REGIONAL DEVELOPMENT

India: 50 years after independence

Healthcare modernization is providing opportunities for domestic and foreign companies developing medical and biotechnology products.

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At the fiftieth anniversary of independence from British rule, India is truly at a crossroads. Healthcare is playing a signficant role in efforts by the Indian government to modernize the country and at the same time to provide needed care for a population of nearly one billion. Modernization is also providing opportunities for domestic and foreign companies developing medical and biotechnology products to serve India's population. If market-oriented policies continue to grow as they have since the early 1990s, economic growth will continue to push an improved healthcare infrastructure.

After years of a socialist government, early in the 1990s, India began to embrace privatization, which included lifting price controls on drugs and allowing Indian firms to enter into strategic alliances with foreign partners. This freedom has attracted the attention of investors around the world, who are betting on India as the next emerging economy.

Today, healthcare in India has the distinct imprint of Western markets. Health insurance plans are being developed for urban dwellers and privately funded hospitals; research and medical centers are beginning to be built throughout the country. Efforts are underway to improve the efficiencies of public healthcare, and pharmaceutical companies are focusing increasingly on R&D as price ceilings on many drugs are lifted. And India's intellectual property protection seems to be coming into line with international law, as mandated by India's membership in the World Trade Organization.

The government of India has reduced tariffs on medical product imports, established public research and funding agencies to develop new technologies for transfer to private firms, and has set up government-sponsored venture capital funds such as Biotech Consortium India Ltd. (BCIL). The government has also instituted an aggressive national healthcare program it calls Healthcare For All by 2000 AD, a program designed to improve public healthcare facilities through greater efficiency and availability, as well as cleaning up alleged corruption at government-run facilities. Still, the government falls short in spending, with a meager 1.5% of its GDP, as compared to 10% in most Western nations.

Pharmaceutical manufacturers, who for many years faced mandatory government-imposed price ceilings on their drugs and formulations, have received relief on 73 of the 145 drugs formerly available only to government-run public sector companies and medical facilities. Since the 1995 Drug Price Control Order, both domestic and foreign multinational companies are able to market these drugs at prices set on the open market. This new policy has resulted in greater interest on the part of pharmaceutical manufacturers in basic and applied research which, until recently, was a low government priority. In the past, Indian drug companies simply copied formulations or imported products.

Today, the larger Indian pharmaceutical companies are investing 5–6% of annual sales in basic research. For example, in 1995, one of India's largest pharmaceutical companies, Wockhardt Limited, invested heavily in biotechnology R&D, and raised its R&D budget from 1% to 7%.

Private healthcare is taking hold in India as greater affluence provides those in cities with more choice in the type of care they receive. This sector, which is estimated to include over 260 million Indians, is increasingly opting out of the public clinic system, and is switching to private providers for better care, which will fuel the development of private health insurance. A recent federal budget allows private sector insurance companies to offer expanded services such as prehospital diagnostic services, organ transplants, emergency medical treatment, and maternity benefits. This trend is also fueling an increased demand for better drugs and medical devices, which should benefit both domestic and foreign biotechnology companies.

Within the public health arena, two primary programs have been instituted by the government to address the needs of rural Indians: the Minimum Needs and the National Health Programs, which have been designed to control communicable diseases such as malaria, leprosy, tuberculosis, AIDS, hepatitis, guineaworm, and river blindness. While the government has promoted these programs widely, only $183 million was dedicated to these programs in 1995—additional evidence that while the government's objectives are notable, still, the Indian Government falls short in its spending for healthcare, with a paltry 1.5% of its GDP compared to 10% in most Western countries.

The government has also launched a disease eradication program designed to strengthen rural health centers, give assistance to allopathic and homeopathic hospitals, and provide therapies for the control of noninfectious disease like cancer, diabetes, iodine deficiency, cardiac disease, and mental health problems. Toward this end, the government of India has announced that it will increase the number of Public Health Centers (PHCs) and subcenters throughout the country. According to the government, over 500 PHCs and 200 subcenters will be built between 1995 and 2000 to serve the nearly 700 million Indians who rely on government-sponsored programs to meet their healthcare needs.

It is also important to note that the Indian system of medicine, which includes centuries-old techniques known as ayurveda,

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unani, and sidha, maintain their popularity in India. Modern biological principles are being applied to improve these popular medical practices and several government-sponsored institutes are focusing on the use of traditional medicines in India. According to the Pharmacopoeia Laboratory for Indian Medicine, a drug standard testing laboratory for traditional medicines, there are over 1,500 plant species in India reported to have medicinal properties.

Vaccine development

The vaccine industry in India is growing at more than 10% annually. While India is producing many vaccines domestically, many major vaccines for the treatment of hepatitis A and hepatitis B are imported. In 1993, total sales of vaccine products in India amounted to $40 million. Both the private and public sectors are involved in vaccine development, production and marketing efforts, but the immunization practices are controlled by the government. Vaccination to all newborns and young children is one of the major goals of the government in order to prevent infectious diseases, and the government is also placing increasing emphasis on establishing domestic R&D facilities to meet the demand.

Since its inception, the Department of Biotechnology (DBT) has been attempting to develop vaccines for polio (OPV and IPV), measles, and rabies. To date, hepatitis B vaccine demands have been met entirely through imports, but now the larger Indian pharmaceutical companies are developing hepatitis B vaccines in India. Typhoid vaccines are available domestically and through the import market. According to industry experts, the whole cell-based cholera and typhoid vaccines produced locally had poor performance in the field.

In 1994, India's new drug policy mandated that genetically engineered drugs and cell culture-based drugs be free from mandatory price ceilings for five years from market entry. This policy was instituted in an attempt to increase the supply of vaccines in the market as the public sector vaccine facilities were not meeting domestic demand. These public sector pharmaceutical manufacturers develop vaccines to address all communicable diseases and often work in conjunction with India's national public health bodies. The ICGEB has been actively involved in vaccine R&D, but has yet to develop a commercially viable vaccine product.

International collaborations involving vaccine development are underway in India, such as the Indo-US Vaccine Action Program (VAP), a $10 million joint bilateral vaccine program initiated in 1987 between the governments of the United States and India. VAP is conducting joint research to develop vaccines to address viral hepatitis, rotavirus, cholera, *E.coli*, typhoid, pertussis, pneumococci, hemophillus, rabies, RSV, and polio. India also has ongoing collaborations in vaccine development with France, Belgium, and Russia.

Discussions are underway among Southeast Asian countries to participate in vaccine technology transfer programs, and between the governments of India and China to produce vaccines against hepatitis A, hepatitis B, hepatitis C, and hepatitis E. The International Vaccine Institute (IVI) being set up by the United Nations Development Program (New York) and the Korean government is negotiating with a number of Indian research institutes to collaborate in vaccine development. IVI already has ongoing collaborations with India's National Institute of Biologicals (NIB), the ICGEB, the Ministry of Health, and public and private vaccine companies in India.

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Several international pharmaceutical companies are developing and marketing vaccines to serve the Indian market, including SmithKline Beecham, Hoechst Marion Roussel, GlaxoWellcome India, Pasteur Mérieux, and Rhône-Poulenc India. Private Indian pharmaceutical companies involved in vaccine development include Cadila, Serum Institute of India, Bharat Serum & Vaccines, Wockhardt, Lupin, and Indian Immunologicals. Indian pharmaceutical companies will benefit from more market-oriented economic policies, and will no doubt play an important role in drug development to serve India.

The indigenous pharmaceutical industry will also benefit from the increasing number of off-patent products coming into the market in coming years. The growth rate for the pharmaceutical industry in India is estimated at 25–30% annually.

Biotechnology in animal health

Many domestic pharmaceutical companies have animal health divisions, and international companies such as GlaxoWellcome, Pfizer, Hoechst, and Bayer have targeted animal health as their primary area of interest in India. Biotechnology and genetics are being used to develop poultry vaccines both within the private companies and at national research labs such as the Indian Veterinary Research Institute (IVRI).

Salmonella vaccines for animal and human care are in great demand in India and include several nonrecombinant and recombinant vaccine constructs based on defined genetic mutations. The vaccines will be live or killed and can be easily administered through food, water or aerosol sprays. Some important joint ventures in the animal health area include a collaboration between Venkateswar Hatcheries, Ltd., India's largest poultry company, with two US-based companies, Tri-Bio Labs and ISA Breeders, Inc. Kegg Farms, another leading poultry producer is collaborating with US-based Immunogenetics to produce and market poultry vaccines.

India is the second largest producer of milk in the world, and has one-third of the world's cattle population. Yet, while India is a large producer of milk, yield per animal is the lowest in the world. The National Dairy Research Institute (NDRI), India's premier dairy research center, has already commenced large-scale commercialization of embryo transfer technology. An Eli Lilly/Monsanto collaboration has targeted the Indian market and Eli Lilly will soon be marketing Monsanto's recombinant bovine growth hormone (rBGH), which is responsible for higher milk yields. In addition, the Indian diary industry suffers from poor hygiene, poor fodder, outdated processing techniques, and lack of proper storage. The National Dairy Development Board (NDDB) and Gujarat Cooperative have played an major role in promoting dairy industry in India.

Agricultural biotechnology

India exported $5 billion worth of agricultural products in 1995—a 20% increase over the previous year. The exports included food grains, fruits, vegetables, seeds, processed food, flowering and ornamental plants.

The Indian commercial seed market has been estimated at close to $300 million and is expected to grow to $1.4 billion by the year 2000. The government has established what is called its new seed policy, which will promote the entry of multinational corporations into India to establish R&D and marketing of seed products. There are currently about 40 Indian private companies involved in the development and marketing of agricultural seed products.

It is expected that, within a few years, several genetically engineered agricultural products will enter the Indian market including transgenic canola, cotton, potato, soybean, squash, tomato, and seeds.

Several foreign firms are involved in agriculture biotechnology. Hindusta Lever Ltd., a subsidiary of Unilever, has established an R&D center in Bangalore employing 200 scientists, and DuPont (Wilmington, DE) is awaiting clearance to open its agriculture R&D facility. Monsanto India has set up a life science and agriculture facility in India and also markets agrochemicals. India has proven to be a vast market for many of Monsanto's agrochemical products and transgenic crops.

India is the largest producer of fruit in the world, and the second largest producer of vegetables after China. However, India accounts for only 1% of world exports of fruits and vegetables. Some industry experts believe that if India can modernize its agriculture processes, the country could become the world's largest exporter of fruits and vegetables—over 20%—by the year 2020. For both the domestic and export markets, the ability to improve food processing and packaging will have an enormous impact on India. Already, advances in agriculture biotechnology have impacted this sector. Over 382 organizations—both public and private—conduct research into commercial applications of biotechnology as it relates to food processing. Of these, 200 are research institutes or university laboratories, 137 are private firms, and 45 are equipment suppliers. The estimated market for biotechnology products and services for food processing was $40 million in 1996.

An important subsector of the Indian biotechnology market deals with enzymes, amino acids, and flavors. Packaging and storage of foodstuffs in India has a huge market potential for domestic and foreign companies alike.

Approximately, $2 billion worth of fruits and vegetables are lost in India due to inadequate postharvest technologies. During the next ten years, total investment in agriculture biotechnology in India could reach $100 million. Much of the public funding going to agriculture biotechnology is funneled through the Indian Council of Agricultural Research (ICAR), which operates under the purview of the Ministry of Agriculture. ICAR has targeted cereal, pulse, vegetable, and floricultural crops, and funds approximately 200 agricultural projects at 15 institutions and 28 universities in the country. The DBT has substantial investment in plant biotechnology research and development. The Indian Agricultural Research Institute (IARI), which is supported by ICAR, has established the National Research Center for Biotechnology, which focuses on plant genetic engineering related to agriculture.

Other important research institutes involved in agriculture biotechnology include the Indian Institute of Horticulture Research (IIHR), Tata Energy Research Institute (TERI), Central Rice Research Institute (CRRI), and the National Bureau of Plant and Genetic Research (NBPGR). It is estimated that by the year 2005, healthcare biotechnology investment will reach over $225 million, with $57 million invested in agriculture biotechnology. With the advent of new technologies, Indian agricultural scientists are incorporating recent methodologies, including biotechnology for the improvement of crops and to sustain germplasm. Various research institutes, both private and public, are developing hybrid tomatoes, brinjal, transgenic plants, plant tissue culture technology, seed technology, and biopesticides. The Indian subcontinent has over 7,000 plant varieties and is an invaluable source for gene banking. The National Facility For Plant Tissue Culture Repository is setting up a gene bank, which will have the capacity to store 10 million plants.

Population growth trends point to the need for increased yields in food grains from the current 200 million tons of annual production today to 300 million tons per year by 2000. Hybrid seed technology for sunflower, rice, wheat, corn, tomato, and vegetable crops are currently under development. Other public and private research projects underway include the development of disease-resistant plants, cloning genes for floral meristem initiation, and tagging genes of agronomic importance.

Intellectual property protection

Market-driven economic policies and India's membership in the WTO will have a tremendous impact on intellectual property protection in India. WTO membership requires that India tighten its intellectual property (IP) protection to comply with WTO standards by 2005. Under WTO guidelines, member countries must grant product and process patents for 20 years. This protection will also apply to industrial designs—which is important for the medical device and instrumentation industry. These changes are already having an effect on basic research in India and will likely lead to more products developed in India to serve the domestic market. However, both domestic and foreign companies must remain cautious.

There are factions within the country who oppose IP protection on the grounds that is will cause the price of medical treatments to soar, effectively pricing the poor out of the healthcare market. Also, the Indian government continues to face charges by the United States Trade Representatives Office (USTR) of "foot-dragging" in restructuring its IP protection laws.

The patenting of natural resource-based discoveries is not permitted in India, and this is likely to continue to be enforced, even as patent protection of food and drugs are strengthened. Under the terms of the Biodiversity Treaty, signed in Rio de Janeiro in 1992, India would have sovereign rights to plant genetic resources found in India. Still, processes and products derived from plant and biological discoveries will be patentable by domestic or foreign organizations. Multinational pharmaceutical companies hold the highest number of patents in India for biotechnology processes.

Currently, while India enjoys a rather strong leadership position in plant tissue culture R&D, the country has not been able to harness the strong commercial potential for certain Indian flora. Instead, foreign pharmaceuticals have benefited from development of the shrub apocynacae, which yields several alkaloids and is an active ingredient in tranquilizers, sedatives, and antihypertensive drugs.

The Council of Scientific and Industrial Research (CSIR) and ICAR are setting up a "patent-watch" section to halt what is called "biopiracy" or "genetic colonialism". CSIR has begun a project to characterize all ayurvedic medicines as a means of detecting the scientific principle behind these traditional medicines and identifying their essential ingredients.

Indian government officials are keeping a close eye on foreign pharmaceuticals and are attempting to control indigenous plant and biologicals, with some charging foreign researchers with exporting important genetic information from India to hasten research in North American and Europe. The government recently set up several institutes designed to maintain genetic libraries and maintain cryogenically preserved tissues to assure that Indian companies and research institutes maintain first rights on these discoveries. The institutes include the National Facility for Plant Tissue Culture Repository, the National Bureau of Plant and Genetic Resources, the Central Institute of Medicinal and Aromatic Plants, and the Tropical Botanical Gardens and Research Institute.

Conclusion

As India celebrates its fiftieth anniversary of independence, the government is laying the foundation for modernization, of which healthcare plays an important role. This new attention to improved healthcare, with its emphasis on basic research, will have multiple benefits for India. Improvements in India's healthcare system will encourage breakthrough discoveries by Indian scientists, support new and better hospitals, and will provide the impetus for a medical equipment and biotechnology industry that is sure to impact India's economy. Finally, and most importantly, a modernized medical sector will significantly improve the health and well-being of millions of Indians as the country enters the next century. ///