INVESTMENT AND COLLABORATION OPPORTUNITIES IN BIOTECHNOLOGY WITH INDIA

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Biotechnology has revolutionised the current status of knowledge of a number of biological pathways and processes applicable to the biological principles for human welfare and better quality of life. Key developments from which modern biotechnology has emerged are based upon our understanding of the structure and function of living cells, how they retain and transmit genetic information, and how they respond to chemical and physical signals. Biotechnology has already made substantial contributions to development through better healthcare, enhanced food productivity through sustainable agricultural practices, improved bioprocess technologies, efficient industrial development processes for transforming raw materials and the detoxification of hazardous material. Its greater impact in the area of human health has been through development of vaccines, bioactive compounds, immunomodulators, new pharmaceuticals, delivery systems, diagnostics and other medical products.

Indian Biotech Scenario

India has been practising conventional biotechnology for several decades using classical technologies of fermentation: production of vaccines, sera and diagnostics; recovery of metabolites through downstream processing; use of microbes or enzymes for producing value added products, plant breeding etc. However, in the past decade products manufactured by the use of modern biotechnological methods using genetic engineering, immunological techniques, cell culture methods and hybridoma technology are increasingly being used and indigenous research in these areas has been intensified. The scientists in the country are actively engaged in fermentation based activities, production of valuable biologicals from microbial, plant or animal cell cultures, marker assisted selection and breeding, value addition, prospecting of biological resources, molecular taxonomy and micropropagation methods for producing high quality, genetically superior planting materials.

India has a well-established biotech industrial base, with more than 800 companies operating in various sub-sectors of biotechnology producing conventional and modern biotech products. The Indian strength lies in its having a large consumption market and its stable democracy and thus a better playground for Foreign Direct Investment in all branches of scientific industries in general and biotechnology industry in particular.

The country today has excellent expertise in biotechnological processes, facilities and tools in many corporate R & D houses, industries and teaching institutions including the universities. Core competence exists in the country for handling of labile biomolecules and compounds efficiently using downstream processing and unit process methods; production and handling of fermentation based products including foods, pharmaceuticals, geneticeuticles etc.; extracting value added products of high purity from plant and animal parts; use of plant/animal cell and tissue culture and microbial culture techniques; and, conventional plant/animal breeding techniques for variety improvement. The country has competence in the construction of bioreactors and processing equipment of diverse nature. The pharmaceutical formulation sector and handling of sophisticated biotech products under GMP has been developed to a high degree of proficiency.

In 1995 the requirement for pharmaceuticals in India was $3,600 million compared to the world

figure of $2,691,000 (0.134%) and for diagnostics the figure was $68.8 million in comparison to world figure of $18,300 million (0.41%). Nearly $830 million worth of recombinant therapeutic proteins were imported and used.

The demand for existing and new biotech products in India has increased with the increase in population as well as increase in awareness in the people about availability of such products. Out of the total consumption of biotech products conservatively estimated worth of US $1500 million in 1997, in all areas of biotechnology viz. human & animal healthcare products, agriculture (including seeds), industrial products and other allied biotech products, nearly 70 percent was produced based on local capabilities and skills. It is estimated that this production will rise with time to about 80 percent by the year 2005 to meet the demand. The average estimates in US dollars on demand of biotech products in India in 2005 would be for human & animal healthcare 1,150 million (39.5%), agriculture 954 million (32.8%), industrial 730 million (25.0%) and other biotech products 80 million (2.7%).

The demand of biotech products is increasing and as the volume of local consumption is significant, the scope of trade as well as new investment is considered enormous. Opportunities do exist for teaming up between Indian Institutes of Excellence and multi-national companies/ foreign investors for jointly developing biotech products that are research based. India has competitive advantage in attracting FDI for joint development of products/processes in healthcare area as well as in agriculture through FDI and institutional teaming up for utilisation by the private industries.

Human and Animal Health

Vaccines: Sufficient capacities have already been created in the country for the production of vaccines against tetanus, diphtheria, pertussis (and combinations thereof like DPT and DT), BCG and measles. Polio vaccine bulk is being imported, blended and used. Genetically engineered as well as human plasma derived hepatitis B vaccines are being marketed in the country partially through indigenous production and the rest through imports. Similarly human diploid cell culture based and vero cell culture based rabies vaccine and the improved cell cultured vaccines against measles, mumps and rubella (MMR), and influenza are being imported and consumed to meet the total requirement. The current imports of these vaccines is low and vary between 0.5 to one million doses per annum, primarily due to their high unit cost. Several other vaccines like attenuated oral as well as Vi antigen based injectable typhoid vaccine, H. influenza type B, meningitis and vericella (chicken pox) vaccines are also required in the country in sizeable quantities although these are not being manufactured in the country. Injectable Vi antigen based typhoid vaccine has been introduced from imported sources.

There are opportunities for the setting up of basic production facilities for MMR, measles, cell cultured rabies, recombinant hepatitis, oral and injectable typhoid (Vi antigen based) and certain other vaccines as the demand is increasing. Investment opportunities also exist in production of cocktail vaccines of DPT with Hepatitis-B, Hepatitis-A with B, influenza, vericella and meningitis vaccines. In the meantime, if vaccines for Hepatitis-E, Hepatitis-C, HIV and malaria become available globally, for which great scientific developments have already taken place elsewhere, as also in India, there would be considerable demand for these vaccines in India.

Human Genetics: The human genome map already announced is widely expected to revolutionise the practice of medicine. India being 20 percent of the world's population, endowed with endogamous ethnic groups with isolated gene pools, rich in genetic diversity has unique genetic material for research on complex genetic diseases like schizophrenia, cystic fibrosis, Duchenne muscular dystrophy and retinoblastoma

Animal & Poultry Vaccines: Currently vaccines against foot and mouth disease, anthrax, BQ, MCC, enterotoxemia, rinderpest, rabies, and sheep pox are being produced in abundant quantities. Several other vaccines and diagnostics like IBR, PPR, blue tongue virus etc, are being developed. The poultry industry is also developing fast in the country. Several viral vaccines for poultry like infectious bronchitis, fowl pox, New Castle disease, Marek's disease etc, are also being produced in large quantities; dominant producers are, however, in the private sector. The area has grown steadily and considerable scope exists for fresh investments.

Diagnostics: The diagnostic market in the country is increasing gradually. The turnover of diagnostics industry in India, which was estimated to be about US$ 135 million during 1992, increased to over US$ 720 million in 1997. The current estimated requirement of tests in million are early pregnancy (30), ovulation (3), T3/T4/TSH/Sex hormones (3), tuberculosis (20), leprosy (5), typhoid fever (5), amoebiasis (5), diarrhoeal diseases (E. coli, rotavirus, cholera) (10), filariasis (25), hepatitis-B (12), HIV(I+II) (12), malaria (25), venereal diseases (12), rheumatic diseases (3) and cancer (cervix, colon, prostate, lungs, mouth) (5). It is expected that this industry in the existing environment will grow much faster.

Bioactive Therapeutic Proteins: Currently several recombinant (r-DNA) products like human insulin, interferons, human growth hormone, streptokinase, erythropoietin, GM-CSF, G-CSF, bovine somatotropin, hepatitis B vaccine, tissue plasminogen activators etc. are being marketed globally. In India, insulin, alpha interferon, hepatitis B vaccine, GM-CSF, G-CSF, blood clotting factor VIII, streptokinase, human growth hormone and erythropoietin are already approved for marketing; only hepatitis B surface antigen based vaccine is being produced in the country and all other products are being imported and consumed.

The demand of the four major recombinant proteins being marketed in India in 2000 was human insulin (150 Kg), Hepatitis B vaccine (45 million doses), interferon alpha (5 million doses) and erythropoitin (1 million doses).

Targeted Drug Delivery Systems: Vehicles being used to target specific sites include liposomes, virosomes, pharmacosomes, hydrophilic nano particles, targeted polymeric chimera etc. These products are finding the number of applications and have revolutionised the pharma industry. Liposomal formulations are already available in the Indian market through imports and have a lot of investment opportunities. Simultaneous R&D efforts have already been launched in this area in India.

Blood Products: The country is currently using nearly 3-4 million units of blood for transfusion, as against the actual demand of around 5-6 million units. Few processing plants in the private sector are producing plasma albumin and globulin, albumin, IgG, Factor VIII, Factor IX and fibronectin. There is enough scope for setting up economically viable blood fractionation units.

Antibiotics: Considerable progress has been made in India towards antibiotic production. The country consumes over 30 bulk antibiotics and produces 13 by fermentation technologies. Large quantities of rifampicin and chloramphenicol are being synthesised from imported intermediates. Currently the scope for the export of semi-synthetic penicillins, derivatives of erythromycin and formulations of rifampicin have increased considerably.

The requirement of major antibiotics in 2000 was penicillin (6300 MMU), injectable cephalosporins (60 MT), cephalosporin-C (150 MT), rifampicin (300MT), tetracyclin (300 MT), oxytetracycline (200 MT), gentamycin (14900 Kg) and erythromycin (150 MT).

Agriculture

Crop Biotechnology: The first generation of transgenic plants has largely focused on important traits that benefit the farmers. Increasingly large areas of transgenic maize, soybean, potato, tomato and cotton are being commercially grown worldwide for human use and consumption. In these crops genes for improving crop productivity and manipulating starch/protein/oil quality and quantity, resistance to pests and diseases, environmental stresses such as temperature and drought, are being isolated and studied. The area under transgenics increased from 11 million hectares in 1997 to about 40 million hectares in 1999. Biotechnology companies are investing billions of dollars in consolidations to ensure access to these rapidly growing markets as well as to further research and development and there is enough scope for investment in this sector.

Hybrid Seeds: The current total global business in seeds is estimated to be US$ 20 billion of which nearly 40 percent is accounted for by sale of hybrids. Indian turnover of seeds in 1995 was estimated to be US$ 461 million only and the hybrid seeds constituted about US$ 185 million. India has paid considerable attention to the development of this sector in the country for distribution of

certified and quality seeds for crops including cereals, pulses, oilseeds, fibre, fodder and other species. Nearly 5 million kg of hybrid vegetables including tomato, cabbage, peas, cauliflower, ladies finger and cucumber were consumed. There is good scope for setting up plants for organised production of hybrid seeds especially in vegetables.

Tissue Culture raised Planting Materials and Cut Flowers: In India, plant tissue culture techniques are being extensively used for the production of elite cultivars for flowers, ornamentals, tubers, bulbs and fruit plant species. Flowering plants include lily, carnation, chrysanthemum, orchids etc. Elite planting materials raised through tissue culture are being used for banana, pomegranates, peaches, berries, papaya, tamarind and pineapples among the horticultural plants and eucalyptus, sandalwood, teak, populous and bamboos among the forest plants. The Government has extended several incentives like automatic industrial approvals and refinancing facilities through certain banks. To exploit full potential additional efforts could enable India to contribute significantly in the global business in this area.

Biopesticides: Biopesticides based on Bacillus thuringensis (Bt) and Bacillus sphericus (Bs) are already being produced. Production techniques are being used for multiplication and formulation of Nuclear Polyhedrosis Virus (NPV) to control cotton bollworm (Heliothesis armigera) and tobacco caterpillar (Spodoptera litura); Granulosis Virus (GV) for sugarcane shoot borers (Chilo infuscatellus); Chrysopa for aphids, white flies and bollworms; Trichogramma for lepidopteran pests; and Trichoderma and Glioladium for root rot and wilt diseases. Controlled field level demonstrations in farmer's fields have been conducted and so far nearly 55,000 hectares have been covered in the fields of cotton, sugarcane, tobacco, tomato, chickpea, groundnut, pigeonpea, other pulses, sunflower and cauliflower at multi locations.

Biofertilisers: Nearly 4,000 tonnes of rhizobium useful for leguminous crops are being produced. The consumption of rhizobium biofertilizers in the country in the next 5-8 years is likely to rise by 8,000 to 10,000 tonnes per annum covering 50 to 60 percent of the 30 million hectare land being used for leguminous crops. Location specific cultures have been isolated and more than 600 production ponds are being operated for growing BGA for field trials in rice cultivation and nearly 7,000 field demonstrations have been organised to popularise its use. The use of algal biofertilisers demonstrated increased rice yield by 7 to 9 percent; at the same time use of chemical fertilisers could be reduced up-to 30 percent. The biofertilizer industry has high economic potential.

Mushroom Production: Currently, out of 2000 edible species known, only 25 are being cultured on commercial scale. In India, the Button and Oyster mushrooms contribute to the major share of production while Volvariella is grown to a certain extent in the tropical belts of India. Only few large-scale production units have been established, although, many small entrepreneurs and individual cultivators have taken up the profession of mushroom cultivation. Local markets are still unattractive and small industry is not fully developed and require further boost.

Animal Improvement: The milk production target to reach 85 million metric tonnes in 2000 AD from 51.5 million metric tonnes in 1990 is already met. Similarly production level of meat, wool and grease has increased. The genetic stock of animals specially cows and buffaloes is being improved through embryo transfer and other technologies. Cross breeding programmes have been intensified. Progeny tested sires of selected elites are being used for semen collection and preservation. Elite females of proven high milk production capacity are being identified for super-ovulation and raising of elite calves. Investment opportunities in various aspects of animal improvement such as production of bovine somatotropin and other hormones embryo banking, animal feed concentrates etc., seem enormous.

Industrial Products

Nearly 1300 million litres of alcohol is being produced from molasses in more than 250 distilleries. A yeast strain capable of tolerating 25-28 percent sugar (w/w) producing 9-12 percent alcohol (w/w) was developed indigenously. Citric acid is being produced by fermentation from molasses; the current consumption is around 8,000 tonnes annually of which more than 5,000 tonnes is produced locally. About 150 tonnes of lactic acid is being locally produced but the demand is expected to rise sharply. Nearly 95,000 MT of glucose and dextrose are being produced from tapioca starch using alpha amylase and amyloglucosidase. Cheese production, which is currently about 8,000 tonnes

annually, is gradually becoming popular and is being produced using imported microbial rennet. Penicillin acylase required for conversion of potassium penicillin G/V into 6-APA or 7-ADCA is increasingly being produced locally. The acylase is isolated from bacterial sources by fermentation. The current total consumption of all the enzymes in the country is of the order of about US$ 8 million only which is anticipated to go up substantially within the next few years.

Other Biotech Products

Restriction endonucleases, oligonucleotides, linkers, adopters, biochemicals, culture media, plastic-wares, pipettes, tips, petridishes, etc. required for biotech research are being produced in increased quantities locally in addition to imports. Solid-state fermentation of agricultural wastes into vitamin rich products as well as conversion of such wastes into probiotics for enriching poultry and animal feeds is also picking up fast. Techniques are being perfected for microbial leaching of copper pyrites, microbial benefaction of high silica containing bauxite and magnesite, using appropriate strains. Most of these efforts are at low stage of industrialisation and it is anticipated that these areas would make sizeable biotech impacts only after six to eight years.

Indian Industry and Government Initiatives for Biotechnology

The Indian government paid enormous attention to the regulation of economy and the industrial wealth including the private sector with an aim to promote public sector industries, setting up of high capital intensive public sector undertakings, nationalisation of major banks, central planning for the diversion of resources and introduction of industrial policy to boost public sector. These policies strengthened and the private sector regulated with the introduction of various Acts and other conservative policies like Foreign Exchange Regulation Act, Monopolies and Restrictive Trade Practices Act, The Indian Patent Act (1970), enactment of Control and Distribution of Essential Commodities Policy, Price Control Policy etc. Apart from these the small-scale sectors were given concessions at various levels. It was until late 1980s that the Government's initiative towards its industrial policy changed with new incentives. The growth of biotechnology research and development in the country started through "National Biotechnology Development Board" set up in 1982 which was changed in to an independent Department for Biotechnology in 1986 by the Union Government.

The Department of Biotechnology

Department of Biotechnology of the Ministry of Science and Technology established in February 1986, has helped in the promotion of biotechnology research and development in the country in modern biology, medicine and DNA technology. As biotech research is multidisciplinary, biotech research has been linked with various other scientific ministries and departments and over 4000-5000 scientists interact with the department in different capacities each year. Significant achievements have been made through its multi-pronged activities and a number of indigenous technologies have been developed and transferred to industry.

Major activities of the department include research and development in multi-disciplinary areas of agriculture, medical sciences and brain research, human genetics & genome analysis, vaccine and diagnostics, animal biotechnology including transgenics and embryo transfer technology, aquaculture & marine biotechnology, environment etc.; Biotechnology Product and Process Development & Technology Transfer; Biosafety aspects including GMOs; Intellectual Property Rights and Patenting; Human Resource Development; Setting up of infrastructure facilities, support services, advanced centres in biotech research and facilities; Biotechnology based programmes for the society; International Collaborations; Bioinformatics etc. The Department has already set up seven autonomous institutions looking into specialised areas of biotechnology. Biotechnology entrepreneurship development with industries and scientists teaming up for technology packaging and commercialisation is rapidly progressing.

Technology Development and Transfer

The Department, with its extramural research efforts has been successful in generating a number of indigenous technologies and their transfer to industry with careful monitoring of their absorption.

Department has assured that such technologies are not only transferred but absorbed and the product is brought out for the use of common man. The Department has been putting its resources to promote research within the country mostly in public funded institutions.

Government policies and Biotech Industry

The Central Government, with the objective of developing a globally competitive industrial sector, adequately modified the previous developmental policies from July, 1991 onwards. The licensing policy was substantially liberalised with the enactment of simpler policies over the years. To attract foreign investors the Ministry of Industry further liberalised the licensing policy through the establishment of Foreign Investment Promotion Board (FIPB) during 1997-98 and Foreign Investment Implementation Authority (FIIA) in 1999 to facilitate the flow of foreign investment in the country. In all this process the biotech sector also got the boost with the liberalised industrial policies.

In today's scenario of the liberalised policies, the industrial licensing allows automatic registration process. There is 100 percent rebate on R&D expenditure by a company and 125 percent rebate if the research is contracted through a public funded R&D Institution. These policies infused the corporate sector to set up their own R&D units to develop their own technologies. Today 100 percent foreign equity investment is possible in all industrial sectors. In the pharmaceutical sector 74 percent foreign equity investment is automatic and over 74 percent equity is also considered by the Union Government on case-by-case basis to promote this sector. This has led to the establishment of various technology parks in various sectors especially in the knowledge-based industry like Drugs & Pharmaceuticals, Information Technology and Biotechnology. There are over 55 research and development laboratories in the public sector and more than 20 are engaged in conducting research in the frontier areas of biotechnology where the Government has invested over US$ 200 million for creating R&D infrastructure and skilled manpower. These facilities can be teamed up by the private sector to perfect their technologies that cannot invest large amounts to create their own sophisticated infrastructure.

Department of Biotechnology has been working in close interaction with the Ministry of Industry on the promotion of Biotech industry in the country. The Department is the Administrative Ministry for Biotech Industry and heads the Fast Track Committee (FTC) of Foreign Investment Implementation Authority for the single window clearances of all mega projects costing more than US$ 20 million as Foreign Direct Investment (FDI) in the country.

Export Potential

Indian economy has undergone major restructuring since July, 1991 after the liberalisation policy of the Government was announced to integrate its economy with global economy including boosting its export. With the introduction of export friendly trade policy, an upward trend in consumption of Indian products has been seen in the international market. India has certain advantages for the lower production cost and abundant availability of skilled and qualified manpower. A number of diagnostics, group blood products etc. are available for commercialisation. With proper selection of products, India could also be a global player through export to certain countries, which may include neighbouring countries, middle-east countries, Southeast Asian countries and certain developed countries.

To Conclude

Biotech industries are at the forefront of other technological revolution. It is estimated that in India in the first decade of the new millennium, approximately US$ 4,000 would be invested mainly in the areas of health-care, agriculture, environment and the food processing industries. The demand for human and animal health care products would increase which would have potential opportunities for the biotech industry for further development.

Indian laws and the government policies are changing fast with the opening up of the economy. The scope of free trade and industrial approvals have been significantly broadened and liberalised and unnecessary procedural controls have been eliminated. New policies are in the offing especially

pertaining to intellectual property rights, right to information, foreign direct investment, customs and excise duties etc.

The country is pursuing an active programme of research and development cooperation in biotechnology with number of developed and developing countries including European countries. Opportunities are available for developing biotechnology related industrial products and processes through direct participation or through industrial and institutional framework.

The views expressed here are those of the author and do not necessarily convey the views of the Department of Biotechnology, Ministry of Science & Technology, Government of India.

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