimaraes Jr., Director

Tel/fax: +55 31 3233-3108

Mobile: +55 31 9185-3904

E-mail: [carlos@ferrararing.com.br](mailto:carlos@ferrararing.com.br)

Ferrara was set up in the early 1990s by Dr Paulo Ferrara, a Brazilian eye specialist who devised a ring to be implanted into the corneal stroma for treatment of keratoconus – deformation of the cornea leading to serious impairment of vision, a disorder affecting one in five hundred individuals world-wide. Other indications are ectasia (damage by laser). The technique has a high treatment success rate, and can be performed without need for general anesthesia. In addition to the ring itself, the company manufactures sophisticated electronic equipment to aid surgeons in performing the technique, and

provides regular training courses and workshops. The patent has expired, but they dominate the market through the back-up services they provide, there being only one competitor based in US. The ring is marketed world-wide, and Ferrara is looking for a distributor in the UK.

### **Biocancer Clinical research (Belo Horizonte, MG)**

[www.biocancer.com.br](http://www.biocancer.com.br)

Dr Alberto J. A. Wainstein, Director

Tel/Fax: +55 31 3224 2030

E-mail: [alberto@biocancer.com.br](mailto:alberto@biocancer.com.br)

Biocancer fills a gap in the 'red' biotech environment in Brazil, providing a commercial facility which is able to conduct and/or oversee phase I and early-stage phase II clinical trials. Originally set up to work on cancer, the organisation has close links with a private specialist cancer hospital capable of accommodating 24 trial patients at a time; it also works in the Hospital das Clinicas in Belo Horizonte – one of the largest hospitals in Brazil. The Brazilian regulatory system, ANVISA, and the ethical commission, COEP, are modelled closely on FDA principles (including an equivalent of the fast-track orphan drug programme); Glaxo and Roche plan to conduct trials in Biocancer shortly and feasibility studies have been concluded with Quintiles. The unit is highly competitive cost-wise, and is able to link up with UFMG (q.v.) for preclinical studies. A facility in Ceará (UNIPAC) can do toxicology work, as well as bioequivalence and compatibility studies. Four cancer trials are on-going (including one using liposomes) and other studies in the pipeline are in the area of antibiotics, sinusitis, gastroenterology and neurology.

Some other Biominas companies described to the UKTI Scoping Mission Team to Brazil in September 2005 include:

**Dialab** ([ww.dialab.com](http://www.dialab.com)), develops and manufactures products for clinical diagnosis and molecular biology; **KATAK Biotech** ([www.biominas.org.br](http://www.biominas.org.br)), specialising in liquid-stable reagents for immunodiagnosics and clinical chemistry; and **ALVOS** a JV with the New York based Ludwig Institute for Cancer Research.

### **FIR Capital (Belo Horizonte, MG)**

[www.fircapital.com](http://www.fircapital.com)

Guilherme Emrich

Tel: 55 31 3074 0020

This is one of the first VC companies in Latin America and has pioneered investment in early-stage and expansion-stage biotech companies. FIR holds a wide ranging portfolio in the biotech and IT sectors and is one of the main driving forces behind the success of the Biominas cluster. The company funded Biobras to become the world's fourth largest insulin producer before the very profitable trade sale to Novo Nordisk. FIR is interested in the prospects of doing business with UK companies and in building UK-Brazil alliances.

### **FK BIOTEC (Porto Alegre, RS)**

[www.fkbiotec.com.br](http://www.fkbiotec.com.br)

Fernando T. Kreutz MD/PhD, Director & Founder

Tel: +55 51 3352 6863

E-mail: [fkreutz@fkbiotec.com.br](mailto:fkreutz@fkbiotec.com.br)

This company was set up 1999 originally to manufacture and market immunoreagents for diagnosis of HIV/AIDS, using flow cytometry as well as more conventional methods. Recently it has diversified into the cancer vaccine area, and is currently trialling a cellular vaccine (autologous cancer cells from patients) in 56 prostate cancer patients. With 11 vaccinated so far, a 40% response rate has been observed, with PSA levels measured for 300 days.

## Public Research Foundations:

### **Instituto Butantan (Sao Paulo)**

[www.butantan.gov.br](http://www.butantan.gov.br)

Dr Paulo Lee Ho,

Tel: 55 11 3726 7222

E-mail: [hoplee@butantan.gov.br](mailto:hoplee@butantan.gov.br)

Instituto Butantan, founded in 1901, produces and supplies 80% of vaccines used in Brazil in the public sector. It is directly linked to the State office of Public Health, and is self-funding through sales of products. It is a major producer throughout Latin America of diphtheria, tetanus, pertussis, hepatitis B and BCG vaccines, (188 million doses in 2003). Researchers here collaborate with FIOCRUZ in production of certain multivalent vaccines, and has an agreement with Aventis Merieux to purchase and distribute 'flu vaccine, with technology transfer for production after five years. Butantan is also well known for work in the area of antivenoms, and produces many anti-sera for treatment of snakebite. In a recent initiative, the Institute has committed to producing an avian flu vaccine in the next three years, and has capability for GMP production of monoclonal antibodies. There are also plans for preparation of recombinant therapeutic proteins such as insulin and EPO. Scientists at Instituto Butantan have also played a key role in sequencing of the transcriptome of *Schistosoma mansoni*, which has been used successfully to identify antigens for a candidate vaccine. A thriving research arm in both applied and basic research boasts 121 investigators.

### **FIOCRUZ (Rio de Janeiro)**

[www.fiocruz.br](http://www.fiocruz.br)

Dr. Carlos M. More, Scientific Coordinator

Centre for Technological Development in Health (CDTS)

Tel: 55-21-3885.1754

E-mail: [morel@fiocruz.br](mailto:morel@fiocruz.br) or [cmmorel@terra.com.br](mailto:cmmorel@terra.com.br)

FIOCRUZ is the main driver for public health research in Brazil, with an annual budget of \$US 300 million pa, and 15 technical institutes and local research centres across the country. With 60 projects underway, and major successes (such as isolating the first strain of HIV in Brazil, and producing over 90 % of the world's yellow fever vaccine), FIOCRUZ publishes around 400 papers a year and holds 43 patents. Researchers here are also trying to identify new diseases originating in the jungle. There is an emphasis on new business opportunities and developing facilities to incubate new businesses. FIOCRUZ would welcome technology transfer opportunities and for partnerships with UK companies interested in licensing technologies and participating in Framework VII projects.

### **FUNED (Belo Horizonte, MG)**

[www.funed.mg.gov.br](http://www.funed.mg.gov.br)

FUNED is a not-for-profit public foundation, focussed on R&D and the provision of vaccines, sera and diagnostics for the public healthcare sector. Activities include the characterisation, purification and cloning of poisons, molecular diagnosis of viruses and cytogenetic assays against tumours and parasites. They are one of only 3 institutes in the country authorised to produce antivenom serum.

### **FAPESP (Sao Paulo)**

[www.fapesp.br](http://www.fapesp.br)

Carlos Henrique de Brito Cruz, Scientific Director

Tel: 55 11 3645-2417

Email: [dc@fapesep.br](mailto:dc@fapesep.br)

FAPESP is the State of Sao Paulo Research Foundation, with an annual budget of \$US 350 million its mission is to translate the State's R&D output and technical innovation into business opportunities. They have an on-going programme funding development in around 500 small companies, of whom 25 – 33 % are biotech based and located in the state of Sao Paulo.

### **EMBRAPA (Brasilia)**

[www.cenargen.embrapa.br](http://www.cenargen.embrapa.br)

Dr Mauricio Antonio Lopes, Head of Research and Development

Tel: (61) 3448-4603/4604

Email: [mlopes@cenargen.embrapa.br](mailto:mlopes@cenargen.embrapa.br)

Most plant biotechnology in Brazil is conducted in partnership with EMBRAPA, the state owned company for agricultural R&D. With 40 centres in the network located across Brazil, R&D priorities within EMBRAPA include:

- molecular markers, gene / trait mapping
- genetic modification for stress tolerance and new products
- genomic sciences (coffee, eucalyptus, meat)
- advanced animal reproduction (breeding, germplasm enhancement, IVF).

EMBRAPA is the first institute in Latin America to develop cloned cattle and has a leading position in developing *in vitro* and *in vivo* fertilisation techniques.

EMBRAPA has more than 170 patents and is keen on establishing international relationships.

### Bioincubators/Technology Parks:

#### **BIO RIO FOUNDATION (Rio de Janeiro, RJ)**

[www.biorio.org.br](http://www.biorio.org.br)

Fernando Steele da Cruz (job title)

Fundação Bio-Rio

Tel: 55 21 3867-5501

Fax: 55 21 3867-5514

E-Mail: [fsteele@biorio.org.br](mailto:fsteele@biorio.org.br)

Bio Rio is a not-for-profit technology park and incubator established in 1986, next to the campus of the Federal University of Rio de Janeiro to promote commercial activity in the area of biosciences, covering in particular all areas of biotechnology. There are twenty companies currently occupying the site, of which approximately half are in the bioincubator. The total area is 116,000 square metres, is serviced by an optical fibre communication network, and includes a central support facility with a quality control lab, meeting rooms and project management facility. Tax incentives are available for clients through CODIN (Companhia de Desenvolvimento Industrial) including exemption from industrial products tax, State government tax and importation tax. Bio Rio is the most well established of a network of similar enterprises across the centre and outskirts of Rio de Janeiro city, all of which are vigorously supported and promoted by state and government agencies.

### **PETROPOLIS TECNOPOLO (Quitandia, RJ)**

[www.petropolis-tecnopolis.com.br](http://www.petropolis-tecnopolis.com.br)

Johnny Klemperer, Project Coordinator.

Tel: 55 24 2243 7200

E-mail: [jklemperer@sarraon.com.br](mailto:jklemperer@sarraon.com.br)

Petropolis-Tecnopolis is being established by a large consortium of government, public and private stakeholders as a high-tech city with IT and Biotech developments well to the fore. Already large companies such as Microsoft, Sun and IBM have built R& D centres. Two major centres are driving the formation of a new cluster in the former imperial capital city; namely the National Laboratory for Scientific Computing (LNCC) (which has played such a pivotal role in Brazil's whole genome sequencing programmes) and a new centre for ethnobotany, phytotherapy and human health planned by the Bio Atlantica Institute.

### **Biominas (Belo Horizonte, MG)**

[www.biominas.org.br](http://www.biominas.org.br)

Eduardo Emrich Soares, Executive Director

Tel: +55 31 3486 1733

Fax: +55 31 3486 1619

E-mail: [eduardo@biominas.org.br](mailto:eduardo@biominas.org.br)

Biominas is an industry organisation set up in 1990 by biopharmaceutical companies in the state of Minas Gerais to develop the biotech sector in the state, and generate new business. Minas Gerais is one of the four states heavily involved in biotech in Brazil and has 90 biotech companies, with a labour force of 3,300. Of these companies, 70% are in healthcare and these generated sales of US\$185 million in 2003. Biominas also runs a very successful bioincubator in the centre of Belo Horizonte (the state capital).

### Industry Organizations:

#### **ABRABI - Brazilian Biotechnology Association**

[www.abrabi.org.br](http://www.abrabi.org.br)

Joao S.B.Paes De Carvalho, Executive Director

Associacao Brasileira das Empresas de Biotecnologia

Tel: 55 21 2220 1109

Email: [jsbpc@abrabi.org.uk](mailto:jsbpc@abrabi.org.uk)

#### **AnBio – National Biosafety Association (colour of title?)**

[www.anbio.org.br](http://www.anbio.org.br)

Dr Leila Oda, President

Associacao nacional de Biosseguranca

Tel: 55 21 2220 8327

E-mail: [secretaria@anbio.org.br](mailto:secretaria@anbio.org.br)

#### **SBBiotec – Brazilian Biotechnology Society**

[www.sbbiotec.org.br](http://www.sbbiotec.org.br)

Luis Antonio Barreto de Castro, President

Tel: 55 61 3223 0845

### Appendix 4: Generic pharmaceuticals

Below is a table of a few drugs launched with company being involved in Brazil, with headquarters in the country. Note that any other company doing work in Brazil would not be recorded here. These are all chemically synthesized molecules rather than Biologicals or natural products.

Generic Name	World Status	Originator	Originator Country	Licensee Company	Licensee Country
clindamycin, ResiDerm	Launched	Access	USA	ProStrakan Astellas Clinuvel Pliva Biosintetica	UK Japan Australia Croatia <b>Brazil</b>
alizapride	Launched	Sanofi-Aventis	France	Vita, Italy Almirall-Prodesfarma Espasil	Italy Spain <b>Brazil</b>
flutrimazole	Launched	Uriach	Spain	Menarini Il-Yang Biosintetica Galenica, Greece	Italy South Korea <b>Brazil</b> Greece
leuprolide acetate, Atrigel	Launched	QLT	Canada	Sanofi-Aventis Mayne Pharma Astellas Tecnofarma Biosintetica Sosei Akzo Nobel Key Oncologics Ranbaxy	France Australia Japan Chile <b>Brazil</b> Japan Netherlands South Africa India
nifedipine, Elan	Launched	Elan	Ireland	Biosintetica Orion Pharma	<b>Brazil</b> Finland

**Table 30: Some launched generic drugs per Originator Company and Licensee Company**

Source: PharmaProjects online database which shows all the products in the pipeline and market.

## Appendix 5: Vaccines

### *Instituto Buntantan*

The following data is from the Butantan Institute.

Butantan was created by Vital Brazil in 1901 to produce anti-pest sera to fight a bubonic fever epidemic. It maintains, since its origins, the model of Louis Pasteur for the Pasteur Institute in Paris, and the Center for Biotechnology has about 30 researchers. It is the main producer of vaccines, anti-sera and other biopharmaceuticals in Latin America. The production was directed for the needs of Public Healthcare, and supplied to the Ministry of Health. To operate this large program, a not-for-profit organization was established, the Fundação Butantan, today supplying more than half a million vials of 13 different hyper immune sera, and produced in 2003 188 million of vaccine antigens.

Vaccines produced in Brazil (2003)  
In million doses

Vaccines	Butantan	Fiocruz	A.Paiva
Diphtheria	66		
Tetanus	66		
Pertussis	26		
Hepatitis B	28		
BCG (intradermal)	2		15
Yellow fever		30	
<b>Total</b>	<b>188 (81%)</b>	<b>30 (13%)</b>	<b>15 (6%)</b>

Vaccines from bulk (2003) that will be produced in 2005-6

Rabies	1.4	
Influenza	16.6	
Hemophilus B		16

Vaccines from bulk (2003) that will still be imported

Oral polio	83
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**Table 31: Vaccines produced in Brazil in 2003**

Today Butantan masters a number of basic technologies which will allow the implementation of new or next generation immunobiologicals:

- Large scale aerobic and anaerobic bacterial fermentation
- Long term animal cell cultivation for production of viruses and recombinant proteins
- Large scale protein purification by chromatography methods
- Large scale purification of polysaccharides
- Large scale continuous and gradient centrifugation
- Tangential and molecular filtration
- Construction of recombinants and expression
- Biologicals and vaccine assays and regulatory assays
- Design of GMP plants
- Complete genomics

**Vaccines in production:**

Anti-bothropic  
Anti-crotalic  
Anti-bothropic-crotalic  
Anti-scorpion  
Anti-lachetic  
Anti-elapidic  
Anti-lonomia  
Anti-arachnic  
Anti-Africanized bee  
Anti-diphtheria  
Anti-tetanus  
Anti-botulinic A,B & E  
Anti-rabies  
Immunoglobulin Anti-timocitária  
Anti-human thymocitic

**Vaccines**

DTP-Hib and DTP (Pediatric)  
DT (adult)  
DT (pediatric)  
TT  
Recombinant Hepatitis B **surface antigen**  
BCG (intradermal)  
Rabies (produced in VERO cell cultures)

**Biopharmaceuticals**

BCG (intravesical)  
Monoclonal Anti-CD3  
Erythropoietin EPO  
Lung surfactant – a new technology was developed for the production of lung surfactant at a fraction of its present cost. The clinical trials should be ready soon and the surfactant will be supplied free to all public health maternities. A second generation of lung surfactant, containing vitamin A is under development.

**Hyper-immune sera**

New Projects:

- Cholera vaccine
- Whole cell single strain pneumococcal vaccine
- Pneumococcal conjugated vaccines for strains antibiotic resitant
- Schistosoma new vaccine based on the complete genome
- Leptisospira vaccine based on complete genome
- Freeze stable vaccines: DTP-Hep B and DTP-Hep B with vitamin A
- Hep B vaccine for expressed health personnel over 50 years old

For more information see <http://www.butantan.gov.br> in Portuguese.

## **Foundation Oswaldo Cruz / FIOCRUZ**

The following data is from the Foundation Oswaldo Cruz website, <http://www.fiocruz.br>

Inaugurated on May 25, 1900 under the name of Federal Serotherapy Institute, Fiocruz was given the mission of fighting the great problems of public health in Brazil. Therefore, Fiocruz became a think tank concerned with Brazilian reality and experimental medicine. Today the institution is noted for its excellence in a wide range of health activities, including research development, hospital and ambulatory care services; production of vaccines, drugs, reactants, and diagnostic kits; human resources teaching and training; information and communication regarding health, science and technology; quality control of products and services, and the implementation of social programs. It has over 7,500 employees and health professionals with different engagements, a workforce proud of being at the service of life.

### **Democracy and diversity**

Fiocruz is located on a 800,000-square meter campus at Manguinhos, a suburban area in the North Side of Rio de Janeiro. Around three historical buildings of the old Federal Serotherapy Institute – the Moorish Pavilion, the Watch Pavilion and the Mews -, there are ten of Fiocruz's thirteen technical-scientific units and all the technical and administrative support units. Another five units are located at Rio de Janeiro, Belo Horizonte, Salvador, Recife e Manaus.

Apart from these fixed units, Fiocruz presence is seen in the whole country, through its support to the Unified Health System, its proposals on public health policy-making, its research actions, its scientific expeditions, and the extent of its services and health products.

## **Vaccines production: BIOMANGUINHOS Immunobiologicals Technology Institute**

Bio-Manguinhos is the biggest producer of yellow fever vaccine in Latin America. It produces an attenuated virus vaccine for Yellow fever

The Immunobiological Technology Institute (Biomanguinhos) at Fiocruz plays a crucial role in the National Immunization Program (PNI) of the Ministry of Health. Biomanguinhos is one of the country's largest centers for the development and production of immunobiologicals. It produces around one third of the vaccines used in the country and 43 percent of the diagnostic reagents. Therefore, the institute can significantly contribute to diminishing Brazil's dependence on health input products, which presently represents a 3.5 billion dollar deficit on the country's trade balance.

Biomanguinhos is the largest world producer of the vaccine against yellow fever and is the only Latin American laboratory to be certified by the World Health Organization to produce this vaccine. Between 2001 and 2004, the institute produced around 320 million vaccine doses against yellow fever, measles, meningitis types A and C, MMR, Hib (against the Haemophilus influenzae type b) and DTP + Hib, which started to be produced by Biomanguinhos in 2001 in a partnership with the Butantan Institute.

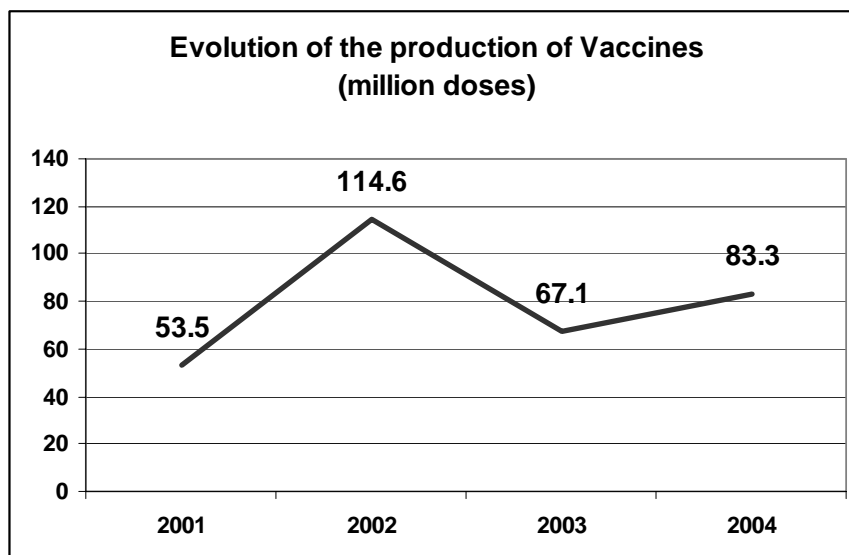


Figure 23: Evolution of the production of vaccines at BioManguinhos/FIOCRUZ

### Drugs production: FARMANGUINHOS - Medicines and Drugs Technology Institute

In 2004, in an unprecedented governmental initiative both in the country and abroad, the Federal Government invested around six million dollars in purchasing GlaxoSmithKline's pharmaceutical plant. The plant comprises high-technology facilities in a 1,130 million square feet area, 430 thousand of constructed area. It is located in the neighborhood of Jacarepaguá, in the west zone of Rio de Janeiro and was merged to Fiocruz's Drug Technology Institute (Farmanguinhos) in August 2004. The plant was entitled the Technological Drug Complex (CTM) and will allow a fivefold increase in the production capacity of the Foundation and a broadening of Fiocruz's research on and development of new drugs.

Between 2001 and 2004, more than 5.5 billion pharmaceutical units (among tablets, pills, ointments and creams) were produced. Gross sales for the four years were of around 320 million dollars. Farmanguinhos is the major public pharmaceutical laboratory in the country and its production represents 36 percent of the Ministry of Health's purchases.

From 2007 on, the production is estimated to reach ten billion pharmaceutical units (including pills, tablets, caplets, ointment and cream tubes, etc.). Farmanguinhos will now be able to expand its product portfolio and include products with different pharmaceutical properties and in other presentations, such as the fixed dose combinations (combinations containing two or more active ingredients in only one medication) used for the treatment of Aids, tuberculosis, among other diseases. Farmanguinhos is also already planning to produce oral contraceptives, cholesterol reducers and drugs against asthma, including aerosols.

Among the products already manufactured by Farmanguinhos are anti-inflammatory, anti-infective, anti-psychotic, analgesic and antiulcer drugs, as well as drugs against Aids, malaria, schistosomiasis, tuberculosis, leprosy, filariasis, onchocerciasis, anemia, diabetes, hypertension and cardiovascular and central nervous system diseases.

Farmanguinhos provides, since 1998, the technical support the Ministry of Health requires for developing effective and egalitarian public health policies. Today, the institute produces nine of the 17 anti-HIV/Aids drugs. The annual cost of one Aids patient dropped from 4.7 thousand dollars in 2000 to 2.5 thousand dollars in 2002, making Brazil an international example in the struggle against HIV/Aids.

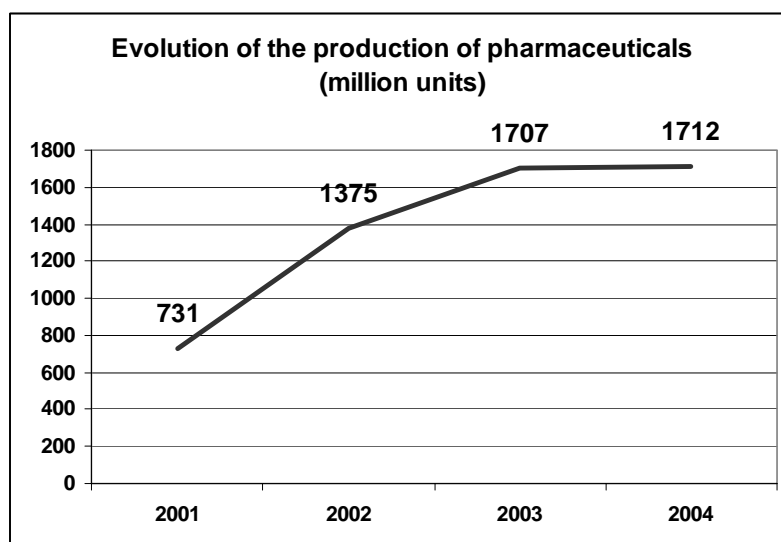


Figure 24: Evolution of the production of pharmaceuticals at FarManguinhos/FIOCRUZ

### Diagnostic kits

Between 2001 and 2004, Biomanguinhos produced 9.2 million diagnostic kits for diseases such as leptospirosis, leishmaniasis, viral diarrhea, Chagas disease, leprosy and dengue fever, among others. Fiocruz began producing the quick test for diagnosing HIV types 1 and 2, which is distributed to the National Program for STDs/Aids.

In 2003, Biomanguinhos signed a technology transfer agreement for the production of the quick test for HIV with the American company Chembio. Biomanguinhos will absorb the technology over three years, producing around 300 thousand tests annually. Nationalizing the production will generate a 50 percent economy compared to importing the product. Besides that, the technology will also be applied to other diseases such as dengue fever, leptospirosis and leishmaniasis.

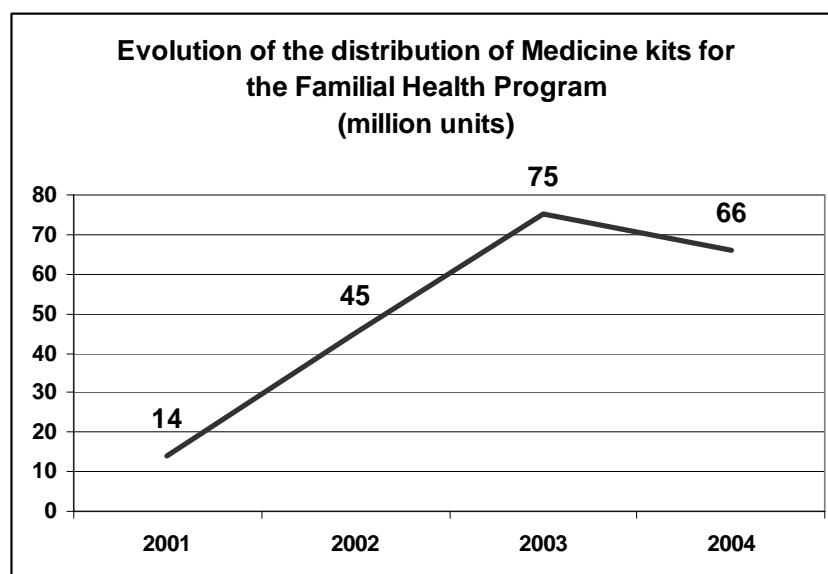


Figure 25: Evolution of the distribution of medicine kits for the Familial Health Program

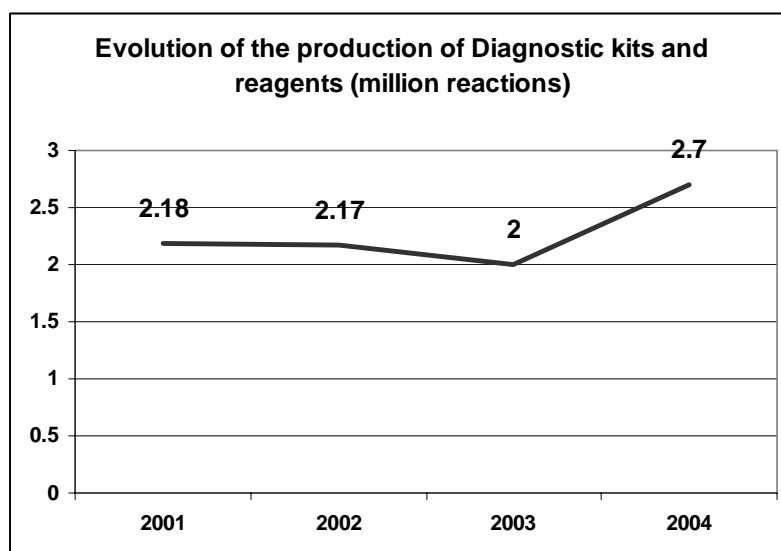


Figure 26: Evolution of the production of diagnostic kits and reagents