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GUEST EDITORIAL

Biomedical research in India: paradigm shift to translation

Biotechnology, a word coined in 1919 by the Hungarian Engineer Karl Ereky, was used to denote products derived from raw materials with the aid of living organisms. It evolved from brewing and fermentation industries to address requirements in almost all facets of day-to-day life: health and disease, food and agriculture, environment and industry. The elucidation of the DNA structure in 1953 and the advent of genetic engineering tools in the 1970s have provided an unlimited scope for the application of this technology. Growth in the biopharmaceutical sector would give a rough measure of the rate of growth of biotechnology globally. The US Food and Drug Administration (FDA) had approved only five products by 1988: synthetic insulin, human growth hormone, hepatitis B vaccine, alpha-interferon and tissue plasminogen activator. This number reached to over 125 products by the end of 1990s. The FDA approvals have been around 30 products on an average in the last 10 years, reaching to over 40 products in the last two years. Biotechnology, genetic engineering (GE) in particular, has also significantly influenced agriculture in the US. GE technology in agriculture is a seriously debated issue. This Guest Editorial is confined to the health sector.

Pasteur Institute, Conoor, King Institute of Preventive Medicine and Research, Chennai, Central Research Institute, Kasauli and Haffkine Institute, Mumbai with origins in late 1800 and early 1900 pioneered in several vaccines (examples: Small Pox, polio, cholera, rabies, anti-snake venom and other conventional vaccines). These have a chequered history but have been restructured to tackle infectious diseases in the present day as well. Hindustan Antibiotics, established in 1954, was the first public sector company in the area of drugs and pharmaceuticals, and made antibiotics such as penicillin, streptomycin, gentamicin, amoxicillin, etc. and had to be restructured in later years. Serum Institute of India was founded in 1966 by Cyrus Poonamwallah with the objective of making immuno-biologicals. It is the largest vaccine company in the world in terms of the number of doses of vaccines made and supplied to 140 countries. The story of Biocon is a heart-warming one, where a woman entrepreneur, Kiran Majumdar Shaw, stood against all odds to establish a true biotech company in 1978. It is indeed a saga where she started in a shed with making enzymes for the brewery and grew up to be a major biopharmaceutical company making statins, insulin and therapeutic monoclonal antibodies. Biocon became the first biotechnology company in India to issue an IPO. Indian Immunologicals Ltd was established in 1983 by National Dairy Development Board to make veterinary vaccines and is a leader in the manufacture of foot and mouth, and rabies vaccines. Shantha Biotechnics was established in 1993 in Hyderabad by Varaprasada Reddy and is the first Indian company to put a recombinant product in the market, hepatitis B vaccine. Bharat Biotech was established in 1996 by Krishna Ella and Suchitra Ella, and is devoted to the development and manufacture of modern vaccines. Astra Research Centre, Bengaluru, was established in 1986 by Astra-Sweden, which operated as Astra-Zeneca since 2003 in its new premises. The centre was devoted to drug development against tuberculosis and malaria, till it was decided to close down the operations a couple of years ago. This Centre gave rise to a few start-ups such as Bangalore-Genei and Xcyton companies.

Government of India recognized the importance of biotechnology early enough and established the National Biotechnology Board (NBTB) in 1982, which became a full-fledged Department of Biotechnology (DBT) in 1986. DBT contributed significantly to the growth of life sciences research in the country by establishing new research institutions such as the National Institute of Immunology, New Delhi; National Centre for Cell Science, Pune; Centre for DNA Fingerprinting and Diagnostics, Hyderabad, and five other institutions spread across the country. It also created infrastructure in various other institutions such as the Indian Institute of Science (IISc), Bengaluru; IITs, CSIR and ICAR laboratories. There was a major thrust on human resource development through internal and overseas training as well as the Master's programmes in biotechnology. DBT also took major efforts to enact the regulatory regime to carry out recombinant DNA research in the country. In terms of translation, mission-mode programmes were initiated to generate modern vaccines, biologicals and diagnostics.

The initiatives of DBT set the stage for generating biotech products. The annual budget of DBT has risen from Rs 6 crores in 1986 to Rs 1800 crores in 2016. The quality of life sciences research in the country has improved substantially. Even so, the successful translational efforts were essentially in the industry sector and the participation of mainstream academia as such was not significant,

except for a few examples such as recombinant hepatitis B vaccine made at IISc and cholera vaccine and streptokinase (to dissolve blood clot) developed at the Institute of Microbial Technology, Chandigarh. The industry essentially took to body-shopping from abroad, but made substantial contribution to downstream processing in product manufacture. Thus, India is a global leader in vaccine supply. It is catching up with the manufacture of biogenerics (molecules out of patents) such as insulin, interferons, growth factors and clinical-grade enzymes such as streptokinase and uricase. Biotech industry has grown at a healthy 20% and with a turnover around 6–7 billion USD. The health sector accounts for more than 60% of the turnover. Even so, all these numbers only account for 2% of the global biotech market. In addition, there is the greater challenge of making vaccines, biogenerics and diagnostics affordable to poorer sections of the community.

A paradigm shift took place with the setting up of Small Business Innovative Research Initiative (SBIRI) almost a decade ago. It was the brain-wave of M. K. Bhan (former Secretary DBT), to take the initiative to fund industry directly to carry out translation research with or without academia collaboration, the only requirement being that the industry should invest 50% of the cost of the total project. SBIRI is based on a similar initiative in the US, with appropriate changes in the Indian context. While SBIRI was started to establish the proof-of-principle, soon it was realized that the successful projects need to be taken forward with larger funding and thus was born the Biotechnology Industry Partnership Programme (BIPP). A major initiative was the setting up of Biotechnology Ignition Grant (BIG) to attract young, potential entrepreneurs with or without a Ph D, who may have ideas, but not the money to invest. A BIG grantee can get up to Rs 50 lakhs as grant to test out an idea within 18 months in any incubator or industry. BIG partners at Benglauru (c-CAMP), Hyderabad (IKP Knowledge Park), Pune (NCL Venture Centre), Delhi (FITT at IIT) and Bhubaneswar (KIIT-TBI) are involved in evaluating and mentoring the BIG projects. An important step has been the setting up of Biotechnology Research Assistance Council (BIRAC) as a section-8 company (not-for-profit) under DBT about four years ago encompassing all the components, a unique venture in the Government system. In the last four years BIRAC has fuelled the innovation pipeline through nurturing young entrepreneurs to take the path of BIG, SBIRI and BIPP, with lateral entries for established companies as well. It has also created incubators for start-ups. A dramatic shift is taking place in terms of the attitude of academia to collaborate with industry, and a Contract Research Scheme (CRS) allows the large-scale validation of discoveries made in the academia by the industry. Interestingly, BIRAC has funded 509 projects with a total funding of Rs 1442 crores, with industry–academia collaboration accounting for 115 projects involving 88 academic institutes. The performance of BIRAC has received encomiums from the Government and an impact assessment gives the following picture: companies supported 346, entrepreneurs supported 170, new start-ups supported and scaled up 104; small and medium-sized enterprises (SMEs) strengthened 100; early stage technologies 25; affordable products, technologies developed 29 and IP generated 100. More than 20% of the entrepreneurs/start-ups are now being able to attract follow-on funding and also series A/B investor funding. A few of the successful projects to be quoted as examples relate to: devices and diagnostics (e.g. ELISA-based tests for HIV and hepatitis; micro PCR to detect malaria, dengue and typhoid; digital oncopathology slide scanner, a device for tumour ablation); vaccines and clinical trials (e.g. rotavirus vaccine, JE vaccine and H1NI pandemic influenza vaccine); drugs and drug delivery (e.g. C-Met kinase inhibitors against cancer, Galnobax for diabetic foot ulcer, novel inhibitors for drug-resistant *S. aureus*). BIRAC has expanded its scope and has joined hands with Bill and Melinda Gates Foundation, Wellcome Trust, USAID, CEFIPRA and French Embassy, Department of Electronics and Information Technology and other Departments of the Science Ministry. BIRAC has also created several networking platforms for start-ups and SMEs inside and outside the country. The projects range from personalized medicine to SPARSH (Social Innovation programme for Products: Affordable & Relevant to Societal Health). About 175,000 sq. ft of bioincubation space has also been created in 15 locations across the country along with five university innovation clusters.

The initial success of the BIRAC mission has spurred the government to set a target of USD 100 billion for turnover by 2025. Traditionally, the strength of the industry has been in downstream processing of biogeneric molecules. Now, there has to be an emphasis on upstream innovation, and this would need participation of academia. Synthetic biology has emerged as a major discipline to generate novel molecules in different sectors. The tremendous enthusiasm created by BIG and other programmes to attract young entrepreneurs and foster more academia–industry collaboration beckons a bright path ahead. An exponential growth would be necessary and this would require a huge increase in start-ups in a conducive atmosphere, more manufacturing facilities and a sensitive regulatory environment for approvals. The challenge is to graduate from import substitution to innovative new products. A greater challenge is to make them affordable.

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