Indian Biotechnology Developments in Public and Private Sectors - Status and Opportunities

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Reminiscence

The year 1982 was a landmark in the history of biotechnology in India. The Government of India, in order to promote biotechnology, relevant to the needs and priorities, constituted an agency, viz. the National Biotechnology Board (NBTB) under the Ministry of Science and Technology, as an apex co-ordinating body to identify prorities, coordinate, oversee and plan for required manpower, integrated industrial development and large scale use of biotechnology products and processes. A unique feature of this board is that all the existing S&T organizations and allied agencies have participated in formulating the objectives and organization of the structure of the board as well as made financial contribution for the core funding of the Board. In terms of identification of needs and priorities in biotechnology in India, the board had a unique international interaction through the formation of Scientific Advisory Committee (North America) [SAC(N)] in 1983.

Accordingly, various programmes for integrated manpower development and establishment of essential infrastructural facilities, realizing the need

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for capacity building through strengthening of existing laboratories, training of young scientists abroad, introducing course curriculum in biotechnology, etc. were initiated.

Establishment of Department of Biotechnology

Coinciding with the production of first transgenic farm animal and first approval of controlled experimental release of genetically engineered organism into the environment, in the year 1986 the NBTB was upgraded into a full fledged separate Department under the Ministry of Science and Technology, viz. Department of Biotechnology (DBT), in recognition of the need for having a focal point in the administrative structure of the Government of India for the purpose of planning, promotion and coordination of biotechnological programmes.

Present Scenario

Setting up of the separate Department of Biotechnology has given a new impetus to the development in the field of modern biology and biotechnology in India and has paid rich dividends.

Human Resource

Trained manpower and expertise in India belong to classical and modern biology/biotechnology. While in many developed countries it has become difficult to find young generation of classical biologists to supplement the inter-disciplinary modern biotechnology research, India has still adequate expertise in the fields like biochemistry, organic chemistry, taxonomy, pharmacology and traditional systems of medicine. Most of the present day modern biologists have long or short-term training in the laboratories of the USA and Europe. The programme of the government to award short - or long-term overseas fellowships, post-doctoral fellowships, etc. has resulted in the creation of trained manpower of more than 1000 scientists in a period less than 20 years. The post-graduate programmes in 47 universities and institutions train about 1000 students every year. Tailor-made industrial attachment and training programmes add value to the

technical skills of these students so as to make them suitable for advanced R&D and production activities. India has also a vast network of 60 bioinformatic centres, with more than 10,000 users and 100 databases. Post-graduate and diploma courses at some of these centers train more than 100 students every year in the field of bioinformatics (refer map).

Biotech Infrastructure

Since 1986, concerted efforts have been made by the Government of India towards capacity building, both in terms of human resource and sophisticated infrastructure for R&D. As a result, India has world class facilities for DNA sequencing, protein engineering, bioprocessing, crystallography, molecular graphics and modelling, PL3 and PL4 level containment for work on dangerous pathogens, prescribed glass/animal houses for transgenic animal/plant research, repositories of micro-organisms important in agriculture, healthcare and industry, *ex-situ* and *in-situ* gene banks for crops and endangered medicinal and aromatic plants, medium and high throughput screening facilities for drugs and pharmaceuticals, biosensors, nuclear magnetic resonance machines, different mass spectrometers for various purposes, GM testing labs and recently micro arrays, automated DNA sequencing as well as robotic plasmid isolation equipment. Most of the facilities could be shared by both the public and private research laboratories at a cost comparable to that of developed countries. There are about 200 laboratories with state-of-the-art equipment and facilities for recombinant DNA research. Many private sector R&D facilities also have sophisticated equipment in most of these areas and some of them are paid-up service facilities for researchers. The biotechnology equipment market in India is about Rs.1500 million and is growing at the rate of 2 to 3 per cent and the demand is shifting from public research laboratories to the private sector.

International Cooperation

India has signed several bilateral agreements for implementing joint projects and human resource development programmes. The earliest among them has been the Indo-US collaboration known as “Vaccine Action

Programme" focused to develop jointly vaccines and diagnostics for communicable diseases, followed by the Indo-USSR programme on assisting manufacture of Oral Polio Vaccine (OPV) resulting in establishment of a public sector vaccines company, viz. Bharat Immunological and Biological Corporation Ltd. (BIBCOL) near New Delhi. The BIBCOL has supplied several million doses of OPV to national immunization programme. There are now several ongoing activities with both developed and developing countries, such as Germany, UK, Switzerland, Sweden, Japan, France, Israel, Sri Lanka, Myanmar, ASEAN countries and the countries from SAARC region. India also hosts one of the centers of International Center for Genetic Engineering and Biotechnology (ICGEB) at New Delhi for training and research needs of developing countries in particular.

The main objective of the biotechnology international collaboration is to assist in implementation of national programmes; acquisition of knowledge in areas of specialization not available within the country; share expertise and large scale facilities; participation in joint R&D programmes; and add to the economic wellbeing of the country through private sector participation in product and process development, technology transfer and communication.

Research

At a given time in a year, there are at least 1500 R&D projects implemented by all S&T agencies. The trend has shifted from individual investigator projects to multi-disciplinary and multi-institutional projects involving industry and scientists from even traditional sciences wherever needed. In India, in the context of biotechnology, the areas of core competence are bioprocess engineering; gene manipulation of microbes and animal cells; downstream processing and isolation methods; extraction and isolation of plant and animal products; recombinant DNA technology of plants and animals; stem cell biology; bioinformatics; proteomics and genomics; traditional and molecular marker assisted breeding of plants and animals; fabricating bio-reactors and processing equipment; human and animal health products; agriculture biotechnology; industrial and other biotechnology products, etc.

Institutional Framework

India is signatory to the WTO and the country is taking steps to enact the provisions of the WTO both in letter and spirit. More regulatory dictums within the framework of the international commitments made by India to the WTO and Convention on Biological Diversity (CBD) are in the offing. These include enactment of Plant Varieties and Farmers' Rights Bill and creation of Plant Quarantine Authority of India. The Plant Varieties and Farmers' Rights Bill will seek to protect currently unprotected plant varieties that are novel, distinct, uniform and stable, for a period of 15 year from the date of registration. The Biological Diversity Bill has been framed with the intention of protecting India's rich bio-diversity and associated knowledge against the use by foreign individuals and organizations without sharing the benefits that arise out of such use. The Indian Patent laws were significantly amended in 1999 as part of India's commitments to the WTO. Recently, India signed Budapest Treaty and established International Depository Authority at Microbial Type Culture Collections at Chandigarh. The Department of Biotechnology has also published Ethical Document entitled "Ethical Policies on Human Genome, Genetic Research and Services" prepared by the National Bioethics Committee. The document bans any research on human cloning and germline interventions by Indian investigators.

Regulatory Mechanisms for rDNA Products

The Indian rules and regulations as well as procedures for handling of the genetically modified organisms (GMOs) and rDNA products have been formulated under the Environment (Protection) Act (EPA) 1986. The rules enforced since 1993 cover manufacture, use/import/export and storage of hazardous micro-organisms, genetically engineered organisms or cells. However, a set of rDNA guidelines were issued in 1990 covering genetically engineered organisms, genetic transformation of plants and animals, mechanism of implementation of biosafety guidelines, containment facilities at lab level under three risk groups, etc. The guidelines have been reworked and issued as Revised Guidelines for Safety in Biotechnology matching with the newer aspects of technology. In order

to provide special thrust to genetically engineered plants "Revised Guidelines for Research in Transgenic Plants and guidelines for Toxicity and Allergenicity for Evaluation of Transgenic Seeds, Plants and Plant Parts" came into force in 1998.

With coming into force of the above regulatory mechanisms so far 10 r-DNA drugs have been approved for marketing, four industrial units are manufacturing recombinant hepatitis vaccine, and locally and indigenously produced erythroprotein and G-csf are also available in the market. Several novel processes to produce r-DNA vaccines and drugs are in the advance stages of development. Under plants category, cotton with insect-resistant Bt gene was given approval for commercial release in March 2002. Following the regulatory procedures, at least 165 institutions are working in r-DNA research in India, which include 55 institutions engaged in transgenic plant research, both in public sector (42) and private sector (13). A large number of private institutions engaged in r-DNA therapeutics – about 25 out of 85 are doing basic research.

Regulatory policies in general are compliance friendly. However, the major criticism in this respect is that at present there are too many agencies involved in giving regulatory clearances. To address the concern of both public and private sector, efforts are under way to establish a single window regulatory mechanism or to put in place a structure which could promote speedy commercialization of recombinant products and processes. Over all, the system is relatively open and transparent yet precarious in its approach. In nutshell, there is enough expertise in technology and risk assessment of GM plants and therapeutics in terms of safety to environment as well as human and animal health. Keeping up with the recent trends/public perceptions on GM foods, appropriate measures and mechanisms are being evolved to label the same within the scope of CODEX alimentaries. GM detection and analytical food safety laboratories have been established to facilitate generation of scientific data. Similarly, containment facilities at the biosafety levels three and four are also available for both research and *in vivo* evaluations.

Technology Transfer

Since the early initiatives for biotechnology transfer of research leads, protocols and technologies to industry have been spearheaded by the Government S&T organizations, particularly the Department of Biotechnology. The process was accelerated with establishment of Biotechnology Consortium India Limited (BCIL), in 1990, to act as an agency for forging effective linkages between research, financial and industrial institutions and the policy making framework at the government level. So far more than 60 technologies and research leads from the Government funded R&D projects have been transferred to Indian industries for scale up, validation and commercialization. Some of these products such as leprosy vaccine, HIV and hepatitis diagnostic kits, natural streptokinase, veterinary diagnostics, etc. are already in the market and some others are in pipeline. With a view to encourage the institutions to file patent applications on their innovations, and to motivate them to transfer their technologies for commercialisation, and facilitate them to reward their inventors, some more instructions were issued during 2002 for institutions receiving funds for research projects from the Ministry of Science and Technology.

The institutions have been permitted to retain the benefits and earnings arising out of the IPR. The IPR generated through joint research by institution(s) and industrial concern(s) through joint efforts can be owned jointly by them as may be mutually agreed to by them through a written agreement. The institution and industrial concern may transfer the technology to a third party for commercialisation on exclusive/non-exclusive basis. The institution shall set apart not less than 25 per cent of such earnings for crediting into a fund called Patent Facilitating Fund. This Fund shall be utilised by the institution for updating the innovations, for filing new patent applications, protecting their rights against infringements, for creating awareness and building competency on IPR and related issues. The funding agency shall have a royalty-free licence for the use of the intellectual property for the purposes of the Government of India.

The general practice in many cases is to transfer technology through bidding by interested companies. Depending upon the stage of technology, market potential, and the cost effectiveness, transfer agreements typically contain clauses on payment of upfront lump sum (Rs 0.2 to Rs 20 million) royalty on sale proceeds (1 to 5 per cent) and exclusive or non-exclusive rights for a periods of 3-7 years.

Reforms in Science Funding and Management

India is among the few countries where S&T funding agencies are completely managed by qualified, scientists with specialization in the field being dealt by them. From time to time, several measures have been taken to institute expert-based priority setting process, peer review mechanisms, reducing project processing periods from submission to sanction, simple accounting systems for monitoring physical and financial progress, etc. Further, in most of the cases, all stakeholders are involved in decision-making.

Recently, national awards for biotechnology research and career development, special awards for women scientists, biotechnology product and process and commercialization have also been instituted by the government to recognize the innovation and excellence of scientists both in public and private sectors. However, there are some nagging problems at laboratory/institution/individual scientist level related to tedious and time consuming procedures for utilization of sanctioned funds, placing orders for equipment/chemicals, placement of research scholars, collaborating with laboratories abroad, visit to foreign countries for training or participation in international conferences. The problems are similar to all other disciplines and not specific to biotechnology. However, biotechnology being knowledge-intensive, tool and technique based, delay in implementation procedures often discourage investigators to take up innovative projects requiring timely decisions. Further, dual or erratic/ higher pricing policy of consumables and equipment by many foreign suppliers and their Indian vendors makes research in advanced areas unaffordable even though manpower is relatively cheaper. Appropriate measures, therefore, are needed to alleviate the problems faced by scientists in dealing with these matters so as to accelerate the pace of research and development and create work atmosphere.

Investments

Investment in Indian biotechnology began with the early initiatives of government and setting up of a separate department of biotechnology. Five year plans are made for such investment by the department for promoting biotechnology R&D, human resource development, establishment of biotechnology facilities, product and processes development and other activities. Since the establishment of the Department during the financial year 1985-1986 to March 2002, an investment of Rs.12.95 billion has been made. Fifty per cent of this investment has been made in the last five years and the same is increasing approximately by 30 per cent. In the early years most of this investment was made for human resource development and establishment of infrastructure. Since, 1997-98, the annual allocations for R&D are almost more than 60 per cent. Medical and agriculture research receive maximum funds.

Besides the Development of Biotechnology, other government S&T organizations agencies such as Indian Council for Agricultural Research (ICAR), Council of Scientific and Industrial Research (CSIR), Indian Council of Medical Research (ICMR), University Grants Commission (UGC) and Department of Science and Technology (DST), also support R&D programmes in biotechnology. Since in all of these organizations there is no separate data pertaining to biotechnology, it is difficult to provide the actual figures of investments made by these agencies. However, normally the contribution or sharing of cost in most of the projects is about 30 per cent, and, therefore, it can be presumed that the contribution by all these organizations would be around Rs.4.00 billion since 1985 till date.

Private Sector

Private sector investment has also been picking up since 1997 and became particularly visible after the announcement of the draft human genome sequence in the year 2000. There are no authentic statistics on the investment in the private sectors. This is because the definition of biotechnology and its indicators vary for different estimations. An Indian directory prepared by Biotechnology Consortium India Ltd. (BCIL) in

January 2001 includes biotechnology activities of about 176 companies in private sector whose products range from those in agriculture, environment and healthcare. On the other hand, estimates have also been made that about 800 companies are operating in various sectors of biotechnology, based on the definition that biotechnology includes basic industry such as food processing and highly sophisticated recombinant products. Employing the same definition one estimate says that 10 per cent (80) of these companies are operating in modern biotechnology sectors while according to another conservative estimate there are only 20 companies engaged in sophisticated biotechnology business. Similarly, it is also estimated that the industry employs 10 to 20,000 people and generates roughly a revenue of US$ 500 million annually. The Indian share of the biotechnology market was estimated at US$ 800 million in 1999 and has risen approximately to US$ 2.5 billion this year. Consumtion of biotechnology products is expected to touch the figure of Rs.14.6 billion.

Notwithstanding these figures by various estimations, it can be concluded that India's burgeoning biotechnology sector is an oasis of rich picking for investors as the government leads the drive to develop the industry. Building a biotechnology industry is a part of knowledge economy strategy of the government. A growing number of high quality Indian biotechnology investment opportunities exist for both early and late stage investors. Some of the major investors include, Connect Capital, ING Barings, Dresdner Kleinwort Benson, London and Warburg Pincus are evaluating Indian biotechnology investment opportunities. And that is not all; a London Stock Exchange-listed biotechnology company (with a market capital of US $125 million) is keen to ally with an Indian biotechnology firm, possibly via a merger. It has also been predicted recently by both Indian and US Business leaders that US stock market listings by Indian technology companies could explode to 100 or more new issues within the next five years.

Venture Capital Funding

With the increased role of established private sector as well as start-up companies investing in biotechnology, several financial institutions/

agencies, both in public and private sectors, have launched venture capital funding mechanism. The Ministry of Science & Technology created these opportunities through the establishment of Technology Development Board (TDB) in 1992 for providing financial assistance to industrial concerns and other agencies attempting development and commercialization of indigenous technology or adopting imported technology for wider domestic application.

The board has been particularly helpful in promoting several new start-up companies. Since its formation, the board has signed 100 agreements with commercial enterprises/agencies with a total projects cost of Rs 15.00 billion and there is a commitment of Rs.3.58 billion financial assistance to areas of health and medicine, engineering and electronics, chemicals and lubricants, agriculture and biotechnology, waste utilization, etc. Companies such as M/s. Shanta Biotechnology and M/s. Bharat Biotechnology, producing recombinant hepatitis vaccine, and M/s ABL biotechnology in marine biotechnology, are some known and successful beneficiaries.

Venture capital (VC) funding in India for biotechnology projects picked up with success stories of the technology development board (TDB). Six or seven prominent VC firms, including ICICI (Industrial Credit and Investment Corporation of India), Morgan Stanley, and Small Industries Development Bank of India (SIDBI) are active. The venture capital is mostly available to companies whose product and market are clearly identified and research leads are already available for commercialization. During 2001, the biotechnology venture capital committed by different financial agencies other than the Technology Development Board (TDB) amounts to a total of Rs.2.80 billion during the year 2001.

Foreign Direct Investments (FDI)

FDI is seen as a means to support domestic investment for achieving higher level of economic development through technology upgradation, access to global managerial skills and practices, optimum utilization of human and natural resources, making Indian industry internationally competitive, opening up of export markets and providing linkages and access to

international quality goods and services. Due to several steps taken by the Government of India, in terms of encouraging foreign investments in general, the approved Foreign Direct Investment (FDI) in biotechnology sector during 1999-2002 amounts to a total of Rs.1478 million for 26 cases. This amount is very meager compared to total FDI of all sectors which amounts to several million thousands of US dollars. This is due to inadequate awareness on the part of the foreign investors about the latest policy of the Government of India for the development of industries in all sectors including biotechnology (refer Box).

Incentives for investment in biotechnology industry and R&D

- ❑ 100 per cent foreign equity investment is possible in almost all sectors.
- ❑ 100 per cent foreign equity investment is automatic in drugs and pharmaceuticals sector, and over 74 per cent is on case by case basis.
- ❑ Fast Tract Clearance route for FDI.
- ❑ Depreciation allowance on plant and machinery set-up, based on indigenous technology.
- ❑ Customs duty exemption on goods imported for use in Government funded R&D projects.
- ❑ Customs and Excise duty exemption to recognized Scientific and Industrial Research Organisations (SIROs).
- ❑ 125 per cent weighed tax deduction on R&D Expenditure.
- ❑ Three-year excise duty waiver on patented products.
- ❑ 100 per cent rebate on own R&D expenditure.
- ❑ 125 per cent rebate if research is contracted in public funded R&D institutions.
- ❑ Joint R&D projects are provided with special fiscal benefits.

For details: www. techno-preneur.net
www. dbtindia.org

Biotechnology Activities in the States

With several major advances in biotechnology taking place in the last few years, it is natural that state governments wish to take part in the ongoing biotechnology revolution and benefit from the same.

States of Karnataka, Andhra Pradesh, Maharashtra, Uttar Pradesh, Madhya Pradesh, Gujarat, Himachal Pradesh, Kerala and Orissa have shown keen interest in the concept of developing biotechnology parks. Karnataka and Himachal Pradesh have set up separate Departments of Biotechnology at the state level. Others have set up Biotechnology Boards/Task Forces, respectively to make detailed plans. Tamil Nadu, Karnataka, Kelara and Andhra Pradesh have already announced their biotechnology policies.

State governments are also setting up biotechnology development funds of their own and earmarking significant amounts to invest in the companies located within their respective boundaries. Andhra Pradesh Industrial Development Corporation (APIDC), Kerala Venture Capital Fund (KVCF) and Karnataka State Industrial Infrastructure Development Corporation (KSIIDC) are some of the examples of the venture capital commitments amounting from Rs 100 to 500 million. Among them, State Government of Karnataka has been quite forward with total investment of Rs 13.00 billion during 1999-2002, while Andhra pradesh signed MOUs with biotechnology firms such as Proximare, Bioserve, Genetics and Sun Microsystems in San Francisco for putting in place concrete programme of research collaboration. In general, state governments have also announced incentives related to exemption of sale tax, concessions for land allotment, water and electricity and labour laws. The basic objective of these State Government initiatives is to promote bio-industry preferably based on local resources. Local people are also expected to benefit from the resultant employment generation.

Conclusion

The initiatives taken by the Government of India in the field of accelerating the growth of biotechnology sector since last two decades have paid rich

dividends. India has developed competence in selected biotechnology areas and come out with policies which provide the entrepreneurs an edge over other countries to set up viable and competitive biotechnology industry in certain areas. With its large resource pool of modern/molecular biologists, statisticians and software programmers, India seems well placed to capture most of the biotechnology market. Many Indian companies have introduced products of original research through technology transfer from R&D institutions of India in the field of vaccines, diagnostics and reagents. Some Indian have also teamed up with foreign collaborators for sourcing technologies and are experimenting new products produced with the help of foreign technologies with a view to introducing them into the Indian market within the framework of Indian laws. This situation is satisfactory to begin with, but there is tremendous scope to come up with innovative products that would be original and would have a cutting edge impact in the global context. Fresh investment of about US $1.00 billion in India could hold the potential of providing turnover of US$1.50 to 2.00 billion during the next 5 to 7 years, that could contribute to import substitution, augmentation of local production and introduction of some new products for global marketing in the areas such as diagnostics, vaccines therapeutics, pharmacogenomics, bioinformatics, agriculture biotechnology, industrial biotechnology, and also provide inputs to the industry (hardware suppliers - instrumentation and chemicals), marine biotechnology, biodiversity and bioprospecting and environment-focused biotechnology. India is expected to emerge as a strong player in both manufacturing and consumption market of biotechnology products in the coming years.

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