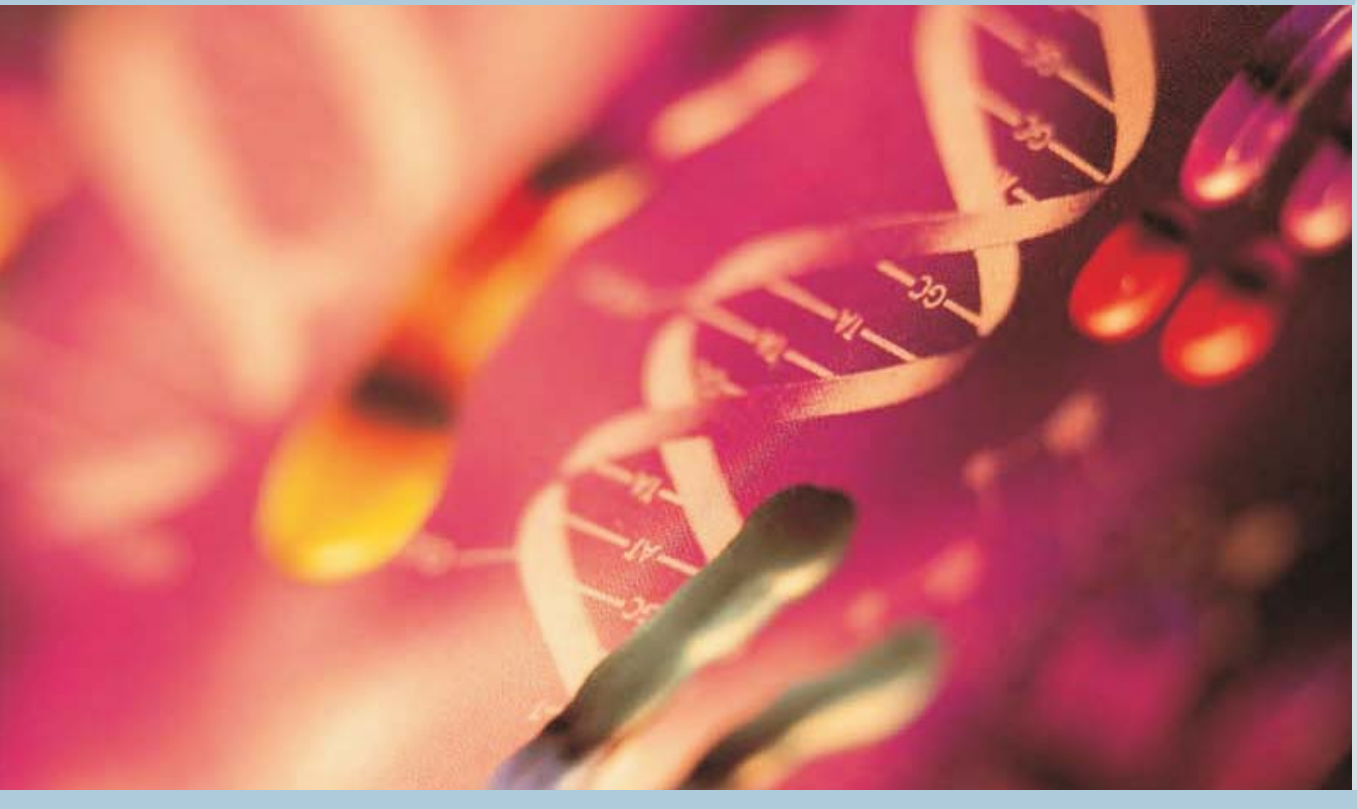
BIOTECHNOLOGY



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A report by Ernst & Young for IBEF

Market Overview

Indian biotech industry crosses the US$ 1 billion threshold

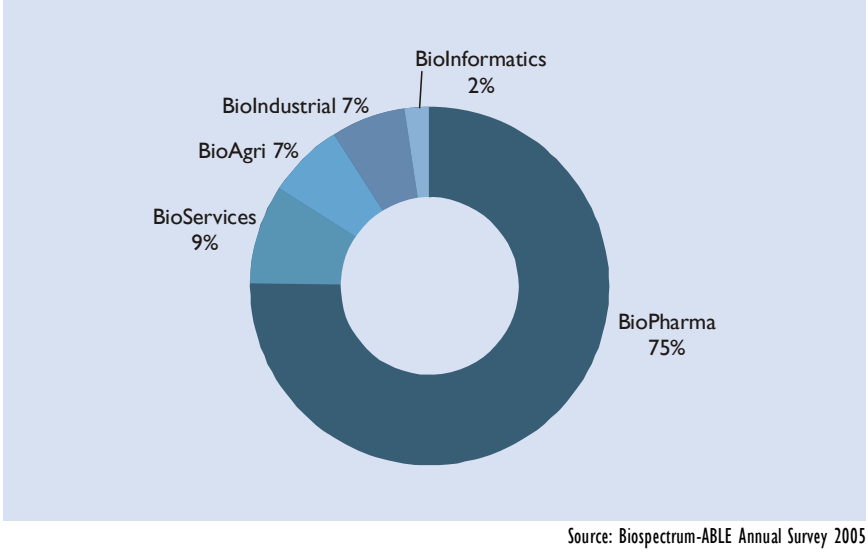
The Indian biotech industry reached a major milestone by crossing the US$ 1 billion dollar mark in 2004-05. The industry grew by an impressive 36.5 per cent over the previous year.

Biotech exports from India stood at US$ 455 million (million), contributing over 42 per cent of the industry revenues.

Segment	Sales (US$ million) 2003-04	Sales (US$ million) 2004-05	Growth (per cent) 2004-05
Biopharma	625.45	811.36	29.72
BioServices	62.50	96.59	54.55
Agribiotech	29.55	75.00	153.85
Industrial Biotech	54.09	72.73	34.45
BioInformatics	18.18	22.73	25.00
Total Industry Size	**789.77**	**1078.41**	**36.55**

Source: Biospectrum-ABLE Annual Survey 2005

Biopharma – the largest pie of the market; Agribiotech – the fastest growing



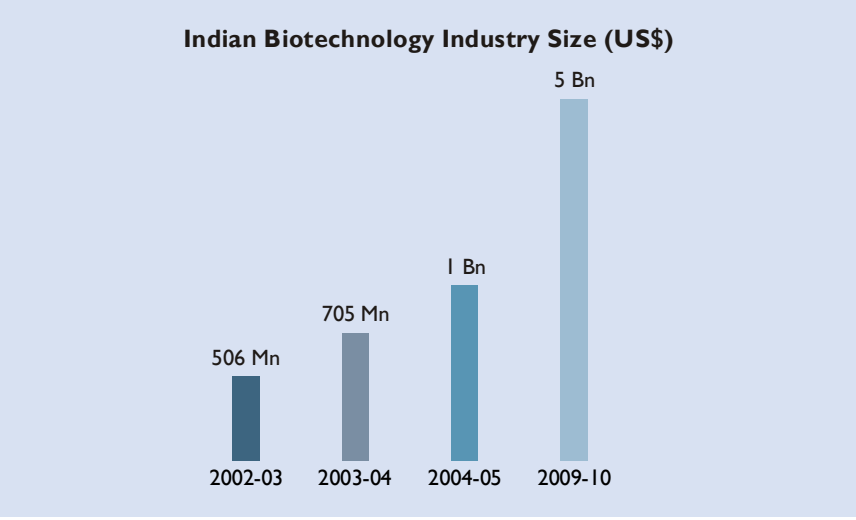
Source: Biospectrum-ABLE Annual Survey 2005

Biopharma, with revenues of about US$ 811million, accounts for three-fourths of the biotech market. This segment registered a 30 per cent growth, driven primarily by the vaccine business.

Agribiotech, contributing a mere 7 per cent of market value, was the fastest growing segment at 154 per cent driven by the revenue growth of leading Bt cotton companies.

Indian biotech market pegged to reach US$ 5 billion by 2010

The Indian biotech industry today comprises over 280 companies with six of them generating revenues of over US$ 22.7 million. With the new product patent regime in place and a national biotech policy set to be notified soon, the Indian biotech industry is set to touch US$ 5 billion in revenues by 2010.



Source: Biospectrum

Strong multinational presence in industry top order

In 2004-05, the Top 20 biotech companies in India represented 60 per cent of the total industry revenues, with six MNCs occupying a position on the list.

Rank among Top 20	MNC	Revenue 2004-05 (US$ million)
6	Novo Nordisk	30.68
8	Aventis Pharma	19.16
10	Chiron Behring Vaccines	17.73
11	GlaxoSmithKline	17.69
14	Novozymes	15.68
15	Eli Lilly & Co.	15.54

Source: Biospectrum-ABLE Annual Survey 2005

India becoming a partner of choice for biotech, globally

India's rising prominence in the field of biotechnology is making it a coveted partner for bilateral technical cooperation in this field. India and Denmark have signed a Memorandum of Understanding (MoU) for developing a long-term cooperation in biotechnology between the two countries and for facilitating joint collaboration on specific areas of interest. The MoU envisages exchange of scientists, technicians, training of young scientists as well as joint execution of scientific research and development projects.

India has also signed a MoU with Netherlands for cooperation in biotechnology in the areas of agriculture and health. The MoU was signed between the Department of Biotechnology (DBT) and Netherlands' Institutes of Higher Education (NIHE). The activities will be aimed at tailor-made biotechnology products, processes, techniques and policy matters based on local needs. The project also includes cooperation in transgenic technology in crops. DBT will contribute US$ 1.6 million, while NIHE will contribute US$ 2.2 million at the outset. The intellectual property generated by the joint research would be shared.

Sweden too has signed a MoU with India for cooperation in the field of Science & Technology. With biotechnology being one of the main areas of focus, the MoU will include a high level of cooperation through joint research, greater academic exchanges and facilitation of industrial research and development.

India's Value Proposition for Biotech

- More than 300 college level educational and training institutes across the country offering degrees and diplomas in biotechnology, bioinformatics and the biological sciences
- A knowledge pool in biosciences and engineering of over 3 million graduates, 700,000 post graduates and 15,000 PhDs
- A strong multinational presence offering Indian talent exposure to cutting age technologies and opportunity to work on state of the art research projects
- A robust IT industry which has already established India's credentials as a viable investment destination
- Presence of a well-defined base industry, that is the pharmaceutical industry

Key Opportunities

Biopharmaceuticals

With gross revenues of US$ 811.36 million in 2004-05, the Biopharma segment was the single largest contributor to the Indian biotech industry.

Biopharma, comprising of vaccines and therapeutics, including diagnostics and other products such as statins, registered a growth of about 30 per cent in 2004-05.

Segment	Sales (US$ million) 2003-04	Sales (US$ million) 2004-05	Growth (per cent) 2004-05
Vaccines	294.32	379.32	28.88
Therapeutics	94.32	113.64	20.48
Others	144.32	181.82	25.98
Diagnostics	92.50	136.59	47.67
Total Industry Size	**625.45**	**811.36**	**29.72**

Source: Biospectrum-ABLE Annual Survey 2005

Vaccines

The vaccines business is a major pie of the Biopharma market accounting for close to 47 per cent. While the human vaccines business saw close to 28 per cent growth, the animal vaccines business has grown by over 75 per cent. India produces most of the known vaccines within the country, including those for Tetanus Toxoid, Polio, DPT, Typhoid and Hepatitis B (recombinant).

Hepatitis B vaccine market estimated at US$ 22.2 million and growing at 20 per cent

India is the largest producer of recombinant Hepatitis B vaccine in the world today. The Hepatitis B vaccine market in India is growing at a rate of 20 per cent and is presently estimated at US$ 22.2 million.

Several domestic biopharma companies are manufacturing and marketing recombinant human Hepatitis B vaccine in India at affordable prices. Early movers in this product category include Shantha Biotechnics, Bharat Biotech International and Wockhardt. The other Indian players in this segment include Biological E, Panacea Biotec, Serum Institute of India and VHB Life Sciences.

Even multinationals such as Aventis, LG Chemicals, GlaxoSmithKline and Wyeth India have their own brands in the Hepatitis B vaccine market. In all, there are over 10 brands available in India.

As the government plans to include Hepatitis B vaccine under the national immunisation programme, many government agencies and non-government organisations are supporting/ pushing the growth of the market in India. The market is growing in terms of volume, but in terms of value it is experiencing slower growth because of some agencies which are selling the vaccine free of cost.

India emerging as the vaccine capital of the world

India is emerging as the vaccine hub of the world. Several vaccines are being procured from India in large volumes by GAVI (Global Alliance for Vaccines and Immunisation). Exports are therefore a major contributor to India's vaccine sales.

Domestic companies have developed strong capabilities in vaccine development and manufacturing. Serum Institute, one of India's largest vaccine players, recently announced the launch of its unique rabies vaccine, Rabivax, claimed to be the only indigenously developed Human Diploid Cell (HDC) rabies vaccine in India. Panacea Biotec, another leading player, has developed "thermostable" vaccines in collaboration with Cambridge Biostability, a UK based research company. The new 'stable liquid' technology will help in the production of a pentavalent childhood vaccine, which can be stored without refrigeration.

An interesting trend in the Indian vaccine market is that animal healthcare companies are expanding their manufacturing expertise to human healthcare in a big way. For instance, Indian Immunologicals, a leading animal healthcare company and one of the largest manufacturers of foot and mouth disease vaccine in the world, has filed seven international patents on novel combination DNA rabies vaccine.

Global companies tying up with domestic manufacturers for Indian foray

Several Indian companies are now partnering foreign companies to manufacture and market their vaccines in India. Acambis plc, a vaccine developer based in Cambridge, UK has established a manufacturing and marketing agreement with Bharat Biotech International Limited, relating to its investigational vaccine against Japanese Encephalitis. Under the agreement, Bharat Biotech will be responsible for end-stage fill/finish processing at its facilities in India and, once the vaccine is approved, it will market and distribute the vaccine in India and neighbouring countries.

Sanofi Pasteur recently introduced Vaxigrip, its global preventive vaccine against influenza for the season 2005-2006 in India. Vaxigrip is produced by Sanofi Pasteur in Lyon, France and is marketed in India by Sanofi Pasteur and Ranbaxy.

Panacea Biotec has formed a joint venture with Chiron Vaccines, USA, the world's fifth largest vaccine company, to provide breakthrough combination vaccines to the Indian market. The two companies together were the first to develop the breakthrough fully liquid pentavalent combination vaccine, which will protect against five potentially life threatening infectious diseases: diphtheria, tetanus, whooping cough, Hepatitis-B and H.Influenzae type b.

New focus on combination vaccines

Recognising the emerging opportunity, a number of other domestic companies are in the process of developing combination vaccines. Shantha Biotechnics recently launched its four-in-one vaccine, *Shantetra,* a single vaccine for protecting children against four life-threatening infections including diphtheria, tetanus, pertussis and hepatitis B. Similarly, Serum Institute has announced an indigenous DTP and Hepatitis B combination vaccine, *Q-Vac*.

Several new vaccines being worked upon in Public R&D laboratories

Various R&D institutes in the country have been doing R&D on vaccines for cholera, tuberculosis, rabies, HIV, malaria and Japanese Encephalitis, among others.

Scientists at the Indian Institute of Science (IISc), Bangalore along with Indian Immunologicals Ltd, have developed the world's first combination rabies vaccine for control of rabies in dogs. The vaccine was found to confer 100 per cent protection in experimental animals.

Scientists at the National Institute of Immunology (NII), New Delhi have developed a vaccine based on the Indian strain of Japanese Encephalitis Virus (JEV) and the technology has been transferred to Panacea Biotec for further testing and commercialisation.

A prototype candidate vaccine for the HIV-I Subtype 'C' has been developed based on plasmid DNA and MVA (Modified Vaccinia Ankara) approaches at the All India Institute of Medical Sciences (AIIMS), New Delhi. The prototype vaccine is now ready for preclinical toxicological studies.

Therapeutics

The therapeutics market recorded 20 per cent growth and grew to US$ 111.1 million in 2004.

At present, over 50 recombinant therapeutic products have been approved globally for commercial use and one fourth of these have already made inroads into India with about 14 recombinant biotech products receiving government approval for marketing in the country.

Indigenous expertise in over seven recombinant therapeutics

About 40 companies, both Indian and multinationals, are involved in one of the many activities such as R&D, importing, manufacturing and marketing of recombinant biotech products in India.

Local companies such as Bharat Biotech, Dr. Reddy's Labs, Panacea Biotec, Shantha Biotechnics, Wockhardt, Biocon and Intas Pharmaceuticals etc. have acquired the expertise to indigenously develop and manufacture seven recombinant biotech products namely Hepatitis B Vaccine, Streptokinase, Human Insulin, G-CSF, Erythropoietin, Human Growth Hormone and Interferon alpha 2b.

The indigenous production of these products by local companies has resulted in the drastic reduction of prices and at the same time led to increased consumption. The entry of Indian firms, with their own brands of recombinant products, has changed the dynamics of the domestic market in India. The Indian biotech products are not only taking the leading global brands head on in terms of quality, but are also increasing their market shares.

Indian biopharma companies eyeing the global biogenerics opportunity

Companies in India are also looking keenly at the global biogenerics space as a large number of biologicals are set to go off patent. Companies such as Wockhardt, Dr. Reddy's Labs and Biocon are looking at entering the regulated market in Europe, which has a regulatory system in place for the biogenerics. Wockhardt has received 17 registrations for its biopharmaceuticals and 36 registrations are being pursued in various overseas markets such as Russia, South America, North Africa, Central Asia and South East Asia. It has also formed majority joint ventures in Mexico and South Africa and has set up a subsidiary in Brazil.

India becoming attractive both as a biopharma market and partner for global companies

While Indian companies are making significant investments to improve and expand their manufacturing facilities in order to enter regulated markets, global players are eyeing India to set up their manufacturing bases in the country.

Some Indian companies are already manufacturing these recombinant products on contract for global pharma firms. For instance, Sun Pharmaceuticals and Torrent Pharmaceuticals are into contract manufacturing of recombinant products for multinationals such as Eli Lilly and Novo Nordisk respectively.

With IPR legislation now firmly in place in India, opportunities exist for speeding up production facilities, based on licensing and other forms of cross-border relationships. The growing number of applications for import/ clinical evaluation/ manufacture and market applications in the sector is strong evidence of the opportunity in biogenerics in India.

Novartis India intends to import Xolair (omalizumab) in finished formulations from the US for marketing in India and has sought the permission of the Genetic Engineering Approval Committee (GEAC) for the same. Xolair is a recombinant humanised monoclonal antibody (protein) indicated for the treatment of asthma and is administered via subcutaneous injection.

India has a huge market potential for biogenerics. It is estimated to be in the region of about 1000 crore by 2007-08, including exports. The aggregate investment in this segment in the next five years is estimated to be in the region of US$ 111.1 million.

Erythropoietin, a US$ 16.7 million opportunity

Observing the trends and increase in the number of reported cases of chronic renal failure in India, the Erythropoietin (EPO) market in the country is set to grow rapidly. The EPO market has been growing at a rate of 20 per cent and is currently estimated at about US$ 16.7 million. Several brands are available in India in the EPO space. The companies that are marketing EPO include Shantha Biotechnics, LG Life Sciences India, Ranbaxy, Johnson & Johnson, Emcure Pharma, Wockhardt, Zydus Biogen, Hindustan Antibiotics and Intas Pharmaceuticals. Except Wockhardt, Shantha Biotechnics and Intas Pharmaceuticals, other Indian companies have entered into agreements with different multinationals for marketing and licensing rights to offer recombinant EPO to Indian patients. Hindustan Antibiotics has a tie-up with Elanex Pharmaceuticals, USA. Emcure Pharmaceuticals has entered into a marketing and licensing agreement with Dragon Pharmaceuticals Inc., Canada for distribution of EPO in India.

Human Insulin market showing blistering growth at over 40 per cent p.a

Human insulin was imported to meet domestic demand until Wockhardt became the first Indian company to launch human insulin under the brand

Wosulin in 2003. Biocon and Shreya Life Sciences are the other domestic companies which market human insulin. Now India has as many as six Indian companies with manufacturing capabilities.

The Indian market for Insulin is highly competitive with global majors such as Novo Nordisk, Eli Lilly and Aventis strongly entrenched. In the human insulin space, there are as many as seven brands of both Indian companies and multinationals.

A number of new products are in the research pipeline in the Indian market. Pfizer's inhaled insulin drug candidate, Exubera, which is targeted at the treatment of Type 1 and Type 2 diabetes, and is currently in Phase III clinical trials abroad, has been given the permission to conduct the trials in India as part of its global trials.

Biocon has entered into an agreement with Nobex, a US biotech firm, for research collaboration relating to joint development of an oral insulin product for the global anti-diabetes market. The project involves using Biocon's manufacturing expertise in recombinant Insulin, which would be modified and converted into oral form using Nobex's proprietary technology.

The insulin market in India is about US$ 55.8 million and the human insulin market is growing at the rate of 40.5 per cent. The market for animal insulin products is coming down as a result of this increase.

Other biogenerics show robust growth

In the **Streptokinase** space, India has a couple of brands marketed by local companies including Bharat Biotech International, Shantha Biotechnics and Kee Pharma. At present, the Streptokinase market is estimated to be in the region of US$ 17.8 million and has been growing at a rate of 25 to 30 per cent.

In the **Human Growth Hormone** space, India has both multinationals and Indian companies marketing their brands. None of the Indian companies are manufacturing this drug locally. Foreign players include Eli Lilly, LG Chemicals and Novo Nordisk.

In the **Granulocyte Colony Stimulating Factor (G- CSF)** space, Indian companies such as Intas Pharmaceuticals and Dr Reddy's Labs have set up their facilities to manufacture this drug. Emcure Pharma and Kee Pharma too are marketing G–CSF. The Indian market for G-CSF is modest and is estimated to be in the region of US$ 5.6 million and growing at the rate of 25-30 per cent.

In **Follicle Stimulating Hormone (FSH),** India has only two brands in the recombinant space marketed by LG Chemicals and Serum Institute of

India Ltd. Similar to the G-CSF market, the FSH market is about US$ 4.4-5.6 million, growing at 20 per cent.

In the **Interferon** domain, India has a few brands from both multinationals and local companies. Shantha Biotechnics is the only Indian company that has been manufacturing Interferon alpha. Launched in April 2002, Shanferon is claimed to be the only Interferon Alpha 2b in the world to be cloned and expressed in *Pichia pastoris*, a eukaryotic new generation host, having immense advantages over prokaryotic *E. coli* host. Companies including Zydus Biogen, LG Chemicals, Fulford India (an affiliate of Schering-Plough) and Glenmark Labs are marketing the drug. The present market size for interferon is about US$ 12.2 million and is growing at the rate of 30-40 per cent.

There are also other recombinant products available in the country. The hemophilia patients receive the **Blood Factor VIII** through Hemophilia Federation of India. In **Tissue Plasminogen Activator** and in **Alpha Drotrecogin**, German Remedies and Eli Lilly & Company (India) have their brands. Bharat Biotech has launched Regen D, a recombinant **epidermal growth factor** for diabetic ulcers and for burns and skin grafts.

Diagnostics

With over 50 companies, the Indian diagnostics sector in 2004-05 was estimated at US$ 137 million, accounting for 16.5 per cent of the total biopharmaceutical sector. The diagnostics sector witnessed an almost 48 per cent jump in revenues compared to that in the previous year. The market can be categorised into two major categories-one being reagents and allied business and the other being the instruments business. The figures mentioned above include mostly the kits and reagents and not instrumentation.

Indian diagnostics market largely import driven

In 2004, there were about 25 companies manufacturing diagnostic kits in India. These companies have been manufacturing and selling kits mainly in the areas of pregnancy, ovulation, estimation of T3, T4 & TSH, HIV, HBV and HCV infection, rheumatoid diseases and disorders, cancer (cervix, colon, prostate, lung and mouth etc.), kidney function and liver function. The Indian diagnostics market is still largely import-driven. High import duties, elaborate custom clearance procedures, difficult logistics, slow pace of approvals from statutory authorities and lack of a robust national laboratory network for evaluation and approval of new products are some of the factors slowing down the pace of indigenisation.

Policy push creates high growth expectations

The National Biotechnology Development Strategy Draft makes a reference to "diagnostics for emerging medical paradigm" in the sectoral road map. The strategic actions include establishing a cell for diagnostic biotechnology to encourage and support studies into the clinical application of pharmacogenomics. With the diagnostics sector getting the strategic attention, the industry expects to register close to 30 per cent growth every year for the next few years.

R & D Activity in Biopharma

Active research is going on in genomics, proteomics, pharmacogenomics, stem cell biology, nanobiotechnology and other frontier areas. The product development focus is on new generation vaccines, diagnostic kits and therapeutics.

Considerable headway in medicinal plant research

In the area of isolation and characterisation of new therapeutic agents, about sixty medicinal plants have been screened for anti-cancer, anti-diabetic and immunomodulatory activity using in vitro bioscreens under a multi institutional programme at Anna University, Chennai; NII, New Delhi and Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow. 30 lead molecules including 12 anti-cancer, 3 anti-diabetic and 15 having immunomodulatory properties, have been identified.

Strong biopharma R&D capabilities in academia

Several institutes in the country have the potential for development of commercially viable technologies for production of rDNA therapeutics. These include Institute of Microbial Technology (IMTECH), Chandigarh; Centre for Biochemical Technology (CBT), New Delhi; M. S. University, Baroda; and International Centre for Genetic Engineering and Biotechnology (ICGEB), New Delhi, among several others.

ICGEB, for instance, is working towards development of a malaria vaccine by partnering closely with industry and with funding from the Department of Biotechnology (DBT) and Malaria Vaccine Initiative (MVI). It is also working towards development of a diagnostic kit for Dengue.

Innovation spurs patenting of new discoveries

With India embracing the product-patent regime in January 2005, the sector is seeing a subtle shift from generics to innovation led research. In

keeping with the times, Indian companies have recognised the importance of patenting and commercialising their technologies and products. GangaGen Biotechnologies, a biotechnology company focused on the development of bacteriophage-based products for prevention and treatment of bacterial infections, has received two US patents for its proprietary bacteriophage technologies. ReGenesis, the Assisted Reproduction Facility of Reliance Life Sciences, has recently filed for a worldwide patent for a novel diagnostic test to detect genetic defects. The new diagnostic test is used to detect 'gonadal mosaicism' or low-grade genetic abnormalities of ovaries which are usually not reflected in the blood test.

India is a rising star in stem cell research

In India, there has been increasing activity in the area of stem cell research over the past few years in both the public and the private sector. Stem cell technology is being encouraged in India and there are no fundamental political or faith-based objections to it.

As per the draft guidelines on stem cell research submitted by the Indian Council for Medical Research (ICMR) to the Drug Controller General of India for final approval, human cloning is barred while therapeutic cloning is allowed subject to IRB (Institutional Review Board) clearance. The guidelines recommend setting up of a regulatory apex body for monitoring purposes.

Over 15 institutions in the country are known to be working on stem cell research currently. Most of the work is being carried out in public research institutes, while a few initiatives exist in the private sector. It is estimated that about US$ 4.5 million is being spent annually on stem cell research in India.

Some of the leading Institutions involved in stem cell research in India include LV Prasad Eye Institute, Hyderabad; CMC (Christian Medical College), Vellore; National Centre for Cell Sciences, Pune; National Centre for Biological Sciences, Indian Institute of Science and Manipal Hospital, Bangalore; and Reliance Life Sciences, Mumbai among others.

Embryonic stem cell (human and murine) research is being carried out in a few centres, with focus on the genetics and biology of differentiation signals.

Indian institutions have managed a few breakthroughs in the field of stem cells. Adult stem cells (limbal and conjunctival) have been harvested (autologous or from donor), explant cultured on processed human amniotic membrane to produce a transparent, stitchable corneal epithelium, and used to successfully reconstruct the damaged ocular outer surface of burn victims and restore vision of over 200 patients at the LV Prasad Eye Institute, Hyderabad. This is claimed to be the largest human trial of stem cells anywhere.

Global companies focusing on stem cells are noticing India now. Histostem, a South Korean biotechnology company engaged in researching and developing stem cell lines for therapeutic purposes, has planned to enter into a joint venture with the Maharashtra government to set up an US$ 19.1 million cord-blood and stem cell bank and process centre near Mumbai.

Bio-Services

Bio-Services have emerged as the second largest pie of the Indian biotech sector today, with India acquiring the reputation of a leading destination for clinical trials, contract research and contract manufacturing. In 2004-05, the bio-services sector witnessed a 54.54 per cent growth in revenues over the previous year.

Recent initiatives of leading global players validate Indian bio-services opportunity

The acquisition of Lotus Labs, one of India's leading CROs, by Actavis Group, a European generic drug manufacturer was a significant development. Actavis has expanded its presence in the Indian pharmaceutical market through this acquisition. Another important development was Quintiles Transnational's opening of a data management centre in Bangalore. The company has announced its intention of moving most of its global data management activities to this centre. Quintiles is the second largest bio-services company in India with total revenues of US$ 14.3million.

Several leading global pharmaceutical companies such as GSK, Pfizer and Novartis have scaled up their clinical data management centres in India. GlaxoSmithKline (GSK) is not only launching new vaccines in India but also shifting the clinical research and development of vaccines to India. GSK India has been supporting GSK Biologicals in its vaccine development process through its clinical data management centre in Bangalore for over 10 years. Now, GSK Biologicals is looking at developing India as a global hub for clinical research and development. It had lined up global trials of four vaccines - two vaccines for Rotavirus, one for cervical cancer, and a combination DPT vaccine in India during 2005.

Biocon's subsidiary, Syngene International, which offers early stage drug discovery and development to its global clients, has entered into a contract research agreement with the R&D arm of Novartis, the Novartis Institutes for Biomedical Research Inc. Syngene will conduct research to support new drug discovery and development, primarily in the early stages, involving small molecules in oncology and cardiovascular segments.

Bioinformatics

In 2004-05, the Indian bioinformatics sector registered revenues of US$ 22.2 million, of which about 40 per cent was from the local market and the rest from exports. India's entry into the product patent regime in 2005 has boosted the bioinformatics sector in 2004-05. The sector is expected to grow to a US$ 120 million opportunity by 2006 and is likely to have a major slice of the global bioinformatics pie in the next few years.

At present, there are about 45 companies in this space concentrated mainly in southern cities in like Bangalore, Chennai and Hyderabad. Of these about 35 companies are involved in developing bioinformatics tools and products while the rest are only into marketing of the tools. In addition to Indian companies, multinationals such as Accelrys (a subsidiary of Pharmacopeia), Tripos etc. also have a presence in this sector in India.

Indian bioinformatics players going global with their services

Some Indian bioinformatics enterprises have already been acknowledged in the US and European markets for their cost saving potential. These companies have demonstrated cost savings to the extent of 30-40 per cent in the drug development process. With this, Indian firms are getting product enquiries and business related to data mining, scientific visualisation, information storage, retrieval of special structure data and simulation of long DNA sequences.

AlphaGene Inc. has entered into a collaboration to use bioinformatics technology from Questar Bioinformatics Ltd. to mine AlphaGene's protein library. Questar will provide support for structure determination, pathway identification, and small molecule library development.

Tata Consultancy Services (TCS), a leading Indian technology services company, has entered into an agreement with Congenia, a biotechnology start-up promoted by Italy's Genextra Spa group. The Life Sciences R&D division of TCS will work on "P66", a target protein identified by Congenia as a key protein involved in several age-related diseases and will develop optimised drug leads based on it. TCS will be using modules of its own product "Bio-Suite" to work on the target protein. The optimised lead molecules produced by TCS will be further developed by Congenia through animal trials and eventually human clinical trials.

Strand Life Sciences has entered into a research collaboration with Elan Pharmaceuticals aimed towards supporting Elan's drug discovery efforts. This collaboration allows Elan to access Strand's technologies and achieve customised solutions for internal research programmes. The agreement incorporates access to Strand's extensive in silico technology portfolio including predictive modeling for efficacy and ADMET, custom library

design, QSAR and pharmacophore modeling, structure based drug design, data and visual mining and consulting experience.

India has the potential to assume global leadership in genome analysis. India has several ethnic populations that are valuable in providing information about disease predisposition and susceptibility, which in turn can help in drug discovery. The Institute of Genomics & Integrated Biology (IGIB), New Delhi is in the process of developing a database of genetic profiles among diverse Indian populations in terms of ethnicity, demographics and ancestral roots.

LIMS tools, a big opportunity

With the new IPR regime in place, sponsors are looking at companies in India to outsource their work and this has opened up the market for Laboratory Information Management Systems (LIMS) tools. The market for LIMS products in India is picking up. At present, the market is estimated to be in the range of US$ 13.3-15.6 million and growing at a healthy rate of 30-40 per cent. In India, LabVantge, Ocimum Biosolutions, Persistent Systems and Agaram Industries are some of the leading players offering LIMS products to companies. Multinational biosuppliers such as Thermo Electron Corporation and Perkin-Elmer are also offering LIMS products in India.

Agribiotech

The Agribiotech sector in 2004-05 registered a growth of over 150 per cent with a value of US$ 73.3 million as compared to US$ 28.9 million in 2003-04. Bt Cotton seeds sales accounted for 76.75 per cent of this market, with bio-pesticides, bio-fertilisers etc. accounting for the rest. Total Bt cotton seeds revenues in 2004-05 were US$ 56.3 million, recording a growth of 369 per cent compared to 2003-04. Mahyco-Monsanto, the first company in India permitted to sell Bt cotton, was estimated to have grown by over 208 per cent to end the year at US$ 37 million.

Bt Cotton, a trailblazer success in India

2004-05 was a watershed year for Bt Cotton as the apex regulatory body, the Genetic Engineering Approval Committee (GEAC), approved six new varieties of transgenic cotton in several other Indian states. The total tally of Bt cotton hybrids approved for cultivation has climbed up to 17. The area under Bt-Cotton has increased over 20 times in the last three years soft its commercial cultivation.

With the success of Bt Cotton, the Government has woken up to the enormous potential of such technologies and is keen to put in place policies and regulations which will promote responsible crop biotechnology.

Floodgates open to the transgenic opportunity

Many seed companies in the country are beginning to invest significantly in crop biotechnology. Several of them already have capabilities to leverage Marker Assisted Selection technologies to augment their crop improvement programmes. They are now moving towards crop genetic transformation approaches, either by building the capabilities in-house, or by striking partnerships with other institutions. By 2010, India has the potential to become a major grower of transgenic rice and several genetically engineered vegetables.

In the area of agribiotech research, the Delhi University is pursuing studies on production and characterisation of osmotic stress tolerant transgenic plants of *Brassica juncea*. The Indian Agricultural Research Institute (IARI) and the National Centre for Plant Genome Research (NCPGR) are jointly working on development of molecular marker based linkage map for chickpea. NCPGR has also developed nutritionally enriched potato lines by transfer of Ama1 gene of Amaranthus.

Meanwhile, the University of Delhi, South campus, and IARI have spearheaded the Indian Initiative on Rice Genome Sequencing. The 28-member team contributed to about 10 per cent of the global sequencing effort.

The Indian government has already started a US$ 8 million functional genomics project, which will help to identify/mine the useful genes. This project has created a critical pool of trained scientists, infrastructure and capability to conduct genome wide research on a range of agronomically important crops.

Biofertilisers and Biopesticides coming into focus

The total market for the biopesticides and biofertilisers is estimated at US$ 17.8 million. The biopesticides market is growing at a rate of 25-30 per cent.

Many programmes are currently running to control major weeds and pest diseases of important crops, vegetables, plants and to increase their productivity through various biocontrol agents.

A number of universities and institutes are working in the area of biofertilisers. The University of Hyderabad, National Research Centre for

Plant Biotechnology, IARI; BARC Mumbai and TERI are working on development of transgenic microorganisms with high efficiency for nitrogen fixation, and phosphate solubilisation.

Scientists at the New Delhi based International Centre for Genetic Engineering and Biotechnology (ICGEB) have developed a microbe-based biopesticidal formulation for the control of a range of agricultural pests. The formulation has been found effective in controlling diamond-back moth in cabbage and cauliflower; white woolly aphids in sugarcane; mealy bugs in grapes, citrus and mango; and white ants in teak plantations. The formulation is being commercially launched by its industry partner in 2005.

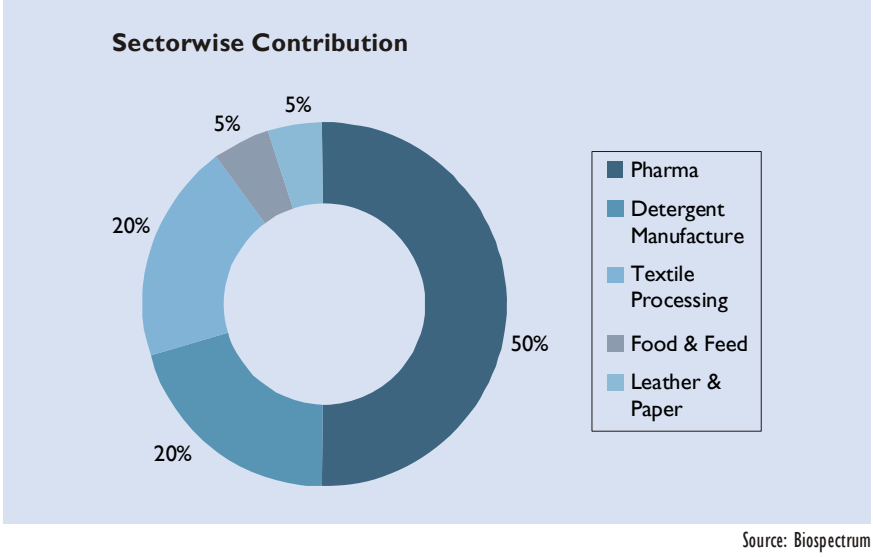
Global cooperation in agribiotech picking up

India and the US have signed a five-year agreement in the area of agribiotech research. The agreement signed is tripartite in nature, wherein the nodal agencies will be the USAID and the Department of Biotechnology (DBT), Government of India. The research will be pursued with support from Cornell University, USA.

Industrial Biotech

The Industrial Biotech sector, which predominantly comprises enzyme companies, was estimated to be worth US$ 71.1 million in 2004-05, registering a 34.45 per cent growth.

The food processing and detergent industries are expected to substantially increase the consumption of enzymes. The government is encouraging establishment of wine parks for processing of grapes for value addition.



Source: Biospectrum

The textile industry is another sector that is consuming large quantities of enzymes.

Global enzyme players take notice of Indian opportunity

Leading global players such as Novozyme, Genencor International, Enzyme Development Corp., Dyadic International and Quest International have a direct or indirect presence in the country. Global enzymes giant, Novozymes, is one of the other major players in the country and the company is estimated to have done a total business of US$ 15.3 million in 2004-05. Genencor, a global leader in the enzyme market and having presence in India since 1996, is planning to enter the Indian market on its own.

Indian players scaling up capacities

Several domestic biotech manufacturers in the enzymes sector are building new facilities. Advanced Biochemicals Ltd, Mumbai which has been manufacturing and exporting cellulase enzyme for the last nine years is setting up a 100 per cent Export Oriented Unit and is planning to invest over US$ 24.4 million at Indore SEZ to manufacture cellulase, alkali protease, amylase, catalase, xylanase, acid and neutral protease enzymes. Similarly, Maps India Ltd, a leading producer of enzymes and microorganisms, has signed an MoU with the Government of Gujarat for investing US$ 2.2 million for production of new enzymes and microorganisms during the current year.

India preparing to become a bio-diesel economy

India imports 70 per cent of its oil requirement. In 2004, India's crude oil import was in excess of US$ 30 billion. About 70 per cent of the total petroleum fuel consumed in India is diesel and 30 per cent is petrol. Even if one-tenths of the oil import is substituted with bio-diesel, it is worth approximately US$ 3 billion a year at 2004 oil prices.

The recent notification of the Bio-diesel Purchase Policy by the Ministry of Petroleum and Natural Gas provides for purchase of bio-diesel by oil marketing companies at a reasonable price with effect from January 1, 2006, at about 20 purchase centres in 12 states. The blending of bio-diesel at a maximum of 5 per cent will be undertaken initially at these 20 centres depending on its availability.

The National Mission Bio-diesel Programme envisages achieving 5 per cent bio-diesel blend in diesel in nine states followed by a pan-India rollout. Later, the bio-diesel blend percentage will be increased to 10 per cent across the country and further towards more than 10 per cent blend in the entire country.

Many states have formed nodal agencies for bio-diesel development and announced draft bio-diesel policies, for example Chhattisgarh, Uttaranchal, Rajasthan, Andhra Pradesh and Tamil Nadu. These states have initiated plantation programmes. For instance, the Uttaranchal Bio-fuel Board has planted Jatropha in over 10,000 hectares in 2005.

In the public sector, bio-diesel pilot plants have been set up at the IITs, IIP (Dehradun), IOC (Faridabad), PAU (Ludhiana), IISc (Bangalore), Railways and CSIR institutes (IICT, CSMCRI) .Trial runs on 5 per cent bio-diesel blend with diesel are being undertaken by Indian Railways, Haryana Roadways (IOCL) and BEST Buses (HPCL).

The role of the private sector in this area is at a relatively nascent stage. Automobile companies such as Daimler-Chrysler and Tata Motors Ltd. (TML) have been conducting trial runs with bio-diesel, in addition to doing R&D on process technology, etc. Daimler-Chrysler has been testing the bio-diesel produced by the Central Salt and Marine Chemical Research Institute (CSMCRI) in Bhavnagar for about a year. DaimlerChrysler is now testing Jatropha biodiesel in two Mercedes-Benz cars and one Viano van in the Himalayan terrain for consistency in results and also to test run the vehicles for more mileage.

Some private companies have taken initiative in planting Jatropha and setting up bio-diesel production facilities. Southern Online BioTechnologies, a Hyderabad-based company is setting up 10,000 tons per year bio-diesel project in Chautupal, Nalgonda district, Andhra Pradesh. The requisite technology support will be provided by Lurgi, Germany. The company is all set to conduct the trial runs in February 2006 and commercialise the biofuel by the first quarter of 2006. This is the first bio-diesel project to get the host country approval from the Ministry of Environment, Government of India. This is the also the first bio-diesel project to get a grant from GTZ, Federal Government of Germany.

The UK-based diesel manufacturing company, D1 Oils, will be investing US$ 2 million in India for setting up a 8,000 ton per annum capacity refinery at Chennai, which is likely to be commissioned by 2007. D1 Oils has formed a joint venture with Mohan Breweries and distilleries and has begun large-scale Jatropha cultivation in Tamil Nadu, Andhra Pradesh and Chattisgarh. The company plans to have five million hectares of land under Jatropha cultivation and to produce 2.7 metric tons of oil per hectare within five years. Earlier, D1 has announced a partnership with Labland Biotech, a Mysore-based plant biotech firm, to produce some 100 million tissue culture-derived Jatropha plants.

Bio-Suppliers

During the last two years, the Indian pharma and biotech companies have focused on increasing their R&D spend and expanding their manufacturing capacities. These developments have spurred the biotech supplies industry in a big way.

There are approximately 120 companies in India that supply technology products to the Indian biotech industry. The life sciences suppliers are supplying over 800 products, ranging from consumables like test tubes, reagents, and pipettes to high-end equipment such as bioreactors, fermentors, HPLC and LCMS.

The total business of the suppliers to the Indian life sciences industry in 2004-05 stood at US$ 273.3 million, up by 39.77 per cent compared to the previous year's figure of US$ 195.6 million. In fact, India has been one of the fastest growing regions for several leading global bio-suppliers. The LSCA business of Agilent Technologies in India is now the fourth-largest country of business in Asia, and one of the fastest growing for Agilent.

Global bio-suppliers scale up in India

The Board of Directors of Alfa Laval (India) Ltd has given its approval to Alfa Laval Holding AB, Sweden, to establish a wholly owned subsidiary in India. Similarly, Cambrex too has firmed up its position in India by combining its different divisions under one umbrella, Cambrex India.

Sartorius AG, the German-based laboratory and process technology major in biotechnology and mechatronics, is planning to make a major capital investment in India towards setting up an integrated production facility as well as an R&D laboratory. The projects in India will be implemented in multiple phases, with an initial investment of US$ 5 million. The company will also look into an expansion of the R&D team in India with more scientists and engineers.

Further, with the suppliers segment finding favour with the government on customs duty reduction, the market is expected to grow further. The Union Budget 2005 has announced reduction of custom duty to 5 per cent on nine specified equipments. These R&D equipments are used extensively in the pharma and biotech sectors.

Policy Initiatives

National Biotech Strategy Guidelines

Salient features of the Draft National Biotech Strategy are as follows:

Fiscal and trade policy initiatives

- Exemption of import duties on key R&D, contract manufacturing/clinical trial equipment and duty credit for R&D consumer goods
- Extending the 150 per cent weighted average tax deduction on R&D expenditure under section 35 (2AB) until 2010 and to permit costs incurred with regard to filing patents outside India for weighted deductions
- Removal of customs duty on raw materials imported into India, where the finished product is imported duty-free.
- Simplification and streamlining of procedures for import, clearance and storage of biologicals, land acquisition, obtaining environmental and pollution control approvals within shorter time lines
- R&D collaboration and generation of joint IP through global partnerships would be fostered.
- Efforts would be strengthened to promote acceptance of Indian regulatory data internationally.

Biotech Parks

- The Department of Biotechnology will promote and support at least 10 biotech parks by 2010.
- The Department of Biotechnology will support creation of incubators in biotech parks promoted by private enterprise or through public-private partnership in the form of grant upto 30 per cent of the total cost or upto 49 per cent in the form of equity.
- Concessions to biotech companies located in biotech parks
- Duty free import of equipment, instruments and consumables.
- Tax holiday under Section 10A/10B of the Income Tax Act
- Biotech companies located in biotech parks to be allowed a five-year time frame to meet the export obligation norms under the SEZ scheme.

Regulatory mechanisms

- A competent single National Biotechnology Regulatory Authority (NBRA) proposed with separate divisions for agriculture products/transgenic crops, pharmaceuticals/drugs and industrial products; and transgenic food/feed and transgenic animal/aqua culture.

Single Window Clearance

- Department of Biotechnology will act to facilitate a single window clearance mechanism for establishing biotechnology plants.

Mashelkar Report on Recombinant Pharma

Having realised the potential of the biopharmaceutical sector, a Task Force was set up in 2004 under Dr. R A Mashelkar, Director-General, Council of Scientific and Industrial Research (CSIR), to formulate a modern and efficient regulatory regime for recombinant DNA pharma products.

The report of the Mashelkar Task Force on Recombinant Pharma has been submitted to the Ministry of Environment and Forests (MoEF) for action.

Officials at the Ministry of Environment and Forests expect most of its recommendations to be implemented in the coming months and the industry could start getting the benefits of the Mashelkar recommendations from January 2006.

Salient points of the tabled report include:

- Task force takes 90 per cent of LMOs (Living Modified Organisms) out of GEAC purview
- National Biotech Regulatory Authority (NBRA), as unified regulatory body, suggested
- Timelines set for regulatory approvals
- DBT to play major role in biotech regulation

The Patent Act (Third Amendment), 2005

India amended its Patent Act in 2005 to usher in a new product patent regime. Provisions in the amended Act which relate specifically to biotechnology include:

- Plants and animals, seeds, including essentially biological processes used for propagating plants and animals are not patentable. The area of patentability in relation to microorganisms is not clear. Going by the US and European precedents, it would appear that only such microorganisms that are the result of human intervention would be patentable.
- Synthetic genes (as distinct from naturally occurring gene segments) too would now be the subject matter of patentability.
- Genetic inventions will include SNP (single nucleotide polymorphism), vectors, recombinant products such as vaccines, enzymes, hormones, etc.

- In order to get a patent, the Act requires the deposit of biological material with the International Depository Authority (IDA). IMT, Chandigarh, is the IDA in India for some of biological materials such as bacteria and plasmids.

Bioinformatics Policy of India (BPI–2004)

The Department of Biotechnology, Government of India, has identified bioinformatics as an area of high priority during the Tenth Plan period to ensure that this sector attains levels demanded in the international arena. The BPI has its focus on resource building in bioinformatics using the infrastructure already available and to ensure venture capital funding for public-private partnership in bioinformatics. The objective of the policy is to create a sustainable niche for India in bioinformatics by the end of 10th Plan period.

Policy focus on Stem Cell research

Stem cell research is coming into strong focus from a policy point of view. Indian scientists have mooted the setting up of a "national stem cell priority fund" to finance research on stem cells and enhance manpower in the area. The National Task Force on Stem Cell Research has proposed to utilise funds from the Indian Council of Medical Research, Department of Biotechnology and other agencies, including the Defence Research and Development Organisation and the Department of Science and Technology for the priority fund. The Task Force is mooting stem cell "city clusters" that would link all publicly and privately funded research groups in a city, enabling them to share facilities, ideas and opportunities. The Department of Biotechnology is also in the process of finalising a road map for stem cell research.

States leading from the front in bio-policy and infrastructure support

In recent years, several Indian states have come to the forefront to create a conducive environment to attract biotech investments and leverage the vast talent pool and rich biodiversities in their states.

Karnataka was the first state in the country to announce a "millennium" biotechnology policy as early as 2001 to promote the nascent biotech sector. Maharashtra, Tamil Nadu, Himachal Pradesh and Andhra Pradesh followed it with their own biotechnology policies during the year. Later other states like Haryana (2002), Punjab, Kerala, Madhya Pradesh (2003), Uttar Pradesh, Rajasthan (2004) and Gujarat (2005) joined the ranks by announcing their respective state policies.

These policy announcements have provided a major thrust to the development and promotion of biotechnology infrastructure in these states. One of the salient features of these biotech policies is setting up of dedicated biotech parks. The state governments are supporting the industry players setting up their units at the parks by offering incubation facilities, tax holidays, incentive packages, venture funding support and other forms of facilitation.

Four states viz. Andhra Pradesh, Tamil Nadu, Maharashtra and Kerala have taken the lead to develop biotechnology through a concerted and cohesive approach, setting up dedicated parks. Today, there are over five biotech parks in the country which are operational and most of these are in the above-mentioned states.

About 11 other states are either in the process of developing or have announced their intention to develop biotech parks. These include: Karnataka, Gujarat, Haryana, Himachal Pradesh, Madhya Pradesh, Punjab, Rajasthan, Uttar Pradesh Uttaranchal, Orissa and West Bengal.

Several states have planned more than one biotech park. Kerala is considering setting up two parks. Tamil Nadu and Andhra Pradesh are setting up marine biotech parks besides biotech parks at Chennai and Hyderabad respectively. With already one park in Pune, Maharashtra has decided to have another park for agriculture at Aurangabad, the seed capital of India. The Central and State governments are keen to replicate the success of IT in biotechnology. As a result, India is expected to have a total of 23 biotech parks in the next few years.

CONTACT FOR INFORMATION

Information on the market and opportunities for investment in the biotechnology sector in India can be obtained from the Confederation of Indian Industry (CII), which works with the objective of creating a symbiotic interface between industry, government and domestic and international investors.

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