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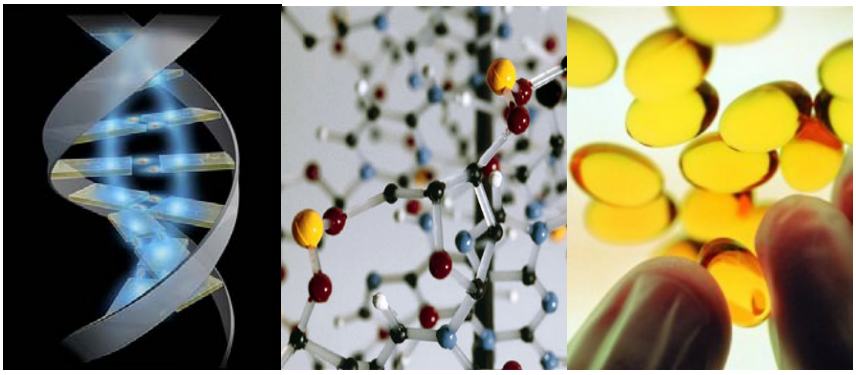
The Biotechnology Industry in India
Profile 2009



BIOTECHNOLOGY SECTOR IN INDIA

Overview

India, which has earned a name worldwide as the most preferred destination for global Information Technology outsourcing and software services firms, is gradually making a mark in another high-tech sector – biotechnology. This sunrise sector, which has seen the entry of many new players both Indian and international, is poised to take the country to the big league with investments flowing in from all corners. The country has traditionally done well in the pharmaceutical and drug industry. As an offshoot of the pharmaceutical industry, the biotechnology sector took shape over the last 10 years with many entrepreneurs making substantial investments in it.

Biotechnology, the application of science and technology to modify biological systems for specific uses, encompasses many fields from biopharma to agri-bio and biofuels, to cite a few. Several Indian companies have started inventing and producing biotechnology-based drugs for diseases such as cancer and diabetes. Agriculture is beginning to gain momentum as well, with a focus on transgenic rice, corn, chickpea, and several other food crops, most notably in the area of genetically modified crops such as Bt cotton as well as bio-fuels. India is already building a global leadership profile in Bt cotton where it has the largest area under cultivation, over six million hectares, which is twice that of China. In 2006, India also ranked first in terms of growth in the transgenic crops sector where it registered over 200 per cent compared to the global average of 13 per cent.

The industry – currently expanding at 37 per cent per annum – is growing phenomenally, and this can easily be sustained. It is projected to burgeon into a $5 billion sector by 2010. From a small beginning 25 years ago, the sector has emerged as a dominant one providing employment to hundreds of thousands of skilled and qualified people. Its revenues crossed the $2 billion-mark last fiscal (2006-07). The 30-plus percent growth rate is faster than the worldwide industry average. Exports in the sector increased by a massive 47 per cent.

Sector Breakup

- **BioPharma -** vaccines, therapeutics, diagnostics and animal health care products
- **BioServices** - clinical research, contract research and contract manufacturing
- **BioAgri -** Bt cotton seeds, bio-pesticides, bio-fertilisers (excludes hybrid seeds)
- **BioIndustrial** - enzymes, organic amino acids, yeast, yeast-based products
- **BioInformatics** - tools for genomics, proteomic databases, sequence analysis, database searches

The biopharma segment, accounting for over two-thirds of the industry, reported sales of US$ 1.46 billion, representing a growth of 27 per cent. The bioservices sector registered 53 per cent growth; the bioagriculture sector grew by 55 per cent, and the bioinformatics and bioindustrial sectors by 21 per cent and 5 per cent respectively. Homegrown companies led the biotech revenue sweepstakes and for the first time in the past five years, the top five companies are all of Indian origin. The total exports from the sector amounted to $250 million.

THE BIOTECH BREAK-UP

SEGMENT (Rs. Crore)	REVENUES (2006-07)	% GROWTH	REVENUES (2005-06)	REVENUES (2004 -05)
BioPharma	5,600	20	4,700	3,570
BioServices	1,000	38	720	425
BioAgri	1,100	50	580	330
BioIndustrial	400	20	375	320
BioInformatics	130	20	110	100
Total	8,300	30	6,485	4,745

Source: ABLE-Spectrum Survey, 2007 (* Rs.1 crore – Rs.10 million; $1 – Rs.40.5)

Of the 325 biotech companies in the country, nearly 40 per cent operate in the biopharma sector, followed by bioservices (21 per cent), bioagriculture (19 per cent), bioinformatics (14 per cent) and bioindustrials (5 per cent).

It is not just multiplying revenues, however. The biotechnology sector also witnessed the emergence of new companies and investments. Out of the total 340 biotech firms in the country, 183 of them are located in Karnataka, with 137 in Bangalore alone. The rest of them are evenly spread in other Indian cities such as Ahmedabad, Panaji (Goa), Mumbai, Pune, Vadodra, Hyderabad and Kolkata.

BioPharma and BioAgri companies constitute the top 10 in the industry

Rank	Company	Sales($mn)	Key focus
1	Serum Institute	156.2	Vaccines; global leader in MMR vaccines
2	Biocon*	152.9	Statins, immunosuppressants and enzymes
3	Panacea Biotec	97.3	Vaccines
4	Mahyco Monsanto	86.9	Bt cotton seeds
5	Rasi Seeds	68.8	Genetically modified seeds
6	Venkateshwara Hatcheries	62.2	Poultry health products
7	Novo Nordisk	38.9	Diabetes treatment
8	Mahyco	26.2	Marketing of transgenic Bollgard cotton
9	Aventis Pharma	25.4	Diabetes treatment
10	Indian Immunologicals	22.8	Animal health; one of the largest producers of Foot and Mouth Disease vaccines

**Group companies also include Syngene International (custom research), Clinigene (clinical research) and Biocon Pharmaceuticals (new molecule developments)*

In an effort to support the biotechnology industry, the Government of India has chalked out an ambitious programme. The focus is on public-private partnerships and a lot of projects have been cleared. Last year, about two-dozen projects had been initiated, and countries like Australia, Sweden and Denmark had partnered with

India. Several states have also announced their own programmes to pursue biotechnology as a major investment sector.

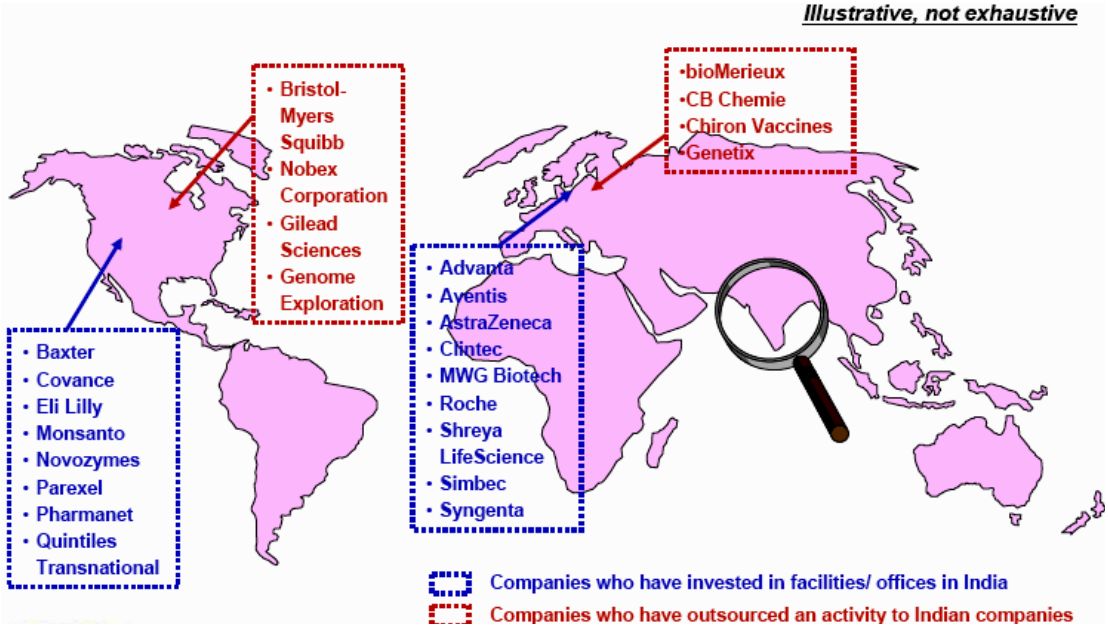
According to a study by the biotechnology industry body ABLE (Association of Biotechnology-led Entrepreneurs) and BioSpectrum, India's cost and skill base supports affordable drug development. The scientific headcount has doubled to about 16,000 from the previous fiscal. India is an emerging preferred hub for contract research organisations and contract manufacturing organisations. The transnational partnership models of global firms are suitable to Indian firms. Over 200 multinationals have set up their operations in India, because of the low-cost-high value proposition.

Discovery research is leading to new molecules in place of generics. Pre-clinical development and presence of large animal facilities is set to attract investments in biopharma and bio-agritech segments. The challenges before the sector are about securing private and public funding despite risk aversion among VCs (venture capital funds).

The industry is lobbying for the need to improve the regulatory infrastructure, bio-manufacturing standards, clinical development capabilities, research and development (R&D) collaborations with US/European Union firms and acceptance of Indian clinical data by the US Food and Drug Administration and the European Agency for Evaluation of Medicinal Products of Europe.

Gearing up to meet Global Challenges

India is poised for stupendous growth in the biotechnology sector. India is following the correct current global strategies to win more deals. India's cost and skill base supports affordable drug development.



Source: IBEF

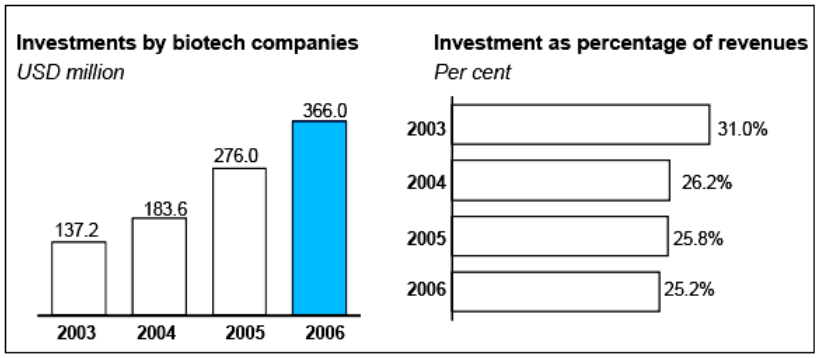
There is a trend of increasing availability of trained and skilled human resource. A number of Indian scientists with regulatory expertise are returning to this country. The regulatory infrastructure is fast improving. From the companies' perspective, the

standards of bio manufacturing are improving. The companies are also increasing capabilities in clinical development. They are also increasing R&D collaborations with US/EU companies. Indian biotechnology sector is rapidly climbing up the drug development path.

The country is fast attaining global leadership in BT cotton cultivation. India is an emerging preferred hub for contract research organisations and contract manufacturing organisations. The transnational partnership models with Indian companies are on the rise.

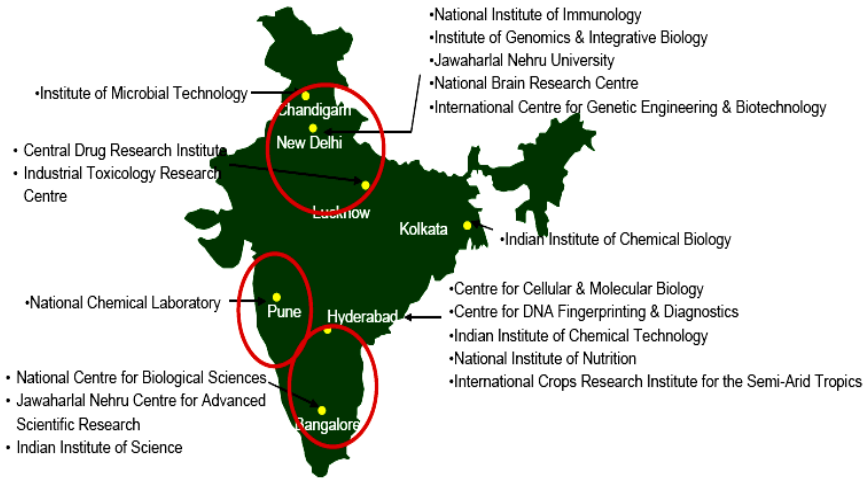
Investments in Research & Infrastructure

Bulk of the investments of the biotech companies have gone into setting up infrastructure, followed by R&D. Industry has continued to invest 25% of its revenues or more over the last few years, with investments crossing USD 360 million in 2006. The Planning Commission has also outlaid USD 448 million for biotech spending



Source: IBEF

A strong infrastructure of biotech focused research institutes exists in the country. The Biotech industry has support from world-class scientific institutions like the National Centre for Biological Sciences (NCBS), Indian Institute of Science (IISc) and Centre of Cellular and Molecular Biology



Biotech Parks

The boom in the biotechnology sector is driving the growth of biotech parks across the country, as state governments try to lure both international and domestic investors to these clusters. According to the Department of Biotechnology, nearly a dozen such parks are expected to come up in the country over the coming months. Over half a dozen parks housing biotech and life sciences companies are already operational. They include one of the biggest, Genome Valley on the outskirts of Hyderabad, a sprawling, 600-sq km complex that includes the Shapoorji Pallonji Biotech Park and the ICICI Knowledge Park. Other ambitious parks include the Bangalore Helix, the International Biotech Park at Hinjewadi in Pune, the Ticel Biopark near Chennai and the Lucknow Biotech Park. Genome Valley is a natural cluster for biotech research, training, collaboration and manufacturing activities, and offers state-of-the-art infrastructure to over 100 biotech companies. Genome Valley was recently issued a registration for the certification mark (intellectual property rights) by the United States Patent & Trademark office, Virginia. About two years ago, it had been granted a community trademark in the European Union.

Other state governments, including Tamil Nadu and Uttar Pradesh, Himachal Pradesh, Haryana, Punjab, Uttarakhand, Madhya Pradesh, Rajasthan and Kerala have unveiled plans to set up biotech parks and clusters.

Soaring Investments

A number of far reaching changes are taking place to facilitate growth in the biotech sector further. India is becoming one of the most favoured destinations for collaborative R&D, bioinformatics, contract research and manufacturing and clinical research as a result of growing compliance with internationally harmonised standards such as Good Laboratory Practices (GLP), current Good Manufacturing Practice (cGMP) and Good Clinical Practices (GCP). A well-defined regulatory framework, along with an emerging stringent IPR regime is also contributing to this trend.

Investments in the Indian biotechnology sector crossed US$ 580 million in 2006-2007 with Bangalore alone witnessing more than US$ 243.9 million outlay from companies like Jubilant, AstraZeneca, GE Healthcare and Biocon. The biotechnology companies' expenditure on research and development (R&D) amounted to an average 3 per cent of sales.

A large chunk of the sector's revenues are expected to come from opportunities in the US$ 4.5 billion Indian pharmaceutical industry which is growing at the rate of over 8 -9 per cent per year. An increasing number of Contract Research Organisations (CROs) in the country bears evidence to this. The CRO market in India is worth US$ 250 million and is growing at 30-40 per cent year on year. Ranked fourth globally in terms of volume and 13th in terms of value, the country has the highest number of manufacturing plants approved by the United States Food and Drug Administration (USFDA).

INDIAN BIOTECHNOLOGY SECTOR: SOARING INVESTMENTS

YEAR	INVESTMENT (Rs. Crores)*	GROWTH
FY 2000-01	250	------
FY 2001-02	504	101%
FY 2002-03	635	26%
FY 2003-04	850	34%
FY 2004-05	1215	43%
FY 2005-06	1650	36%
FY 2006-07	2270	37%

Source: ABLE-Spectrum Survey, 2007 (* Rs.1 crore – Rs.10 million; $1 – Rs.40.5) (# FY – financial year).

While global generic pharmaceutical majors such as Teva, Mylan and Actavis have set up Indian bases to leverage the low-cost availability of raw materials here, the emerging opportunities in clinical trials is driving the biotech majors towards the country.

Some of the major biotechnology companies, which are on an expansion mode, include Biocon, Jubilant, Advinus, AstraZeneca, GE Healthcare, Avesthagen, Agilent and SRA Security. Many firms are spending an average of three per cent of their sales on research and development activities. According to Ernst and Young, India ranks third after Japan and South Korea in the Asia Pacific Region in the biotechnology sector. A number of merger and acquisitions have also taken place in the sector in recent years. Reliance Life Sciences acquired 74 per cent majority stake in the UK-based GenMedix. Mumbai-based Nicholas Piramal, the second-largest pharmaceutical health care company in India, acquired UK's Avecia Biopharma. Biocon acquired the intellectual property assets of US-based Nobex Corp. It also entered into co-development of Intranasal Insulin with Bentley Pharma of the US. Another international company, Merrieux Alliance, picked up a 60 per cent stake in Hyderabad-based Shantha Biotechnics, for global vaccine production. And the Tata group-promoted biotech firm Advinus inked a $150 million research deal with Merck.

Biotech companies have also been attracting investments. Avesthagen attracted over $40 million from a leading European venture capital. Indian entrepreneurs have started a number of new companies in the biotechnology sector.

Riding the wave of Innovation

According to a report by Ernst & Young titled "On the Threshold: The Asia Pacific Perspective Global Biotechnology Report", India now has the twelfth most successful biotechnology sector in the world as measured by the number of companies. If the current rapid pace of progress of the health biotechnology industry is any indicator, India holds great promise at the national and international level in producing innovative drugs at a cheaper price.

Indian pharmaceutical and biotechnology companies are impacting the global health care sector through affordable innovative drugs. While one dose of R-human insulin is priced in the international market at $30 for 100 IU vials, the average Indian price per dose is $6.50, an 80 per cent difference in price. Similarly, EGFR antibody costs $25,000 per treatment in the international market while the same in India is $6,000 per treatment. Also, as against $150 per vial of Recombinant Streptokinase in the global market, it is priced at $10 per vial in the Indian market, a 95 per cent difference in price. The success of Indian biotech companies in producing innovative products has attracted the attention of multinational companies. For instance, Advinus inked a $150 million research deal with global leader Merck. In a similar

agreement, Biocon co-developed Intranasal Insulin with Bentley Pharma, USA. Merrieux Alliance picked 60 per cent stake in Shantha Biotechnics for global vaccine production after witnessing the company's stupendous success in innovation.

Innovative Indian Pharmaceutical & Biotechnology Products

SECTOR	PRODUCT NAME	APPLICATION	PRODUCER
Vaccine	Shanvac-B	Hepatitis B	Shanta Biotechnics
	Revac-B	Hepatitis B	Bharat Biotech
	Gene Vac-B	Hepatitis B	Serum Institute of India
	Tybar V1	Typhoid	Bharat Biotech
Theraupetics	Wosulin	Diabetes	Wockhardt
	Epox	Anemia	Wockhardt
	Shanferon	Cancer	Shantha Biotechnics
	Shankinase	Cardiovascular	Shantha Biotechnics
	Fungisome	Visceral Leishmaniasis	Lifecare Innovations
	Gramstim	Neutropenia	Dr Reddy's Laboratories
Diagnostics	HIV-TRI DOT	HIV-1 & HIV-2	J Mitra
	HIV-HCV Combo	HIV & Hepatitis C	Bhat Biotech India
	HEP Chex C	Hepatitis C	Cyton Diagnostics
	Cysti-Chex	Neurocysticercosis	Cyton Diagnostics

SOURCE: Association of Biotechnology-Led Enterprises of India

It is not just drugs and biotech products that the pharmaceutical and biotech firms are engaged in. Indian companies have gone ahead to play a pivotal role in developing innovative biotechnology services and bioinformatics. Some of the big names in the Indian IT industry have forayed into this sector. IT giants such as Infosys Technologies of Bangalore and Tata Consultancy Services of Mumbai, Ocimum Biosolutions of Hyderabad and Strand Genomics of Bangalore have produced world class Bioinformatics products. Strand Genomics, India's first bioinformatics company, launched Avadis 2.0 version, a homemade product for the biotech industry. Besides, the Institute of Genomics and Integrative Biology has indigenously developed bioinformatics software called PL Host. Research institutes and laboratories are critical to India's pharmaceutical and biotechnology sector. For instance, the Indian Institute of Science (IISc), established in Bangalore, has become a big time contributor to innovative research in biotechnology. It has a division of biological sciences, consisting of various departments, a centre and a unit, all of which are involved in diverse research projects, many relevant to health. The Department of Biochemistry in IISc is working on immunology, reproductive biology and plant development as part of the study of such diseases as malaria, rabies and tuberculosis. Of the 15 most active Indian universities publishing in the innovative field of biotechnology in international journals, IISc ranked first.

Certainly, the innovation quotient in the Indian pharmaceutical and biotechnology sector is on the increase.

Emerging Business Models

Several Indian companies are entering the market for biogenerics – generic therapeutic products produced through a process using modern biotechnologies – with a view to becoming a competitive provider for the global market, an ambition comforted by the current commercial success of Indian chemical generic drugs. At the same time, a growing number of emerging companies are developing new

business models based on the mastering of hedge technologies with the ambition of becoming privileged partners offering an attractive cost advantage at various stage of the complex chain of development of new drugs, and trying to emulate the development of the IT sector with a model of international outsourcing. These evolutions have been initiated quite recently and the industry can still be considered in a phase of emergence of new models of organisation. These models of organisation do not only refer to the positioning of Indian companies on value chains destined to feed the domestic market. They also refer to the relations of the Indian companies with downstream and upstream foreign public or private partners, as well as the targeting by Indian companies of foreign markets.

Strategies for technology and competency development or acquisition are the central factor determining the success of these ventures. Indian policy of research support and human resource development through the funding of several public research and teaching institutions is of course a critical factor determining the technology availability. The interactions between those public institutions and the Indian companies were the object of a specific analysis. It appears that Institutions and Companies are learning to work together and the effects of this collaboration can help the companies at various stage of their development. Companies often adopt alternative solutions to collaboration with Indian institutes such as collaborations with foreign companies or institutions. The personal networks built by the managers of these Indian firms – many of them have had an international academic or corporate carrier – are the main determinant of those international connections.

Concerning the funding of biotech projects, most of the projects started so far have been supported either by industrials or by individuals. The lack of venture funds with the money and competency necessary to support efficiently the development of an innovative Indian biotech industry has already been signalled by many analysts. Changes are occurring from the public and private side towards an increasing of the availability of venture funding, and the next years would show if intermediated funding actually increases the rate of company creation.

Companies entering the market for biogenerics are targeting foreign markets, and the most ambitious plan to enter the most regulated markets (US & Europe). As for the companies with business models based on research partnerships with other companies involved in drug development, their business is almost purely export oriented.

Intellectual property regime in India

Indian intellectual property regime has witnessed its most important change in 19704. The 1970 Act was designed to facilitate cheap technology acquisition and to enhance technological self-reliance. It differed from the Paris Convention Standards in three main areas: patent protection, period of protection, and importation of patented products. In the case of food, chemicals, and pharmaceuticals, the 1970 Act restricted the range of patent protection concerning drug, food, and chemicals to only process patents. Namely, this excluded from protection the patents on products themselves. This legal background has been the starting point for the development of the Indian pharmaceutical industry that used reverse engineering competencies to develop generic drugs destined to the Indian market.

The length of patent protection provided under the 1970 Act was of 7 years for food, chemicals, and pharmaceuticals and of fourteen years for the other products,

another difference from the Paris convention that granted a twenty-year protection for all kind of products.

Concerning the statute of the importation of patented goods; the 1970 Act did not recognize the importation of patented goods as sufficient for the working of the patent and permitted the revocation of the patent in such a case.

As a consequence of these provisions, India was not part of the Paris convention, for several years. However, as part of the founder countries of the WTO in 1995, India had to sign the Agreements regarding Trade Related Aspects of Intellectual Property Rights (TRIPs). These agreements negotiated as part of the Uruguay Round became effective with the creation of the WTO on the 1st January 1995. It requires all the members of the WTO to comply with the most recent version of the Paris Convention for the Protection of Industrial Property.

Developing nations were given a ten-year period to harmonise their domestic laws and institutions with the WTO standards. India has now to comply with all the provisions of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) before the 1st of January 2005.

The main elements of these provisions are:

- Enforcement of product patent protection in all branches of technology, including drugs.
- 20 years of protection instead of 14 or 7 in the case of the Indian patent Act.
- No discrimination between imported and domestic products.
- Compulsory licensing.

The first amendment in this direction was adopted in March 1999; it establishes a "mailbox facility" for accepting product patent applications for pharmaceuticals during the pipeline protection period from 1.1.1995 to 31.12.2004. A new amendment has been recently adopted to confirm the evolution of Indian patenting environment toward the WTO standards.

The debate on generic drugs

Generics drugs - chemical as well as biological – are at the centre of one of the fiercest debate of the international scene. On one side, the pharmaceutical companies defend their right to be rewarded for their innovation and insist on the necessity of setting strong incentives for innovation through the settlement of a strict and global enforcement of the Intellectual Property Rights (IPR). The WTO has followed this logic while elaborating the TRIPS. On the other side, the poorest countries are denouncing a system which allows private firms to sell at a monopoly price a product that can save lives, such as tritherapies for AIDS or antibiotics. Indeed, in the absence of any national health system in those countries, the monopoly prices adopted by the patent owning companies simply prevent most of the people to buy the medicines. By signing the TRIPs agreements without insuring the development of an efficient health system, the leaders of the poorest nations take a risky bet. Once the TRIPs agreements in action, either they will be able to exploit the flexibility of the international regulation to import or produce generic drugs, either they will have to face the discontent of the local populations deprived from life saving drugs. The most optimistic view is that the TRIPs will allow multinational pharmaceutical firms to invest in, or to collaborate with research and production unities based in developing countries, and doing so, reducing dramatically the cost of drugs.

In this debate, India occupies a very special position. Indeed, India is already both one of the largest market for generic drugs, and the Indian pharmaceutical Industry is the world largest exporter of generic drugs, the strategy of copying of existing companies adopted by Indian companies being considered by most of the Western Pharmaceutical companies as piracy.

Controls

R&D activities control

The DBT as well as the state-level departments of biotechnology pursue an objective of "single window agency". Following recommendations from the Confederation of Indian Industries (CII), the DBT has established a simplified process for the treatment of new applications concerning new research projects by the different committees (Review committee on genetic Manipulation (RCGM), Genetic Engineering Approval Committee (GEAC), Drugs & Pharma Approval Committee (DPAC), and Biotech Foods Approval Committee (BFAC)). Similarly, the state governments are developing simplified procedures of examinations for new applications, such as applications for the settlement of a biotech manufacturing plant.

Drug approval

In the case of biogenerics, not only the Indian approval process but the specific process of each country representing a potential market for the Indian companies has to be taken into account. Opening the world largest market, and being one of the most rigorous approval process, the United States Food and Drugs Administration (U.S.–FDA) system of drug approval is used as a reference for the Indian companies having a global strategy. On the government side, the Union minister of health & family welfare has recently claimed its desire to see the central drug organisation evolving in the pattern of the USFDA.

Public-Private Partnership

Apart from being a potential pool of entrepreneurs, public institutions can also play a critical role in the early days of a new biotech project by offering a shelter for the newborn project. This interaction, called incubation is relatively loosely defined. It consists generally in the provision of a working space and the possibility for the incubated company to use some equipment from the incubator institution. Avesthagen and Genotypic (Genomics), Shanta (recombinant therapeutics) and XCyton (Peptide-based Diagnostics) have used this model of collaboration.

Private Company Involved	Public Partners
Avesthagen	NCBS
	University of Agricultural Science
	ICRISAT
Bangalore Genei	CCMB
	IBA - ICAR
Bharat	DBT – AIIMS – NIH - CDC Atlanta - Stanford
	ICGEB - AIIMS
	CBT
Bigtec	IMT
Biological E.	CCMB
	IISC
	ICGEB
	Christian Medical College
CDC Linux	CSIR project team
Genotypic	CBT
	IISc
	Madhurai University
IAHS	NRCPB
Ingenovis	IICT - CCMB
	CCMB
Monsanto	IISc
	TERI
Nicholas Piramal	CBT
Rallis	ICGEB
	IISc
	University of Madurai
Shanta	Osmania University
	CCMB
	IISc
	JNU
	BARC
	CCMB
	AIIMS
	NII
	IICB
	Anna University
	Tata Memorial Hospital
	NDRI
SP Biotech Park	IICT
	CCMB
	CDFD
Strand Genomics	IISc
TCS	CSIR project team
	CDFD
Themis	CDRI
	IIT
	CBT
Wockhardt	ICGEB
Xcyton	NIMHNS
	IISc
	NIMHNS
	ICGEB
	AIIMS

The offer of incubation services is considered as a critical factor for the enhancement of the rhythm of company creation in the field of biotechnology. That is why the creation of an incubator is part of the various projects of Biotech Park in India (Bangalore, Chennai, Hyderabad). In the case of Hyderabad, the incubator is being

set up in collaboration by the biotech park - a joint venture between the state of Andhra Pradesh – and the Indian Institute of Chemical Technology (IICT).
A multitude of models exist for the interaction between a public institute with a certain technological competency, and a firm eager to use this competency. First, research institutions can take profit of a technology already developed by transferring or licensing it to the industry. The industry can also use the research capacity available in the research institutions through contract research or collaborative research. Institutions can also support private companies by signing memorandum of understanding for competency sharing or by providing specific training to newly hired people from a certain company.

Bioinformatics: Research Institutions as competency pools

In the case of companies entering the bioinformatics sector, the common trend is the demand from the companies' side for general competency in biology as their initial competency lies rather in information technology. Therefore they are keen on building flexible relations enabling them to tap in the competency pool provided by the institutes when required. This competency can be used for training. For example the new employees of the bioinformatics team of Tata Consulting Service (TCS) are trained at the Centre for DNA Fingerprinting and Diagnostics (CDFD) Hyderabad. Ocimum Biosolutions, a bioinformatics company implanted in Hyderabad offering bioinformatics training uses teaching material developed specially by the Michigan Technological University (MTU). This competency can also be used in the development of a tool for which the institute can formulate the needs and conduct the testing. This model has been applied by Ingenovis in its collaborations with institutions such as Cambridge University, CCMB, or IICT. In the case of Bigtec, a bioinformatics company from Bangalore, a Memorandum of understanding has been signed with the Institute of Microbial Technology, Chandigarh for general competency sharing.

Diagnostics: different positions toward collaboration

The development of a diagnostic kit is composed of two main stages that can be handled separately: the first consists in identifying the short nucleic acid sequence that can be used to detect a certain disease, and the second phase consists in developing a commercially viable kit. In some cases the company has simply bought a sequence already developed, and in other cases it has collaborated with institutes during the work on the peptide sequence. Once the peptide sequence is identified, the company can undertake the kit development on its own, or in collaboration. The same kind of articulation between the isolation of a certain protein and its insertion in a kit can be found in the case of recombinant diagnostics.

Recombinant proteins: learning how to collaborate efficiently

The market opportunity for recombinant therapeutics manufactured in India is now well known and there is a large demand from all the local companies with connected competencies for the technology enabling them to produce such products. Nevertheless, it seems that the bridge between the technology developed at the lab scale in the public institutions and the industrial competencies of the firm is difficult to build.

Genomics: an emerging field

The main interactions between firms involved in genomics activities and research institutions were discussed in the section on collaboration at the earliest stage of development. The reason for this is that all these companies are considered to be at their very stage of emergence. Nevertheless, considering the impressive rate of

creation of new companies in this field, one may wonder whether this dynamic will create a demand of collaboration toward public research institutes.

Recombinant Therapeutics

The recombinant products market has been led so far by imports of established global brands and marketing of the products either by local subsidiaries (*SmithKline Beecham (SKB)*, *Novo*), or through marketing arrangements as in the case of *Nicholas Piramal* and *Roche*. This trend is changing thanks to the massive entry of local competitors with a critical cost advantage.

Indian market for recombinant therapeutics (US$ millions)

Product Name	Year		
	1997	2000	2005
Insulin	7.1	16.7	26.9
Streptokinase	3.1	52.7	9.0
Erythropoietin	2.0	4.1	6.5
Hepatitis B	30.6	45.9	92.3
Human Growth Hormone	1.0	2.3	3.7
Granulocyte colony stimulating factor	4.1	15.3	24.7
alpha-interferon	12.2	16.3	26.5
gamma-interferon	N.C.	0.1	0.2
blood factor VIII	N.C.	0.2	0.3
FSH	N.C.	3.1	4.9
TPA	N.C.	N.C.	N.C.
Total	60.2	109.3	195.4

Source: TIFAC "recombinant DNA therapeutic products" January 2002.

The main strategies observed for technology acquisition can be classified as follows:

· **In house R&D:**
- Basic R&D
- Process scale-up R&D

· **Collaboration with a public institute:**
- Project funding
- Incubation
- Platform sharing

Technology transfer: A technology transfer can be defined by the precision of the contract. In this case, the contract defines precisely what the transferring part has to bring (cell line, scale up, support) and when the transfer ends.

- **Joint Venture:** A joint venture (50/50 is the general case) is a well defined financial structure allowing flexibility in the inputs of each parts, considering that each part has the same interest in the venture. For a given company involved in the production of recombinant products, there are several characteristics defining its marketing strategy:
- **Bulk compound / finished products:** the company may choose to market the purified protein as a component bought by other companies formulating the final drug.
- **Comprehensive marketing / Distribution Agreement:** In the case of finished products the company may choose between marketing itself its product and using the marketing force of an integrated pharmaceutical company. This "pharmaceutical marketing force" constitutes an important

asset in the pharmaceutical value chain, it is composed of a comprehensive network of representatives in close relation with every medical actor in the country, this can represent between 500 and 1200 people for a country like India.

- **Geographical range:** In the case of a Bulk Compound marketing strategy, the choice will be made between selling this compound to Local Pharmaceuticals Companies or Foreign Pharmaceuticals Companies.

In the case of a finished product the choice will be between addressing the Indian market and targeting the global market.

Drug Development

In the case of a company involved in a chain of research and development in the medical sector, the identification of the business model requires the definition of several classes of characteristics that can be determined in the following order.

- **End-use products** – to one end use product is associated one value chain with several stages.
- **Central development stages** – in the process of developing a new drug with the tools provided by the biotechnology, a stabilised sequence of stages seems to have emerged, which is common to every research programs. Identifying the achievement of which of these central development stages the work of a certain company contributes can be used to locate the business model vertically on the value chain.
- **Exchangeable goods –** The nature of the inputs and outputs actually exchanged by the company with its partners.
- **Assets** - The nature of the assets on which the company bases its model of value creation.

Business Models: Technology driven companies start with a specific technological competency, and the will to develop revenue models based on this competency. Opportunity driven companies are created with the general goal of taking advantage of India's cost effectiveness to take part in the drug development chain.

Bioinformatics

Although bioinformatics has been a critical element of the advances made so far in the fields of genomics and proteomics, its role is taking know an even greater importance. Here are the reasons why India should have a role to play in this industry:

The development of the Indian Software industry has provided the country with:

- An increased awareness of the growth opportunities in high tech outsourcing.
- The evolution of the regulatory bodies in order to facilitate the expansion of the sector.
- The development of bandwidth and other infrastructures required by IT enabled services.
- The development of an extensive skilled manpower base in informatics.
- An India inc. Brand recognizing for the quality of the services provided by the local industry.

The development of the local Biotech sector brings:

- Public bodies with a clear mission to make Indian Biotech industry a success story similar to the IT industry.

- Public initiatives specifically directly towards bioinformatics as a part of the Central Biotech policy. (Biotechnology Information System sponsored by the DBT, academic programs of bioinformatics)
- A strong academic knowledge in the public institutes in the fields of biology.
- Industry leaders eager to seize the opportunity the bioinformatics may offer.
- A general enthusiasm towards all the biotech-related fields.

Bioinformatics companies in India

Company	Financial / Organisational Backing	Business model
Avesthagen	Biotech company	services + databases
Astrazeneca	Pharmaceutical company	in-house
Bigtec	Private	Solution
CDC Linux	High Performance Hardware	Hardware + Integration
DSQ Biotech	IT + Biotech	
GVK Biotech	Biotech company	Training + Services
Ingenovis	IT Company (I-Labs)	Products
Jubilant Biosys	Chemicals (Jubilant)	
Kshema technologies	BI division IT Company	
Landsky solutions	Private	Products + Services + databases
Mahindra - British Telecom	BI division of an IT Company	
Metahelix	Biotech company	services + databases
Molecular connections	Pharmaceutical company Dr Reddy's	Projects
Monsanto	Biotech company	In-house
Ocimum biosolutions	Pharmaceutical company Saraca Group	Products
PrayogNet Computing	Private	
Questar Bioinformatics	Pharma company Gland Pharma	
Reliance Life Science	Biotech company	
Satyam	BI division of an IT Company	
Strand Genomics	Private Spinn of from IISc	Products
Spectramind	BI division off an IT Company	
Syngene	Biotech company	Services
SysArris	BI division of an IT Company	
TCS	BI division of an IT Company	CSIR Joint Program
Wipro	BI division of an IT Company	

Business Models: Bioinformatics companies can adopt the following kind of model:

Integration: The company provides its customers with a ready-to-use and coherent computing system composed of hardware and software. The company offering integration services can be also involved in providing some components of the final system.

- Computing services: The company takes information under a certain form and returns it in a more valuable form.
- Solution: A solution contract implies the delivery by a company of a tailored product answering the specific needs of the customer.
- Product: While some company offer standard products (i.e. software), most of the companies offer, along with the basic product, services in integration and customisation.
- Intellectual Property Development: Although the development of bioinformatics tools does not constitute a central stage of the drug development chain, the specificity and the value added by a certain tool can be allow the access to intellectual property applied on the final product (therapeutic or agricultural)
- Intellectual property relevant to the final product is the best way for a bioinformatics company to access to high returns.

At the stage of emergence, the business model is strongly determined by the financial constraints of the bioinformatics firms. Whereas firms with a strong corporate backing can allow themselves to adopt a long term strategy of competency building, small independent firms must cope with the requirement of external funding, i.e. rapid generation of cash flow.

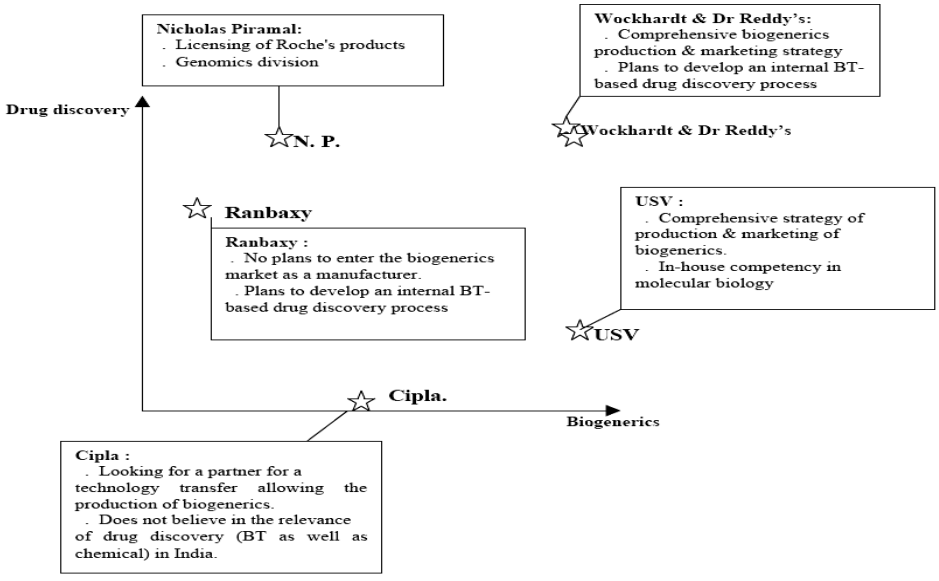
Clinical Trials

Clinical trials are the most expensive stage of the drug development chain and India possesses resources that should allow the country offering clinical research services at a very competitive cost.

Several companies have already taken the initiative to develop an activity of contract driven clinical trials in India. For example the global major Quintiles has already settled three centres in the country and some Indian companies having activities in Biotech and pharmaceuticals have launched their own division for contract clinical trials. Indeed, the enzyme manufacturer Biocon has set up a new subsidiary, Clinigene to conduct clinical research under contract, so did the pharmaceutical companies Nicholas Piramal with its subsidiary WellQuest, and Ranbaxy with SRL Ranbaxy. Siro Research was founded in 1995 as a clinical research organisation. Catalyst Clinical Services is another clinical research organisation settled in India. All these companies are looking for large scale contracts with foreign partners and they are working on their practices in order to comply with the international standards such has the Good Clinical Practices (GCPs) defined by the International Conference on Harmonisation (ICH).

On the regulatory side, the process of convergence of the Indian institutions in charge of the control of the clinical trials carried out in India - the Drug Controller General of India (DGCI) under the tutorship of the Central Drugs Standard Control Organisation (CDSCO) – toward the international standards has been already initiated.

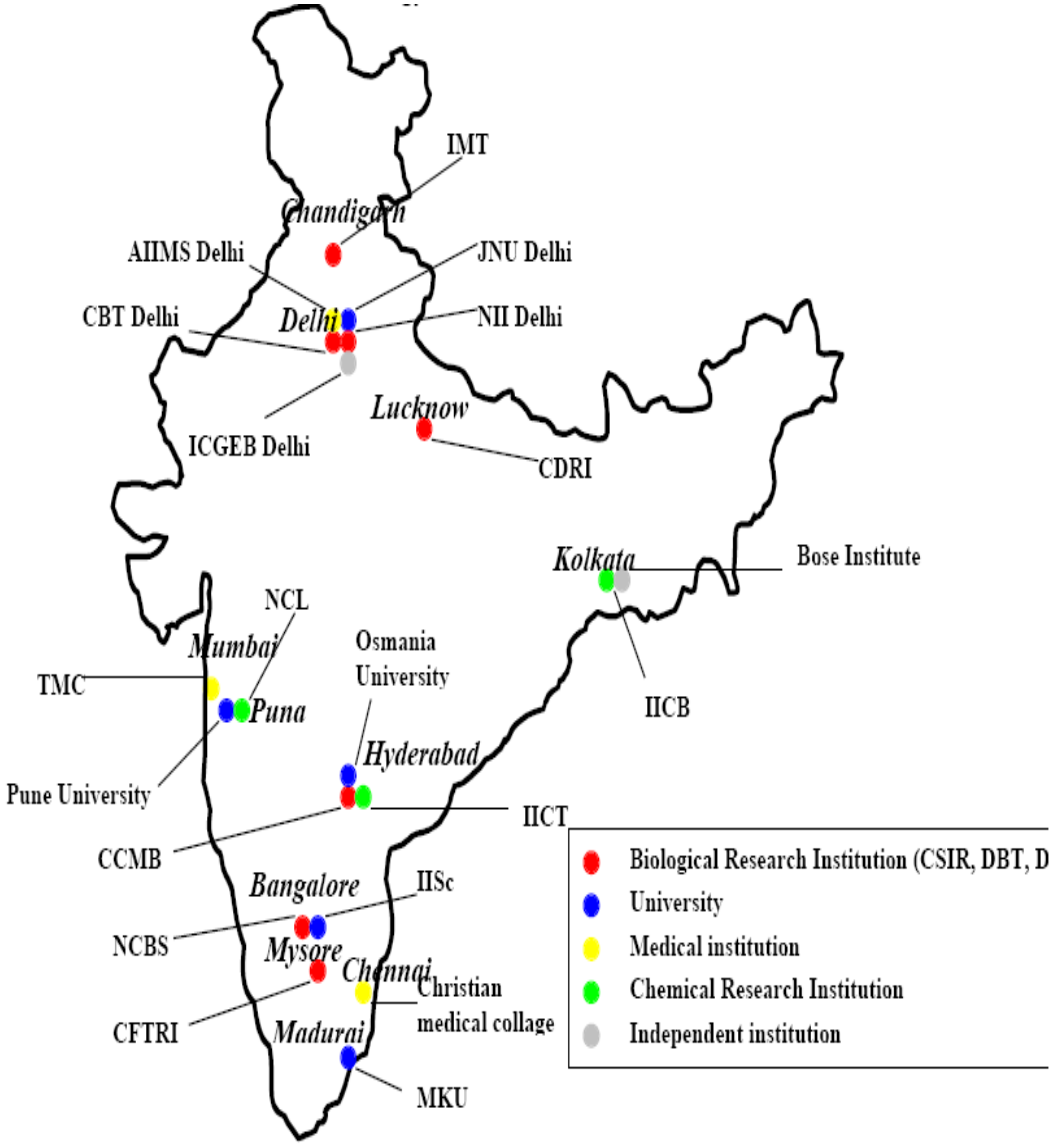
Biotech Strategies of some leading Indian Pharma companies



Concentration of Biotechnology Industry in major Indian cities

The location of the Indian modern biotechnology sector provides interesting insights on the emerging metropolises in India. Various factors can explain the presence of BT industry in cities such as Mumbai, Delhi, Bangalore, Hyderabad and Chennai. Among them are the presence of better than average infrastructure, the presence of public research institutes and the facilities provided by State policies that aim at encouraging new sectors for development.
However, this location is certainly linked to the new forms of industrial organisation that are a requirement for the Biotechnology sector where the importance of networks is crucial for the innovation process.

Geographic repartition of the main research institutions mentioned in fields related to biotechnology



Institutions Identified as national Centres of Excellence

Name of the institution	Affiliation	Location	Interactions
Centre for Cellular and Molecular Biology (CCMB)	CSIR	Hyderabad	Bangalore Genei (Bangalore)
			Biological E. (Hyderabad)
			Ingenovis (Hyderabad)
			SP Biotech Park (Hyderabad)
Centre for Biochemical Technology (CBT)	CSIR	Delhi	Bharat (Hyderabad)
			Genotypic (Bangalore)
			Nicholas Piramal (Bombay)
			Themis (Bombay)
Indian Institute of Science (IISc)	UGC	Bangalore	Biological E, (Hyderabad)
			Genotypic (Bangalore)
			Monsanto (Bangalore)
			Rallis (Bangalore)
			Shanta (Hyderabad)
			Strand Genomics (Bangalore)
			Xcyton (Bangalore)
International Centre for Genetic Engineering and Biotechnology (ICGEB)	UNIDO	Delhi	Biological E, (Hyderabad)
			Rallis (Bangalore)
			Xcyton (Bangalore)
			Wockhardt (Mumbai)
			Bharat (Hyderabad), AIIMS (Delhi)
All India Institute of Medical Science (AIIMS)	ICMR	Delhi	Bharat (Hyderabad), DBT (Delhi), NIH (USA)
			Bharat (Hyderabad), ICGEB (Delhi)
			Shanta (Hyderabad)
			Xcyton (Bangalore)

Government Initiatives

India is among the first few countries in the developing world to have recognised the importance of biotechnology as a tool for advancing growth in the agriculture and health sectors. The Government established the National Biotechnology Board (NBTB) in 1982 as the apex body to identify priority areas and evolve a long-term plan for the development of biotechnology. Later, in 1986, NBTB graduated to a full-fledged government department called the Department of Biotechnology (DBT).

The DBT is the only agency fully dedicated to biotechnology, and it is hard to assess the share of the presented allocations from the other institutions that have been dedicated to biotechnology.

Budgetary allocations of major funding agencies (Rs. Million)

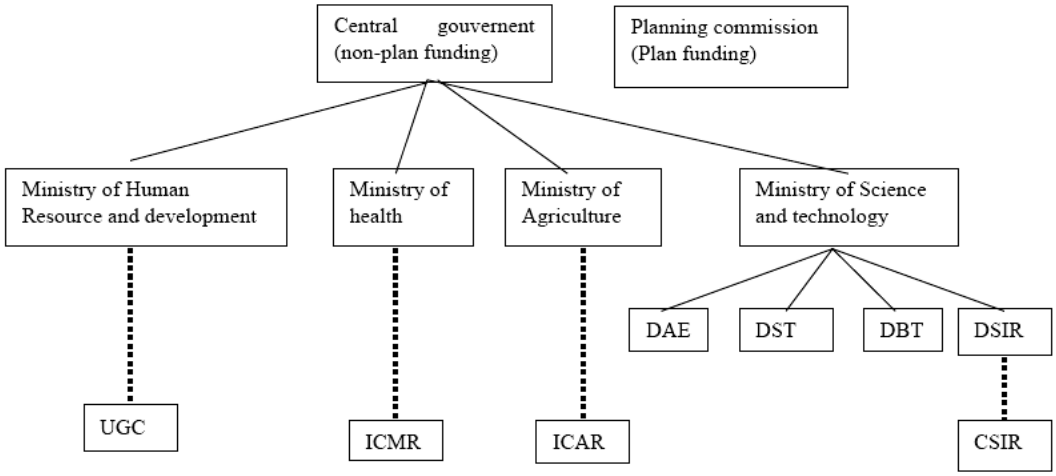
Agencies names	1990/91	2000/01	Growth (%)
Department of Scientific and Industrial Research (DSIR)	131	584	446
Council of Scientific and Industrial Research (CSIR)	2351	9120	388
Department of Science and Technology (DST)	2589	7798	301
Department of Biotechnology (DBT)	655	1391	212
Indian Council of Agricultural Research (ICAR)	3236	13990	432
Indian Council of Agricultural research (ICMR)	396	1470	371
University Grants Commission (UGC)	3495	14070	403

Source : RIS based on budgetary papers of relevant years, Ministry of Finance, Government of India.

While the DAE, DST, DBT and DSIR are full fledged government bodies, the UGC, ICMR, ICAR and CSIR are independent bodies affiliated respectively to the ministry of human resource and development, ministry of health, ministry of agriculture, and

Department of Scientific and Industrial Research - ministry of science and technology. Those different entities have several programs and autonomous research centres under their supervision.

Administrative organisation of the main public agencies involved in the funding of public research.



Incentives for investments in the Indian biotechnology industry include:

- 100 per cent foreign equity investment allowed in manufacturing of all drugs except recombinant DNA products and cell targeted therapies.
- DBT provides a single window processing mechanism for all mega biotechnology projects involving Foreign Direct Investment (FDI) of US$ 22 million or more under the Foreign Investment Implementation Authority (FIIA) with its Fast Track Committee (FTC).
- Depreciation allowance on plant and machinery.
- Customs duty exemption on goods imported in certain cases.
- 150 per cent weighted tax deduction on R&D expenditure.
- 3 year excise duty waiver on patented products.
- 100 per cent rebate on own R&D expenditure.
- 125 per cent rebate if research is contracted to public funded R&D institutions.
- Customs duty on import of reference standards has been reduced from 25 per cent to 5 per cent.
- Joint R&D projects are provided with special fiscal benefits.
- Recently announced tariff and non-tariff measures by the Government are set to further stimulate market development in the biotechnology.

Advantage India

<u>Availability of Skilled Manpower</u>

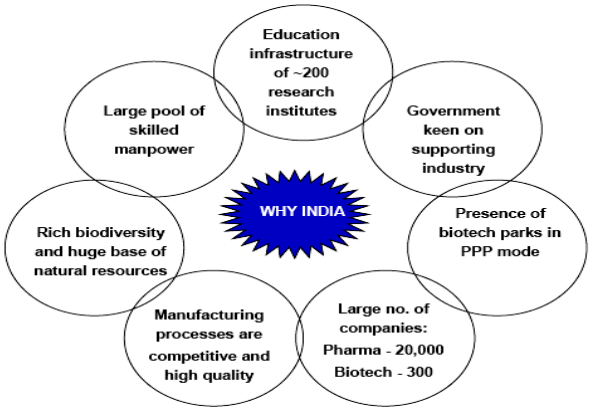
- India has the largest English speaking population, after the US
- Science/Engineering stream in India produces 3 million graduates, 700,000 post graduates and 1500 PhDs every year
- 15,000 scientists are engaged in the biotech sector
- Manpower costs much lower in India vis-à-vis competing nations

High Quality Standards in Manufacturing

- Outside the US, India has the world's highest number of FDA approvals
- World-class facilities for generic manufacturing that comply with internationally harmonised standards such as Good Laboratory Practices (GLP), current Good Manufacturing Practice (cGMP) and Good Clinical Practices (GCP)
- Well-recognised for low cost fermentation technology and generic biologicals

Genetic Profile of Indian population

- Clinical trials can be outsourced to India as the Indian population has similar genetic profile as US and European patients due to joint Aryan descent
- Moreover low penetration of medical treatment in the country and the resulting speed of patient enrollment for trials is an advantage



SWOT Analysis

STRENGTHS • Trained manpower and knowledge base • Good network of research laboratories • Rich biodiversity • Well-developed base industries (e.g., pharmaceuticals, seeds) • Extensive clinical trials and research • Access to vast & diverse disease populations	WEAKNESSES • Missing link between research and commercialization • Lack of venture capital • Relatively low R&D expenditure by industry • Doubts about the ability of Indian products to meet international standards of quality
OPPORTUNITIES • The large Indian market can be captured by gaining IP protection. • There will emerge new revenue streams from patent licensing and litigation. • Strong IP protection increases the lucrativeness of India as a destination for contract research.	THREATS • Existing business models will not work. • Fresh investments need to be made in new directions (strategic R&D set up, IP protection).

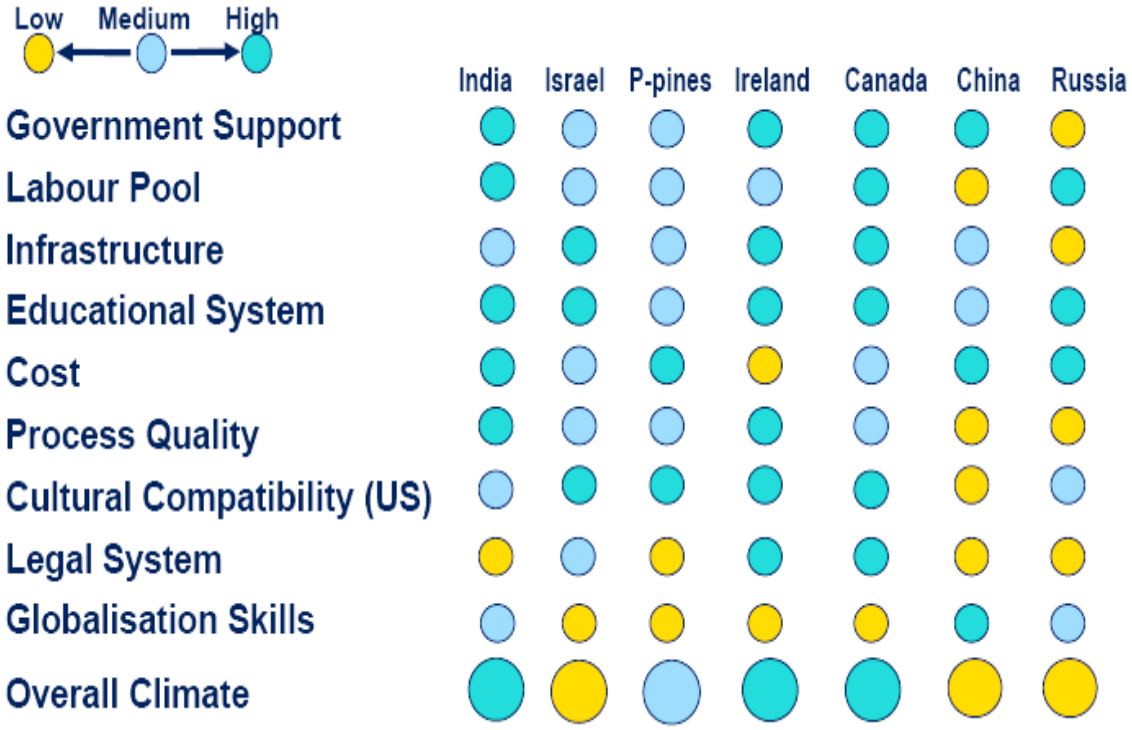
Opportunities in the Indian Biotech Sector

By 2010, the Indian Biotech industry is expected to achieve revenue of USD 5 billion and create 1 million jobs.

New Business Models are emerging:

Collaborative R&D	Indian companies can partner with foreign players to enter into collaborative R&D efforts as an initial step towards developing an R&D focus.
New revenue streams	Revenues from patent licensing and litigation can re-define existing business models completely, and shift them to a higher value-generation plane.
Emerging business opportunities	India will become a highly lucrative option for contract research once strong IP protection legislation is introduced.
Capturing the Indian market	Indian companies can introduce entry barriers for foreign players in the Indian market by using IP to protect their own innovations.

Advantages in R & D Sourcing



Source: Gartner

BioPharma - custom manufacturing in India

- Indian companies have proven manufacturing strengths in making generic equivalents of bio drugs
- Indian vaccines have huge market in developing markets

Bioservices - outsource from India

- Services like clinical trials, contract research, data management, clinical development services, site management

BioAgri - sell in India

- Area under Bt cotton only 8% of total cotton cultivation, immense opportunity for further sales
- Another modified genetic crop approved in India is brinjal (expected to be commercially released by 2007 or 2008). Other biotech crops approved for multi-location trials - cabbage, cauliflower, corn, peanut, mustard/rapeseed, okra, pigeon pea, rice, and tomato
- Huge potential for biofertilisers and biopesticides

Medical Technologies

- Market size 2006 - $1.32 billion
- Market size 2010 - $1.70 billion
- Though the industry ranks in the top 20 in the world, per capita spending on medical devices is very low at less than USD 1
- Infrastructure for health care still in a nascent stage
  - Currently only 0.7 hospital beds and 0.6 physicians per 1000 population
  - Public health system unable to cope with changing disease patterns
- Growing investments in private sector healthcare infrastructure, with corporates establishing premium hospital chains offering world-class healthcare
- Imports dominate costly and high-end medical equipment, whereas medical supplies and disposables are dominated by domestic producers

Cancer Diagnostics & Treatment Equipment

- Cancer diagnostic and treatment equipment (CD&TE) is the largest segment in medical devices with market size of ~ USD 270 million, accounting for more than 20% of market
- Incidence of cancer (oral, pharynx and cervix) is on the rise because of very high usage of tobacco (almost 40% men and 15% women have tobacco-related cancer)
- Both Government and private sector are adding to hospital capacity in India
- Almost 70% of the CD&TE is imported - linear accelerators, CT scanners, cobalt and branch therapy systems, X-knives, simulators for treatment planning systems, mammography and fluoroscopy systems
- Low-end CD&TE is manufactured in India

In-vitro Diagnostic Equipment

- In-vitro diagnostic equipment and reagents market in India estimated at ~USD 150 million, of which equipment comprises 40%
- Overall market estimated to grow at more than 25% annually with increasing health awareness and developing clinical research market; almost 60% of equipment and supplies are imported
- ~30,000 laboratories in the country servicing about 1.25 million patients per day

- High end laboratories (offering automated chemistry and hematology systems) account for 30% of patients, second-tier regional laboratories account for 40% of patients
- Corporate players establishing diagnostic centres in small towns will drive future growth of imported systems and reagents

Medical Equipment

- Growth in medical equipment and supplies market to be driven by to be driven by investment in healthcare spend in India
- Sales prospects good for cancer diagnostic, medical imaging, ultrasonic scanning, plastic surgery equipment and polymerase chain reaction technologies
- Way to enter India is by way of technically trained distributor, who would also offer service support for all medical equipment
- International companies present in India include GE, Siemens, Philips, Baxter, Bayer, Hewlett Packard, Water, Miles, Bohrienger Mannheim, Pickers and Coulter

PUBLICATIONS

- **Biospectrum** (monthly biotech magazine)

401, 4th Floor, MBC
134 Infantry Road
Bangalore - 560 001
Website: www.biospectrumindia.com

- **Chronicle Pharmabiz** (weekly newsletter)

Ipharma India Ltd
Manek Mahal,
5th Floor,
90 Veer Nariman Road,
Churchgate
Mumbai - 400 020
Website: http://www.pharmabiz.com

- **Express Pharma Pulse**

Business Publications Division,
Indian Express Newspapers (Bombay) Ltd.,
Express Towers, 1st floor,
Nariman Point
Mumbai - 400 021
Website: http://www.expresspharmapulse.com

Monthly Newsletter by ABLE: http://ableindia.org/html/newslet/newslet.html

CONTACT LISTS

Trade Associations

Association of Biotechnology Led Enterprises (ABLE)
No. 13, 2nd Floor, 4th C Block
10th Main Road, Koramangala
Bangalore – 560 034
Tel: +91 80 2553 3938
Email: info@ableindia.org
Website: www.ableindia.org

Confederation of Indian Industry (CII)
Plot 249 F, Sector 18
Udyog Vihar - Phase IV
Gurgaon - 122 015
Tel: +91 124 5014060-67
Email: ciico@ciionline.org
Website: www.ciionline.org

The Associated Chambers of Commerce & Industry of India
ASSOCHAM Corporate Office
1, Community Centre, Zamrudpur
Kailiash Colony
New Delhi - 110 048
Tel: +91 11 46550514
Website: http://www.assocham.org/

National Government Bodies

Department of Biotechnology
Department of Biotechnology
Block No. 2, Floor 7
CGO Complex, Lodi Road
New Delhi - 110 003
Website: http://dbtindia.nic.in

Council for Scientific and Industrial Research
Anusandhan Bhawan, 2 Rafi Marg
New Delhi – 110 001
Tel: +91 80 23737889
Email: dyr@csir.res.in
Website: http://www.csir.res.in

Department of Science & Technology
Technology Bhavan
New Mehrauli Road
New Delhi - 110016
Tel: +91 11 26567373, 26962819
Fax: +91 11 26864570, 26862418
Email: dstinfo@nic.in
Website: http://www.dst.gov.in

Intellectual Property & KnowHow Informatics (Patent) Division
National Informatics Centre
Department of Information Technology
A-Block, CGO Complex
Lodi Road
New Delhi - 110 003
Tel: +91 11 24363239
Fax: +91 11 24362628
Email: bali@nic.in
Website: www.patinfo.nic.in

Controller General of Patents, Designs & Trade Marks
Bhoudhik Sampada Bhavan,
Near Antop Hill Head Post Office
S.M. Road, Antop Hill
Mumbai – 400 037
Tel: +91 22 24123311
Fax: +91 22 24123322
Website: www.ipindia.nic.in