ADVANCES IN Biopharmaceutical Technology in *India*

Eric S. Langer, Editor

Society for Industrial Microbiology
BioPlan Associates, Inc.

Advances in Biopharmaceutical Technology in India

January 2008

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Cover photos courtesy of Shantha Biotech

ISBN 978-1-934106-07-5

Acknowledgment

This project would not have been possible without the exceptional efforts of the many people involved. In particular, we would like to thank:

Yibing (Eliza) Zhou, Project Director, Enterprise
John Morrow, Project Director, Scientific
ES Illustration and Design, Inc., Production Manager, cover graphics.

We would also especially like to thank our reviewers, whose expertise ensured this volume addressed today's most important issues:

Prof. P.S. Biesen, Director, Madhav Institute of Technology and Science, India
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Dr. Scott Wheelwright, President, Strategic Manufacturing Worldwide, Inc., USA

We also extend our sincere appreciation to Shantha Biotech, and Ms. Sravanthi Reddy for her support and use of cover photos and graphics.

Thank you for your efforts, and your recognition of the importance of this study.

Eric S. Langer
Managing Editor

Preface

This study was undertaken, managed and coordinated by BioPlan Associates, Inc., a biopharmaceutical management and marketing research consulting firm in Rockville, MD, based on nearly 20 years experience and knowledge of the market segment. BioPlan surveyed the industry to identify required content, and then selected subject matter experts to author relevant chapters to this study.

The Society for Industrial Microbiology (SIM), in recognizing the importance of applied sciences in biotechnology processes, has lent its name to this endeavor. The Society for Industrial Microbiology is a nonprofit professional association dedicated to the advancement of microbiological sciences, especially as they apply to industrial products, biotechnology, materials, and processes. Founded in 1949, SIM promotes the exchange of scientific information through its meetings and publications, and serves as liaison among the specialized fields of microbiology. Membership in the Society is extended to all scientists in the general field of microbiology.

India is one of the fastest growing economies in the world. The country has invested heavily in advancing its pharmaceutical and biopharmaceutical technologies to improve its healthcare systems, its population's general health, and its overall economy.

Both scientists and entrepreneurs in India have made important contributions to advancing the field at many levels. This study provides a framework from which both those new to India's rapid advancements in biotherapeutics and vaccines, and those with long histories can recognize the potential, and plan for the future. The findings of this study support worldwide public health and economic policy.

Each chapter provides unbiased, peer-reviewed perspectives of the current state of the science and technology associated with biopharmaceuticals in India. While no single work can encompass all the advances being made in the field, this study offers a comprehensive assessment of the technological and economic advancements in India.

The intended audiences include decision-makers at biopharmaceutical research organizations, biotherapeutic manufacturers, contract manufacturing organizations, suppliers to the industry, policy-makers, and international entities evaluating this market. We plan to keep this study current by providing regular updates as technologies, and the industry advance.

Advances in Biopharmaceutical Technology in India

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Prasanta K. Ghosh, PhD, FIE, C. Chem, FRSC, received his Master of Technology in chemical engineering and a Ph.D., University of Calcutta, and has worked in various government departments since the late 1960s. Actively involved in policy-making for the production & pricing of drugs and pharmaceuticals, he also developed biotech policies relating to industrial development, IPR protection in publicly-funded institutions, technology transfer and policies relating to use of genetically-modified organisms. With hands-on experience in the production of antibiotics, sera and vaccines respectively, fermentation, handling of blood & blood products and separation of biomolecules using various separation techniques, his primary research interest is in the production of hydrophilic polymeric nanoparticles made up of synthetic as well as natural polymers. He heads the biotech division for Cadila Pharmaceuticals Ltd., Ahmedabad, India, and has more than 80 publications to his credit, including several U.S. Patents.

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ABSTRACT

Throughout its history, the Indian government has created policies to help enable the manufacturing of conventional and modern biotech products at affordable prices. Presently, private companies in India dominate the biomanufacturing sector, while new and existing institutes are being created and funded by the government. To educate and train future workers, biotech courses are being offered at graduate, postgraduate, and Ph.D. levels; private institutions are also supporting these efforts. The Indian government is working to create an alliance between private industry and research institutes. With the help of local governments, biotech parks are being created to assist small and medium level enterprises with startup funds. With private companies investing little for research and development, alliances between private industry and institutes for basic research has been small, even with help from the Indian government. However, in the next decade, with collaboration from the Indian government and private companies, there should be a significant increase in the development of conventional biotech industry, and modern biotech drugs may be produced once Intellectual Property Rights (IPR) expire.

Prospects for Modern Biotechnology in India

Introduction

Biotechnology applies to organisms, or parts thereof, and the techniques to produce, identify or design substances, or to modify organisms for specific applications. Modern biotechnology consists of: recombinant DNA technology, hybridomas production, cell fusion techniques, protein and carbohydrate engineering, along with structure based molecular design. Modern biotechnology has advanced significantly in the past decade with the use of computer-aided informatics, aided by the use of structural and functional genomics with proteomics.

Conventional biotechnology includes: fermentation processes and the conversion of substrates into desired products by biological processes; downstream processing for recovery of metabolites; use of microbes or enzymes for producing value-added products; sera, vaccines and diagnostics produced by conventional methods; reproduction, artificial insemination and embryo transfer technology for animal breeding; methods for fish spawning induction; plant cell or tissue culture; plant breeding for producing better seeds or plants cultivars; bio-fertilizers; bio-pesticides; plant growth stimulants; extraction and isolation of active principles from plants or animals or parts thereof; bio-diesel production from natural vegetable oil obtained from diverse sources; ethanol and/or biogas production from agricultural and forest based wastes; treatment of solid or liquid wastes rich in organic matter by microbes; or specialty plants to minimize the polluting load; and rehabilitation of degraded land by growing plants utilizing the knowledge of symbiotic association of microbes with such plants etc.[1,2]

India's Independence as Catalyst for Change

The Indian government is currently working towards developing a sound biotech base to help minimize foreign dependence, especially in high-tech areas. After India's independence in 1947, the country attempted to procure the basic technologies for the production of several lifesaving drugs such as antibiotics, sulfonamides, antimalarial drugs, antidiarrhoeal drugs, antituburcular drugs, antileprotic drugs, analgesics, antipyretics, vitamins and others; however they were unattainable due to high costs. India contended with the belief from other developed nations that it was not yet adequately developed enough to set up infrastructures to manufacture basic chemicals or bulk drugs (active pharmaceutical ingredients.) Due to a legal stipulation that existed at the time, India was denied the right to produce tetracyclines on the pretext of exclusive products patent rights. One particular Indian company that developed a novel method for the production of an antidiabetic drug was prevented by the Indian courts from producing the drug because a transnational company owned the Intellectual Property Rights (IPR) India had many problems, including poor healthcare for its citizens, high infant mortality rates, prevalence of several infectious such as microbial and diarrhea-related diseases, malnutrition, tuberculosis, malaria etc., which caused many deaths, and allopathic medicines were too expensive for the mainstream public.

In order for the Indian government to afford the basic starting materials for the pharma industries, production increased in petrochemical industry during the 1960s and 1970s.

In the early 1950s, Indian politicians, under the leadership of Pandit Jawaharlal Nehru, then Prime Minister of India, obtained assistance from international help organizations including UNICEF in order to obtain a strain of penicillin, which was then used to start a national pharmaceutical company named Hindustan Antibiotics Ltd. (Pune). This undertaking also included a state-of the art R&D unit. Later, in the early 1960s, with a supply of technological knowledge given to India from the former U.S.S.R., several public companies, subsidiaries Indian Drugs and Pharmaceuticals Ltd., were built and supplied with strong R&D units. In order for the Indian government to afford the basic starting materials for the pharma industries, production increased in petrochemical industry during the 1960s and 1970s. Also during this time, the private pharmaceutical industry in India increased its production towards self-sufficiency. In the agriculture sector, dwarf, disease-resistant plant cultivars and seeds were imported and crossed with the local cultivars to generate hybrids and self-pollinated varieties that revolutionized productivities of rice, wheat and several cereals in the 1970s. The private Indian sector also made significant contributions in these efforts. Several international institutions provided enormous assistance in these developmental efforts. The Indian government soon realized that efforts by companies in the country, piloted by the government, could help elevate India to great economic heights. In turn, the Indian government modified its policies to help steer the country towards prosperity.

In the late 1980s, the Indian government realized it placed too many restrictions on the creation of monopolies of private ownership of wealth, thereby restricting wealth accumulation and wealth control. This was done as a move towards equitable distribution of wealth among the people of India to help bridge the divide between the poor and the rich people, as a means to help poorer citizens with education and acquisition of work skills. However, with very few people in the country considered wealthy, limitations were placed on creating efficient public infrastructure and public goods. To rationalize the restriction of accumulating wealth by its citizens, Indian government enforced the following policies during the late 1960s through the late 1970s:[3]

a. Central planning to divert resources as per the visions of the Central government.
b. Pronouncement of Industrial policy to boost the Public Sector.
c. Sertorial Reservation Policy in Pharmaceutical industry: to attract foreign investment only in high tech areas in specific sectors of bulk drug production; to allow Indian private sector units to invest in high tech as well as in comparatively low tech areas provided production of bulk drugs was from the basic stage; and to create investments in capital intensive plants in Public sector units only, as investment from private sector units was not forthcoming in these areas.
d. Setting up of highly capital-intensive Public Sector Undertakings in all areas for building and strengthening basic infrastructure.
e. Nationalization of major Private Banks and Insurance Companies to enable mobilization of funds for national development
f. Creation and strengthening of National Institutes, Centers of Excellence, Agricultural institutes, national science &technology teaching institutes like IITs, Regional Engineering colleges, Biotechnological institutes, Universities etc.
g. Regulating the structured growth of Private Sector Industries (including private Indian and foreign Companies) by introducing:
    - Monopolies and Restrictive Trade Practices Act
    - Foreign Exchange Regulation Act
    - The introduction of a revised Indian Patents Act 1970 to abolish Product patents in certain vital economic sectors like drugs and chemicals, and non-patentability clauses in areas of agriculture
    - Introduction of Price Control in Drugs Pharmaceuticals sectors as also in other vital sectors like cereals, fertilizers etc.
    - Control and distribution of essential commodities including food grains
    - Concessions and fiscal supports to the medium and small scale industrial sectors so that they develop faster and create more goods & services, besides creating many jobs.

These conservative policies enabled the spreading of wealth among Indian citizens, and consequently enabled the rise in population of middle class Indians, and increased their personal wealth. Several small and medium scale

industries were created and a large number of products and services became affordable. By 1980, India grew to be a leader among developing countries by supplying most of the essential drugs to its citizens at much cheaper prices. At the first meeting of the United Nations Industrial Development Organization (UNIDO), Lisbon, Portugal in December 1980, India was applauded for its unprecedented success .

India's policies provided assistance for the development of the Indian economy during its initial period. However, like any other policy, many of them had several shortcomings that were not so visible at the inception; they started showing up later. While India worked towards autonomy in the food and pharmaceutical sectors, new developments in the world began to appear, especially in the pharmaceutical sector. In the early 1980s, companies in other countries began production on several highly effective bioactive therapeutic substances, which were unavailable to India. They first entered India at exorbitant prices. Recombinant human insulin, somatotropin, Hepatitis B vaccine, etc. were the first such products that entered the world market in the 1980s,, along with several conventionally-manufactured fermentation–based products. The fluoroquinolones produced by synthetic methods, captured a sizable portion of the antibacterial market once serviced by antibiotics produced by fermentation, causing loss of growth of fermentation-based antibiotic industries. The new fermentation-based statins reduced the incidence of cardio-vascular diseases resulting from the presence of high lipids and triglycerides in persons who were already ill or others that were at risk. Several other synthetic pharmaceutical products entered into the market that could treat many life-style related diseases more efficiently, and India needed the skills and resources to develop them. The gap once substantially bridged, grew wider with time.

India's policies provided assistance for the development of the Indian economy during its initial period.

Even with the emphasis on R&D in India since its Independence in 1947, and with the help of several policy incentives already in place for conducting research, the emphasis in basic research at the work place was rather lacking; efforts were more directed towards developing alternate processes that were often of less innovative nature. Moreover, the insistence on price controls and the introduction of a dual-pricing system for active pharmaceutical substances took away from incentives for improving efficiency. The profit margins shrunk substantially and there wasn't enough money left for allocation for developmental or even basic research. Efforts by certain transnational companies, started in the 1970s and 1980s, were denied and gradually these companies closed down their basic research facilities throughout the country.. Failing to see the importance of these changes, India was slow in modifying its industrial and trade-related policies in order to remain competent in the international arena.

Strong reliance on public sector initiatives, especially in the late 1960s, 1970s and beyond, however, increased almost insurmountable inefficiencies in R&D operations. Products became more expensive than before. Private sector companies took advantage of this situation. The net effect was that the once

cherished Indian pharmaceutical industry started showing symptoms of weakening. Wherever there were avenues for imports, the Indian producers of pharmaceuticals procured cheaper imports through others that were non-producers. By late 1980s and early 1990s, it became evident that the policies needed to be revised. The World Trade Organization (WTO) policies were in effect at this time, and India became a member of the Treaty in April 1994. In the meantime, the liberalization policy was announced[4] in July 1991 by the Indian government allowing global trade, which would gradually provide equal opportunities for all businesses and sectors involved in the country's economic development.

India has always believed that all of its society should receive equal opportunities in order to allow the poorer class to reap the economic benefits along with the rich. Therefore, from the late 1940s up to the late 1980s, policies created by the government placed major emphasis on creating initiatives that have worked towards an equal distribution of wealth. Entrepreneurs create wealth by deploying capital, labour and technology. Wealth created by entrepreneurs' remains with them if adequate interventions are not exercised by the political system and by governments. India's policies enable it to improve its economy considerably; however, the impact was perceived as too small for a long time. The reasoning behind this perception, by some, included a rise in corruption, the assumption that creation of industries with manufacturing capacities were dispersed regionally without attention to economy of scale, limited scope of further expansion of manufacturing capacities, price protection of commodities to enable industries to recover "cost plus" margins for the goods and services produced by them from a non-competitive market place, and that any additional initiatives favorable for the public or local-industry to promote economic welfare wouldn't be able to last beyond the 1980s. These perceptions in turn caused reserves of foreign exchange to lower and nearly created insolvency in the economy resulting primarily in inefficiencies from productivity in most of the industries but particularly in the public sector undertakings. Consequently, to correct the situation, the Central Government modified the previous developmental policies from early 1990s. The licensing policy was enormously liberalized through the enactment of simpler policies successively over the years through policies by the Foreign Investment Promotion Board of the Union Ministry of Industry in order to attract large foreign investments. The present promotional policy[5] of the Indian Government for the development of industries in all sectors, including the biotech sector, can be summarized as follows:

India's policies enable it to improve its economy considerably; however, the impact was perceived as too small for a long time.

- Industrial licensing policy has been liberalized for accommodating automatic registration.
- 100% foreign equity investment is possible in all sectors
- Fast Track Clearance route created for Foreign Direct Investment
- Rationalizing of customs duties, central excise duties, special excise duties and value added tax

- Central Government playing proactive role in creating conditions for easing open field experiments with genetically modified organisms including plants to enable industry/entrepreneurs to take products from lab to the market faster
- Creation of level playing field for all sectors of entrepreneurship: public sector, private sector or foreign entrepreneurs
- Government investment to date is approximately Rs 28 billion (US$650 million) in biotechnology for developing skilled manpower, creating R&D infrastructure and providing extramural R&D support to publicly funded institutions.
- Full rebate on R&D expenditure from expenses, and more than 100% if research is contracted in publicly funded R & D institutions
- Over 50 R&D labs in public sector are in place and over 20 are conducting research in frontier areas of biotechnology: these facilities can also be used for joint entrepreneur/industry research;
- Joint R&D projects are promoted with special fiscal benefits
- Special funds have been created for industries and small entrepreneurs for research conducted in specific areas of biotechnology, either as grants or with very low interest rates.

The tools utilized by the government include infrastructure development, funding of research, human resource development, creation of industry-development policies, networking, promotion of public goods, related activities like biotech parks, creation of various regulations to ease industry development including intellectual property rights, plant variety protection, use of genetic biodiversity for research and applications, bio-safety measures emanating from use of genetically modified substances and products, fiscal incentives, trade regulations, investment facilitation and others.

Indian foresight by the government dates back to 1982 when a small division was created in the Department of Science and Technology of the Central Ministry of Science and Technology.

Indian foresight by the government dates back to 1982 when a small division was created in the Department of Science and Technology of the Central Ministry of Science and Technology. In February, 1986, a full fledged Department of Biotechnology was created that could independently pilot multifaceted development in biotechnology in the country. The mandate[6] of this department as approved by the Indian Parliament is summarized below:

- To promote large-scale use of biotechnology
- To support R&D and manufacturing in biology
- To promote and to take responsibility for autonomous institutions
- To promote university and industry interaction
- To identify and set up Centers of Excellence for R&D
- To develop an integrated programme for human resource development
- To serve as a focal point for specific international collaboration in biotechnology
- To establish infrastructure facilities to support R&D and Production
- To develop biosafety guidelines for recombinant DNA products and

substances and to be the responsible agency in all policy matters relating to import, export and use of such products for research use
- To evolve guidelines for manufacture and applications of recombinant DNA products, including cell-based vaccines
- To serve as the focal point for the collection and dissemination of information relating to biotechnology

The Central Government provided major allocation of funds through several of its major departments, with emphasis on the Department of Biotechnology. The Table below summarizes annual allocations[7] over a decade, comparing them in 1990-91 and 2000-01 (Table 1):

Table 1: Allocation of funds by different funding agencies for promoting biotechnology in India.

Unit: million Rupees

Funding Agencies	1990-1991		2000-2001		% Growth over 10 years	
	Tot.	Biotech	Tot.	Biotech	Tot.	Biotech
Department of Biotechnology (DBT)	655	655	1391	1391	212	212
Council of Scientific and Industrial Research (CSIR)	2351	24	9120	182	388	758
Department of Science and Technology (DST)	2589	26	7798	234	301	900
Department of Scientific and Industrial Research (DSIR)	131	1	584	6	446	600
Indian Council of Agriculture Research (ICAR)	3236	3	13990	280	432	9333
Indian Council of Medical Research (ICMR)	396	15	1470	15	371	100
University Grants Commission (UGC)	3495	35	14070	704	403	2011
TOTAL	**12853**	**759**	**48423**	**2812**		

As seen in Table 1, the DBT remained the leading department used by government to promote biotechnology; several other scientific departments also started taking more interest with time in developing this area. However, the majority of money allocated by major departments like ICAR for agricultural research in biotechnology, ICMR for medical research in biotechnology and other departments like Ministry of Human Resource Development, University Grants Commission (UGC), All India Council for Technical Education (AICTE), etc for engineering research in biotechnology was lower. Up to the present time, this trend continues and DBT remains the main funding organ of biotechnology development in the country. The combined expenditure in biotechnology from all the funding agencies of the government up to the end of 2006 is approximately Rs. 28000 million (US $650 million).

Indian Commitments to Globalization in all Aspects of Biotechnology

India is a signatory to the WTO: the objectives of WTO are:[8] (Figure 1)

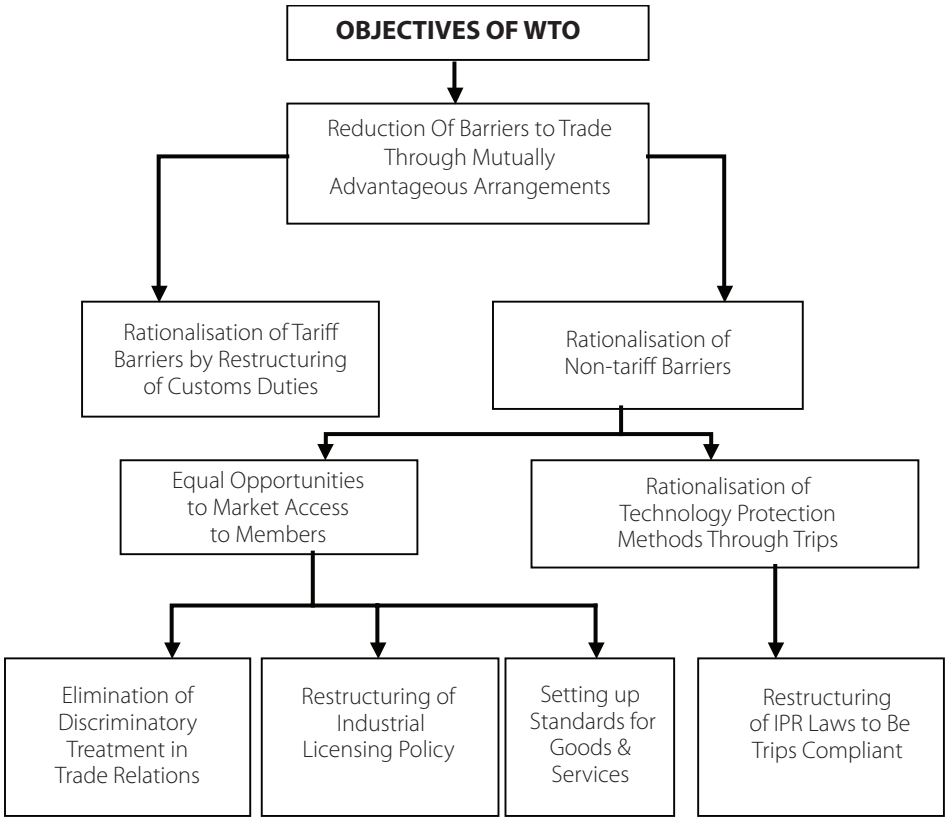

Figure 1: Flow sheet depicting the objectives of WTO.

The Indian government has taken steps to fulfill the objectives of WTO. Steps have been taken commensurate with maintenance of a rationale that does not create an imbalance in the core competence of the country. No actions have been initiated that create a virtual collapse in any industrial sector. Among the objectives of WTO, changes in the Indian IPR laws are considered as the most crucial and this aspect is still under watch by several countries the world over. The main controversies between the WTO-and the Indian IPR are summarized below:

a. Data protection provision for efficacy trial of drugs not built-in
b. Micro-organisms are not defined
c. Plant variety protection provisions not precise; farmers' interests take predominance
d. Animals of any kind are not protected by IPR

e. Mere discovery of a new property of any known substance is not patentable.
f. Ethical issues could be interpreted based on societal customs that have no bearing on IPR issues
g. Discovery of natural products are not patentable
h. Biological diversity (genetic) cannot be used for inventions without prior consent

None of the above factors require inclusion in the IPR acts and rules as per the provisions contained in the WTO document. However, some countries and companies find the absence of these provisions in the revised Indian Patents Act to be obstructions to innovation and free trade. The Trade-Related Aspects of Intellectual Property Rights (TRIPS) of the WTO seeks from member countries assurances on compliance of certain minimum provisions; it does not advocate creating a model IPR law because of infeasibility with regard to economic situations prevailing in different countries. It remains to be seen how the TRIPS compliant Indian Patents Act will fare in the global context.

Some salient features of the TRIPS compliant Indian Patents Act:.

a. Definition of inventive step in the Patents (Amendment) Act 2005 was changed to incorporate a new section, which is section 2(1)(ja). This section reads as under:
b. *"A feature of an invention that involves technical advances as compared to the existing knowledge or having economic significance or both and that make the invention not obvious to a person skilled in the art.*"
c. The definition of Patent was changed to mean "*a patent for any invention granted under this Ac*t."
d. Sec. 3 of the Indian Patents Act 1970 was amended to include Section 3 (j) which reads:
   "*Plants and animals in whole or any part thereof other than micro-organisms but including seeds, varieties and species and essentially biological process for production or propagation of plants and animals"* (June 25, 2002 Amendment) (cannot be patented).

Sec 3(d) of the amended Patents Act defines what is non-patentable:

i) the mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance.
ii) the mere discovery of any new property or new use for a known substance.
iii) the mere use of a known process, machine or apparatus – unless such process results in a new product or employs at least one new reactant.

The provisions in the amended Sec 3(d) would prevent the "ever-greening" effects of continuing product-patenting rights by the first inventors, allowing continued protection of IPR rights with regard to new uses or new useful properties.

e. Sec 92 A (1) of the new Patents Act has expanded the scope of compulsory licensing grounds

f. India signed the Paris convention and became a party to the Budapest Treaty before December 31, 2004.

All the above amendments and actions are TRIPS compliant. The above amendments were introduced on strong grounds of consideration of such factors as: concerns for food security, livelihood security and the availability of modern life-saving Biotech Medicines to the masses. The main reasons for concerns were India's lack of adequate resources, lack of adequate scientific and technological skills, inadequate incentives for R&D and inadequate for creating expensive R&D infrastructure.

The TRIPS of WTO requires member countries to comply with other aspects of IPR in the areas of protection of plant varieties, protection of undisclosed information, trademarks and geographical indications, all the areas of which have bearings in biotechnology. A Plant variety is a genotype within genera and within a species. It is developed by a breeding process. It can also be developed by genetic engineering. All germplasms in a country are owned by the country if they are not yet owned by any individual or organization under the law. A public or a private entity under the Plant Variety Protection Act (PVPA) can own a plant variety. In order to own a variety for a limited period, the inventor / breeder has to prove that the variety is Distinct (New), Uniform (with regard to features of its vegetative propagation or sexual reproduction) and the variety is Stable in its essential characteristics.

The Indian Plant Variety Protection Act, enacted to comply with the provisions of the TRIPS of WTO allows farmers to grow and retain the cultivated propagules including seeds, under farmers' rights.

The Indian Plant Variety Protection Act, enacted to comply with the provisions of the TRIPS of WTO allows farmers to grow and retain the cultivated propagules including seeds, under farmers' rights. All protected plant varieties in India must be registered with the authority. Trademarks are signs or combination of signs that are capable of distinguishing goods and services of one undertaking from others. Such distinguishing features constitute protectable subject matter under the TRIPS of WTO, which also stipulates that compulsory licensing of Trademarks is not allowed. Indian laws on Trademarks were accordingly modified and notified on 30.12.1999; the revised law is fully compliant with TRIPS. Geographical indications refer to obligations of member countries to provide legal means for interested parties to prevent the use of certain marks for commercial gain to mislead buyers for goods being purchased by them by designating or presenting such goods that suggest that the goods had originated from a geographical area, while actually the goods originated elsewhere. A new law for protection of geographical indications was enacted by India on 30.12.1999 and the Rules promulgated on 8.3.2002 in order to be TRIPS compliant.

As a signatory to the Convention on Biological Diversity (CBD), India is committed to protecting its genetic biodiversity and concurrently it would have to consent to enabling access to people or parties to its genetic biodiversity. The objectives of CBD are stated in a flow diagram[9] (Figure 2). As a signatory country to CBD, India has enacted its Biodiversity Law and has consti-

tuted its designated Authority for accessing Indian Genetic Biodiversity by the CBD member countries. More regulatory dictums within the framework of international commitments of India to WTO and CBD are imminent. These include the creation of the Plant Quarantine Authority of India and some such laws, all of which may cut across the interests of the biotech industries. The enacted procedures are to be user friendly so as to enable access to genetic biodiversity faster by all applicants in order to promote and cut down the time of innovation.

The future holds many opportunities for the entrepreneurs on how the laws and rules will be framed and how society would benefit from these in their quest for information about biodiversity.

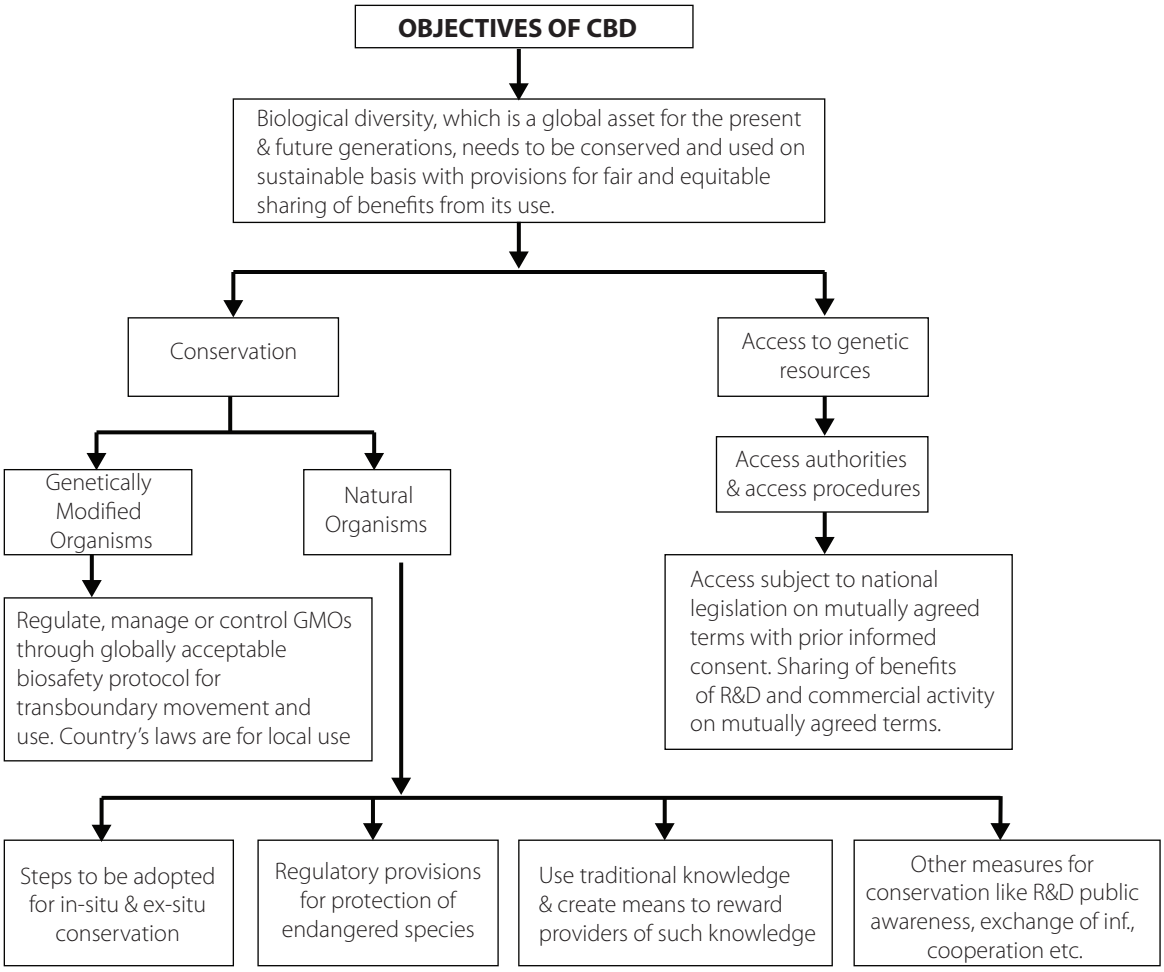

Figure 2: Flow diagram depicting objectives of Convention on Genetic Biodiversity (CBD).

Indian Regulations for Genetically-Modified Organisms and Substances

Use of all genetically modified (GM) substances is regulated under the Environment (Protection) Act, 1986 and Rules, 1989. Guidelines have been issued over time to ease the application process. Genetically modified organisms (GMOs) can be living as in the case of micro-organisms, plants and animals (GM edible yeast or lactobacillus or a host of agricultural produces such GM corn, potato, tomato, soybean, wheat, rice, mustard/rape seed, etc.) as well as substances derived from GMOs that are non-living like inactivated GMOs, or substances derived from GMOs such as proteins, nucleic acids, carbohydrates, lipids. Rules require that all GMOs and products thereof are introduced only after they are found to be environmentally safe as well as safe for use by human and animals. The clearance of GMOs is accorded under Rule 7-10 of the Environment (Protection) Act, 1989, which reads as "Rules for Manufacture, Use, Import, Export and storage of hazardous micro organisms/Genetically Engineered Organisms or Cells" and notified under the Environment (Protection) Act, 1986. All clearances are conditional and are for a limited period; renewal is required after the period is over. The law is based on precautionary principle. Fig. 5 shows the regulatory structure[10] and the applicable rules while handling different kinds of genetically modified substances.

The Cartagena Protocol is consistent with the Indian Rules on GMOs; Indian Rules also cover products produced from GMOs and is thus wider in its scope.

India is also a signatory to the Treaty on Cartagena Protocol which regulates the trans-boundary movement of genetically modified organisms. The Cartagena Protocol is consistent with the Indian Rules on GMOs; Indian Rules also cover products produced from GMOs and is thus wider in its scope.

Indian Scientific & Technological Institutes of the Government to Promote Biotechnology

The government created a large number of Institutes and Centers of Excellence with adequate regional balance to promote both basic and applied research in biotechnology in the country. The major ones are listed in Table 2.

As seen in Table 2, the government is funding a large number of institutions. The emphasis on R&D projects in these institutions varies considerably. Consequently, concerted efforts do not seem to be in place to develop products and services with a view to take them from laboratory to the market sooner. Moreover, the R&D efforts are built around expertise of individuals and are not synchronized with the needs of the common man and the market. A nationally coordinated committee or an autonomous institution studying, advising and monitoring the efforts at various institutions to reach a common goal within a time-frame may bring better results of applications.' However

creating such a body is not easy because of diverse interests and social compulsions. There is presently no such centralized coordination among the different government departments.

Table 2: Major Indian Institutions Involved in Biotechnology Research.[11]

Institutions	Main Area of Research
DBT funded institutions	
National Institute Of Immunology, New Delhi	To undertake research in basic and applied immunology & to develop new vaccines and diagnostics. To serve as a National Reference Centre for immunology.
Centre For DNA Fingerprinting And Diagnostics (CDFD), Hyderabad	DNA fingerprinting, diagnostics, genome analysis and bioinformatics form the major service components. Basic research in the above areas of modern biology is an integral component of this institute.
National Centre for Cell Sciences, Pune	Repository for different cell lines including mammalian cell lines. Basic research in the area of cryopreservation technology for bone marrow, development of bio-equivalent skin for transplantation in burns and vitiligo cases, development of cell cultures from commercially important invertebrates and vertebrates etc.
National Brain Research Centre (NBRC), Gurgaon	Neuroscience research and networking of the existing groups and creating satellite units to catalyze the overall growth of neurosciences.
National Centre For Plant Genome Research (NCPGR), JNU, New Delhi	Application of genomics to study the crop species including chickpea genomics & development of transgenic plants including protein rich potato.
Institute of Life Sciences, Bhuvaneswar	To conduct basic and applied research in frontier areas of Life Science & to provide training to M.Sc. students leading to M.phil and Ph.D degrees.
Institute of Bioresources and Sustainable Development (IBSD), Imphal, Manipur	Management of bioresources in the Indo-Burma Biodiversity Hotspots.
CSIR funded institutions	
Institute of Genomic and Integrative Biology (IGIB), New Delhi	Allergy, immunology and human genomic research including nucleic acid research.
Indian Institute of Chemical Biology (IICB)	Basic and Applied Research in cell biology, physiology, molecular & human genetics, structural biology, bioinformatics and diagnostics.
Central Drug Research Institute (CDRI)	Design and development of biotech drugs, diagnostics & vaccines besides synthetic drugs.
National Chemical Laboratory (NCL)	Besides basic work in chemicals and rheology of plastics, plant tissue culture, enzyme production, membrane separation etc in biotechnology.
Institute of Microbial Technology (IMTECH)	Microbial products including thrombolytic agents, growth factors, antibody based diagnostics, site specific drug delivery systems for tropical diseases, development of endocrine disorders model system and gene targeting. Bioinformatics is also a strong area of research.
Centre for Cellular and Molecular Biology (CCMB)	DNA Fingerprinting, Cell Biology, Microbial Genetics, recombinant DNA products, Molecular Biology Biochemistry & Biophysics.

Central Institute of Medicinal and Aromatic Plants (CIMAP)	Genetic manipulation of essential oil bearing plants for high yield, Morphine deficient and hyper morphine-codeine yielding genotypes for alternate methods of opiate alkaloid production.
National Botanical Research Institute (NBRI)	Plant molecular biology, tissue culture of economically relevant Plants, biodiversity, ex-situ conservation of plants etc.
Regional Research Laboratory (RRL), Jammu	**B**io-prospecting of natural molecules; biotechnology- fermentation and enzyme technology, microbial biodiversity, molecular biology and gene cloning; natural products chemistry; cultivation & **u**tilization of drugs and essential oil bearing plants and **c**hemical **e**ngineering & **d**esign backup for packaging of technologies.
Regional Research Laboratory (RRL), Jorhat	Plant tissue culture for medicinal, perfumery and endangered plant species, agro-technologies and isolation of potent anti-malarial drugs from plant sources besides chemistry, chemical engineering and other areas of research.
Regional Research Laboratory (RRL), Trivandrum	Agro-processing, chemical sciences, materials & minerals, biotechnology and process engineering and environmental science & technology.
Institute of Himalayan Bioresource Technology (IHBT)	Improvement in productivity and Quality of Hill Area Tea.
DST funded institutions	
Bose Institute, Kolkata	Advancement of knowledge in science and technology through six departments including Plant Molecular Cellular Genetics, Animal Physiology, Microbiology, Biochemistry, Biophysics, Botany and other divisions.
Agharkar Research Institute, Pune	Microbial, Plant and Animal Sciences with emphasis in biotechnological solutions.
Indian Association for the Cultivation of Science, Kolkata	Besides physics and chemistry, some work is done in enzymes, natural polymers, anticancer drugs, biosensors etc.
Sreechitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram	Promotion of biomedical engineering and technology, high standards of patient care and the development of post graduate training programs in advanced medical specialties and in biomedical engineering and technology.
ICMR funded institutions	
National AIDS Research Institute, Pune	Biomedical research on HIV/AIDS.
National Institute of Virology (NIV), Pune	WHO Collaborating Centre for arboviruses reference and hemorrhagic fever reference and research. Also the National Monitoring Centre for Influenza, Japanese encephalitis, Rota , Measles and Hepatitis.
Vector Control Research Centre (VCRC), Pondicherry	Entomology of vector borne diseases.
Institute of Immunohaemotology (IIH), Mumbai	Hematopoietic stem cell biology, hybridoma, red cell serology etc.
National Institute for Research in Reproductive Health (NIRRH), Mumbai	Reproductive Biology and Assisted Reproductive Techniques.

National Institute of Cholera and Enteric Diseases (NICED), Kolkata	Community studies and epidemiological investigation, molecular epidemiology, biochemistry and molecular biology, clinical research, microbiology, virology and parasitology, Immunology, ultrastructure analysis and histopathology of cells.
National Institute of Nutrition (NIN),Hyderabad	Study of dietary and nutrition problems prevalent among different segments of the population.
National Institute of Malaria Research (NIMR), New Delhi	Malaria related vector biology and control, genetics and cytogenetics, parasitology, pharmacology and epidemiology.
Tuberculosis Research Centre (TRC), Chennai	Studies on the domiciliary application of chemotherapy in the treatment of pulmonary tuberculosis. Training in controlled clinical trials and laboratory aspects of tuberculosis. Immunology and molecular biology of tuberculosis.
National JALMA Institute for Leprosy & Other Mycobacterial Diseases (NCJILMD), Agra	Thrust on leprosy, tuberculosis and HIV. Studies on leprosy through nerve ectrophysiology, pathology and immunopathology of disease process using immunological, molecular and electron microscopic tools. Microarray facility and DNA as well as protein sequencing in understanding the above diseases. Study of relationships between HIV & leprosy and HIV & tuberculosis.
ICAR funded Institutions	
Central Institute for Cotton Research, Nagpur, Maharashtra	Research in improvement, production and protection of cotton crop.
Central Plantation Crops Research Institute, Kasaragod, Kerala	Research in improvement, production and protection of coconut, cocoa and arecanut plants.
Central Potato Research Institute, Shimla, Himachal Pradesh	Collection, conservation, evaluation and propagation of potato germplasms. Development, breeding & release of blight & insect resistant, heat tolerant and high yielding genotypes of potato.
Central Research Institute for Jute and Allied Fiber, Barrackpore, West Bengal	Developing high yielding varieties of jute and allied fiber crops.
Project Directorate of Rice Research, Hyderabad	Multi-location testing of genetic lines and technologies for rice crop production and protection.
Indian Agricultural Research Institute, New Delhi	Utilization of plant genetic resources, conservation of microbial, cyanobacterial and insect resources. Generation of hybrids, crop modeling, use of nuclear tools, molecular biology and biotechnology for crop and plant improvement.
Indian Grassland and Fodder Research Institute, Gwalior, Jhansi	Programs on all aspects of forage production and development.
Indian Institute of Horticultural Research, Bangalore, Karnataka	Productivity increase of fruits, vegetables and flowers of economic value.
Sugarcane Breeding Institute, Coimbatore, Tamilnadu	Collection, maintenance, evaluation and documentation of sugarcane germplasm. Repository of the largest collection of sugarcane germplasm in the world.
National Bureau of Animal Genetic Resources, Karnal, Haryana	Characterization, evaluation and development of Information System on Livestock and Poultry Genetic Resources. Gene Bank established for preservation of somatic cells and semen doses of few important breeds of cattle and buffaloes.

National Bureau of Fish Genetic Resources, Lucknow, Uttar Pradesh	Assessment and conservation of fish genetic resources. Database development, genotyping, registration of aquatic germplasm, genebanking and evaluation of endangered and exotic fish species.
National Bureau of Plant Genetic Resources, New Delhi	Molecular fingerprinting of released varieties and genetic stocks of crop plants. Collection, maintenance, evaluation and documentation of plant germplasm.
National Bureau of Agriculturally Important Microorganisms, Distt. Mau, Uttar Pradesh	Promote and co-ordinate systematic scientific studies in agriculturally important microorganisms. identification of indigenous species, strains, races and types of microorganisms.
National Research Centre for Agroforestry, Jhansi, Uttar Pradesh	Horticulture, silviculture and silvipasture for social forestry and improved soil conditions.
National Research Centre for Cashew, Puttur, Karnataka	Cashew Field Gene Bank, micropropagation of cashew nut and programs related to improvement of cashew nuts.
National Research Centre on Camel, Bikaner, Rajasthan	Basic and applied research for the improvement of camel including cryo-preservation, artificial insemination & embryo transfer technology.
Central Institute for Research on Buffaloes, Hissar, Haryana	Basic and applied research for the improvement of buffaloes including cryo-preservation, artificial insemination & embryo transfer technology.
Central Institute of Freshwater Aquaculture, Bhubaneswar, Orissa	Nutrition, physiology, genetics, pathology, pond environmental monitoring & aquaculture engineering for developing intensive and extensive warm freshwater farming systems for commercially important finfish and shellfish.
National Research Centre for Medicinal & Aromatic Plants, Boriavi, Gujarat	Biotechnological approaches for production and cultivation, Mass multiplication and molecular characterization & Karyotype analysis for medicinal plants.
National Research Centre for Orchid, Pakyong, Sikkim	Collection, maintenance, micropropagation, evaluation and documentation of orchid and bulbous plant germplasms.
National Research Centre on Seed Spices, Ajmer	Collection, evaluation and conservation of major and minor seed spices germplasm.
National Research Centre for Soybean, Madhya Pradesh	Germplasm augmentation, marker assisted selection, molecular, biochemical and morphological characterization of soybean varieties.
Central Institute for Research on Goats, Farah, Uttar Pradesh	Basic and applied research for the improvement of goat including cryo-preservation, artificial insemination & embryo transfer technology.
Central Avian Research Institute, Izatnagar, Uttar Pradesh	Conservation of indigenous fowls and creation of genetic stocks, Development of DNA restriction profiles of layers, broilers, quails, guinea fowls etc.
Indian Veterinary Research Institute (IVRI), Izatnagar	Pioneering institute in the development of sensitive and specific diagnostics and immuno-prophylactic veterinary vaccines used to treat a wide range of animals.
Indian Institute of Pulses Research (IIPR), Kanpur	Genetic enhancement for yield and grain quality, Integrated pests and diseases management, Germplasm collection, evaluation and conservation etc.

National Dairy Research Institute, (NDRI) Karnal	Development of high milk producing strains of cattle, ***in vitro*** maturation and ***in vitro*** fertilization, embryo transfer technology, hybridoma technology, cytogenetic profile of various breeds of cattle, buffaloes and goats established.
Other Centrally Funded Institutions	
Indian Institute of Science, Bangalore	Basic and application oriented research in various aspects of biotechnology.
Indian Institute of Technology (IIT), New Delhi	Application oriented biotech research in areas covering industrial biotechnology.
Indian Institute of Technology (IIT), Kanpur	Application oriented biotech research in areas covering industrial biotechnology.
Indian Institute of Technology (IIT), Kharagpur	Application oriented biotech research in areas covering industrial biotechnology. Plant tissue culture related work as well as genetic engineering of microbes and plant cells.
Indian Institute of Technology (IIT), Roorkee	Application oriented biotech research in areas covering industrial biotechnology.
Indian Institute of Technology (IIT), Mumbai	Application oriented biotech research in areas covering industrial biotechnology. Also concentrating on protein structures, proteomics and genomics.
Indian Institute of Technology (IIT), Assam	Application oriented biotech research in areas covering industrial biotechnology.
Indian Institute of Technology (IIT), Madras	Application oriented biotech research in areas covering industrial biotechnology.
Various Central Universities & Engineering Institutions at various locations	Application oriented biotech research in areas covering various aspects of biotechnology.
Various State funded Institutions and universities.	Application oriented biotech research in areas covering various aspects of biotechnology.

Manpower Development

Biotechnologists use molecular keys, biological tools and mathematics including different algorithms to understand biological relationships among biomolecules, cells, tissues, organisms, environment and ecosystem to produce tangible and intangible wealth. The following flow chart (Figure 3) covers how biotechnologists[12] across the world create wealth in different sectors such as health care products, agriculture, bio-industrial products and sustainable environment management practices.

One of the few countries to initiate an integrated program of human resource development in biotechnology was India. The courses are comprised of postgraduate teaching programs, short term training courses in India and abroad as well as long term overseas courses to develop better faculties. The postgraduate courses were initiated in 1985 in collaboration with UGC , ICAR and the Department of Ocean Development. The curriculum contained most of the areas and elements mentioned above in Figure 3, but in different institutions.

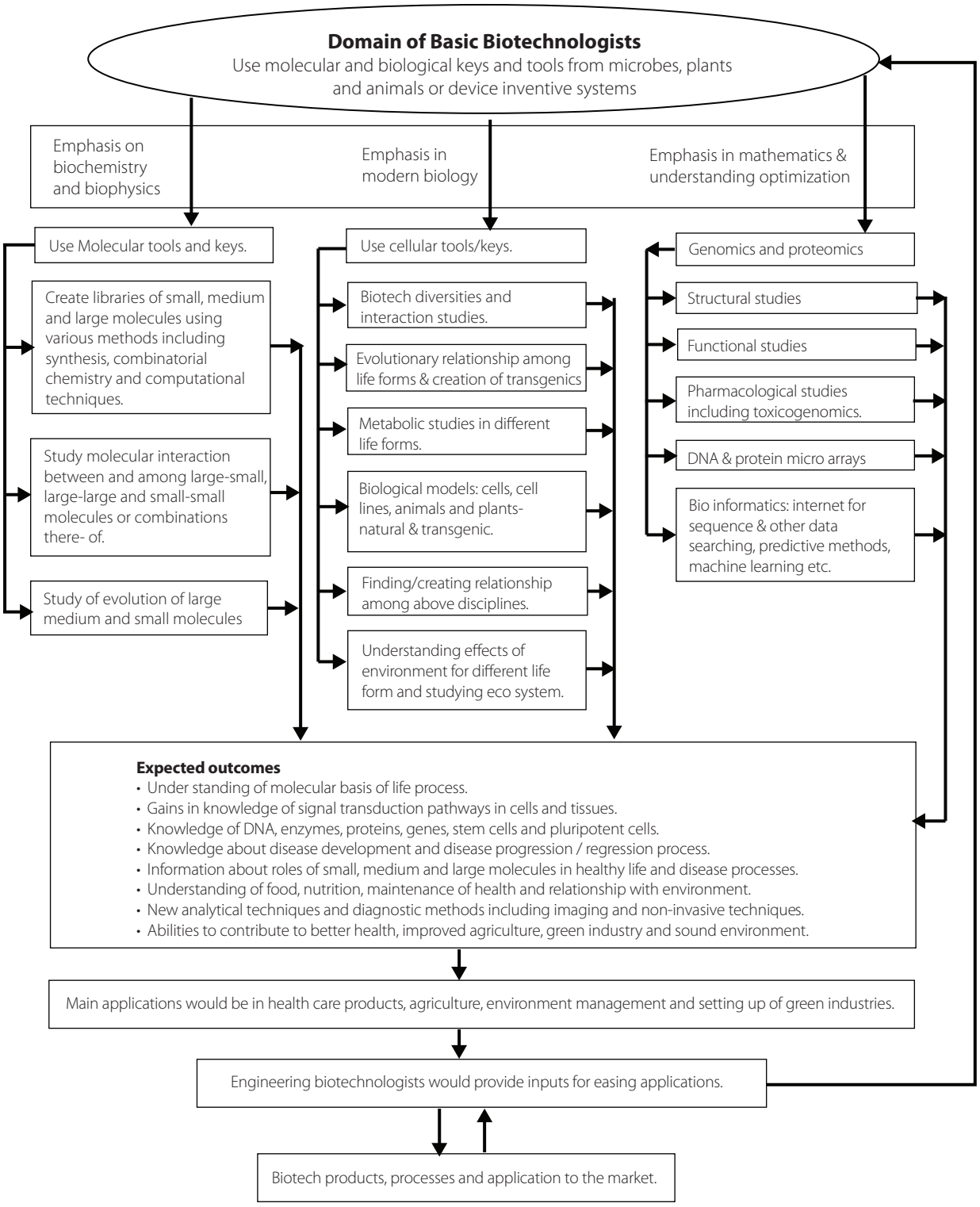

Figure 3: Domain of Biotechnologists (Schematic).

The teaching program is continuously monitored by the government to ensure minimum and uniform teaching standards. Currently the DBT is supporting 30 institutions for teaching General Biotechnology, seven in Agricultural Biotechnology, one each in Medical and Marine Biotechnology, as well as Diploma courses in Biochemical Technology and Molecular Biology. The total student output annually is around 800. The Indian Institute of Science (IISc), Bangalore, has also been involved in selecting quality students for certain areas through written examination. All the students qualifying in the DBT sponsored programs are provided fellowships .

To further knowledge and research areas of interest, Indian scientists are exposed to newer cutting-edge areas in biotechnology R&D by the DBT through overseas associateships as well as short-term training courses. Full-fledged departments of biotechnology are being set up in various institutes all over India. Besides the efforts of the DBT, the AICTE has approved graduate degrees (B. Tech) programs in biotechnology in several colleges/institutions. Other than higher educational institutions, expansion of biotechnology as a subject has been planned at school level also by the AICTE and UGC with the introduction of a specific module on biotechnology. The Ministry of Human Resource Development is also promoting biotechnology programs in various institutions. The total output of students in biotechnology from the government endeavor is anticipated to be about 1200-1500 annually.

[T]otal number of biotech students educated by the country by various institutions is estimated to be approximately 2200-2500.

Besides government efforts, great interest has been taken by several private entrepreneurs to set up institutions to teach biotechnology at graduate and post-graduate levels. Some private engineering colleges are also offering graduate degrees (B. Tech) in biotechnology. With private institutes producing nearly 1000 additional students who are trained in biotechnology, total number of biotech students educated by the country by various institutions is estimated to be approximately 2200-2500.

Biotechnology students are taught a wide range of subjects including: Biochemistry, Bioenergetics, Molecular Genetics, Microbiology, Cell Biology, Biophysics, Structural Biology, Molecular & Developmental Biology, Enzymology & Enzyme Technology, Biology of Cloning Vectors, Immunology & Immunotechnology, Plant Molecular Biology, Recombinant DNA Technology, Bioprocess Technology, Biochemical Engineering, Bioinformatics, Marine Biotechnology, etc., depending upon the institutes they study at. Some institutes also give basic training in Intellectual Property Rights & legal aspects, regulatory aspects such as rules for handling genetically modified substances and training in cGMP practices in biotechnology. Research areas for the Ph.D. students in biotechnology include and may be designated as Gene Cloning, Regulation & rDNA technology, Functional Genomics, Immunology and Immunodiagnostics, Microbial Genetics, Molecular Biology, Genomics & Proteomics, Stem Cell Research, Signal Transduction Pathways, DNA Fingerprinting, and Bioinformatics.

Table 3: Major public and private sector biotechnology institutions in the country.[13,14]

India's Top Biotechnology Institutes offering various courses like integrated Ph.D, M.Sc, M.Tech & B.Tech degrees			
Publicly Funded		***Privately Funded***	
Name of Institute	**City/State**	**Name of Institute**	**City/State**
Indian Institute of Science (IISc)- Integrated 5 y PhD.	Bangalore	Jaypee Institute of Information Technology, M.Tech.	Noida
Center for Biotechnology & Bioinformatics Centre, Jawaharlal Nehru University, (JNU) M. Sc. & PG Diploma.	New Delhi	Amity Institute of Biotechnology, Amity University, B.Tech., M.Tech.	Noida
Department of Biochemical Engineering and Biotechnology, Indian Institute of Technology Integrated M. Tech.	New Delhi	The Oxford College of Science, M.Sc.	Bangalore
University School of Biotechnology, Guru Govind Singh, Indraprastha University Integrated M. Tech. 5 ½ y.	New Delhi	Birla Institute of Technology, B. E., M.Sc., PG Diploma.	Ranchi
School of Biotechnology & Bioinformatics Centre, Madurai Kamraj University M. Sc. & PG Diploma.	Madurai	Jaypee Institute of Information Technology, B. Tech.	Solan
School of Life Sciences, University of Hyderabad M. Sc.	Hyderabad	Arunai Engineering College, B. Tech.	Tiruvannamalai
Institute of Chemical Technology, University of Mumbai M. Tech.	Mumbai.	Seedling Academy of Design, Technology & Management & SILAS, B.Tech., M.Sc.	Jaipur
Departments of Biochemistry, Microbiology & Biotechnology Center, The Maharaja Sayaji Rao University of Baroda M. Sc.	Vadodara	Shree Manibhai Virani & Smt. Navalben Virani Science College, M.Sc.	Rajkot
National Institute of Immunology (NII) Ph.D.	New Delhi	Acharya Institute of Technology, B.E., M.Tech.	Bangalore
Indian Agricultural Research Institute (IARI) M. Sc.	New Delhi	Kamraj College of Engineering & Technology, B.Tech.	Virudhnagar
Department of Biological Sciences & Bioengineering, Indian Institute of Technology, Kanpur M. Tech.	Kanpur	Garden City College, M.Sc.	Bangalore
Rajiv Gandhi Center for Biotechnology, Ph.D.	Trivednrum	RV College of Engineering, B. E.	Bangalore
Department of Animal Biotechnology, Madras Veterinary College, Tamil Nadu Veterinary & Animal Sciences University M. Sc.	Chennai	Rajalakshmi Engineering College, B. Tech., M.Tech.	Chennai
University Institute of Engineering & Technology, Punjab University M. Sc.	Chandigarh	Presidency College, M.Sc.	Bangalore
Department of Plant Molecular Biology & Biotechnology, Tamil Nadu Agricultural University, M. Sc.	Coimbatore	Sreenidhi Institute of Science & Technology, B.Tech.	Hyderabad

Publicly Funded		*Privately Funded*	
Name of Institute	**City/State**	**Name of Institute**	**City/State**
University of Pune & its Bioinformatics Center, M.Sc. & PG Diploma.	Pune	T John College, M.Sc.	Bangalore
Center for Biotechnology, Anna University, B.Tech & M. Tech.	Chennai	Sri Bhagawan Mahavir Jain College, PG Degree.	Bangalore
Dr.BC Guha Center for Engineering & Biotechnology & Bioinformatics Centre, University of Calcutta M.Sc. & PG Diploma.	Kolkata	Kumaraguru College of Technology, B.Tech.	Coimbatore
Department of Biotechnology, University of Kashmir, M.Sc.	Hazrathol	Maharani Lakshmi Ammanni College for Woman, M.Sc.	Bangalore
Guru Jambheshwar, University of Science & Technology M.Sc.	Hisar	BMS College of Engineering, B. Tech.	Bangalore
Department of Biochemistry, University of Lucknow, M.Sc.	Lucknow	G M Institute of Technology, B. Tech.	Davangere
Department of Biotechnology, Cochin University of Science & Technology, M. Sc.	Cochin	Ambala College of Engineering, B.Tech.	Ambala
Department of Microbiology, Bangalore University, M.Sc.	Bangalore	Padmashree Institute of Sciences, PG Degree.	Bangalore
National Institute of Pharmaceutical Education & Research (NIPER), M. Tech. & Ph.D.	Mohali	SIES College of Management Studies, PG Diploma (Biotech Business Management).	Mumbai
Department of Biotechnology, Bharathiar University, M.Sc.	Coimbtore	Administrative Management College, PG Diploma..	Bangalore
Department of Biotechnology, Himachal Pradesh University, M.Sc.	Shimla	SRN Adarsh College, M.Sc.	Bangalore
Devi Ahilya Vishwa Vidhyalaya, M.Sc.	Indore	Reva Institute of Science & Technology, M.Sc.	Bangalore
Aligarh Muslim University, M.Sc.	Aligarh	Al-Ameen Arts Science & Commerce College, M.Sc.	Bangalore
Department of Biotechnology, Karnataka University, M.Sc.	Dharwad	SKM Institute of Management & Science, M.Sc.	Bangalore
Department of Biotechnology, Punjab University, M.Sc.	Chandigarh	Guru Nanak Khalsa College of Arts Science & Commerce,	Mumbai
School of Biotechnology, Banaras Hindu University, M.Sc.	Varansi	Nirma University, M. Sc., Ph.D.	Ahmedabad
Banasthali Vidyapeeth, M.Sc.	Banasthali	Manipal Institute of Technology, B.E. (Biomedical Engg).	Manipal
Coshin University of Science & Technology, M.Sc.	Kochi	KLE Society's College of Engineering & Technology, B.E. (Biomedical Engg).	Belgaun

Publicly Funded		***Privately Funded***	
Name of Institute	**City/State**	**Name of Institute**	**City/State**
Gujarat University, M.Sc.	Ahmed-abad	Thapar Institute of Engineering & Technology, M.Sc.	Patiala
Indian Institute of Technology, M.Sc.	Roorkee	Birla Institute of Technology, M. Tech.	Pilani
Bose Institute, Ph.D.	Kolkata	Allahabad Institute of Agricultural Sciences.	Allahabad
International Centre for Genetic Engineering & Biotechnology, Ph.D.	New Delhi		
National Physical Laboratory, Ph.D.	New Delhi		
Sri.Krishnadevaraya University, M.Sc.	Anantpur		
Department of Biosciences, Sardar Patel University, M.Sc.	Vallabh Vidyanagar		
Department of Biotechnology, University of Calicut, M.Sc.	Calicut		
Department of Biotechnology, Government Science College, M.Sc.	Bangalore		
Department of Biotechnology, Gulbarga University, M.Sc.	Gulbarga		
Jamia Millia Islamia, M.Sc.	New Delhi		
Sree Chitra Thirunal, College of Engineering, M.Sc. & Ph.D (Biomedical Technology	Thiruvanan-thapuram		
Department of Studies in Applied Botany & Biotechnology, University of Mysore, M.Sc.	Mysore		
Bhabha Atomic Research Centre (BARC), M.Sc. & Ph.D.	Mumbai		
Bharathidasan Institute of Engineering & Technology, B. Tech.	Tituchirapil-lai		
Guru nanak Dev University, B. Tech.	Amritsar		
Jadavpur University, M. Tech.(Biomed, Food Tech.)	Kolkata		
National Centre for Plant Genome Research, Ph.D.	New Delhi		
Kurukshetra University, M.Sc.	Kurukshetra		
University of North Bengal, M.Sc.	Siliguri		
GB Pant University of Agriculture & Technology, M.Sc.	Pantnagar		
Goa University, M. Sc (Marine Biotechnology).	Goa		
Marathwada Agricultural University, M. Sc.	Parbhani		

Publicly Funded		*Privately Funded*	
Name of Institute	**City/State**	**Name of Institute**	**City/State**
Tata Institute of Fundamental Sciences, M.Sc. (Neurosciences) & Ph.D.(Biotechnology).	Mumbai		
Central Drug Research Institute(CDRI), Ph.D.	Lucknow		
Central Institute of Medicinal & Aromatic Plants, Ph.D	Lucknow		
Centre for DNA Fingerprinting & Diagnostics, Ph.D.	Hyderabad		
Centre for Cellular & Molecular Biology, Ph.D.	Hyderabad		
National Botanical Research Institute, Ph.D.	Lucknow		
National Brain Research Institute, Ph.D.	Gurgaon		
National Centre for Cell Science, Ph.D.	Pune		
National Environmental Engineering Research Institute, Ph.D.	Nagpur		
Dr. Babasaheb Ambedkar Marathwada University, M.Sc.	Aurangabad		

All biotech students graduating from universities face stiff competition in employment in the respective fields, as the industry is at the developmental stage, while publicly-funded institutions and other sectors have limited capacity to absorb new graduates. In order to gain work experience to obtain jobs quickly after graduation study materials should be introduced into the curriculum so that postgraduates can start an independent business. Some demand also exists in protecting intellectual properties in biotechnology; therefore courses emphasizing basic legal principles may assist in creating jobs for some graduates. Presently, the majority of the students who graduate accept low-paying jobs, and many leave the country for better opportunities.

The next flow chart (Figure 4) indicates schematically[15] how entrepreneurs create wealth in many sectors, including biotechnology.

Of all the resources utilized by entrepreneurs for producing goods and services, technology plays a key component. If the technology belongs to a high tech category, the entrepreneurs accrue more bargaining power for charging higher prices; the other factors of value including resources, the organizational structure, the infrastructure and the environment are almost equally shared by different entrepreneurs for their goods and services, therefore, technology becomes the key factor in value addition. In biotechnology this is the main factor which is harnessed by the inventing companies who are developing products and services of high value.

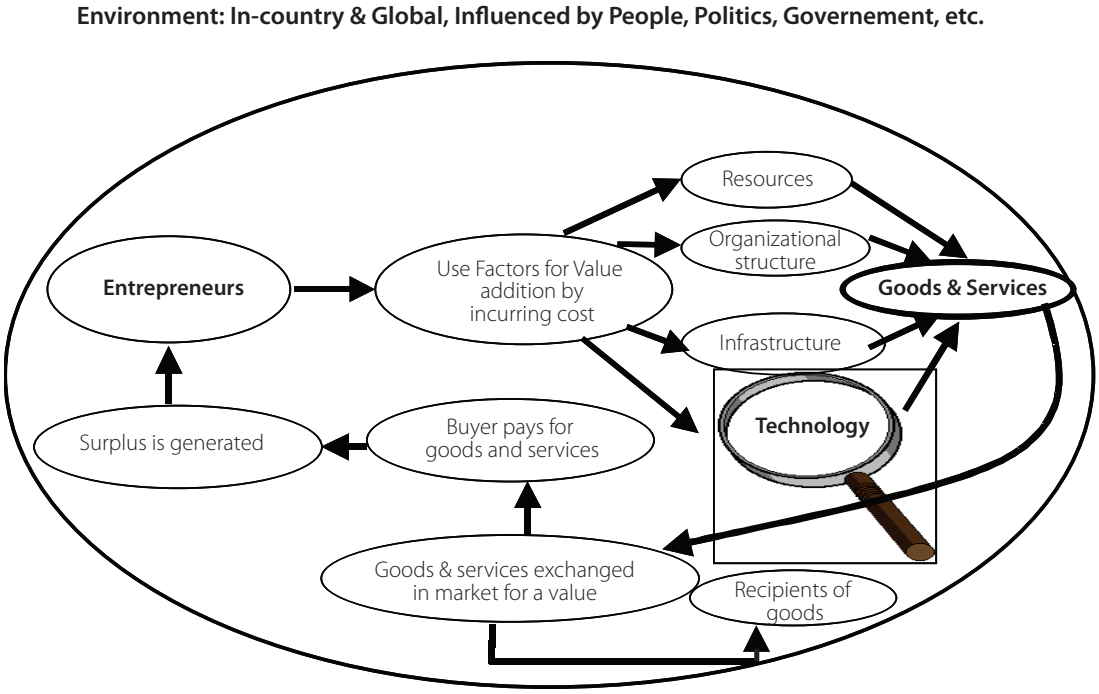

Figure 4: Wealth Creation Model (Qualitative).

Biotechnologists skilled in molecular biology, immunology, chemistry, and chemical engineering sciences, along with good business skills are rare. Courses containing basic biology with chemistry and chemical engineering, or biochemical engineering, should form the core of study, while ancillary subjects should develop business skills that will help with understanding the financial aspect of business Such combinations hold the great potential of taking products of this powerful technology from laboratory to the market, especially in the health care products area and in bio-industrial sector. In agriculture, the breeders must also be part of the team. The curriculum of any teaching institution in India in biology or in biotechnology does not yet combine these disciplines together. The biotech industry can help by financing such initiatives to help future graduates gain marketable skills.

Biotechnology Parks

The Indian government, with the help of biotechnology, has been instrumental[16] in promoting the creation of small and medium industries in biotechnology in different parts of the country. Towards these efforts the government, with the assistance of the state governments, has earmarked land and such zones have been designated as Biotechnology Parks. Such parks have been planned to provide financial & other logistical support to young entrepreneurs who lack the capital to fund such endeavors in the biotech industry, but have the capabilities to develop, design and perfect

new biotech products and processes by utilizing such facilities.

Presently, biotech parks in India have been created and/or proposed in a number of states including Tamilnadu, Andhra Pradesh, Kerala, Karnataka, Uttar Pradesh, Punjab, Maharashtra, Gujarat, Uttaranchal, Rajasthan, Delhi, Orissa, Madhya Pradesh, etc. The total investment to build these facilities is estimated at approximately Rs. 15 billion.

Scenario of Biotech Products in India

India has been practicing conventional biotechnology for several decades. Products manufactured by the use of genetic engineering, immunological techniques, cell culture methods and hybridoma technology has increased during the last five years and local research in these areas has intensified. The following Table 4 gives an estimation of the current consumption and future demand of biotech products in value in India. The products include in health-care area, all substances produced by microbial fermentation and cell culture including the recombinant DNA products, vaccines, sera, blood and glandular products of human and animal origin, bioactive substances extracted and purified by special techniques used medically,, diagnostics produced by multiple techniques including synthesis (for peptides, conjugates, oligonucleotides, linkers, etc.), and rDNA technology, immunology etc. Since 2005, 70-75% of the products were locally produced while the rest was imported and locally consumed. Several fermentation-based products including betalactams, erythromycin derivatives, rifampicin and a host of statins and immunosuppressants are also exported. Future consumption and demand is expected to intensify further production from local sources, which is estimated to increase to over 80% by 2010. The agriculture sector includes the turnover of the seed industry including genetically modified seeds (insect resistant cotton), tissue culture raised horticultural plants, sugarcane, seed potato, ornamental plants flowering plants and tubers, processed vanilla beans, biofertilizers, biopesticides and organic fertilizers. The products from the industrial sector include industrial enzymes; cheese produced by using recombinant microbial rennin; fermentation-based organic products, etc. The other biotech products include microbial application methods for the containment of wastes, microbial leaching of minerals, reclamation of soil by microbial methods, and waste water treatment, etc.

Since 2005, 70-75% of the products were locally produced while the rest was imported and locally consumed.

The health care products most likely will dominate the scene and may contribute to about 38.5% of the consumption market by 2010 up from nearly 37.6% in 2005. However, the products portfolio shall undergo a significant change. While in the 1990s biotech products were dominated by fermentation based antibiotics like penicillins, cephalosporins, 6-APA, 7-ACA, 7-ADCA and their derivatives; tetracyclines; streptomycin, gentamycin, neomycin, amphotericin, rifampicin etc., the current shift has been towards local produc-

Table 4: Past Sales of Biotech Products in India and Future Sales Estimates (Rs. In Million).

	Particulars of Biotech Sub-sectors	Actual Sales 2005	Future Sales Estimate 2010
1	Human & Animal Health care Products	35320 **(37.6)**	93540 **(38.5)**
2	Agriculture (including traded varieties & hybrid seeds & other planting materials)	28880 **(30.7)**	78720 **(32.4)**
3	Industrial Products	28500 **(30.3)**	53590 **(22.1)**
4	Other Biotech Products	1300 **(1.4)**	17000 **(7.0)**
	Total	94000 **(100**)	242850 **(100)**

(Figures in brackets indicate contributions as a % of the total)

tion of anti-lipidimic drugs, recombinant DNA based therapeutic substances, an increase in the production of several live-saving vaccines, and modern diagnostic kits requiring recombinant proteins, etc. Most of the facilities for fermentation-based antibiotics production have recently been closed due to economic non-viability arising from fast changes in the adoption of globalization policies. In 2005, the contribution of modern biotech products through local production was about 61% while the balance 39% in value was imported and sold. This scenario is going to lean more towards increased production from local units in future. For conventional biotechnology products however, local production was considerably low representing about 35% of the total value and 65% was imported. This distortion was mainly because of cheaper availability of a wide range of biotech products from developing countries including China.

Contribution of biotechnology in agriculture did not change much except that genetically modified, insect-resistant cotton was approved for cultivation in the country in early 2002 which let to significant increases in cotton lint production, improving its quality and helped contribute to a cleaner environment due to substantial reduction in the use of chemical pesticides in the country. The basic technology of some vital components was imported from the U.S., China and Japan; the insect-resistant genetic trait was introduced in several Indian hybrids. During 2006, nearly 10 million acres of land were brought under the cultivation of Bt cotton using locally produced seeds worth Rs. 7500 million, [17]. More modern biotech seeds and planting materials may be approved in the country in the future which may contribute to increased agricultural output. The present seed replacement practices which stand at around 10% per year for crops and cereals should jump up substantially during the coming years. The farmers may realized the significance of these changes, and such attitudes driven by visible economic benefits (as already perceived by the Bt cotton growers) may be instrumental in increasing demand for better quality of productive seeds. In the case of vegetables such trends are already visible

where seed replacement practices are over 80% presently and should increase further. Contributions in industrial products and other biotech materials may go down from the present 31.7% to about 29.1%, although in monetary terms, the absolute contributions in these areas would rise sizably. The major developments anticipated are in the increased production and use of enzymes in various facets of industrial applications, biodegradation of agricultural, municipal and city-generated market(organic) wastes, and development and planting of stress-tolerant plants and trees to make optimal use of waste and degraded lands, etc.

Leader Countries in Modern Biotechnology During the Next Decades and the Position of India

The U.S. and Canada are expected to lead as modern biotechnology innovators…

Modern biotechnology is the term applied to the skills deployed in producing goods and services that use recombinant DNA technologies, whole genome cloning, genomics, proteomics, bioinformatics, stem cell research, targeted drug delivery, anti-sense technology, cellular and immune based therapies, monoclonal antibodies, gene therapy, etc.

Modern biotechnology is still rather new to India. There is little doubt however that the applications of modern biotechnology will greatly increase as products or processes hold great potential for providing much better solutions to improving the health of people and the quality of life, improving agricultural productivity significantly along with supplying more nutritious food, producing industrial bio-products at much cheaper prices, and improving the quality of the environment more effectively on a sustainable basis.

The U.S. and Canada are expected to lead as modern biotechnology innovators, but developments in other countries especially in Europe will also be significant. Countries such as the U.K., Germany, France, Sweden, Switzerland, Belgium, Denmark, Italy, Finland, Ireland, Russia, Hungary and Poland are poised to make significant progress. Among the Asian countries Israel, Japan, China, India and South Korea are increasing their output of modern biotech companies. India, China and South Korea are expected to emerge as major players towards providing health care products at much cheaper prices than what is currently available. In agriculture, China may be a pioneer in achieving major breakthroughs among developing countries; their results are likely to inspire many poor countries to adopt modern biotechnology in their agriculture. Australian developments in certain sectors are also expected to be substantial. Significant progress is foreseen in South American countries like Brazil, Argentina, Mexico, Cuba and Columbia. Among the African countries substantial developments are expected from South Africa. Globally, major developments are expected in health care products followed by agriculture.

The present consumption and production of modern biotech products in different major nations and the projections for the future years are summarized[18] in the following Table 5.

Table 5: Estimated global consumption and production of modern biotech products.

Global Segment	Estimated consumption in billion US$		Estimated production in billion US$	
	2005	2010	2005	2010
USA & Canada	34.0	50.0	27.0	52.0
Europe and Japan	10.0	15.0	12.2	12.5
Rest of the World	**5.0**	**12.0**	**9.8**	**12.5**
Total	49.0	77.0	49.0	77.0
Overlap of the Segments of the Rest of the World				
India	0.3	1.0	0.2	1.3
China	1.2	3.0	2.9	3.1
South Korea	0.5	1.3	1.1	1.4
Latin American countries and the rest of the world	3.0	6.7	5.6	6.7
Subtotal	5.0	12.0	9.8	12.5

While the developed world will intensify its production specifically in the U.S. and Canada, it is anticipated that the production in Europe and Japan will attain a plateau, while developing countries including India and China are expected to intensify their production and supply their produce for exports. More modern biotech products are anticipated to be produced in the form of bio-generics or bio-similar products. Products exported from the developing countries would have expired patents and will be produced by more economic methods of production, including modifying the basic structure of molecules in order to make the bio-therapeutic products more effective. In turn, they can be converted into different presentable forms such as pulmonary delivery, nasal delivery, oral delivery, etc., or by making them long acting by producing long acting derivatives such as by PEGylation, hyperglycosylation by linking them with albumin – binding fatty acids etc.

It is anticipated that there will be some surprises in the supply of quality, modern biotech drugs from developing countries including India, even though the contribution of modern biotech products from India shall continue to remain small in the global context.

Indian Capabilities in Modern Biotechnology

While there exists over 800 companies operating in all sectors of biotechnology, there are only about 50 companies that are working in modern biotech sectors. Modern biotech products include substances where genetic materials have been or are targeted to be modified by recombinant DNA or other such technologies involving the whole genome cloning, identifying the genes and finding functional relationships with them, determining to understand and apply knowledge on how single or multiple genes operate in cells and tissues, how signal transduction methods could be

understood and applied to repair cells, tissues and organs, creating understanding and applying them to regulate single or multiple genes within the cells, tissues and organs to develop and produce transgenic substances and life forms of diverse nature to use them for human benefits , improve agriculture, upgrade forestry development, and device better environment management systems. Use of bioinformatics to support product development in any of the above areas is also considered as modern biotechnology. Some measuring devices or some services developed or used particularly for the development of modern biotech products and industry are not however, considered as biotechnologies as these have no direct genetic linkage with the life process.

With this in mind, the Indian modern biotech industries dealing with such products include the following major companies[19] as provided in Table 6.

Table 6: List of Indian Modern Biotechnology Industries Statewise.

City, State	
Name of Company	**Name of Company**
Hyderabad ,A.P	
Shantha Biotechnics Ltd.	Dano Vaccines & Biologicals (P) Ltd.
Bharat Biotech International Ltd.	Emco Industries
Ma Gene Ltd.	Fortune Biotech Limited
Biological E. Ltd.	GVK Bio Sciences Pvt. Ltd.
Reddy's Laboratory	Hi-Tech Pharmaceuticals Pvt. Ltd.
Transgene Biotech. Ltd.	Human Biologicals Institute
AsthaLaboratories Pvt. Ltd.	Midas Biotek Pvt. Ltd.
Aurobindo Pharma Ltd.	Trident Pharmaceuticals Pvt. Ltd.
Bacto-Chem Laboratories	TTK Pharma Ltd.
Bactolac Formulations Pvt. Ltd.	Uni-Sankyo Ltd.
Biological and Plant Products	Virchow Laboratories Ltd.
Biomax Lifesciences Ltd.	Zen Biotech Pvt. Ltd.
Crescent Therapeutics Ltd.	Gland Pharma Ltd.
Sathamrai ,A.P	
Behring Pharma (P) Ltd.	
Ranigunta; A.P	
Malladi Drugs & Pharmaceuticals Ltd.	
Pune; Maharashtra	
Emcure Ltd.	Srini Pharmaceuticals Ltd.
HindustanAntibiotic sLtd.	BAIF Labs. Ltd.
Venkateshwaar Health Care Pvt. Ltd.	Serum Institute of India Ltd.
Aurangabad; Maharashtra	
Wockhardt Biotech Ltd.	
Mumbai, Maharashtra	
Schering India Ltd.	HaffkineBio-Pharmaceutical Corp. Ltd.
Artemis Biotech	Kopran Ltd.

City, State	
Name of Company	**Name of Company**
Nicholas Piramal India Ltd.	Novartis Idia Ltd.
Glenmark Pharmaceuticals Ltd.	Pfizer Limited
Aventis Pharma Ltd.	Shreya Life Sciences Pvt. Ltd.
Lupin Laboratories Ltd.	UCB INDIA Ltd.
Aventis Pharma Ltd.	VHB Life Sciences Inc.
Bharat Serums & Vaccines Pvt. Ltd.	Maharashtra Hybrid Seeds Company Ltd.
Boehringer Mannheim India Ltd.	Monsanto India Ltd.
Chiron Vaccines	
Navi Mumbai; Maharashtra	
Clinisearch Biotechnologies	Reliance Life Sciences Ltd.
Ahmedabad; Gujarat	
Torrent Biotech	Concord Pharmaceuticals Ltd.
Zydus Cadila Health Care Ltd.	Atul products Ltd.
Cadila Pharmaceuticals Ltd.	Maize Products
Intas Pharmaceuticals	
Vadodara; Gujarat	
Sun Pharmaceuticals	Alembic Ltd.
A.S.C Ltd.	
Surat; Gujarat	
Span Diagnostics	
Vapi; Gujarat	
Gujarat Themis Biosyn Ltd.	
New Delhi	
Panacea Biotech	Care Well Biotech (P.) Ltd.
J. Mitra & Company	Kee Pharma Ltd.
Ranbaxy Laboratories	Radicura Pharmaceuticals Pvt. Ltd.
Eli Lily Ltd.	Steva Biotech Pvt. Ltd**.**
Bangalore; Karnataka	
Biocon (India) Ltd**.**	Indo-American Hybrid Seeds
KarnatakaAntibiotics& Pharmaceuticals Ltd.	Rallies India Ltd.
Mysore; Karnataka	
Glaxo Smithkline Pharmaceuticals (India) Ltd.	
Gaziabad ,U.P	
Dabur India Ltd.	Bio-Med Pvt. Ltd.
Gurgaon; Haryana	
Pro-Agro PGS	Life Medicare & Biotech Pvt. Ltd.
Kolkata; W.B.	
East India Pharmaceutical Works	Albert David Ltd.
Baddi; H.P.	
M. J. Biogenetic Drugs Pvt Ltd.	
Mehatpur; H.P	
Tulip Laboratories	
Chennai; Tamilnadu	
Amrutanjan Limited	SPIC

None of the Indian companies have introduced any product of original research in Indian market that could be considered as unique. However, some have introduced known products that are tantamount to effective imports substitution. Others have teamed up with foreign companies for sourcing technologies and are experimenting with new products produced by foreign technologies with a view to introduce them into the Indian market within the frame work of Indian laws. Certain companies are also introducing novel and effective but intellectually protected genes into Indian germplasms to increase agricultural productivity or to reduce agricultural production costs.

Modern biotech products are only a few that are being produced currently in the country. They include the following[20] in various biotech sectors:

Table 7: Modern biotech products currently (2006-07) being produced in the country.

Sector	Major Industries Producing	Remarks
Health Care Products		
Hepatitis B surface antigen	Transgene Biotech, Hyderabad did the first experiments in the country to introduce the product based on a recombinant yeast strain by the name ***Hansenula polymorpha*** but subsequently sold the technology to Serum Institute Pune.	The strain and original technology belonged to Rhein Biotech, Germany.
	Shantha Biotechnics produced the recombinant strain in ***Pichia pastoris*** and started producing the pure antigen from the recombinant organism.	The strain and technology was developed with the multiple institutional assistance of Osmania University Hyderabad, Centre of Cellular & Molecular Biology Hyderabad and inputs from certain American Universities.
	Wockhardt Ltd. Aurangabad produced the substance using recombinant yeast strain of ***Hansenula polymorpha.***	The strain and original technology belonged to Rhein Biotech, Germany.
	Bharat Biotech International Ltd., Hyderabad produced the substance in ***Pichia pastoris***.	The company obtained assistance from the Indian Institute of Science Bangalore besides putting its in-house efforts.
	Panacea Biotech Ltd., Delhi produced the substance in recombinant ***Pichia pastoris.***	The technology belonged to CIGB of Cuba.
	Serum Institute of India Ltd., Pune produced the substance using recombinant yeast strain of ***Hansenula polymorpha.***	The technology was obtained from Transgene Biotech, Hyderabad.
	Biological E Ltd., Hyderabad produced the substance using recombinant ***Pichia pastoris.***	The technology was obtained from the IISc, Bangalore.
	Efforts by several other newcomers as well as introduction of the product by direct importers.	Several Indian companies are trying to develop this product to make it more cost effective. However such efforts are likely to raise increased market competition. The direct importers are likely to gat phased out due to severe local competition. Moreover, more of combination vaccines with DPT and Hepatitis B is getting more popular.

Granulocyte Colony Stimulating Factor (GCSF)	Dr. Reddy's Laboratory developed the recombinant E. coli strain and technology for the production of this lifesaving drug for leucopoiesis in various conditions especially in patients suffering from cancer after receiving chemotherapy.	The technology was developed in-house.
	Intas Ltd. Ahmedabad developed the clone and technology in E. coli and had introduced the product in the market.	The technology was developed in-house.
	Efforts by several other newcomers as well as introduction of the product by direct importers.	At least six more companies are trying to develop the product in-house; they are at various stages of development. In addition, the product is being imported and sold by certain companies.
Recombinant Erythropoietin alpha	Wockhardt Ltd. Aurangabad started producing the product using genetically modified CHO cell lines.	The strain and basic technology was of Italian origin.
	Intas India Ltd. Ahmedabad developed its own clone in CHO cell line.	The strain and technology was procured from outside and further developed in-house.
	Efforts by several other newcomers as well as introduction of the product by direct importers.	Several companies are marketing the formulated product by importing from various sources. Some companies are also trying to develop the technology based on the recombinant strain procured from outside. It is anticipated that there would be sever market competition as several entrants have interest in obtaining a market share.
Interferon alpha 2B & pegylated product	The product was developed by Shantha Biotehcnics Ltd. Hyderabad in ***E. coli*** strain.	The technology was developed in-house.
	Efforts by several other newcomers as well as introduction of the product by direct importers.	The companies supplying the material from imported sources are finding more competition from the local producer. Several other companies are trying to develop the pegylated form of the product.
Epidermal Growth Factor	Bharat Biotech Ltd. Hyderabad developed the product in E. coli.	The technology was developed in-house.
Streptokinase	Shantha Biotechnics, Hyderabad; Bharat Biotech Hyderabad, developed this technology in *E. coli*.	The recombinant product is inherently unstable, and therefore, the product could not be marketed.
Recombinant Human Insulin	The product was developed in ***Hansenula polymorpha*** by Wockhardt India Ltd.	The basic technology was procured from Rhein Biotech, Germany.
	The product was developed in ***Pichia pastoris*** by Biocon India Ltd.	The basic technology and the strain was procured from Shantha Biotechnics, Hyderabad and was improved.
	Efforts by several other newcomers as well as introduction of the product by direct importers.	Several Indian companies are trying to develop the basic technology as the product has a very long term demand; diabetes is on the increase and insulin dependent diabetic cases will be on the rise. In addition to the efforts of certain companies to develop the basic technology, the original inventors namely Eli Lily, USA and Novo Nordisk, Denmark are keeping a strong hold on the market by introducing products more convenient to use as also by supplying more potent substances. Several new methods of delivery including nasal spray, inhalers, oral sprays etc. are in the developmental stage, which technologies may take dominant position and make the possessor to have larger market share.

Analogues CETUXIMAB	Biocon Ltd. Bangalore has launched a monoclonal antibody produced by genetic engineering method, which works to block certain receptors of epidermal growth factor that are responsible for proliferation of cancer cells. Excess of production of bio-molecules in the EGF pathway promotes growth and spread of several solid tumors. Epithelial cancers especially colorectal cancer responds well with the drug. The monoclonal antibody interrupting one or more of the intermediate molecules would disrupt signal transduction pathways and immune system will be activated to minimize their production. In the process the tumor growth shall slow down.	Biocon has received the marketing rights for the product in India and after conducting trials have been approved to sell. The drug has been developed under a joint venture with the Cuban Centre of Molecular Immunology (CIMAB).
RITUXIMAB	Dr. Reddy's Laboratory, Hyderabad is introducing the product based on local production and purification. The product is indicated for treating Non-Hodgkin's Lymphoma and Rheumatoid Arthritis.	The technology and the recombinant cell line were procured from U.S.A.
Several New Products & BioGenerics	Many companies are working on different compounds with/without collaborations to develop the technologies to market them. These have been dealt with in the descriptive part of the paper. It is anticipated that several new products would be introduced during the next one decade. Concurrently, imports of many such products would continue.	Basic technologies for genetic engineering have developed to a great extent especially utilizing microbial cultures and certain mammalian cell lines. The development of transgenic animals as well as transgenic plants is yet in the rudimentary stage. Picking up the right gene and the protein in order to discover new molecules through the application of genomics and proteomics techniques are still at the early stage of development.
Agriculture		
Bt Cotton	**Private Sector**	
	Mahyco – Monsanto Hybrid Seeds Pvt. Ltd. Mumbai, is a joint venture of Monsanto U.S.A. and Maharashtra Hybrid Seeds Company Ltd (Mahyco) Mumbai with 50% ownership each. Mahyco-Monsanto obtained approval for producing Bt cotton seeds containing ***Cry1Ac*** gene in March 2002 and started transferring the Bt ***Cry1Ac*** trait into Bt cotton hybrids held by Mahyco. These seeds are being sold to the cotton growers in the country. Later, they introduced ***Cry2Ab2*** gene which is more tolerant to a wide spectra of insects with more sustainable insect resistant properties into Indian cotton cultivars and sold the transformed hybrids to the farmers. Company also researching to generate plants resistance to herbicide glyphosate using CP4 EPSPS gene.	The original technology of insect resistant Bt cotton gene containing plants was developed by Monsanto and the genetically modified seeds were provided for breeding till stable cultivars were produced after four to six cycles. The seeds were then multiplied and sold through Mahyco-Monsanto to the Indian farmers. Later the seeds containing ***Cry2Ab2*** gene were supplied by Monsanto for transforming the Indian cotton cultivars. All the products are in the market.
	Rasi Seeds Company Ltd., Tamilnadu purchased the transgenic seeds containing ***Cry1Ac*** as well as ***Cry2Ab2*** genes from Monsanto-Mahyco and transformed their parental cotton lines to contain the above genes. The stable hybrids produced are being marketed.	Monsanto –Mahyco supplied the ***Cry1Ac*** and ***Cry2Ab2*** genes containing cotton seeds, which were the properties of Monsanto U.S.A. to Rasi Seeds Ltd.

Bt Cotton (Continued)	Nath Seeds Ltd. Aurangabad obtained cotton seeds containing insect resistant genes GFM ***Cry1A*** and transformed their parental cotton cell lines with these. The stable hybrids produced therefrom are being sold to the cotton growers.	The technology was taken from Biocentury Transgene Company, China.
	Syngenta India Ltd., Pune has introduced insect resistant cotton seeds containing Vip-3 gene. This gene codes for a toxic protein similar to Bt ***Cry1Ac***. Syngenta India transferred the gene to its parental cotton lines and produced hybrids which are being sold in the market.	Syngenta India obtained the original technology from its parent company.
	Ankur Seeds Ltd., Nagpur, purchased the transgenic seeds containing ***Cry1Ac*** as well as ***Cry2Ab2*** genes from Monsanto-Mahyco and transformed their parental cotton lines to contain the above genes. The stable hybrids produced are being marketed.	Monsanto –Mahyco supplied the ***Cry1Ac*** and ***Cry2Ab2*** genes containing cotton seeds to Ankur Seeds Ltd, which were the properties of Monsanto U.S.A.
	Krishidhan Seeds Ltd., Jalna purchased the transgenic seeds containing ***Cry2Ab2*** gene from Monsanto-Mahyco and transformed their parental cotton lines to contain the above gene. The stable hybrids produced are being marketed.	Monsanto –Mahyco supplied the ***Cry2Ab2*** gene containing cotton seeds to Krishidhan Seeds Ltd, which were the properties of Monsanto U.S.A.
	Ajeet Seeds Ltd., Aurangabad purchased the transgenic seeds containing ***Cry1Ac*** gene from Monsanto-Mahyco and transformed their parental cotton lines to contain the above genes. The stable hybrids produced are being marketed.	Monsanto –Mahyco supplied the ***Cry1Ac*** gene containing cotton seeds to Ajeet Seeds Ltd, which were the properties of Monsanto U.S.A.
	JK Seeds, Secunderabad, purchased the transgenic seeds containing ***Cry1Ac*** gene from BREF-Bioteck, IIT, Kharagpur & UDSC New Delhi and transformed their parental cotton lines to contain the above gene. The stable hybrids produced are being marketed.	The technology was developed at IIT Kharagpur by BREF-Biotek & UDSC New Delhi.
	Nuziveedu Seeds Co. Ltd., Hyderabad purchased the transgenic seeds containing ***Cry1Ac*** gene from Monsanto-Mahyco and transformed their parental cotton lines to contain the above genes. The stable hybrids produced are being marketed.	Monsanto –Mahyco supplied the ***Cry1Ac*** gene containing cotton seeds to Nuziveedu Seeds Ltd, which were the properties of Monsanto U.S.A.
	Public Sector Institutions	
	Central Institute for Cotton Research, Nagpur is developing plants resistant to lepidopteran pests using Bt***. cry*** genes.	
	National Botanical Research Institute, Lucknow has developed transgenic plants resistant to ***Spodopotera litura*** and ***Heliothisis armigera*** using ***Cry 1E*** and ***Cry 1C*** with terminal altered at C-end.	All the genes have been outsourced.
Rice	**Private Sector Units**	
	Mahyco, Mumbai is generating plants resistant to lepidopteran pests, bacterial blight and sucking pests using genes namely ***CrylAc, Xa21*** and ***GNA*** genes	All the genes have been outsourced.
	Mahyco Research Foundation, Hyderabad is generating plants resistant to bacterial blight using Bacterial blight resistance conferring gene ***Xa-21***	The gene has been outsourced.

Rice (continues)	Hybrid Rice International, Guragaon is generating plants resistant to lepidopteran pests and herbicide tolerance using ***CrylA(b)*** and ***Cry9C*** for insect resistance and bar genes for herbicide tolerance.	The genes have been outsourced.
	Public Sector Institutions	
	Bose Institute, Kolkata is generating plants tolerant to stress using genes coding for S-adenosylmethionine.	The gene has been outsourced.
	Centre for Cellular and Molecular Biology, Hyderabad is generating herbicide-tolerant plants using ***bar*** genes.	The gene has been outsourced.
	Central Rice Research Institute, Cuttack is developing plants resistant to lepidopteran pests, bacterial blight/ disease using Bt***. crylA(b)*** and ***Xa21***	The genes have been outsourced.
	Delhi University, South Campus, New Delhi is generating plants tolerant to flooding using genes coding for Pyruvate decarboxylase and alcohol dehydrogenase. They are also developing plants resistant to biotic and abiotic stresses using ***Coda*** and ***Cor47*** genes.	The genes have been outsourced.
	Directorate of Rice Research, Hyderabad Is generating plants resistant to lepidopteran pestsas well as tolerant to bacterial diseases using ***Xa-21***, ***cryLA(b)*** genes.	The genes have been outsourced.
	Indian Agricultural Research Institute, New Delhi is generating plants resistant to lepidopteran pests using genes Bt***.crylA(b)*** and chitinase	The genes have been outsourced.
	IARI sub-station, Shillong is generating plants resistant to yellow stem borer using gene Bt. ***CryLA(b).***	The gene has been outsourced.
	International Centre for Genetic Engineering and Biotechnology, New Delhi is generating plants resistant to gall midge using gene ***Gm2***.	
	Madurai Kamaraj University, Madurai has developed plants resistant to fungal infection using Chitinase, β-1,3-glucanase and osmotin genes.	The genes have been outsourced.
	Narendra Dev University of Agriculture, Faizabad is generating plants resistant to lepidopteran pests using ***CryLA(b)*** gene	The gene has been outsourced.
	Punjab Agricultural University, Ludhiana is generating plants resistant to yellow stem borers using genes Cry ***1Ab*** and Cry ***1Ac***	The genes have been outsourced.
	Tamil nadu Agriculture University, Coimbatore is generating plants resistant to pests gall midge using ***GNA*** gene.	The gene has been outsourced.
Potato	**Public Sector Institutions**	
	Central Potato Research Institute, Simla is generating plants resistant to lepidopteran pests using Bt. ***crylA(b)***	The gene has been outsourced.
	Indian Agricultural Research Institute, New Delhi is generating plants with controlled fruit maturing using genes ACC synthase	The gene has been outsourced
	Jawaharlal Nehru University, New Delhi is generating nutritionally enriched plants using gene ***Ama-L***	The gene was discovered locally.

Tomato	Private Sector Units	
	Indo-American Hybrid Seeds, Bangalore is generating plants resistant to viral and fungal diseases using Alfalfa glucanase and Tomato leaf curl virus genes.	The genes have been outsourced.
	Proagro PGS (India) Ltd, Guragaon is generating plants resistant to lepidopteran pests using gene *CrylA(b*)	The gene has been outsourced from its foreign collaborator.
	Public Sector Institutions	
	Delhi University, South Campus, New Delhi is developing edible vaccine using genes of ***Ctx-B*** and ***Tep*** of Vibrio cholerae	The genes have been outsourced.
	Indian Agricultural Research Institute, New Delhi is generating plants resistant to viral and fungal diseases using gene Bt.***crylA(b).*** They are also generating plants with controlled fruit ripening using ***ACC synthase***.	The genes have been outsourced.
	Indian Institute of Horticultural Research, Bangalore is generating plants resistant to leaf curl virus using Leaf curl virus sequence and also generating plants resistant fungal disease using ***Chitinase*** and ***glucanase*** genes.	The genes have been outsourced.
	Jawaharlal Nehru University, New Delhi is generating plants resistant to fungal infection using ***OXDC*** gene.	The OXDC gene (oxalate decarboxylase) was discovered by the university.
Corn/Maize	**Private Sector Units**	
	MAHYCO, Mumbai is generating plants resistant to lepidopteran pests using ***CrylA(b***) gene.	The gene has been outsourced
	Syngenta India Ltd, Pune is also generating plants resistant to lepidopteran pests using gene ***CrylA(b***)	The gene has been procured from its parent company.
Brinjal/Eggplant	**Private Sector Units**	
	Proagro PGS (India) Ltd, Guragaon is generating plants resistant to lepidopteran pests using ***Cry1A(b)*** gene.	The gene has been outsourced.
	Delhi University, South Campus, New Delhi is generating plants resistant to diseases using genes encoding Chitinase, glucanase and thaumatin.	The genes have been outsourced.
	Indian Agricultural Research Institute, New Delhi is also generating plants resistant to lepidopteran pests using gene Bt. ***CrylA(b).***	The gene has been outsourced.

Mustard	**Private Sector Units**	
	MAHYCO, Mumbai is generating plants tolerant to herbicide using gene ***CP4 EPSPS.***	The gene has been outsourced.
	Proagro PGS (India) Ltd, Guragaon is developing superior hybrid cultiovars using genes like Bar, barnase and barstar.	The genes have been outsourced.
	Public Sector Institutions	
	Delhi University, South Campus, New Delhi is generating herbicide-tolerant plants, male-sterile and restorer lines for hybrid seed production using genes Bar, barnase and barstar.	The genes have been outsourced.
	Indian Agricultural Research Institute, New Delhi is generating stress-tolerant plants using Arabidopsis annexin gene and also generating abiotic stress-tolerant plants using genes coding for Choline dehydrogenase. They are further generating plants resistant to fungal diseases using genes for chitinase, glucanase and RIP.	The genes have been outsourced.
	Tata Energy Research Institute, New Delhi is generating plants containing high levels of β-carotene using Ssu-maize Psy and Ssu-tpCrtl genes.	The genes have been outsourced.
Pigeonpea	Private Sector Units	
	MAHYCO, Mumbai has started transformation work using selectable marker ***GUS*** gene.	The gene has been outsourced.
	Public Sector Institutions	
	Indian Agricultural Research Institute, New Delhi is generating plants resistant to bollworms and aphids using ***Protease inhibitor*** and ***lectin*** genes	The genes have been outsourced.
Cauliflower & Cabbage	**Private Sector Units**	
	Proagro PGS (India) Ltd, Guragaon was experimenting to generate cauliflower & cabbage plants resistant to lepidopteran pests using ***CrylH/cry9C***. They were also developing superior hybrid cultivars of cauliflower using ***Bar, barnase*** and ***barstar*** genes.	The genes have been outsourced
	Public Sector Institutions	
	Indian Agricultural Research Institute, New Delhi is generating Cauliflower & Cabbage plants resistant to Plutella scylostella using Bt.***crylA(b)*** gene	The genes have been outsourced.
Chickpea	Public Sector Institutions	
	International Crop Research Institute for Semi-Arid Tropics, Hyderabad is generating plants resistant to fungal pathogens using gene ***PGIP***.	The gene has been outsourced.
	AAU, Jorhat is generating plants resistant to bruchids (small beetles) using ***Bean alpha AI*** gene.	The gene has been outsourced.
Groundnut	**Public Sector Institutions**	
	International Crop Research Institute for Semi-Arid Tropics, Hyderabad is generating groundnut plants resistant to peanut clump virus (PCV) through transferring the ***coat protein*** and ***polymerase*** gene of the Indian PCV through Agrobacterium tumefaciens.	The gene has been outsourced.

Black-gram	**Public Sector Institutions**	
	Madurai Kamaraj University, Madurai is developing viral-resistant plants using ***coat protein*** and ***replicase*** genes of Vigna mungo yellow mosaic virus. They are also developing insect resistant and herbicide-tolerant plants using ***dianthin*** and ***bar*** genes respectively.	The genes have been outsourced
Wheat	**Public Sector Institutions**	
	Delhi University, South Campus, New Delhi are developing plants resistant against biotic and abiotic stresses using ***Bar***, ***HV AI*** and ***PIN2*** genes.	The genes have been outsourced
Banana	**Public Sector Institutions**	
	Indian Agricultural Research Institute, New Delhi is developing plants with controlled fruit ripening using genes for ***ACC synthase***	The gene has been outsourced.
Coffee	**Public Sector Institutions**	
	Madurai Kamaraj University, Madurai is developing plants resistant to fungal infection using ***chitinase, β-1,3-glucanase*** and ***osmotin*** genes.	The genes have been outsourced
Muskmelon	**Public Sector Institutions**	
	Indian Institute of Horticultural Research, Bangalore are developing edible vaccines of Muskmelon using ***Rabies glycoprotein*** gene.	All the genes have been outsourced.
	University of Agriculture Sciences, Bangalore are also developing edible vaccines using ***Rabies glycoprotein*** gene	All the genes have been outsourced.
Tobacco	Public Sector Institutions	
	Central Tobacco Research Institute, Rajajmundry is generating plants resistant to Helicoverpa armigera and Sodotera litura using genes Bt. ***crylA(b)*** and ***cryIC***	All the genes have been outsourced.
	Indian Agricultural Research Institute, New Delhi is generating plants resistant to fungal attack using genes for ***chitinase***, ***glucanase*** and ***RIP***.	All the genes have been outsourced.
	International Centre for Genetic Engineering and Biotechnology, New Delhi is generating plants resistant to Spodoptera litura using gene Bt. ***Crylla5***	
Industrial and Other Products	Several Institutes are working to produce enzymes from recombinant organisms. The enzymes being utilized are xylanase and different kinds of proteases, lipases, cellulases, amylases and rennin (for cheese making) and certain enzymes for molecular biology research.	The efforts are indigenous and the genes are being isolated and inserted into different kinds of organisms especially of fungal nature. East India Pharmaceuticals Ltd., Kolkata is trying to increase the copy number of alpha amylase in one fungal system.

In this context, it is necessary to look at the developmental scenario across the world in modern biotechnology. Gene splicing, creation of host compatible constructs initially in prokaryotic organisms followed by using eukaryotic cells for the transcription, translation and post-translational modification to create near natural equivalents of bio-active proteins in 1970s and 1980s revolutionized drug therapy. The decades of 1980 and 1990 had seen phenomenal growth in the production of bioactive therapeutics; the trend is being and would be maintained during another two decades. Concurrently, a large number of technology platforms have been created from increased understanding of signal transduction pathways of cells and tissues; the development of high-throughput screens that provide a wide array of information that facilitate the search for clinically useful compounds; and better understanding of cell based immune rejection thereby facilitating the possibilities of interrupting or delaying rejection, which in turn shall make allotransplantation as well as xenotransplantation of organs increasingly feasible. Stem cell culture, tissue engineering and tissue transplantation are emerging as alternative solutions to organ failure. In agriculture, transgenic plants are expected to ease agricultural production with reduced use of chemical pesticides as well as reduced usage of fertilizers and water; several designed crops are expected to emerge that are nutritionally superior. The environmental pollution problems are expected to be addressed more efficiently by the use of engineered microbes and plants. Biochips are expected to contribute to simple and easy-to-use diagnostic kits for detecting genetic disorders, discovering new drugs and research applications. Proteomics would shed light to genome-encoded events and would contribute to drug discovery and research. Bio-informatics would facilitate the progress of research in pharmacogenomics, biochips and data mining. The lead biotech platforms are combinatorial chemistry, proteomics, biochips, pharmacogenomics, tissue engineering, allotransplantation, xenotransplantation, genetically modified plants and other agricultural biotechnology. Several products and services are expected to be emerging from each of these platforms.

[T]he actual sales of top 25 biotech companies in the world for the year 2005 was reported to be US$40 billion

The global picture of production and use of modern biotech products is very wide .The major health care products already approved globally with their annual sales turnover is placed below[21] in Table 8.

In this context the actual sales of top 25 biotech companies in the world for the year 2005 was reported to be US$40 billion reported below in tabular form along with the year of establishment and country of origin. Interestingly, the table below shows that 25 companies of the world held about 82% of global sales[22] for the year 2005. This indicates that biotech products will remain monopolized by a very small number of players for some time in the future until there is adequate global development.

Table 8: The global major biotech products market by class 2001, 2002, 2005 and projections for 2010.

Class	Sales 2001 (US$m)	Sales 2002 (US$m)	Sales 2005 (US$m)	Estimated Sales 2010 (US$m)
Erythropoietins	6,702	8,426	12,815	17,350
Interferons	3,923	5,731	6,635	8,470
Insulin	3,949	4,400	5,800	10,340
Monoclonal antibodies	2,997	4,150	9,120	18,200
Blood factors	3,188	3,565	4,985	6,360
Colony stimulating factors	2,059	2,739	4,630	5,910
Growth hormones	1,652	1,703	1,860	2,050
Interleukins	173	213	390	630
Growth factors	108	123	180	360
Therapeutic vaccines	50	68	170	340
Others (calcitonins, enzymes, TNF, etc.)	2,080	2,222	2,600	7,000
Total	**26,881**	**33,340**	**49,185**	**77,010**

Table 9: Sales of Leading Biotechnology Companies - 2005 (US$millions).

	Company/Country/Year Founded	Sales – 2005
1	Amgen (U.S. - 1980)	$12,430
2	Genentech (U.S. - 1976)	$6,633
3	Genzyme (U.S. - 1981)	$2,735
4	Serono (Switzerland - 1906)	$2,586
5	CSL (Australia - 1961)	$2,494
6	Biogen Idec (U.S. - 2003)	$2,422
7	Gilead Sciences (U.S. - 1987)	$2,028
8	Chiron (U.S. - 1981)	$1,920
9	MedImmune (U.S. - 1988)	$1,244
10	Cephalon (U.S. - 1987)	$1,212
11	Millennium Pharmaceuticals (U.S. - 1993)	$558
12	Celgene (U.S. - 1980)	$537
13	Actelion (Switzerland -1997)	$533
14	Elan (Ireland - 1969)	$490
15	ImClone Systems (U.S. - 1984)	$384
16	PDL Biopharma (U.S. -1986)	$280
17	MGI Pharma (U.S. - 1979)	$279
18	AEterna Zentaris (Canada - 1991)	$247
19	QLT (Canada - 1981)	$242
20	Ligand Pharmaceuticals (U.S. - 1987)	$177
21	OSI Pharmaceuticals (U.S. - 1983)	$174
22	Enzon Pharmaceuticals (U.S. - 1981)	$166
23	Vertex Pharmaceuticals (U.S. - 1989)	$161
24	Amylin Pharmaceuticals (U.S. - 1987)	$141
25	Berna Biotech (Switzerland - 1898)	$137
	TOTAL TOP 25	$40,036

The above table depicts monopolistic market dominance (obviously through pricing dictated for their IPR protected products) by a handful of companies. This situation may be different for a small number of biogenerics, which will be available from multi-sources in plentiful quantities at competitive prices.

This global monopolistic situation needs to be understood in order to improve the local situation of the developing countries, including India. Monopoly is in mainly from IPR protected products. Such products are the gifts of R&D. In order to understand the dynamics of research across the globe for capturing the major market share it is necessary to analyze what research work is presently going on worldwide. Admittedly, the above 25 companies and a few others are leading global research with a view to establishing new frontiers in the fast growing, potentially competitive market scenario. The development taking place globally in terms of emergence of new products in various areas in the health care products arena[23] is described in Table 10.

Table 10: Number of biotechnology drugs in development.

BIOTECHNOLOGY MEDICINES UNDER DEVELOPMENT BY THERAPEUTIC CATEGORY (up to Dec. 2006)	
Therapeutic Category	**No. of Drugs**
AIDS/HIV/Infection/Related Conditions	22
Autoimmune Disorders	44
Blood Disorders	10
Cancer/Related Conditions	210
Cardiovascular Diseases	22
Diabetes/Related Conditions	15
Digestive Disorders	14
Eye Conditions	6
Genetic Disorders	9
Growth Disorders	4
Infectious Diseases	50
Neurologic Disorders	17
Respiratory Disorders	13
Skin Disorders	7
Transplantation	4
Other	18
Total	**465**

Some details about pipeline drugs targeting/interrupting specific signals or conditions are enumerated below' along with the major companies involved in the development.[24]

Table 11: Biotechnology medicines in development by therapeutic category.

BIOTECHNOLOGY MEDICINES IN DEVELOPMENT BY THERAPEUTIC CATEGORY	
In each therapeutic category several kinds of approaches to produce a wide spectra of drugs are listed below along with the major companies involved in research	
1. AIDS/HIV/Infection/Related Conditions	
MAbs	
Various companies have developed approaches for producing different kinds and stretches of humanized MAbs neutralizing gp41, gp120, other epitopes of HIV 1; interfering with T-cell epitopes like CCR5, CD8 or CD4 proteins; which have shown effectiveness in reducing viral load or infectivity.	
Vaccines	
Various kinds of vaccines such as DNA vaccine, therapeutic vaccine, and recombinant vaccine are under developmental stage to boost both cellular and humoral immunity.	
Immune-based therapy	
Several approaches such as whole-inactivated viral antigen with a synthetic Toll-like receptor (TLR-9) agonist, as also synthetic RNA pieces have been used to boost the immune system so as to increase the CD4 T- cell count.	
Gene Therapy	
Antisense RNA genes have been developed that get delivered to HIV infected blood cells and prevent replication of HIV; however complete stoppage of replication may require very high and continuous dosage.	
Recombinant growth hormone	
Such therapy clinically builds body mass and improves physical function in people with HIV-associated weight loss.	
Major Companies	Sanofi-pasteur, GlaxoSmithKline, Hemispherx Biopharma, Polymun Scientific, AlphaVax, Human Genome Sciences, CytoDyn, Merck, Immune Response, Serono, Targeted Genetics, Tanox, GenVec, VIRxSYS etc.
2. Autoimmune Disorders	
MAbs & Polyclonal Abs	
Many autoimmune disorders arise from antibody production via clonal B-cell proliferation or stimulation. Various companies have developed approaches for producing different kinds and stretches of humanized MAbs neutralizing interfering with WBC epitopes like CCR2, CD20 proteins; which have shown effectiveness in MAbs to CD20+ B cells or B-cell stimulators would reduce such cells from circulation; disorders characterized by such CD20+ cells respond to anti-CD20 therapy or to anti B-cell stimulation therapy. With such concepts several MAbs are being developed. Several cytokines mediate inflammation, bone loss etc. Antibodies against them would incapacitate their activities. Many companies have developed MAbs against specific cytokines like receptor activator of NF-κB ligand (RANKL, which is a ligand initiator for bone loss) and other cytokines like TNF alpha, IL-1, IL-6, IL-12, IL-15and IL-23, IFN gamma, IFN alpha etc with the above concept in view. CCR2 sitting on several WBCs plays an important role in their trafficking to sites of inflammation. The recruitment of macrophages to the arterial wall is a critical step in the development of atherosclerosis. Therefore antibodies to CCR-2 would play a role in curing the disease. With this concept certain MAbs against CCR-2 have been developed. MAbs are useful for modulating or inhibiting induced IgE expression in treatment or prophylaxis of disease conditions including allergic conditions, autoimmune diseases and inflammatory diseases.	

Cytokines	
Cytokines are important protein mediators of a wide range of conditions in the body including inflammation, immunity, fibrosis, cell differentiation and cell proliferation. They have therefore, important role to play in the pathogenesis of autoimmune conditions. Cytokines are incessantly produced by inflammatory cells or by the target cells of autoimmune attack. They reflect ongoing inflammatory and mediation processes. Control of the key cytokines is expected to bring relief to different kinds of autoimmune diseases. With these concepts in view several drugs are being devised. Formulations of various interferons like IFNα, IFN beta-1a, Interferon-tau (IFNτ) are being developed. Substances are also under development to control/trap/neutralize certain key cytokines (e.g. IL-1) before they can attach to cell-surface receptors and generate signals that can trigger disease activity in body tissue.	
Recombinant Protein/Receptor	
Formulations of rh-alpha-fetoprotein, an immuno-modulatory serum protein, are being developed to improve the treatment of autoimmune diseases. In another approach, fusion proteins like abatacept & atacicept are selective co-stimulation modulator in rheumatoid arthritis.	
Vaccines	
Analogs of immuno-dominant epitopes of myelin basic protein are exploited to treat certain autoimmune diseases like multiple sclerosis.	
Cell Therapy/ Gene Therapy	
Targeted but localized protein therapy to inhibit the production of certain inflammatory cytokines like TNF alpha in inflammatory cells of autoimmune diseases is an approach for developing new therapy. Several companies are trying to make use of this concept.	
Immune-based Therapy	
Certain nucleic acid compounds including specific form of mismatched double-stranded ribonucleic acid (dsRNA) where uridylic acid (U) substitutions in the polycytidylic acid chain, act as modulators or molecules that mediate cellular immune activities are being developed.	
Major Companies	Abbott Laboratories, Roche, Amgen, Hemispherx Biopharma, Biogen Idec, Centocor, InterMune, Genentech, Bristol-Myers Squibb. Etc.
3. Blood Disorders	
MAbs	
Certain MAbs block cleavage of the C5 component of the complement system, thereby preventing the final stages of complement activation; using this principle a few products are being developed. F(ab')2 fragment of a murine anti-TNF-alpha antibody is associated with controlling sepsis for a considerable period. Hemolytic uremic syndrome (HUS) a type of blood disorder is believed to be resulting from E.coli infection & its toxins, MAbs to these toxins are being developed.	
Recombinant Protein/Hormone/ Clotting Factor	
Recombinant erythtopoietin or its analogs, activators of erythropoietin receptor etc. are under development to enhance the process of erythropoiesis in different kinds of anemias. B-Domain deleted recombinant clotting blood Factor VIII, Coagulation factor XIII & recombinant human thrombin are under development for use in various disorders.	
Major Companies	Abbott Laboratories, Alexion Pharmaceuticals, Roche, NovoNordisk, Zymogenetics, Teijin Pharma Japan, etc.

4. Cancer/Related Conditions
MAbs
MAbs are targeted to interrupt/modulate signals that promote cell division, which is a major manifestation in almost all kinds of cancers. Mabs are also designed to promote apoptosis of targeted cells. The immunogenicity of murine MAbs limits therapeutic use in chronic or recurrent human diseases; hence the need for humanization. MAbs against cell surface markers CD2, CD4 receptor, CD20, CD23, CD30, CD 33, CD40, CD 44 and CD52, CD80 are useful in the treatment of proliferation of lymphocytes in lymphomas. MAbs against various molecules and antigens like MHC (major histocompatibility complex) class II molecule, Prostate Stem Cell Antigen (PSCA), lymphotoxin-β receptor, TRAIL (tumor necrosis factor-related apoptosis-inducing ligand) receptor 2 (TR-2), membrane-bound MUC1 antigen, NF-κB ligand (RANKL), Death receptor 5, HER2 protein receptors, EpCAM, Lewis Y antigen, cytotoxic T-lymphocyte-associated antigen-4 (CTLA4), integrins, cell surface glycoproteins, "GP-3" OR "GP-9", tumor-associated antigen CA125, glycotope N-linked carbohydrate antigen (RAAG12), fibroblast activation protein etc are also under development for various cancers; different kinds of mechanisms are involved. Certain classes of MAbs are designed to capture /interrupt special substances like phospholipids, aminophospholipids, ganglioside GD2, GM2 ganglioside, GD3 ganglioside and destroy the cancerous cells. MAbs are also designed to bind to and inhibit VEGF, hepatocyte growth factor (HGF), transforming growth factor-alpha, insulin-like growth factor-1(IGF-1) receptor, epidermal growth factor receptor (EGFr), vascular endothelial growth Factor receptor-1 OR 2 in order to inhibit tumor cell proliferation; different kinds of mechanisms are involved. MAbs against certain cytokines (IL-6, IL-13) as wells as some of their analogs like an analog of interleukin-2 (IL-2) would modulate the growth of certain types of cancers. MAbs conjugated to radioisotopes like yttrium-90, Iodine 131; targeting several tumors and cell lines expressing various antigens/substances are also being researched. Cytotoxic proteins or toxins combined with precise antibody fragments that target only cancer cells are approaches under development. MAbs attach to the cancer cells and get internalized into the tissues while the radioactive substances/toxins eradicate them.
Vaccines
Several biomolecules have been targeted which are elevated in cancer patients or which are associated with suppression of tumors. Vaccines encoding full length antigens like carcinoembryonic antigen (CEA) or its part, prostate-specific antigen (PSA), whole gp100 antigen or its specific peptide stretches, anti-EpCAM antibody, **p53 tumor suppressor substances, FUS1 tumor suppressor,** MART-1 (melanoma antigen recognized by T-cells), heat shock protein 65 (Hsp65) of ***Mycobacterium bovis*** conjugated with human papilloma viral (HPV) protein E7, vectors expressing human granulocyte-macrophage colony-stimulating factor (GM-CSF) etc are being developed as new products. Various vectors like replication deficient recombinant fowl pox viral vector, and certain co-stimulatory molecules like, (TRICOM) B7.1, ICAM and LFA3 have been used to promote the expression of many of these substances. Another approach uses irradiated autologous melanoma cells modified with the hapten, dinitrophenyl (DNP) for enhanced and specific immune responses.
Gene Therapy
The aim is to enhance the production of such substances that suppresses the tumor cells. In certain cases, cytotoxic T- cell proliferation is aimed to destroy the cancerous cells. In other approaches immune responses of adaptive and innate pathways are boosted to enable the body to fight back. For all these activities different kinds of vectors have been used that are less toxic and are replication deficient.

Gene Therapy (continued)

Genetically engineered vectors expressing various proteins like wild-type p53 (a tumor suppressor), **mda-7 (a tumor suppressor),** HLA-B7 and ß2 microglobulin, (which together form a Class I Major Histocompatibility Complex, or MHC-I antigen), tumour associated antigen (5T4), CYP1B1, thymidine kinase (tk) , IL-2, IL-12, TNF-alpha, IFN-gamma, HPV type 16 E6 and E7 antigens or MUC1 tumour-associated antigen along with IL-2,etc have been used to develop substances for tumor treatment.

In an interesting concept, human peripheral blood lymphocytes (PBL) or TIL (Tumor infiltrating Lymphocytes) were isolated from a melanoma patient and were engineered to react with the melanoma antigen MART-1 (Melanoma Antigen Recognized by T cells, also called Melan-A) or melanoma antigen glycoprotein 100 (gp100) or to code for IL-2. These PBLs are transfected with a retroviral vector encoding anti-MART-1/anti-gp100 specific T-cell receptors etc, grown in culture, and then transferred back to the patients. These genetically modified PBL or TIL may recognize and halt the growth of MART-1/gp100-expressing melanoma cells. These cells require IL-2 to sustain them when they are transferred back to the patient. With the above concept some drugs are under development.

Gene therapy with dominant negative mutant of the human cyclin-G1 gene, a powerful, essential, and early part of the cell cycle control pathway, results in targeting and aborting the early regulatory components of the cancer cell's universal replication machinery. Some products are under development.

Recombinant Proteins

Cancer cells draw heavily from the bodily nutrients for fast cell division; they require generating new blood vessels within their tissues for drawing nutrients; interruption of angioproteins could hinder the development of new blood vessels. Recombinant Fc-peptide fusion protein (peptibody) targeting angiopoietins or the recombinant proteins derived from the non-collagenous domain of type IV collagen that has anti-angiogenesis properties are examples of these categories. Several types of cancer cells express HER-2 growth factor and therefore, interruption of this protein could control cancer cell growth. Protein vaccines that wipe out HER-2 growth factor are under development. Certain substances like GM –CSF assist in recognition of cancer cells by the immune system; therefore, agents secreting such substance could be beneficial in cancer treatment. Engineered form of HSV **expressing GM-CSF is under development; the recombinant HSV** has tumor selectivity and ability to get the infected tumor cell to be detected by the immune system. Cancer patients treated with highly toxic drugs would benefit if substances could be used that reduce the toxicity of such drugs. Generally, with these ideas several drugs are under development; recombinant glucarpidase is an example where this is being developed to quickly clear the concentrations methotrexate from the blood. Designer molecules consisting of multiparts where one part targets the cancer and other part is a toxin for that cancer are also under development; a single molecule composed a tumor-targeting molecule (IL13) and a cytotoxic agent (PE38) is an example. human keratinocyte growth factor (KGF), MAGE-A3, recombinant human Insulin-like Growth Factor Binding Protein-3, soluble form of the TACI receptor are other examples of recombinant protein based drugs under development.

Immune Therapy

Active immunotherapy platforms have been created to stimulate a patient's own immune system by using various competent molecules; the primary aim is to enable the body to fight the cancer cells by cytotoxic T-lymphocytes as well as by other innate mechanisms. Short synthetic DNA molecules (a single-stranded, 22–base pair (bp) immunostimulatory phosphorothioate) signalling through TLR-9 to suppress Th-2 response and stimulate Th-1 response is one example. Non-toxic peptide combined with nucleic acid and a group of long and short synthetic peptides derived from Wilms tumor antigen 1 (WT1) mixed with adjuvant are other examples which have been tried. Certain immunotherapies have been tried to target various antigens like prostate cancer antigen, prostatic acid phosphatase or HER2/neu by delivering them to Antigen Presenting Cells.

Cytokines	
Cytokines have been used to treat a variety of cancers. They stimulate the normal immune response to fight disease. When a patient is injected with a cytokine, the immune system is activated throughout the body, rather than just at the tumor site. In the process cytotoxic T- cells proliferate to recognize and destroy the cancer cells. The cytokine based therapies that are under development for treating cancers include IL-3, IL-12, IL-18, IL-21, alfa interferon, TNFa . In another approach fusion proteins consisting of an antibody attached to a cytokine are under investigation to combine the specificity of an antibody with the powerful immune-stimulating features of cytokines.	
Major Companies	National Cancer Institute USA, Introgen Therapeutics, Vical, Amgen, Biogen Idec, Genentech, Sanofi-Aventis, Boehringer Ingleheim Pharmaceuticals, Centocor, Cambridge Antibody Technology UK, Chiron, Wyeth, Pfizer, Daiichi Sankyo Japan, Bristol-Myers Squibb, GlaxoSmithKline, Cell Genesys, Human Genome Sciences, Genmab, Aphton Biopharma, NeoPharm, ImClone Systems, Immunomedics, Introgen Therapeutics, Eli Lilly, Medarex, YM Biosciences, Isis Pharmaceuticals, Seattle Genetics, Telik, Transgene, Cell Therapeutics, MGI Pharma etc.
5. Cardiovascular Disease	
MAbs	
The recruitment of macrophages and monocytes to the arterial wall is believed to be a critical step in the development of arteriosclerosis. CCR2 plays an important role in accelerating the trafficking of monocytes and macrophages to sites of inflammation. In cardiovascular diseases, arterial inflammation in the heart is a manifestation of symptoms. Therefore, humanized monoclonal antibody, specifically targeting CCR2 receptors (found on the surface of macrophages and monocytes) could be useful. Some products are being developed with this concept. In another concept, certain serum glycoproteins, like the complement factors, that normally exist in inactive form get activated and stimulate the inflammatory response. MAbs are being developed to bind to complement C5 and block the production of the downstream inflammatory byproducts, substantially reducing white blood cell activation. Through this process, myocardial infarction can be minimized.	
Gene Therapy	
Blood vessels in the ischemic tissues are blocked because of various disease conditions. Therefore, building new alternate blood vessels may bring about normal blood flow to the tissues. With this idea, genes are being constructed that promote the production of certain factors that contribute to building alternate blood vessels. Genes encoding for Vascular endothelial growth factor (VEGF) and its different forms, developmentally regulated Endothelial cell Locus-1 (Del-1), different forms of Fibroblast Growth Factors etc. are under development with suitable delivery vehicles in order to promote angiogenesis.	
Growth Factor	
Arterial diseases including the impairment of coronary arteries as well as peripheral arteries create conditions in certain types of cardiovascular diseases where alternate blood vessel growth becomes necessary to provide blood supply to the blocked areas. With this concept in view several substances like recombinant Hepatocyte Growth Factor (HGF), fibroblast growth factor (FGF) etc are being developed.	
Recombinant proteins	
In coronary artery bypass grafting (CABG) surgery) also known as "bypass surgery", blood is rerouted through a separate cardiopulmonary bypass (CPB) machine and the heart is stopped, while the heart is filled with a compatible solution to keep it still and the function of heart and lungs is taken over by the CPB machine. When a patient's blood comes in contact with the artificial surface of the CPB machine, contact activation of the inflammatory cascade may occur. Human plasma kallikrein, is a key enzyme in the inflammatory cascade, which is a relevant target during CABG surgery. Recombinant proteins with high affinity and specificity for human plasma kallikrein are being designed to inactivate this process of inflammation. In another approach recombinant proteins that inhibit the complement factors so as to minimize the complement-mediated damage following surgery on cardiopulmonary bypass are also being developed.	

Antisense	
Each antisense subunit carries a genetic letter that matches with its pair on the gene target. Several cardiovascular diseases arise from the increased function or dysfunction of genes within the body, either that of pathogens or of one's own genes. When these compounds bind tightly to the disease-causing sequence, the genetic process is inhibited, thus disabling the pathogen or pathogenic process. In coronary diseases reocurrence of stenosis is common. Antisense oligonucleotides targeting the key regulatory gene in restenosis coding for an important proteins can downregulate the production of such proteins and control progression of cell replication in arteries resulting in stenosis. In other approach genes coding for apo-B-100 are being targeted to reduce the production and transport of bad cholesterol, thus is useful in management of cardiovascular disease.	
Vaccines	
There is a need to balance the ratio of LDL cholesterol and HDL cholesterol. Substances that target cholesteryl ester transfer protein (CETP), which is responsible for converting HDL to LDL is blocked so that the balance is maintained. With this concept a vaccine based product is being developed that targets antibodies against this CETP.	
Major Companies	Amylin Pharmaceuticals, Genzyme, AVANT Immunotherapeutics, Vical Dyax, CardioVascular Therapeutics, Collateral Therapeutics, Daiichi Sankyo, Isis Pharmaceuticals, Alexion Pharmaceuticals, AVI BioPharma, Sanofi-aventis, Ark Therapeutics UK, etc.
6. Diabetes/Related Conditions	
MAbs	
Insulin-dependent diabetes mellitus (IDDM) also called as type 1 diabetes is caused by autoreactive T cells. Such cells have CD3 receptors which on interruption would induce tolerance to autoimmunity and inhibit autoreactive T- cells. In such cases the disease may disappear and insulin loss is minimized. MAbs against CD3 are under development; the best one totally inhibiting the auto-reactive properties would be the best bet.	
Recombinant Insulin	
Combination of rapid acting and intermediate acting soluble recombinant insulin is likely to provide better control of glucose levels. With this invite some products are being developed. In another approach, a recombinant peptide of islet neogenesis gene associated protein (INGAP) is under development; this peptide is expected to increase insulin level and lower blood glucose level more efficiently.	
Growth Factor	
Serious and persistent ulcerations in limbs is a know manifestation in strongly diabetic patients. The increased blood glucose level enable the microbes to colonize and spread at the site of ulceration/wounds. These conditions may require amputation of limbs to save the patient. In such situations agents that help develop new blood vessels and growth are beneficial. Various agents like Vascular Endothelial Growth Factor (VEGF), complex of insulin like growth factor-1 & insulin like growth factor binding protein-3, fibroblast growth factor, platelet-derived growth factor-B, epidermal growth factor etc. are under development.	
Gene Therapy	
Like the use of growth factors, gene delivery systems to transcribe and translate Vascular Endothelial Growth Factor (VEGF) are also being attempted to develop to increase the generation of new blood vessels at the site of diabetic foot ulcers.	
Antisense	
One of the causes of type 2 diabetes is insulin resistance. An enzyme PTP-1B, is a key mediator of insulin resistance. Antisense nucleotides are being developed to prevent the formation of this enzyme.	
Cell Therapy	
Pancreatic islets along with Sertoli cells of the patient are co-transplanted with a view to promote the growth of pancreatic cells so that insulin production and secretion is enhanced. Obviously such treatment is to be carried out on patients where there is enough reserve of these cells.	

Vaccine	
In type 1 diabetic patients inflammatory interferon-gamma-producing T helper (Th)1 lymphocytes are being deregulated so that they do not recognize the insulin B chain epitope coded between amino acids B(9-23). This principle is exploited in developing a protein that would down-regulate the Th1 lymphocytes.	
Miscellaneous	
Glucagon-like peptide-1 (GLP-1) secreted from intestines promotes body to make more insulin. Its analogs can mimic the effect and can help to control diabetes (Type 2). In another approach orally-administered agents that inhibit 11-beta hydroxysteroid dehydrogenase type 1 (11ß-HSD1), an enzyme associated with conversion of cortisone to cortisol in the liver, are used to minimize the excessive hepatic glucose production in hyperglycemia.	
Major Companies	Amgen, MacroGenics, Sertioli Technologies, Amylin Pharmaceuticals, Isis Pharmaceuticals, Novo-Nordisk, Genentech, Johnson & Johnson, TolerRx, Corautus Genetics etc.
7. Infectious Diseases	
MAbs	
In order to control the antigen concentration in various life threatening microbial infections, MAbs and poly Abs in combination with MAbs are being investigated. MAbs against protective antigen of ***Bacillus anthracis,*** fungal heat shock protein 90, lipoteichoic acids of ***staphylococcus***, ***S. aureus*** adhesion protein clumping factor A, F protein of respiratory syncytial virus, aminophospholipids whereas, Poly Abs and a combination of MAbs against E2 envelope protein of HCV are under development.	
Vaccines	
Different kinds of vaccines against several diseases are also under development. These include modified attenuated influenza virus, attenuated form of the bacterium ***Vibrio cholerae*** , gene sequence that produces certain proteins found in ***B. anthracis***, phosphoprotein 65 and glycoprotein B of CMV, gene sequence without virulent genes of ***Salmonella typhi*****,** chimeric bovine PIV type 3 (PIV3) that expresses human. PIV fusion (F) and hemagglutinin-neuraminidase (HN) proteins, as well as RSV F protein, DNA-particle mediated epidermal delivery encoding four specific HSV-2 antigens, polyepitope vaccine with MVA for HBV etc.	
Recombinant Vaccines	
Recombinant proteins are being developed that stimulate both adaptive and innate immunity. Several approaches are being tried which include selection of antigen responsible for most of the neutralizing antibodies stimulated by Epstein-Barr Virus; **recombinant hemagglutinin proteins derived from the flu strains;** virus-like particles for the prevention of human papillomavirus; recombinant protein that fuses a part of the ***P falciparum*** circumsporozoite protein with the hepatitis B surface antigen; gD2 subunit of herpes virus together with an adjuvant; novel cell surface proteins of ***pneumococci***; protective antigen of anthrax; fusion protein (Mtb72F) formulated with an adjuvant for tuberculosi; live attenuated Varicella Zoster virus propagated in MRC_5 human diploid cells etc.	
Cytokines	
Interferons are being expressed in different host systems to produce different formulations to combat viral infections. Interferon-alpha is being produced in aquatic plant ***Lemna;*** alfa interferon fused with albumin is another approach. Oral and inhalable interferon-alpha are other delivery technologies under development. Recombinant Interferon-omega (also called interferon-alpha-II1) is being developed to control viral infections.	
Recombinant Proteins	
Various approaches like development of human heat shock protein (HSP) complexed with 32 synthetic peptides of various HSV-2 proteins for genital herpes, **neuraminidase as additive to influenza vaccines,** human Mannose-Binding Lectin (rhMBL), a protein therapeutic for severe infections in MBL deficient individuals undergoing chemotherapy, tissue factor pathway inhibitor (rTFPI) for severe community-acquired pneumonia are under development.	

Gene Therapy	
IL-1Ra gene therapy, is being investigated to re-establish the cellular immune response to the Hep B infected patients during chronic infection.	
Immune-based Therapy / Cellular Therapy	
Immune based therapies are being developed to enhance the immunity of the patients. Several approaches are being investigated. Hepatitis B surface antigen combined with short synthetic DNA molecules, alpha-epibromide immune regulating hormone for HIV, TB, malaria etc are being developed.	
Major Companies	Human Genome Sciences, Antigenics, Hemispherx BioPharma, Nabi Biopharmaceuticals, NeuTec Pharma England, MedImmune, AVANT Immunotherapeutics, Vical, GlaxoSmithKline, Dynavax Technologies, Protein Sciences, Hollis- Eden, Intarcia Therapeutics, Peregrine Pharmaceuticals, Chiron, CuraGen, etc.
8. Growth Disorders	
Growth Hormone	
Several formulations of hGH are used to correct growth disorders using various approaches are under development. Formulations are being developed which are injectable as well as oral.	
Recombinant Growth hormone	
Oral formulations using various expression systems producing recombinant human growth hormone (rhGH) are under development.	
Major Companies	Altus Pharmaceuticals, Skye Pharma, EmiSphere Technologies, LG Lifesciences S.Korea, etc
9. Neurologic Disorders	
MAbs & recombinant antibody	
Among the neurologic disorders Alzheimer's disease is most prevalent as this is also age related. Presently, a large population of aged people is seen in every society. In this disease excess of beta-amyloid aggregates and forms plaques inside the brain. MAbs against beta-amyloid are considered as potential candidates for controlling the disorder. Pain is another severe cause of discomfort in several conditions including osteoarthritis. MAbs against nerve growth factor stop it from stimulating nociceptors and help in controlling pain. Recombinant antibody against myostatin for the treatment of muscular dystrophy is under development.	
Various Other Agents	
Several other agents like an anti-amyloidotic agent is believed to act by reducing the deposition of amyloid by binding to soluble Aß peptide in Alzheimer's disease; recombinant plasminogen activator a highly specific to fibrin and which is non-neurotoxic for acute stroke treatment; etc. are under development. For the diagnosis of Parkinson's disease(PD), which is a neurodegenerative movement disorder characterized by the loss of dopamine-producing neurons in the brain, agents like E isomer of [123I]-2b-carbomethoxy-3b-(4-fluorophenyl)-N-(1-iodoprop-1-en-3-yl)nortropane (E-IACFT) a ^{123}I-labeled small molecule with high selectivity for the Dopamine Transporter (DAT) is being developed as an early diagnosis for PD.	
Immune-based Therapy	
Accumulation of the amyloid-b (Ab) plaque in the cerebral cortex is a critical event in the pathogenesis of Alzheimer's disease. Therapeutic antibodies that would bind and clear beta-amyloid is one approach of drug development. In another, antibodies specific for amyloid b peptide (Aβ peptide) are developed which are soluble and can clear plaque in Alzheimer's disease.	

Gene Therapy	
In Alzheimer's disease cognitive loss of neurons occur. Agents that can prevent such loss are one approach of new drug development; genes have been constructed to express nerve growth factor which would prevent loss of neurons in Alzheimers. To restore lost motor function and to protect against further losses in Parkinson's disease, genes have been constructed that express neurturin or glutamic acid decarboxylase. In case of Duchenne muscular dystrophy genes have been constructed that express a protein dystrophin for allowing preservation of the muscle fibres.	
Cell therapy	
Parkinson's disease is characterized by the loss of dopamine-producing neurons in the brain. One approach involves injection of micro-carriers with retinal pigment epithelial (RPE) cells into the brain, to provide a localized continuous source of dopamine in brain regions deficient in dopamine for treatment of Parkinson's disease.	
Major Companies	Boston LifeSciences, Wyeth, Neurochem, Elan, Ceregene, Forest Laboratories, Transgene, Rinat Neurosciences, Titan Pharmaceuticals etc.
10. Respiratory Disorders	
MAbs	
Allergic inflammation of the airways is promoted by secretion of several cytokines and inflammatory substances. Therefore, MAbs against them may provide relief as these agents would not be able to escalate the inflammatory process. With this idea in view MAbs against IL-4, IL-8, IL-9, IL-13, IL-15, IgE, IL-2 receptor, monocytic chemotactic protein-1(MCP-1) are being developed. In another approach MAbs against specific tissue factor (a component of the extrinsic coagulation pathway), is being developed for providing relief in acute respiratory distress syndrome.	
Antisense Gene Therapy	
Lead understanding has revealed the commonality of sequences shared by cellular receptors for several inflammatory mediators like IL-3, IL-5, RANTES, GM-CSF, eotaxins 1,2,3, and Monocyte chemotactic proteins-3 & 4. Therefore, interrupting the common sequence is anticipated to block several such mediators. With this idea in view antisense nucleotide sequences are being developed.	
Recombinant protein	
Multiple recombinant proteins against several substances such as TNF alpha receptor or clara cell secretory protein are being developed to either minimize inflammation or improve lung functioning.	
Immune-based therapy	
Short synthetic DNA sequences in association with immuno-modulating substances are under development to enhance immune responses against foreign pathogens and cancer, and to suppress inflammatory responses caused by allergens.	
Major Companies	Genentech, Topigen Pharmaceuticals, Tanox, Dynavax Technologies, Novartis Pharmaceuticals, Amgen, Protein Design Lab, Wyeth, GlaxoSmithKline etc.
11. Skin Disorders	
MAbs	
Among the skin diseases Psoriasis is a cause of major concern for several individuals. Psoriasis is an immune-mediated, genetic disease of the skin. Several approaches are being tested to bring relief to the infected. MAbs against inflammatory cytokines like TNF alpha, IL12, IL23, and interruption of receptors like CD3 with MAbs are being tested to control the disease.	
Recombinant Protein	
Like MAbs, certain proteins that can bring relief to inflammation in Psoriasis are also being developed through recombinant DNA technology. Examples are rDNA version of human alpha-fetoprotein.	

Antisense	
In Psoriasis, besides local inflammation there is overgrowth of cells at the site which creates discomfort. Antisense drug designed to block the synthesis of insulin-like growth factor-1receptor, (IGF-1R) is expected to control the overgrowth of cells. With this concept Antisense drugs are being developed.	
Growth Factor	
Wound healing on the skin requires angiogenesis for the healing process to occur as more blood flow would facilitate the healing process. Certain growth factors like Fibroblast growth factor-1 are under development to accelerate wound repair on the skin.	
Miscellaneous	
Skin cancers are the results of several impaired factors like damage of the DNA from sun exposure which requires repairing. Drugs enhancing this repair process like DNA repair enzyme T4 endonuclease V entrapped in liposomes are under development for topical application.	
Major Companies	Antisense Therapeutics Australia, Centocor, AGI Dermatics, Abbott Laboratories, Merrimack Pharmaceuticals etc.
12. Transplantation	
MAbs & Polyclonal Abs	
In transplantation process one of the impediments is auto-reactive basis of organ rejection. Certain auto-reactive T cells play a major role. Therefore MAbs are being developed that inhibit the intensity of auto-reactive T cells by blocking their CD3 receptors. In another approach Polyclonal Abs against thymocyte globulin are being developed to suppress immune cells responsible for acute organ rejection in transplantation of renal and liver transplant patients.	
Recombinant soluble receptor	
The immune system's normal response to a transplant is to recognize the new organ as foreign and to signal production of hyperactive T-cells to destroy it. A second, co-stimulatory signal is required before the T-cells attack the transplanted organ. Recombinant substances are being developed which block this co-stimulatory signal process without suppressing the immune system's normal response to viruses and pathogens. An example of this strategy is the development of recombinant fusion protein made up of Fc fragment of a human IgG1 immunoglobulin linked to the extracellular domain of CTLA-4 which is important for T-cell co-stimulation.	
Cell Therapy	
Graft vs. Host Disease (GVHD) is a life threatening immune condition that can affect cancer patients who have received a bone marrow transplant. Mesenchymal Stem Cells (MSCs) have the capacity to form a variety of highly specialized cell types including bone, cartilage, muscle, tendon, fat, liver and many others. Human mesenchymal stem cell therapy is being developed for the treatment of GVHD and to repair damaged tissue. Identification and use of MSCs is an important challenge in this kind of treatment.	
Major Companies	Bristol-Myer Squibb, Johnson & Johnson, Osiris Therapeutics, Genzyme etc.
13. Digestive Disorders	
MAbs	
For treating different disease conditions in digestive disorders various MAbs are being developed. MAbs for treating inflammation in Crohn's disease are being developed to control/block integrin alpha4beta7, CD3, IL12/IL23, TNF-alpha, pegylated anti-TNF alpha etc. In inflammatory conditions of ulcerative colitis MAbs against chemokine IP-10 are under development. In other approaches MAbs against Toxin A and Toxin B of *Clostridium difficle* and other toxin producing organisms are being developed.	

Vaccines	
In digestive disorders a hormone Gastrin 17 is a stimulator of gastric acid secretion and is a growth factor in situations of pancreatic, stomach and colorectal cancers. Substances that would neutralize or scavenge the above hormone are expected to minimize its interaction with disease causing cells. With this concept a vaccine is under development utilizing a chimera of a synthetic peptide and Diptheria Toxoid. The synthetic peptide is partly similar to the natural gastrin 17 hormone and therefore antibodies to the chimera would capture the hormone.	
rDNA	
In inflammatory bowel diseases an analog of glucagon-like peptide-2 (GLP-2) with longer half-life, is being developed that would stimulate growth, proliferation and maintenance of cells, which are lining the gastrointestinal tract. In the process the absorption will be enhanced and mal-absorption disorders can therefore be treated.	
Antisense	
In inflammatory disorders like ulcerative colitis, Cellular Adhesion Molecules like ICAM-1 have been known to be overexpressed on cell surfaces and to influence inflammation through lymphocytes and cell trafikking. An antisense DNA targeted to inhibit expression of ICAM-1 is under development to minimize the inflammation.	
Cell Therapy	
Crohn's disease (CD) is a digestive disorder characterized by inflammation and ulceration of the small intestine and the beginning of the large intestine. Human mesenchymal stem cell (MSC) therapy is under development for the treatment of such inflammatory disorders and to repair damaged tissue. MSCs are derived from healthy adult volunteer bone marrow donors and are universally compatible and may be used without tissue-type matching. MSCs are thought to interact with the immune cells, which help in reducing inflammation and assist in tissue repair.	
Miscellaneous	
Clostridium difficle releases various toxins in the body during infection and damages the intestine. Approaches using non-absorbable polystyrene sulfonate beads that selectively bind the *C. difficle* toxin are under development.	
Major Companies	Abbott Laboratories, Isis Pharmaceuticals, Centocor, Aphton, Medarex, Millenium Pharmaceuticals, PDL BioPharma, Osiris Therapeutics, NPS Pharmaceuticals, Genzyme, Biogen Idec etc.
14. Genetic Disorders	
Gene Therapy	
Several approaches are under evaluation. Alpha 1 AntiTrypsin Deficiency defects (AAT) cause loss of lung function; genes coding for AAT are incorporated through a proper vehicle to treat the disease. A protein known as cystic fibrosis transmembrane conductance regulator (CFTR) is either defective or deficient in cystic fibrosis (CF). Genes coding for the CFTR protein are under development for delivering with appropriate vehicles at the deficient cell sites. Other genes with delivery mechanisms are under development to produce iduronate-2-sulfatase in case of hunter syndrome and glucocerebrosidase in Gaucher disease.	

Recombinant Protein	
Hereditary angioedema (HAE) is an acute inflammatory condition characterized by painful swelling affecting the extremities (hands, feet, face, etc.), the gastrointestinal tract, the genitalia, and the larynx. The disease is caused by the deficiency of C1 esterase inhibitor (C1-INH), which is a naturally occurring molecule that inhibits kallikrein. Kallikrein is a key enzyme in the inflammatory cascade affecting the above extremities of the body. Recombinant small proteins are under development that inhibits kallikrein to prevent the above disease conditions. Inflammation in the airways of Cystic Fibrosis patients is characterized by persistent and excessive neutrophil infiltration, which release large quantities of destructive oxidases and proteases, including human Neutrophil Elastase (hNE). Recombinant small proteins are under development that inhibits neutrophil elastase for controlling the inflammatory process.	
MAbs	
Paroxysmal nocturnal hemoglobinuria (PNH) is a chronic disease where a portion of a patient's oxygen-carrying red blood cells (RBCs) are missing the normally present complement inhibitors. Therefore, such RBCs are abnormally fragile and get destroyed by normal complement activation. MAbs against C5 complement component are under development which are anticipated to block the complement-mediated destruction of PNH red blood cells.	
Cell Therapy	
Neuronal ceroid Lipofuscinosis (NCL) is a rare neurodegenerative disease that affects infants and young children. It is characterized particularly by the lack of two enzymes namely, palmitoyl-protein thioesterase 1 (PPT1) and tripeptidyl peptidase I (TPP-I). Human central nervous system stem cells have been shown to produce both the PPT1 and TPP-I enzymes. Therefore such stem cells are under isolation and use for treating NCL.	
Enzyme Replacement Therapy	
Several enzymes are produced and delivered into the digestive system from pancreas. Deficiencies in pancreas result in diminished availability of such enzymes and are manifested through conditions of malabsorption and diminished digestion. In order to correct such situation mixtures of enzymes such as lipase, protease, and amylase are being produced and delivered orally to benefit the affected patients.	
Major Companies	Applied Genetic Technologies, Copernicus Therapeutics, Dyax, Shire, StemCells, Alexion Pharmaceuticals, Altus Pharmaceuticals etc.
15. Eye Conditions	
MAbs	
Uveitis is an inflammation of the uvea. The uvea is the layer of the eye between the sclera and the retina. Inflammation is caused primarily though inflammatory mediators like TNF alpha. Therefore, MAbs against TNF alpha are being developed to treat uneitis. "Wet" type of age-related macular degeneration (ARMD), a common form of age-related vision loss is characterized by growth of new leaky blood vessels resulting in excessive fluid leakage in eye. MAbs against VEGF are under development to resist/prevent vision loss caused by ARMD.	
Gene Therapy	
In ARMD the growth of abnormal blood vessels in the center portion of the retina (the macula) occurs which results in loss of vision. This can be prevented by gene delivery method wherein a genetically modified adenovector containing genes coding for Pigment Epithelium - Derived Factor (PEDF) is delivered at the eye. Once the transgene is expressed, the resulting PEDF facilitates normal blood vessel growth and protects the photoreceptors. The action of VEGF is suppressed. New drugs are developed with the above concept.	

Cell Therapy	
In another approach for ARMD, where the retinal photoreceptors are getting degenerated, genetically modified cells containing genes that express ciliary neurotrophic factor (CNTF) that are embedded in a semi-permeable hollow fibre membrane implant are used. The modified cells draw nutrients from the recipient and continuously secrete the CNTF which diffuses out and activates dying retinal photoreceptors and protects them from degeneration.	
Miscellaneous	
Active substances derived from ***Combretum caffrum*** tree have been found to target VEGF and prevent it from forming leaky blood vessels in macular degeneration disorders of the eye. Formulations are under development.	
Major Companies	OXiGENE, GenVec, Centocor, Genentech, Neurotech, Regeneron Pharmaceuticals etc.
16. Others	
There are more than a dozen new drugs under development for various other disease conditions which do not fall in the above categories. Interested readers may go into the individual websites after obtaining the preliminary details from the PhRMA website indicated below.	
Major Companies	Amgen, Neurochem, Insmed, GlaxoSmithKline, Curacyte, Amylin Pharmaceuticals, Savient Pharmaceuticals, MedTronic, Aastrom Biosciences, Dynavax Technologies, Amatillo Biosciences, QLT Canada, Genentech etc.

It can be seen that a wide spectra of biotech drugs are under development; major R&D work is being carried out in U.S.A. Unfortunately, in developing countries like India there is no product worth mentioning that would qualify to be rated as unique and comparable to the new products being developed globally. India would therefore have to change its research strategies considerably to create innovative capabilities that would match the current global standard in at least some sectors of research and developmental capabilities.

In agriculture, some work to develop recombinant DNA plants and planting materials is being carried out in India[25,26,27] as has been indicated earlier in Table 7 Global development is, however, moving much faster and several types of genetically modified plants are being invented that are safe environmentally and safe to consume. Such developmental work is a continuous process. If India wishes to participate, extensive alliances may have to be created. The strength of India lies in its genetic biodiversity, as well as in several parental lines developed in agriculture that have proven to be more efficacious in productivity and resistant to stressful conditions. In the development of industrial products through modern biotechnology, India is still at the rudimentary stage as has been in Table 7.

Developing a modern biotech product from scratch and testing its efficacy to be effective and safe within the framework of law in any, country including India, is time consuming and expensive and technologically difficult.

Biotechnology is highly skill based requiring expensive infrastructure especially in terms of expensive instruments and high quality of work-space. India is lagging in most, if not all, areas. Research is the backbone of new product development. Therefore, new inno-

vation based initiatives must be taken.. It is from past experience that there is no adequate incentive for biotech innovators. There is very little framework to facilitate alliance between academia and industry where the academia can have financial interest in new companies. Biotech companies are still family owned and run by hired professionals.

Most of the Indian companies pursuing modern biotechnology do not have PhD programs for their young employees and retaining talented young people often becomes difficult. While the country has basic capabilities in chemistry and a strong cultural history of using biodiverse natural products in various facets of life, provisions for assessing their utility does not adequately exist. For example, various cell lines and animal models for assessing the bioactivity of chemicals and analogs derived from nature, is inadequate. The screening facilities for new biological compounds are poor and therefore, intellectual properties cannot easily be created. Gene banks for biodiversities need to be created for different kinds of life forms including plants (forestry, arid zone plants, cereals etc.), marine biodiversities, high altitude life form biodiversities etc. The public perception of modern biotechnology is not clear; there is a negative attitude toward acceptance of new products, especially in agriculture. The country does not yet have adequate expertise in creating and upgrading standards for modern biotech products and services. Complete protocols for the conduct of experiments for the use of transgenic products commercially are not yet developed for different materials that may be emerging. The regulatory clearances require simplification. There is no mechanism to identify the potential marketability of discoveries and inventions at the stage of "proof of concept" or to take them further for development.

Future Trends of Development of Biotechnology in Various Sub-Sectors in India

Scenario 1:

India already has developed competence in selected areas that provide the entrepreneurs an edge over other developing countries to set up viable and competitive biotech industry in certain areas.

The Indian Government continues to play a significant role in the promotion of biotechnology in all its facets. The efforts of DBT during the initial years in transferring institutionally developed technologies to the industry have been summarized.[28] These efforts have been instrumental in developing competence within the country. The areas of core competence in India in the context of biotechnology are:

- Capacity in handling sterile fermentation processes
- Skills in handling microbes and animal cells
- Skills in plant cell/tissue culture
- Experience in application oriented microbiology e.g., production of antibiotics by microbial fermentation
- Expertise in downstream processing, including handling of various kinds of centrifuges, micro-filters, chromatographic techniques utilizing different kinds of columns, membrane filtration methods, use of molecular weight cutoff membranes, gel filtration techniques, freeze drying, and other processing methods

- Skills in cloning of desired organisms through rDNA technology utilizing available plasmids and DNA constructs, using established methods. Cloning of *E. coli, Aspergillus niger,* various yeast like *Pichia pastoris, Saccharomyces cerevisiae*, *Hansenuella polymorpha, Zymomonas mobilis* etc., growing of various insect and mammalian cell lines and multiplication of chosen viruses in cell lines
- Skills in preservation and maintenance of cell lines and microbial life forms.
- Infrastructure and skills in fabricating bioreactors and processing equipment of diverse kinds
- Competence in chemical synthesis
- Proficiency in general immunology
- Skills in extraction and isolation of plant and animal products
- Competence in plant and animal breeding
- Skills in mathematics and statistics

Existing and new entrepreneurs will expand their activities and introduce bio-similar or bio-generic products in the health care area and genetically modified plants, (using available genes and constructs) into agriculture. Indian productive parental lines for hybrids and varieties (for self-pollinated crops) will be extensively utilized in producing GM plants for use in agriculture. Expansion will also be taking place in conventional biotech activities in all sectors of biotechnology.

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The almost nonexistent basic research infrastructure in existing industry would not e likely to result in the invention or discovery of new products that would have high sales volume (e.g., annual sale more than US$1 billion). But expertise already exists in many areas such as in the deployment of microbial fermentation processes, and in many other areas such as the following: modest capabilities in downstream processes for recovering milligram or microgram quantities of metabolites from liter quantities of fermented broth using, especially standardized micro-filtration and chromatographic techniques as well as membrane filtration methods. Other promising areas are where products or processes require very little basic research input and where complex product characterization services requiring inputs from sophisticated instruments such as RP-HPLC, MALDI-TOF, DNA sequencing, capillary gel electrophoresis, etc are available on hire. In such areas, many entrepreneurs will invest in value added bio-pharmaceuticals, which can be expected to be produced in sizeable quantities locally.

Concerted efforts would be made especially for products where the selling prices are several times higher than their manufacturing costs and the availabilities are still in the hands of a few foreign companies that are yet monopolizing the world market, while the product patents have expired. Several companies would likely be involved in such endeavors and once in into the business endeavor, entrants would need to invest in R&D in order to become more productive. It is anticipated that market competitiveness and the moti-

vation to remain efficient would drive sizeable investment in creating R&D capabilities in biotechnology in the industry sector. This situation would be fuelled and stimulated by several government departments and institutions by extending technical assistance and providing some capital to certain classes of activities and entrepreneurs.

The Indian market scenario in the immediate span of next five to seven years is further elaborated:

Human and Animal Health Products:

The human and animal health care products would grow substantially. There would be increase in the production of more effective but known vaccines. The cocktail vaccines of DPT with hepatitis B and/or HIB, tetanus toxoids with hepatitis B, hepatitis A with B, vericella and meningitis vaccines have been introduced during the last 5 years; more market competition in this area is anticipated. There would be substantial export of many of these products from India, as the quality is high and the prices are extremely competitive. There is need for increased availability of effective typhoid vaccines. It is anticipated that better carbohydrate based vaccines as well as heat-shock proteins based vaccines may evolve in this area. There is an unmet demand for several animal and poultry vaccines. There are also opportunities for developing vaccines for protection against hepatitis C, hepatitis E, HIV, malaria, tuberculosis and leishmaniasis; these developments are closely related with a long term planning on research and adequate teaming up between the institutions and the industry. There are also opportunities for developing recombinant viral vector vaccines and DNA vaccines, especially for imparting protection of animals against rabies, anthrax, etc and for human against typhoid fever, viral encephalitis etc., as the basic knowledge exists in some institutions.

There are also opportunities for developing vaccines for protection against hepatitis C, hepatitis E, HIV, malaria, tuberculosis and leishmaniasis.

Disease diagnostic areas are growing fast although the country has neglected investment opportunities for local production. Most of the diagnostic products are imported, even though local skills could be developed for competitive global advantage. Diagnostics based on monoclonal antibodies, synthetic peptides and recombinant antigens or antibodies could be made locally, as skills exist. The requirement of membranes could be met from local sources by providing encouragement to skilful local producers. These areas are already growing, though slowly. The requirement of specialty plastics could also be met from local capabilities. The intervention in policies could play a vital role in developing this industry locally. A little adjustment to provide a level playing field to local producers and direct importers of certain products, would be needed to encourage investment in diagnostics to create a globally competitive local industry. Opportunities exist for the setting up of facilities for developing diagnostics devices for detecting HIV, HCV, HEV, Papilloma, Malaria and Tuberculosis. Further, opportunities exist for quantitative estimation of hormones such as T3/T4/TSH, hCG, LH, FSH, Progesterone, Testosterone,

Corticosteroids, Alpha fetoprotein and prostatic inhibin. Still further opportunities exist for setting up facilities for producing diverse biochemicals required in health care products like diagnostics such as monoclonal antigens/antibodies, recombinant antigens/antibodies for various conditions including cardiac markers, peptides, nucleotides, specialty plastics, membranes of different molecular weight cut off, polyclonal antisera, various conjugates and specialty enzymes.

The production of therapeutic recombinant proteins is steadily growing locally, but the speed of development is slow. Opportunities exists for taking up production facilities for interferons, insulin & its analogs, human growth hormone, G-CSF, GM-CSF, erythropoietin, blood factors VIII and IX, urokinase, tissue plasminogen activators (both whole length glycosylated as well as the non-glycosylated truncated product), streptokinase, several interleukins and tissue necrosis factors. As the patents on these products expire (on some products, patents have already expired) they would be produced locally to meet part of the export markets.

[S]ignificant demand exists for the production of different monoclonals, peptides, hyaluronic acid and other animal products, besides effective biotechnological drug delivery systems including liposomes, virosomes and nanotechnology.

In the antibiotics area, opportunities for future investment are not presently bright, especially in view of the core competence of some Asian countries. Some products like erythromycin, vancomycin etc., could be produced; erythromycin serves as a basis for conversion into several value added macrolides while vancomycin as such is required to treat certain life-threatening conditions arising from microbial infection. In order to survive economically, some existing units may produce conventional antibiotics like penicillins, streptomycin, gentamycin, rifampicin and amphotericin-B for internal consumption. However, production of value added anti-lipedimic drugs and immuno-suppressants by fermentation will need to increase substantially as the products would be required on a large scale to meet the global market at competitive prices. Lovastatin, simvastatin, pravastatin, tacrolimus, mycophenolate, pimecrolimus are being produced in the country from the basic stage of microbial fermentation; the capacities are being enlarged to cater to increasing export demand. India would be able to fare well in this area as skills in conventional fermentation processes are of high a order.

There also exists fair opportunities for fresh investment in setting up facilities for the fractionation of blood and blood products into cellular and non-cellular components, and sensitized immunoglobulins. Able blood donors are plentiful. The placental blood goes almost totally to waste. Separately, significant demand exists for the production of different monoclonals, peptides, hyaluronic acid and other animal products, besides effective biotechnological drug delivery systems including liposomes, virosomes and nanotechnology. Investment in these areas is expected to be increased in the coming years as demand exists, profitability is thus ensured and little basic research infrastructure is required to be created.

Stem cell banks and tissue banks would also be set up to play the role of

supplier of such materials to a cross section of clients who would pay for the preservation costs.

Agriculture Biotechnology:

In agriculture, a major contribution is anticipated from the local production of increased quantities of hybrid seeds and high-yielding varieties. Already core competence exists for developing varieties and hybrids; the cheap labor force available locally is of great advantage. Unfortunately this area has not grown because it has not been possible to bring home the great merits in the replacement of productive seeds every year. Genetically modified plants/ seeds are expected to emerge in the coming years and would capture markets in specific sectors of seed industry. Genetically modified seeds have been subjected to too much negative criticism by certain NGOs. With time, as the merits of such seeds in developed countries would be confirmed, acceptance level would increase. Substantial work on producing transgenic seeds of different kinds is being carried out in several publicly funded institutions and universities; these efforts could negate considerably the present non-acceptance environment in years to come. One important consideration while dealing with cross pollinated crops is the effect of transgenic pollen flow; to do away with this factor, the mitochondrial gene manipulation techniques are gaining importance. More research in this area in the public sector is expected to contribute more positively to the acceptance of GM crops in future years.

Substantial work on producing transgenic seeds of different kinds is being carried out in several publicly funded institutions and universities…

There would also be an increase in the usage of bio-pesticides including botanical pesticides. Formulations based on Bt, different viruses like NPV and GV as well as need-based pesticides would be increasingly used locally and would also expand to exports.

Industrial and Other Biotech Products:

The sector represented by industrial products will remain primarily based on conventional biotechnology although recombinant microbial strains are expected to contribute substantially to the production of bio-catalysts (useful for complex chemical reactions like esterification, deacylation etc.), industrial enzymes, food-grade enzymes, milk clotting microbial rennet from recombinant *E. coli* and production of simple microbial metabolites such as organic acids and amino acids. Investment opportunities are being harnessed by creating or expanding facilities for the production of proteases, lipases and cellulases that are tolerant to acidic or alkaline conditions. These products are formulated for use in textiles, leather and detergent industries. Alpha amylase, amyloglucosidase, pectinase and diastase are being produced in increased quantities for the food and beverage industry; alpha amylase is also being consumed in increasing quantities in textiles industry for the removal of starch from the fabric after weaving. These areas are expanding fast in the country itself.

There would be a rise in the production of specialty enzymes and oligo-nucleotides in molecular biology research, specialty materials including specialty

plastics for specific uses, analytical materials and reagents for diverse use, and application of biological materials in electronic devices. Opportunities in investment in these areas are clearly linked with India's having sizeable quantities of sugar cane molasses, and also other cheap agricultural substrates like various grades of starches from tapioca, maize, potato etc; corn steep liquor (whose quality can be improved if adequate demand is created), sugar, pea /peanut /soybean meals, and various vegetable oils. In the area of bakers and brewers yeast, opportunities for production of fresh compressed yeast do not presently exist as large capacities have already been created for local consumption and exports are yet negligible; but production of value-added NAD/NADH and specialty enzymes could be explored by using the locally available compressed yeast. In addition to the above areas of investment, there exist reasonable scope for setting up facilities for the recovery of value-added products from wastes such as proteins from milk whey, bio-gas and composted fertilizers from municipal or agriculture wastes, better methods of recycling of organic wastes, production of specialty bio-chemicals and specialty plastics that are bio-degradable.

With the increased usage of the tools of bioinformatics, software packages could be developed for attempting to discover new drugs, applications in clinical diagnostics, study of pharmaco-genomics, use in agricultural biotechnology, as well as in industrial biotechnology.

Scenario 2:

India has a strong mathematical base. People are well trained in physics and chemistry. As a result, bioinformatics has developed to some extent in its various facets. The country has the right kind of scientific skills that encompass capabilities of handling all aspects of biological information acquisition, processing, storage, distribution, analysis and interpretation. The Indian Bio-resource Information Network (IBIN) is documenting country's animal reserves, cereals, vegetables, crop plants, fishes of various kinds, its forest plant reserves & resources, as well as, to a considerable extent its microbial reserves. These documents in themselves would be expanded through the use of data generated by remote sensing satellites. With the increased usage of the tools of bioinformatics, software packages could be developed for attempting to discover new drugs, applications in clinical diagnostics, study of pharmaco-genomics, use in agricultural biotechnology, as well as in industrial biotechnology. There is a need to expand the number of proficient taxonomists to identify the genetic biodiversity wealth from the super-order level to the species level. The institutional strength exists which is globally competitive. If this message is taken across to entrepreneurs, it should be possible to develop a strong bioinformatics market in modern biology in various facets of application. Unfortunately, at present only small operators are working in this field. Moreover, several high profile private institutes are signaling inexact notions across the country by overselling this potential area by producing students who merely learn the tools and techniques of how to use the bioinformatics software without understanding or emphasizing on biology, chemistry and physics. Fortunately, this is not the case in certain premier teaching institutions of the country. There is therefore, a need to promote this area at the national level

with highly concerted efforts by building capabilities around certain competent institutions and by creating strong alliance with the industry. It is anticipated that this area in biology can grow even faster than modern product-oriented biology as the skills are existent in certain fields. If enough effort is not made, the skills would be outsourced to the developed world that would then reap the real benefits.

There are several world class facilities and knowledge pools in some of the institutes of excellence in the country. Table 2 provides information on major Indian institutions involved in biotechnology research. The microbial cell culture banks, the eukaryotic cell lines, the seed resources for cereals and other food crops exist in specific Indian institutions. Basic knowledge of a high order is present in immunology, cell signaling pathways, microarrays, proteomics and genomics in some of the institutions. Knowledge in gene silencing using RNAi technologies also exists in some institutions. The institutions have little involvement with the industry, unfortunately. Moreover, scientists working with specialized skill have not yet been interested in setting up companies nor such provisions freely exist yet in publicly funded institutions; the existing procedures are not simplified, the clearances required from several agencies are difficult to obtain, and to arrange for funds is difficult. Presently, the rewards for innovation are grossly inadequate in terms of monetary benefits. Because of this, translation of basic science into industrial products is almost nonexistent. The knowledge base will acquire value addition only when it is utilized as products and services. This can happen when such structures are created where industry can take benefit of the products developed through joint research conducted at the institutional level as well as the industry level. Only if such efforts are catalyzed by the government, is there a likelihood of Indian products going into the international market.

By the year 2010, the comparative contributions of production from health care products are expected to reach about 39% from the present 38% (2005), while agriculture may rise from 31% to nearly 32%.

Concluding Remarks

Despite obstacles, India is expected to emerge as a strong player in the production and sale of biotech products in the coming years. The local consumption is expected to rise substantially. By the year 2010, the comparative contributions of production from health care products are expected to reach about 39% from the present 38% (2005), while agriculture may rise from 31% to nearly 32%. The other products may drop from about 32% to about 27%, although in monetary terms there would be substantial rise in the consumption in these products as well. The conventional and the patent-expired modern biotech products will be the mainstay of product portfolios if the existing environment is maintained.

India can make a difference by becoming a dominant player in modern biology including in bioinformatics if certain policy changes are made and efforts are used to achieve milestones. This would require changing the existing

mindset of the government, the industry and the academic research institutions. By adopting appropriate government interventions, as profiled in the text, it should be possible to attract sizeable investment in the modern biotech area to create a competitive global industry locally in star products and services over a period of seven to ten years. Conventional biotech industry will grow in any case in the present business environment; bio-similar products will also emerge in the coming years. Such products will meet the local demand and a sizeable portion will be exported. But there are apprehensions about whether any major products would emerge in the next decade from India that would have US$1billion sales or more annually, if the existing environment is not deliberately changed for the better. Wisdom lies in taking more proactive steps to develop a globally competitive local industry that stands on the solid foundation of basic research; some major products could emerge from such efforts over a period of time. Mere facilitation of biotech industries as is done presently would no doubt make economic contributions but these would continue to be minimal in contrast to world developments where companies are moving ahead systematically with more concerted efforts.

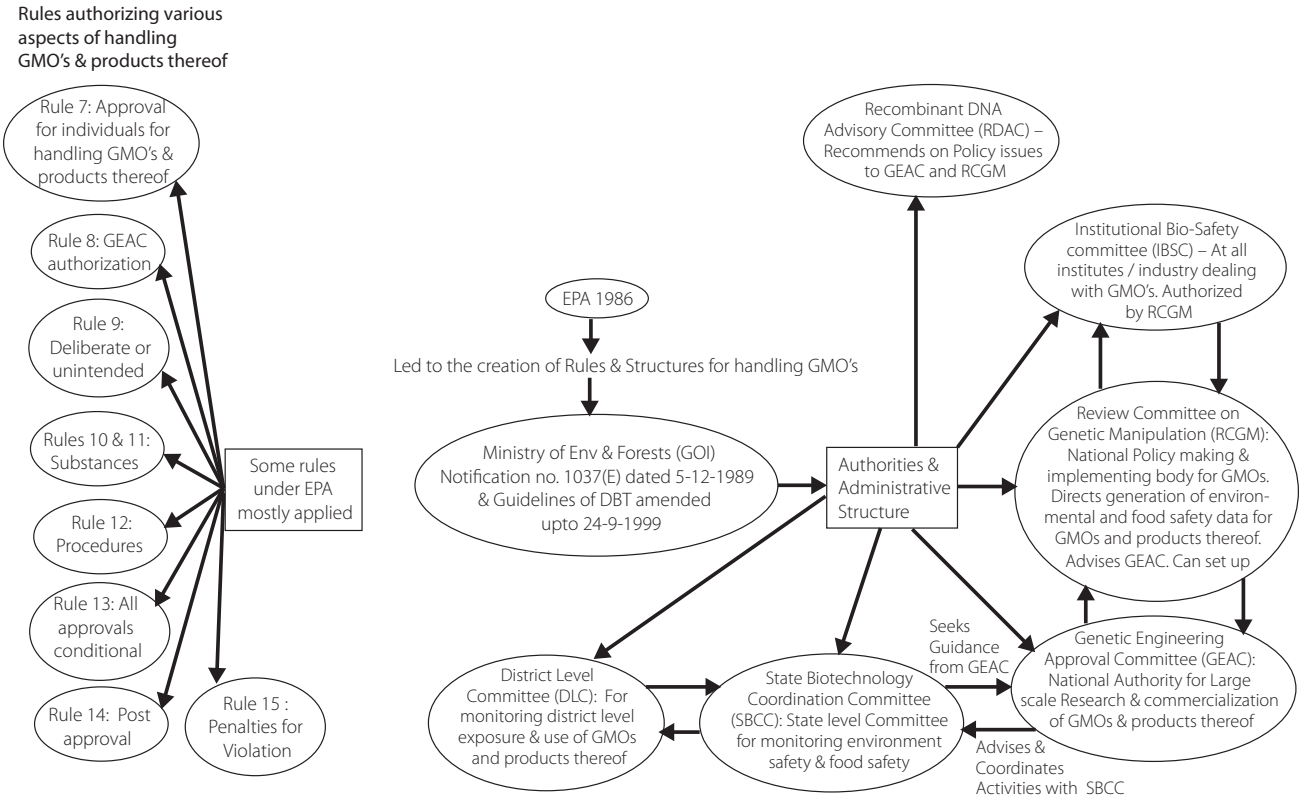

Figure 5: The Rules, Authorities and Administrative Structures for Dealing with GMOs and Products thereof.

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About Advances Biopharmaceutical Technology in India

The biopharmaceutical industry in India has grown dramatically over the past few years, and sales have exceeded US$1.5 billion. This study describes the Indian biopharmaceutical industry, its history, its advantages and opportunities, as well as its challenges and risks. Today, the biopharmaceutical industry in India has brought several protein drugs to market and is developing many more. The next several years will be interesting as India takes its place on the global stage. Biopharmaceutical products have a long history in India, and trace their roots back several thousand years through schools of healing practice. The Indian government is currently working towards developing that experience into a sound biotech industry. The country's objective is to help minimize foreign dependence, especially in high-tech areas. This study describes the industry's history, and the Indian government policies that have helped enable the manufacture of modern biotech products at affordable prices. We discuss the patent factors and history that have shaped the Indian industry, including the industry's reliance on production of outside-of-patent products. As the Indian government continues its efforts to create alliances between private industry and research institutes, the next decade should show a significant growth in the Indian biotech industry, and novel biotech drugs may ultimately dominate. India is expected to emerge as a strong player in the production and sale of biotech products in the coming years, as local consumption rises, and as its local biotech industry takes steps to develop a globally competitive local industry that stands on a foundation of basic research.

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ISBN 978-1-934106-07-5