New Technologies:
An International Perspective

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3

Introduction

The impact of modern biotechnology on the world's economy is becoming increasingly evident, as the past two decades of investments are now resulting in a wide range of new products, processes, and services. Total sales of these new biotechnology-based products in the USA, presently the major market, were approximately $A12 billion ($US8.8 billion) in 1995. It is estimated US sales alone will increase by 12% annually over the next decade, leading to total sales of approximately $A43 billion ($US31.4 billion) by 2006 (Ernst and Young, 1995).

Biotechnology has been defined by the United States Office of Technology Assessment (OTA, 1991) as *any technique that uses living organisms to make or modify products, to improve plants or animals, or to develop microorganisms for specific uses*. It is comprised of a continuum of technologies, ranging from *traditional biotechnology* based on long-established and widely used technologies, such as those used in fermentation, through to *modern biotechnology* based on more recent techniques of recombinant DNA technology to enable the genetic manipulation of living organisms, modern immunology as a basis for new diagnostics and vaccines, and new cell and tissue culture techniques for the production of biological products.

Biotechnology is thus not an industry in itself, but a set of enabling technologies that are being applied to research and product development in several existing industries, notably in the pharmaceutical industry, agriculture and food processing, and in the conservation of the environment.

International Perspective

Evolution of technology and investment

Modern commercial biotechnology originated in the USA in the mid-1970s when the business and scientific community recognized the commercial opportunities arising from the new discoveries in genetics, immunology, and biochemistry. Biotechnology has been described '*as the first business with enough glamour to persuade eminent scientists that the entrepreneurial spirit and academic respectability are not mutually exclusive*' (Wyke, 1988).

The major reason for the greatly increased role of the private sector in modern biotechnology is that for many of the new technologies the process and/or the product are protectable by patents and other forms of intellectual property rights. Thus a company is able to appropriate many of the benefits of its R&D investments in biotechnology, in contrast to previous public good research in biology, from which an individual or organization could not benefit directly from inventions by the commercialization of the intellectual property involved. This new situation means that powerful new discoveries in biology and genetics are able to be developed into valuable commercial products.

In the USA, biotechnology developed as a business initially through the creation of new biotechnology firms, some 400 of which were already established in the USA by the late 1970s. The characteristics of these start-up companies are that they are small, technology-based enterprises, often established in close association with a university. They are usually dependent on venture capital and equity investments. They have a strong R&D component and a long lag time to product development. Many of the new biotechnology firms are loss makers, at least initially, and often need to go to the capital market more than once for venture capital and equity investments.

The major companies in the pharmaceutical industry and agribusiness have also progressively utilized biotechnology in their businesses, in order to develop new products, to reduce the costs of production, to improve productivity, or to conserve the environment. The areas where the major companies are investing in biotechnology are in human health care for new diagnostics, drugs, and vaccines; and in agriculture for products such as new biopesticides and novel crop varieties with improved characteristics, such as improved pest resistance, extended shelf life, or better processing quality. Approximately four times as much has been invested in R&D for biotechnology applications for human health care as for agriculture. Total biotechnology-related R&D expenditure in the USA in 1995 was $A9.6 billion ($US7.0 billion) (Ernst and Young, 1995).

The major companies became involved in biotechnology through both in-house R&D and contract R&D with academic institutions and new biotechnology firms, from which the major companies owned or shared any resulting intellectual property. There has also been a significant public sector investment in modern genetics and related biological sciences, through universities and national research institutes, notably in the USA, Japan, Australia, and several European countries through the 1970s and 1980s, building on the discoveries in recombinant DNA technology and immunology of the early 1970s.

The biotechnology business evolved differently in the USA and Europe, in that approximately two-thirds of all new biotechnology firms were established initially in the USA. Relatively few were established in Europe, where biotechnology has developed primarily through the major European pharmaceutical, chemical, and food companies, especially those from France, Germany, Switzerland and the UK, that operate globally. Similarly, in Japan, the large Japanese companies are the major investors. Australia has a small number of start-up, biotechnology-based companies as well as activity by larger companies, both Australian-owned companies and multinational companies and their Australian subsidiaries.

Changes in the International Environment

There have been several significant changes in the international environment that have led to consolidation and restructuring within the biotechnology sector. As a result of the 1987 stock market crash in the USA and elsewhere and the consequent loss of investment capital, many small, public biotechnology firms either merged, were acquired by larger companies, or went out of business. The constraints on the early start-up companies were: that they lacked sufficient development capital; it took longer and cost more for product development than originally expected; regulatory processes for product approval were slow and costly; and the new firms lacked marketing and distribution channels for new products.

Because of these constraints, most new biotechnology firms that did develop promising technologies and/or products have entered into strategic alliances, joint ventures, or been acquired by major companies, to ensure the successful commercialization and distribution of their products. Having such partners also became important in moving new products through the regulatory channels, a process with which the pharmaceutical and chemical companies were well experienced.

The regulatory process for pharmaceuticals developed using recombinant DNA technology is essentially the same as for conventional drug development, based on chemical technology. In agriculture, the development of suitable regulatory arrangements has been more controversial, due to perceived threats to the environment and to biodiversity by the release of genetically engineered organisms. The US system is based largely on assessing the familiarity of the product and its characteristics. The European system places more emphasis on the process by which it is produced. A safe and efficient national regulatory system with facilities that meets internationally agreed regulatory standards is a comparative advantage for countries investing in biotechnology (Persley *et al.,* 1992; Doyle and Persley, 1996).

Market Size and Trends

In the 1990s there has been a new wave of investment in biotechnology as the first suite of novel products have come to market successfully. Total industry sales in the USA were approximately $A12.4 billion ($US9.1 billion) in 1995, an increase of 21% over the previous year. The estimated sales for 1996 were $A13.5 billion ($US9.8 billion). It is estimated that these sales were for human therapeutics (75%), human diagnostics (17%), agriculture (3%), specialties (3%), and non-medical diagnostics (2%). An annual average growth rate of 12% is anticipated over the next decade, leading to a market of approximately $A43 billion ($US31.4) in the USA alone by 2006.

Pharmaceutical industry

The early biotechnology-based products have been mainly human therapeutics. Product sales in 1996 were expected to reach $A10.7 billion ($US7.8 billion). There are presently 34 products on the market in the USA. These are mainly products for gene therapy and new vaccines. There are approximately 284 potential new pharmaceuticals in clinical trials in the USA, 40% of which are being tested for cancer treatments and 10% being tested against AIDS/HIV (PHARMA, 1996).

Biotechnology is now an integral part of new drug development. It is estimated that by the year 2000, 85% of all new pharmaceuticals will be produced as the result of using biotechnology in both the R&D and production processes.

New diagnostics is an area where new biotechnology companies developing products for niche markets have been especially successful. Diagnostic monoclonal antibodies are being used in drug testing, cancer detection, pregnancy and fertility testing, and the diagnosis of infectious diseases such as AIDS and herpes. Sales of human diagnostics are expected to be $A2.4 billion ($US1.75 billion) in 1996 and grow at least 9% annually.

Agriculture and food processing

Biotechnology now has increasing commercial applications in agriculture and food processing. There are at least 15 new products on the market, with the first recent releases of new varieties of crop plants with novel traits (e.g. cotton with insect resistance, potatoes with disease and insect resistance, and tomatoes with extended storage life; canola with herbicide resistance). In 1996, it was estimated that there were approximately 0.6 million ha of novel crop varieties grown in the USA. Other products on the market include new diagnostics for plant and animal diseases, biopesticides, and vaccines to prevent animal diseases.

Annual sales of the novel agricultural biotechnology products were estimated to be $A380 million ($US277 million) in 1996, with a rapid annual growth rate of 20% predicted over the next decade as the many new products in the pipeline come to market. In the agriculture and food sector, it is recognized that the products of biotechnology will be delivered mainly through seed. The time to commercial release of some products has been delayed by the lengthy and controversial regulatory processes in the USA and the European Union, due to public perceptions of possible risk from the release of genetically engineered organisms into the environment. The regulatory system in the USA and Canada is being streamlined but the EU system continues to be time-consuming and controversial.

Environmental biotechnology

Biotechnology techniques, based on the use of microorganisms, can be used to clean up hazardous waste sites, to degrade industrial waste, to clean up oil spills and to rehabilitate mining sites. While long-standing problems in industrial countries, these environmental problems are also emerging in the newly industrialized countries and new, biologically based solutions are being sought. Environmental biotechnology is a growing segment of the market, with sales forecast to grow from $A300 million ($US219 million) in 1997 to up to $A800 million ($US584 million) by the year 2000.

Biotechnology also offers the possibility of more environmentally sustainable agricultural production, for example by the use of novel biological agents rather than pesticides to control plant pests and weeds, an advantage both to the environment and to the consumer. There are several new biopesticides emerging, with potential for use in integrated pest management systems in a range of crops where pesticide use is presently excessive and damaging to human health and the environment (Waage, 1996).

Production and marketing

The novel products arising from biotechnology have been taken to market mainly by the major pharmaceutical companies and by the agrochemical and seed companies. Many of the technologies were developed either by public sector laboratories or by new biotechnology firms. These technologies have either been licensed to the major firms or the latter have acquired new firms with promising technologies. The major companies have three advantages: (1) a global distribution and marketing network; (2) sufficient cash flow to acquire new firms with their intellectual property; and (3) the funds to continue to invest a proportion of their profits in R&D to develop the next generation of novel products.

This trend towards mergers and acquisitions is particularly evident in agriculture, where much of the enabling technology, intellectual property, patents, knowledge, and investment in the commercial use of agricultural biotechnology now lie with a small number of multinational companies. Access to, and freedom to operate with, the core technologies held by these firms in order to evaluate their applicability to other commodities and problems worldwide is a critical issue in agricultural biotechnology.

Investment Trends

Since 1995 there has been a new wave of private investments in biotechnology as investors try to capture the benefits of the new technologies. Ernst and Young (1995), in their annual review of biotechnology, note that there were approximately 1300 biotechnology companies in the USA, about 650 of which were small biotechnology companies and 260 were large public companies, mainly in the pharmaceutical, chemical, and food industries. There were a further 485 biotechnology firms in Europe, mainly large companies in the UK, France, Germany, the Netherlands, and Belgium.

The major companies are continuing to invest heavily in contract R&D with universities and small biotechnology firms and owning or sharing the intellectual property if any potential commercial products or processes emerge. The new biotechnology firms continue to seek strategic alliances with other companies for product development and distribution. The number of such alliances in the USA increased from 152 to 246 between 1994 and 1995, a jump of 62%. Approximately 30% of these alliances were with overseas partners (Ernst and Young, 1995).

Venture capital remains a major source of funds especially for small and medium-sized biotechnology companies. Venture capital-financed biotechnology companies in the USA raised an average of $US4.7 billion per year in private equity finance from 1992 to 1994. The trend in the USA since 1994 is for venture-capitalists to invest in mature companies when they have developed promising products to a stage close to commercial marketing rather than start-up companies (Ernst and Young, 1995).

Another trend is the restructuring and reduction in public sector expenditure in science in several OECD countries, with greater emphasis on public sector institutions earning a proportion of their income from contract research and the commercialization of their inventions. Several OECD countries have various tax and financial incentives to encourage private sector participation in biotechnology. One of particular interest is the UK initiative on *Biotechnology Means Business*, to which the UK government has committed £10 million ($US16 million). The programme, managed by the Department of Trade and Industry, aims to inform companies of the opportunities and benefits of using biotechnology in their business, with assistance provided through a telephone help line, follow-up technical advice, seminars, publications, and competitive grants, including a new grants scheme to encourage public sector agencies to collaborate in assembling portfolios of intellectual property suitable for commercialization (DTI, 1996).

Several other member countries of the European Union are also promoting biotechnology, through promoting the growth of existing and new biotechnology companies, direct government support, the encouragement of venture capital investment, and the adoption of less restrictive regulatory systems. The UK presently leads Europe in terms of the number of biotechnology-based companies and the promotion of an active financing environment. France and Germany have also begun to examine ways in which they can stimulate the development of local biotechnology-based companies as they recognize their potential impact on employment and sustainable industrial development (Ward, 1997).

Another changing factor is that several developing and newly industrialized countries are now investing substantially in biotechnology for its applications in human health care, sustainable agriculture, and food production. For example, there is increasing interest in investments in biotechnology in Asia, especially in China, India, Korea, Malaysia, and Singapore. The Malaysian Government has established a National Directorate of Biotechnology, with substantial funds to invest in the development and commercialization of biotechnology. Similarly, Singapore has substantial public and private funds to invest in biotechnology as well as various tax and other financial incentives to encourage biotechnology companies to establish operations in Singapore.

The development banks, such as the World Bank, and a number of bilateral agencies and private foundations are assisting many developing countries through grants, loans and technical assistance to develop capacity in biotechnology. The countries include Argentina, Brazil, China, India, Indonesia, Kenya and Zimbabwe, amongst others. Biotechnology is seen as being essential for increasing incomes of people in poorer countries and meeting world food needs into the next century (CGIAR, 1997b).

The World Bank has lent at least $US100 million for biotechnology-related activities, while bilateral development agencies, such as those of the USA, the UK and the Netherlands, and private foundations such as the Rockefeller Foundation, have invested approximately $US200 million in biotechnology R&D over the past decade (Brenner, 1996; IBS, 1994). The international agricultural research centers, sponsored by the Consultative Group on International Agricultural Research (CGIAR), a group of some 50 governments and private foundations, presently spend approximately $US22.4 million per year on biotechnology R&D for crops and livestock important throughout the developing world (CGIAR, 1996).

Emerging Technologies

The emerging technologies that will have most impact over the next decade are: molecular genetics, particularly genome mapping; cellular and molecular immunology, including the role of cytokines in human health and the development of novel vaccine technologies; and new technologies for drug design and synthesis based on knowledge of the structure and function of the drug and its target.

The International Human Genome Project aims to map the entire human genome, at a cost of some $A4 billion ($US3.2 billion) over the next decade. This project is likely to lead to a new generation of human therapeutic products as the genetic basis of various diseases is elucidated. The genomes of economically important livestock and plant species are also being mapped through international collaborative efforts. Such information will improve the rapidity and accuracy of the breeding of new varieties and breeds of plants and animals with improved performance traits. It will also support the production of transgenic plants and livestock with improved performance characteristics not attainable by current breeding technologies.