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Biotechnology-Destination India

Introduction:

Biotechnology is at the threshold of tremendous growth and India is emerging as an important player in the global sector. The present market of approved products has been estimated to be in the range of Rs. 5357 million, which is approximately 1.6% of the world market.

India is incorporating vast changes in order to facilitate growth in the sector. The current consumption of Biotech products in India is in the region of $2186 million, which is expected to grow upto the tune of $4270 million by the end of year 2010. Where the Indian Biopharma sector accounts roughly for 70% of the bulk Biotechnology sector, the Bioindustrial, Bioservices, Bio-agri and Bio-IT approximately account for 13%, 7%, 6% and 4% respectively.

Biotechnology in India: Why is India important?

- The country has a rich human capital, which is backed by a knowledge base that constitutes the strongest asset for this industry. India produces approximately 650,000 postgraduates and 1500 PhD's qualified in Biosciences and Engineering.
- There exists a huge market for Biotech products and services.
- India has a Rich Biodiversity with the most varied size of flora and fauna.
- India possesses one of the largest agriculture sectors in the world, with varied climatic zones that can help in research and development of different agribiotech products.
- Core competency in Bioprocess Engineering, Gene Manipulation of microbes and animal cells, Recombinant DNA technology of plants and animals and has well-developed base industries (e.g. pharmaceuticals, seeds etc).
- There are facilities for extensive clinical trials and research and access to vast and diverse diseased populations.
- Increasing International collaborations in the field.
- Presence of avenues for bilateral cooperation in the sector due to availability of excellent infrastructure at low costs.
- Presence of a sound and widely acknowledged framework of Biosafety Regulations.

Scope of Biotechnology Business in India:

India has started attracting the Global Attention especially in the field of clinical trials, contract research and manufacturing and other services of Biopharma segment.

Some avenues for foreign companies include:

- Entering into contract Research and Manufacturing with Indian companies especially at the Drug Discovery stage of research.
- Forming joint ventures with the Indian companies, enter into partnerships or establish technology transfer agreements or strategic research partnerships with key research institutions.
- There are opportunities in Indian markets to produce and sell vaccines and therapeutics that respond to the needs of the poor in India.
- Deriving benefits through the cheaper qualified workforce, low cost of infrastructure and a base for clinical research.
- Collaborating with and selling products and services in the Biotechnology sub-sectors like Biopesticides and Industrial enzymes.

Modes of doing Business in India:

A new entrant to the Indian market should consider one of the following entry vehicles, depending on the expected volume of business, the nature of business (whether it is an active pharma ingredient/generic bulk drug or a pharma product), mar-

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ket potential and its long-term strategy for the Indian market.

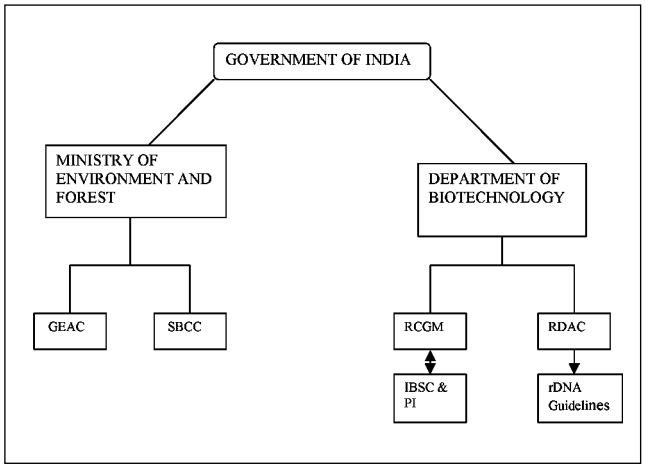
1. Appointing of Distributor/Agent:
2. Opening a Liaison Office:
3. Opening a Branch Office:
4. Project office:
5. Joint Venture Company/Wholly Owned Subsidiary:
6. Contract Research:
7. Partnership Firm:
8. Technology Collaborations:
9. Collaborative/Clinical Research:

Foreign company can also enter for Biotechnology business in India for the purposes of collaborative research or clinical research.

Governing structure in India:

Department of Biotechnology (DBT) Constituted under the Ministry of Science is the nodal agency for policy promotion regarding R&D, International Co-operation and manufacturing activities. Along with DBT Ministry of Environment and Forest (MoEF) is the leading regulatory body in the field of Biotechnology in India. These ministries ensure the compliance of requisite safeguard at R&D level. The guidelines are provided under DBT's Recombinant DNA Safety Guidelines, 1990 that was revised in 1994 & 1998 respectively. Further, various committees has been constituted under the above-mentioned Ministries. They are as follows:

1. Recombinant DNA Advisory Committee (RDAC).
2. Institutional Bio-Safety Committee (IBSC).
3. Review Committee on Genetic Manipulation (RCGM).
4. Genetic Engineering Approval Committee. (GEAC).



- SBCC: State Biotechnology Co-ordination Committee.

Recombinant DNA Advisory Committee (RDAC):

The main function of the committee is to review the developments in Biotechnology at the national and international levels and to recommend the appropriate safety regulations for India in rDNA research works. It functions under the DBT.

Institutional Bio-Safety Committee (IBSC):

IBSC is the nodal point of interaction within a commercial organisation/applicant company involved in rDNA research for the implementation of rDNA guidelines. In the first instance, an applicant company intending to carry out research activities involving genetic manipulation of microorganisms should constitute IBSC comprising of the Head of the applicant company, scientists involved in DNA work, a medical expert and a nominee of the DBT. Institutions carrying out the genetic engineering activity should strictly adhere to the guidelines and may be subjected to inspection by the competent authority.

All recombinant research carried out by the applicant company shall designate a Principal Investigator (PI). The guidelines stipulates three categories of research activity:

i. In case of Category I routine recombinant experiments mentioned in the guidelines, the PI is required to intimate to the IBSC in the prescribed format.

ii. In case of Category II experiments, the PI shall seek permission of IBSC before starting the experiment. IBSC shall intimate its decision to the RCGM before execution of the experiments and the RCGM shall put the information on record.

iii. Category III experiments, where the risk involved in the experiments are considered to be of higher magnitude having the potential of polluting/endangering the environment, the biosphere, the eco system, the animals and the human beings could be conducted only after obtaining clearance from the RCGM and upon being notified by the DBT.

All experiments conducted in green house and open field conditions not belonging to the Category II, would fall under Category III.

Therefore, the IBSC shall review and give clearance to the project proposals falling under the restricted category that meets the requirements under the guidelines. Where the clearance from the RCGM is required, IBSC shall forward its report to the RCGM after screening along with its recommendation.

Review Committee on Genetic Manipulation (RCGM):

The RCGM under the DBT comprises of representatives of a) DBT; b) Indian Council for Medical Research; c) Indian Council for Agricultural Research; d) Council for Scientific and Industrial Research; and e) other experts in their individual capacity.

The function of this committee is to frame the regulations for the institutions involved in rDNA research activities and (i) to review the on-going researches involving hazardous microorganisms, (ii) to visit the experimental site and ensure that the trial is being carried out as per the guidelines, (iii) to advice the custom authority on import of microorganism and G.M. products.

Before conducting the research in rDNA work involving risk categorized as category III and above under these guidelines, the PI/Applicant is required to obtain the permission of RCGM following approval from the IBSC. After reviewing the application, the RCGM may recommend the application to Monitoring cum Evaluation Committee (MEC) of the DBT for agronomic benefits and evaluation. After detailed deliberations, the MEC recommends the modified application back to RCGM. For making its evaluations and recommendations, MEC may visit trial sites, analyze data, inspect facilities and conduct environmental risk assessments.

An applicant shall also seek the permission of the RCGM for conducting green house trials and small-scale field trials to generate data to assess the safety of GM/transgenic crops that are intended to be released into open fields. The safety studies include environmental safety studies (pollen flow, emergence of volunteers, persistence etc.), food safety studies (toxity, allergenicity, pathogen drug resistance, alteration of nutritional value etc.), and the assessment of agronomic advantage over non-transgenic crops. Large-scale field trials would also require the approval of the GEAC.

Genetic Engineering Approval Committee. (GEAC):

In the cases of large-scale field trials, deregulation and commercialization, a permission of GEAC constituted under the MoEF is required in addition to the DBT approval process.

Precisely, approval of the GEAC is required from the environmental angle on:

i. Import, export, transport, manufacture, process, selling of any microorganisms or genetically engineered substances or cells including food stuffs and additives that contain products derived by gene therapy.
ii. Discharge of genetically engineered/classified organisms/cells from Laboratory, hospitals and related areas into environment.
iii. Large-scale use of genetically engineered organisms/classified microorganisms in industrial production and applications. Production can only be commenced after obtaining such approval.
iv. Deliberate release of genetically engineered organisms.

All approvals of GEAC shall be for a specified period not exceeding 4 years at the first instance renewable for 2 years at a time. Experiments beyond 20 liters capacity for researches as well as for industrial purposes are included in the category of large-scale experiments/operations and therefore, require prior approval of the GEAC.

Biosafety Regulations:

Initiatives have been made by several International organizations to regulate biosafety measures. The most ambitious attempt to produce a globally harmonized regime for biosafety has been under the Convention on Biological Diversity (CBD). The Cartagena Protocol on biosafety was negotiated and adopted under the aegis of CBD on 29th January 2000. It seeks to protect the biological diversity from the potential risks posed by the living modified organisms. India is a party to CBD and a signatory to Cartagena Protocol.

In India the research for the genetically engineered organisms is governed by the Indian Recombinant DNA Safety Guidelines, 1990, revised in 1994, which includes biosafety measures for research activities, large-scale environmental release of genetically altered agricultural and pharmaceutical materials. There are safety guidelines to be followed by the Microbiological and Biomedical laboratories. The guidelines also specify the catego-

ry levels of the research activities according to the risks involved for the purposes of obtaining prior approval of intimation of concerned authorities.

The Environment (Protection) Act, 1986 provides for the compliance of the procedural safeguards for the persons or the companies handling hazardous substances and the procedures regarding emission or the discharge of environmental pollutants.

The Rules for the Manufacture, Use, Import, Export and Storage of Hazardous Micro-organisms/Genetically Engineered Organisms or Cells, 1989 prescribes the competent authorities which will review the developments in Biotechnology and monitors the safety related aspects of research activities involving hazardous micro-organisms and restrictions on production or importation of hazardous micro-organisms from the environmental angle. These authorities are RDAC, RCGM, IBSC, and GEAC etc.

The Bio-Medical Waste (Management and Handling) Rules, 1998 requires the concerned Biotechnology company or person involved in research work to take all the necessary steps to ensure that the Biotechnology waste is handled without any adverse effects to human health and the environment. The Bio-medical or the Biotechnology waste is a hazardous waste under the Hazardous Waste (Management and Handling) Rules, 1989.

The non-compliance of the safety guidelines under different authorities would lead to legal consequences and the person responsible would be held liable. A Vigilance Cell for that purpose is functioning under the DBT to keep a check on the functioning of the Biotech companies.

Foreign Direct Investment in Biotechnology Industry

Agricultural Biotechnology:

Under FDI Scheme of the Government of India, a person resident outside India [including foreign companies and Non-Resident Indians (NRIs)] can invest in the Indian company not engaged in agriculture including plantation by way of subscription of up to 100% of its shares, without obtaining any prior approval provided that the person resident outside India does not have a previous financial or technical collaboration in India.

Medical/Pharmaceutical Biotechnology:

Under the FDI scheme of the Government of India, 100% (FDI) is permitted on the automatic route in Drugs and Pharmaceuticals sector provided,

- Activity does not attract compulsory licensing or involve the use of recombinant DNA technology and specific cell/tissue.
- FDI proposal for the manufacture of licensable drugs and pharmaceuticals and bulk drugs produced by rDNA technology and specific cell/tissue targeted formulation will require prior Government approval.
- In case of trading companies, 100% FDI is permitted with respect to Medical and Diagnostic items subject to the provisions of the Export Import (EXIM) Policy.

Import and shipment

All import of seeds and planting material etc. are subject to EXIM policy and the requirement of Plant Quarantine Order 2003 (PQO), and shall require a permit granted by the Plant Protection Advisor (PPA). The importer has to apply to the National Bureau of Plant Genetic Resources (NBPGR) for Phytosanitary clearances after which the Transgenic Crops /GMOs /Germplasm can be imported (subject to the prior approval of GEAC under MoEF). Application for the import of Live Insects / Bio-control agents is to be made to the PPA.

In addition, permits authorizing the import or receipt of regulated materials for research and specifying conditions under which the agent or vector is shipped, handled and used are issued by RCGM while large scale imports for industrial use are regulated by GEAC. The RCGM issues the import certificate after ensuring that it is free from any risk.

Certain Fiscal Incentives and support measures presently available include:

- Income-tax relief on Research and Development expenditure.
- Weighted tax deduction for sponsored research and on in-house Research and Development expenditure.
- Customs duty exemption on capital equipment, spares, accessories and consumables imported for Research and Development by approved institutions/SIROs.
- An excise duty waiver on indigenous items purchased by approved institutions/ SIROs for Research and Development.

- A ten-year tax holiday for commercial Research and Development companies.
- An excise duty waiver for 3 years on goods produced based on indigenously developed technologies and duly patented in any two of the following countries: India, European Union (one country), USA and Japan.
- Accelerated depreciation allowance on plant and machinery setup based on indigenous technology.
- Customs duty exemption on imports for Research and Development projects supported by Government.

Intellectual Property Rights and Biotechnology:

Intellectual Property (IP) defines the amalgamation of Law and Science. IP aids in the facilitation of collaborative activities in clinical trials, drug discovery and other research areas. Being a member of the World Trade Organization (WTO) and a signatory to the Trade Related Aspects of Intellectual Property (TRIPS), India has to follow and abide by the provisions of global intellectual property.

In pursuance of the above matter, the Government of India has made significant amendments to the patent legislation by bringing forth Patent (Amendment) Act, 2002. Following are some of the changes made:

1) Patent protection is available for microorganisms.
2) Inventions relating to the methods of treatment of plants are made patentable.
3) The term of patent is made uniform so as to provide a 20 years protection.
4) The provisions relating to compulsory licensing have been modified to suit the public interest requirements and also to comply with TRIPS Agreement

India being already a member of the Paris convention, Patent Cooperation Treaty, Berne Convention, Convention on Biological Diversity and WTO, is aiming to make the legislation clearer on the patentability of biotechnological inventions. In a significant development, India has repeatedly confirmed its accession to a "product patent regime" by 2005.

Also, a Biotechnology Patent Facilitating Cell under the DBT has been created to assist in writing and filing of patents along with creating awareness and understanding about the intellectual property rights among the researchers and scientists by arranging workshops, seminars, conferences etc.

Future of Biotechnology in India:

- The product patent regime will come into force by the end of 2005 and will provide the strategic inputs for companies to invest in product research.
- There are opportunities for such investments in the Indian Biotechnology sector to an extent of Rs. 8 Billion that could result in a turnover of Rs. 10 billion in the next 5-7 years.
- The Pharmaceutical Market, owing to the emergence of corporatisation in health care, growth of health insurance, deeper rural penetration, development of a strong market and marginilasation of the DPCO, is expected to cross $37 billion by 2010.
- According to the Indian geneticists, the country is slated to become a world leader in "functional biological genomics," and the challenge before the country is to set up an Inter-disciplinary research program under which the molecular biologists, geneticists, computer scientist and even theoretical physicists and synthetic chemist would work together.
- Agriculture being the mainstay of the Indian Economy is expected to grow by 60% in terms of Agri–Biotech products.
- The Neutracenticals market is also expected to grow exponentially in future.
- The Department of Biotechnology is aiming to excel in future in terms of Genome research, stem cell biology, vaccine research, Biomass utilization and Human Resource Development.
- Indian Biotechnology vision 2020 include doubling or tripling of farm production, curing what may now appear to be incurable diseases including HIV, AIDS, and producing non- chemical pesticides with no harmful elements in them. The country is also aiming to generate medications, drugs and pharmaceuticals with the least side effects. Biotechnology also seeks to develop safe preservatives to increase the shelf life of many products.
- India is one of the 1st countries in the world to initiate a Bioinformatics program. The Bioinformatics sector, which is currently valued at $15 million with major share coming from the global market, is presumed to touch $120 million by 2006.
- With a large pool of scientific talent, world-class information technology industry, a vibrant

pharmaceutical sector, tremendous growth in agricultural sector and with remarkable support of the Government, Biotechnology is viewed as a latest revolution in India.

Conclusion:

With a liberal industrial policy coupled with the large pool of scientific talent, world class Informatics Technology industry, a vivacious Pharmaceutical sector, remarkable growth in Agricultural sector, massive Foreign investments, increasing number of Biotech companies, expanding Biotech markets, extensive Clinical Researches, strong Bio-processing skills, the forthcoming product patent regime and remarkable government support both at the Central and the State levels, India is viewed as a potential locale for manufacturing activites and high-level biotechnology research programmes.

Finally, with all lights flashing, signals green and the runway clear, Biotechnology is well poised for its destination India.