Canada

TECHNOLOGY TRANSFER MECHANISMS IN BIOTECHNOLOGY IN THE U.S., U.K., JAPAN AND CANADA

Government of Canada
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Gouvernement du Canada
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IN BIOTECHNOLOGY

IN THE U.S., U.K., JAPAN AND CANADA

Review by country and recommendations for Canada

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EXECUTIVE SUMMARY

The authors (Frank Maine Consulting Limited) have examined the transfer of biotechnology in the United States, United Kingdom, Japan and Canada so as to recommend initiatives which could accelerate the development of the biotechnology industry in Canada. To this end, the extensive recent literature on the subject was studied and the subject was discussed in the four countries with representatives of industry, government and universities. Most of the conclusions are based on these interviews.

The U.S., with its entrepreneurial culture and a comparative abundance of risk capital, is virtually exploding in the expansion of industrially oriented research and development in biotechnology, in the commitment of established firms and in the creation of new biotechnology firms. This will position the U.S. for a certain eventual revolution in raw materials, processing and new products.

The Japanese are developing their biotechnology industry on a well-established base of fermentation technology. Through government support and co-ordination, the established companies are expanding their R&D in biotechnology, acquiring know-how from foreign companies, and making marketing arrangements around the world. Also, the Japanese government has many programs to encourage the development of small or new high-technology firms, which will be used increasingly by new biotechnology companies.

The U.K., without an entrepreneurial culture such as in the U.S., and disappointed in its reliance on established firms, has established a number of programs to accelerate the application of its research discoveries and to encourage the creation of new biotechnology firms. Already, changes can be seen and the U.K. is slowly regaining the position it deserves.

Without an internationally strong research base, with little indigenous industrial research, with the larger companies having a high degree of foreign control, with a small domestic market and apparently lacking in venture capital and entrepreneurship, the development of Canada's industrial biotechnology capability has been rather meagre.

The U.S. and U.K. lead the world in research in biotechnology but, in both countries, there is concern that this lead may be eroded as budgets are reduced. Japan, on the other hand, has recognized its need for more basic research and is expanding research in an attempt to gain world leadership. While Canada produces excellent biotechnology research in its universities and the National Research Council, this research is not keyed to the marketplace and has attracted little attention either in Canada or elsewhere.

Canadian universities, generally, are not well organized either to perform the multi-disciplinary research required for success in biotechnology, or to promote biotechnology. Suitable developed industries are not available to provide the market pull.

In its role as facilitator, the government should take steps immediately to further expand and strengthen the involvement by industry in the commercialization of biotechnology, while ensuring that the universities are able to produce the research and the scientists that will provide biotechnology worth commercializing. The major emphasis should be on improvement of the industrial biotechnology sector in Canada where the economic benefits will be realized.

It is recommended that action be taken to:

- expand access to export markets for Canadian biotechnology products;
- provide an environment, through vigorous DRIE initiatives, which will create many more new biotechnology firms and commercialize foreign biotechnology;
- improve drastically university/industry collaboration;

- establish, in the private sector, an information resource of markets, technology and other data of commercial value to all in the biotechnology industry;
- expand exploratory missions worldwide by the private sector for markets and technology.

BACKGROUND AND OBJECTIVES

The discussions the authors had during the past few months have further persuaded them of the insight expressed in the 1980 Biotechnology Report of a Joint Working Party (Spinks Report):

> "We envisage biotechnology..as creating wholly novel industries, with low fossil fuel energy demands, which will be of key importance to the world economy in the next century. Over the next two decades, biotechnology will affect a wide range of activities such as food and animal feed production, provision of chemical feedstocks, alternative energy sources, waste recycling, pollution control and medical and veterinary care. We are convinced that it will shortly be possible to use microbial and other cells to make a wide range of organic chemicals which either cannot at present be made economically on a large scale or, if they can be made, require extensive inputs of land, energy and capital plant for their production from feedstocks, such as oil, which will become more expensive.

Already animal insulin is being replaced by bio-insulin, bio-pesticides are nearing the market place, and intensive research is under way to develop nitrogen-fixing plants which would reduce the large chemical market. Should a soybean species containing lysine be developed by genetic engineering, the need for synthetic production of this amino acid will be drastically reduced.

Means must be found to place Canada in a position to develop and use biotechnology in the world context. Since Canada, itself, can develop only a small portion of the new biotechnology needed to keep it competitive, it must build an infrastructure suitable for the commercialization of transferred technology as well as a sound base of excellence in biotechnology research.

Biotechnology, in the form of the fermentation industry, has been with us for a very long time. Watson and Crick (U.K.) elucidated the structure of DNA in 1953, and after Cohen and Boyer (U.S.), in 1973, spliced the DNA from one organism into the DNA of another (which passed on the new genetic material to its offspring), the way was opened for the creation of new products both in the fermentation industry and by completely new biotechnological processes.

Both the U.K. and U.S. have made many discoveries through strong biotechnology research efforts. U.S. entrepreneurs and venture capitalists have successfully commercialized basic research from universities. Japan has capitalized on discoveries in areas related to its industrial strength by building on its established manufacturing base through government direction and co-ordination. The U.K., which has contributed valuable research in biotechnology, has been slow to exploit it, and is now endeavouring to regain, through a number of government initiatives, ground lost to the U.S. and Japan.

Market information on biotechnology is scarce and often highly speculative. World markets for biotechnology-derived products by 1990 have been estimated at from $4 billion to $36 billion with the two major market areas being pharmaceuticals and health care and agriculture and food processing. Estimates for the year 2000 are well over $100 billion. The available domestic market for Canada, with a population of 24 million, is small in comparison to Japan with 120 million, the U.S. with 240 million and the European Economic Community with between 200 and 250 million inhabitants.

Canada must export to have a market sufficient to support the industry. The others have large enough domestic markets to warrant the initial development and production costs. Exporting, for them, is a secondary concern.

Canada does not have the research base, the industrial base, the sizeable market nor the entrepreneurial culture of these other nations and so there has been comparatively less activity in the biotechnology field.

The transfer of technology is trade dependent. Increasingly, the success of companies depends on their ability to gain access to world markets and, while the situation varies with different products, this is especially important for Canadian companies in biotechnology. There are four ways to gain such access, all of which involve the transfer of technology:

- to license technology to a foreign company;
- to form a joint venture with a foreign company;
- to manufacture a product through a wholly owned subsidiary in a foreign country;
- to export a product.

Canada's lack of indigenous biotechnology coupled with its economic structure, which is not characteristic of an industrialized nation, will make it very difficult for Canada to catch up to other nations, which it must if it is to maintain its standard of living. However, without a suitable infrastructure, it is extremely difficult to transfer biotechnology to Canada and exploit biotechnology for the benefit of Canadians.

The goal of this limited study is to survey the methods and success of biotechnology transfer in the U.S., U.K., Japan and Canada in order that recommendations may be made to improve the process as it concerns Canada. The situation in the U.K. regarding industries, universities, government and culture, resembles most nearly that of Canada and has, therefore, been examined in greater detail.

The literature has provided background and a perspective of the biotechnology industry as well as some detail on activities of industries, universities and governments. The experience and opinions of the many representatives of universities, institutions, government and industry, with whom discussions were held in the subject countries, form the basis of this report. There was no consensus among all the contacts. Since there is no single solution and initiatives must be taken on many fronts, the authors have tried to incorporate a wide variety of comments and suggestions.

In attempting to outline the problems of technology transfer in each country during the stages from research to commercialization, the authors have been unable to make clear-cut separations because all stages are intimately intermingled and biotechnology firms are still heavily, or often solely, involved in research.

UNITED STATES

INTRODUCTION AND BUSINESS BASE

Early in the 1970s, especially with the successful gene splicing by Cohen and Boyer, a flurry of activity developed in biotechnology. Many small entrepreneurial enterprises were founded to build on this new knowledge in molecular biology. A number of large, established firms began to include the new genetic engineering techniques in their research programs. After a period of uncertainty while the government debated guidelines for this activity, further considerable industrial expansion took place as the small, new firms acquired more substantial financial backing and many of the more established firms began to make a serious commitment to this area. The period of explosive growth of new biotechnology ventures was 1980 to 1982.

Industrially, the United States is very strong in the sectors where biotechnology is expected to have the greatest impact. Although it has been gradually losing its dominance, the pharmaceutical industry, noted for its research and advanced technology, has been a world leader for many years. It is only 15 percent foreign-owned and exports over 40 percent of its production.

The total health care industry is large and growing rapidly. The organic chemical industry, while large and mature, is still in an overcapacity situation due to extensive expansion in other countries and the energy price increase and resultant lower consumption. It is looking for new opportunities. The agriculture and food industries are among the most advanced in the world with substantial exports. The fermentation industry is a strong one, with a large domestic market and considerable exports.

THE BIOTECHNOLOGY SEGMENT

Because they are so dependent on the new technology continually being developed at universities, most of the new biotechnology firms (NBFs) were formed in the San Francisco or Boston areas. Professors engaged in leading-edge research were deeply involved in their establishing the NFBs. As the new firms began to see that their financial resources were insufficient or dwindling, they sought research contracts from government and industry. They found themselves often in the business of developing products for the older established firms. In time, some NBFs were bought up and became part of, or subsidiaries of, larger firms. All of this increased the interest and commitment of the older firms in the growing area of biotechnology.

The main research thrust is in pharmaceuticals and the established companies are becoming increasingly involved. In fact, most of the leading pharmaceutical and chemical companies are now taking active roles in bringing established development and marketing organizations and financial wherewithal into the biotechnology industry. In animal agriculture, the new firms outnumber the old, while in plant agriculture, probably due to their vested interest in the agricultural chemical industry, the old firms outnumber the new.

More than 200 firms are dedicated solely to biotechnology and an additional 200 or so diversified firms have extensive biotechnology activities. Many of the research firms have broad interests, especially in the early stages of their development. A typical breakdown of their interest is -- pharmaceuticals, 54 percent; agriculture and food, 45 percent; specialty chemicals, 12 percent; bioprocessing, 6 percent; energy, 8 percent; instrumentation and supplies, 4 percent; mining, 1 percent.

As they become more firmly established, the NBFs are shifting away from the development of products for larger companies and are doing proprietary research for their own use.

BIOTECHNOLOGY R&D

The NBFs commenced operations as research companies and mainly remain so. As the large established companies become involved in biotechnology, they are using the NBFs as their research arms and may have research contracts placed with several NBFs. For the NBF, these contracts may replace government research contracts (National Institute of Health, National Science Foundation, Defence, Agriculture) or allow the NBF to grow larger. The established company may also initiate its own R&D program so that there is continual growth in this area.

Meanwhile, despite government plans to reduce support, the universities are attempting to maintain the desirable research base upon which the whole future of the industry depends.

In recent years, there has been a tremendous change in the attitude of academia to biotechnology and industry. While in some other disciplines, the university/industry interface has become very close and sophisticated, it is developing slowly in the biotechnology area and varies greatly among universities. Many would like the interplay to increase but, as the relationship becomes more formalized, there appears, to some, to be a greater separation of the two. In some universities, many professors are consulting with one or more companies; in others, they are trying to maintain a purist stance and avoid any relationship with industry.

Generally, the university seems to be less satisfied with the university/industry relationship than is industry. Industry suggests that the financial expectations of academia in this relationship are still too high. There are relatively few no-string grants to universities and these are from the larger biotechnology companies. A number of contracts for specific projects have been placed in universities.

Many scientists have now been trained in the fundamental techniques of biotechnology and there is a fear that either they may become a glut on the market or else provide for a considerable expansion. While few schools are giving specific training in bio-engineering, there is, as yet, little demand for new graduates. Instead, established companies seem to be attempting to retrain their present staff. There is a feeling that government support is swinging from basic to applied research.

In 1982, major government funding for biotechnology research was received from several agencies:

National Institute of Health (NIH)	$380.0 million
National Science Foundation (NSF)	53.1
Department of Agriculture	35.0
Department of Energy	9.2
Department of Defense	6.0
Agriculture Research Service	12.0
Total	$495.3 million

There is an unspecified amount of additional funding provided in unrestricted grants from industry. Furthermore, some firms support specified areas of research or projects at some institutions. Biotechnology clubs or associations, which have been formed at several universities, provide additional funding. By late 1983, at least 22 companies had some 24 agreements with 17 universities.

A number of non-profit foundations have been established to perform research in biotechnology. These are largely funded by government contracts which will be reduced as they are able to license or sell their technology. They find that, without the constraints imposed by the university situation, they are able to advance more quickly in research areas.

Interdisciplinary research can be accomplished more easily. Without the constant retraining of graduate students, scientists can be kept active on the leading edge of biotechnology and thus make more rapid progress.

In some areas of applied research there is evidence that industry is now considerably ahead of academia, which lessens corporate interest in university work -- until there are problems or new requirements.

Attempts are still being made to create biotechnology centres by university groupings. With the commitments already made by biotechnology firms, this is becoming more difficult and requires substantial state and local funding to weather the early years until the centres are viable.

APPLIED RESEARCH TO COMMERCIALIZATION

Many NBFs were started by placing contracts with academic researchers for the commercial development of a laboratory discovery resulting from basic research. In establishing some NBFs, international biotechnology transfer has been a factor. Although well supported by venture capital in the U.S., several have obtained capital in addition to manufacturing and marketing expertise, when these were not available in the U.S., by becoming involved in international ventures, frequently with Japan.

The United States government has a number of programs to support the establishment and growth of NBFs:

* Small Business Innovation Research (SBIR) program, administered by NSF:

  Phase I - Grants to US$40 000 for feasibility research.
  Phase II - Awards average US$200 000 for subsequent research assistance (to two professionals for two years).

Applicable to small business firms with strong science or engineering capabilities for high-quality research proposals in technological innovation, the program encourages links with universities. Areas of U.S. federal interest are specified. This program is highly competitive -- approximately one application in 10 is accepted at Phase I. Special consideration is given in Phase II for projects with contingent private commitment for Phase III (Development to Commercialization), with about one in three Phase I recipients receiving Phase II awards.

The program appears to provide complete support for a limited amount of research on projects which are likely to have commercial potential. If successful, they should provide sufficient information for obtaining ongoing private financing for commercialization. Many projects in biotechnology in universities and small firms need such help over this substantial hurdle.

* Creation of Generic Technology Centres.

* To improve university/industry co-operation in R&D, $29 million.

* Support for establishment of Corporations for Innovation Development to provide, regionally, equity funding for NBFs.

* Small Business Administration (SBA) and Enterprise Development Administration (EDA) general loan programs.

* U.S. Department of Agriculture (USDA) loans to Small and Medium-sized Enterprises (SMEs) for new equipment.

* Department of Energy Appropriate Technology Small Grants Program. There are also many programs for technical assistance and to provide scientific and technical information to business.

* Small Business Innovation Development Act -- federal agencies set aside 1.25 percent of R&D funds for small business.

* Industrial Development Partnership -- tax incentives for Research and Development Limited Partnerships (RDLP). This program is widely used in biotechnology to support R&D.

In addition, encouragement for increased industrial R&D comes through tax provisions:

- tax credit for increased R&D expenses;
- accelerated depreciation for R&D equipment;
- suspension of apportioning R&D expenses to foreign source income
- increased deductions for charitable equipment donations to universities for research.

Most NBFs were founded by university professors with the help of the entrepreneur and venture capital. Typically, the professors retain their jobs as long as possible, keep their research within the university as long as possible and, finally, when they have sufficient support, establish a unit outside but near the university. They will expand as they receive government help through research grants and, when their reputations are sufficient, they will get contracts for applied research and development from other organizations. As they grow, they may become frustrated at doing all this work for others and seek sufficient funding to work to a much greater extent on their own projects.

As various projects develop into product opportunities, they may form limited partnerships with other companies. They will seek companies with appropriate marketing and/or production expertise and with financial strength. They may also chose to license their technology or, in fact, sell to or merge with another company depending on their goals and their assessment of the situation.

The first products resulting from applications of biotechnology in the pharmaceutical industry are now being sold and competition is high among NBFs to capture the market on these and other pharmaceutical products which can be expected in the near future. Products from the application of biotechnology in animal and plant agriculture, specialty chemicals, food, commodity chemicals, energy, the environment and electronics are expected to appear on the market more slowly, and their development can be expected to proceed in different ways in the various industries.

COMMERCIALIZATION

When government provides a suitable climate for entrepreneurs and for the growth of established companies and there is an excellent research base in the universities, there is no real problem in the commercialization of new technology. The informal contacts between scientists in industry and those in universities are responsible for the multitude of biotechnology firms in California.

Ultimately, the success of firms in biotechnology will depend on their ability to market their products. This is why the NBFs are making collaborative arrangements with established firms which have already developed strengths in the marketplace. Where an NBF has identified possible products in different market areas, it is not unusual for it to collaborate with a number of separate companies with expertise in appropriate areas.

More recently, large established pharmaceutical and chemical companies have taken the initiative in funding research and collaborating with NBFs. This has been a major factor in providing the U.S. with an early competitive advantage in the commercialization of biotechnology.

DISCUSSION

In the early years, biotechnology transfer was largely confined to the published literature and the frequent contacts within worldwide academia.

In the U.S., the role of the university in providing and transferring technology consists of:

- publishing scientific papers
- obtaining and licensing patents
- joining research partnerships with a company on specific projects
- being part of a research consortium with a group of companies interested in a common area of research
- sponsoring industrial associates/affiliates programs
- providing consulting contracts
- participating in ownership/founder relationships.

There is a tremendous exchange of technology between university and industry on a personal basis. There are also great opportunities for technology transfer through meetings, seminars, courses, etc., especially in places like San Francisco, San Diego and Boston due to the high concentration of universities, institutes and industry. On some campuses, there are seminars on a particular area of biotechnology research available every day of the week.

The entrepreneurial culture in the United States has made it possible for the excellent research base in biotechnology to spawn a multitude of NBFs. Its strong research-based pharmaceutical industry has slowly picked up on the developments by the NBFs and become intensely involved in the new technology. The large forward-looking chemical companies have also become seriously involved. The universities, which worked with industry in other disciplines, have been able more quickly to establish adequate university/industry ties in biotechnology. Guidelines for university/industry co-operation are becoming more formalized than in other countries and to some extent now are inhibiting that co-operation.

NBFs have been formed by entrepreneurs because of the relative availability of venture capital due to tax treatment and the availability of R&D limited partnerships (RDLPs), as well as the availability of government funding for applied research. Most of the large companies also use these incentives effectively to expand their efforts. With the advanced technology they now possess, many companies are making international agreements and licensing research, production and marketing.

Most biotechnology companies not only have consultants from academia but also scientific advisory boards drawn from the best experts available anywhere in the world. Some bring in experts to lecture to their scientific staff on a weekly or monthly basis. Most of the NBFs are the result of involvement of university personnel, many of whom are still in the university but others have left and are completely immersed in industry. Professors frequently consult with more than one firm. However, many of the NBFs no longer have strong ties with universities and the relationship of industry with the universities is becoming very formalized. Some in academia are still suspicious of industry but, increasingly, it is becoming apparent that the university must look to industry for a greater part of its funding in the future.

There is great apprehension on the part of many in industry that funding of basic research by the federal government is being reduced, while such funding in Japan is being increased. For the U.S., this could eventually lead to the loss of world leadership in biotechnology. There are others who feel strongly that university research should be financed by industry, but how to accomplish this is a matter of conjecture.

Although there is an increasing number of agreements and collaborative arrangements between American and foreign firms, international technology transfer is considered much less important than 1) financing and tax incentives for firms, 2) government funding of basic and applied research, and 3) personnel availability and training. There are no laws governing international joint ventures and technology licensing among U.S. and foreign companies.

As the number of agreements between companies in biotechnology multiplies, it is becoming more difficult to find suitable partners, or to buy or license technology unless something substantial can be offered in exchange. Marketing agreements are made on an area rather than a country basis.

Weaknesses of the American system are related to the entrepreneurial culture which has allowed an oversell to the venture capital market. This has caused financial losses to many people and may result in a more conservative attitude in the future on the part of investors. Growth may be slowed as a result. The cost of government support has been substantial, although it may not have been particularly wasteful, and apparently the economy could afford it.

Should government support for the research base diminish before industry is willing or able to take up the slack, the United States could lose its cherished lead to Japan or even a European country.

As the result of the U.S. system, the biotechnology industry has become very dynamic and gained a good deal of momentum. There has been tremendous activity which has resulted in the formation of many NBFs, the failure of many, takeovers and considerable movement of personnel between companies. All of this activity is aimed at commercial goals. Everywhere there is enthusiasm. Now, as products begin to reach the marketplace and the larger older firms are becoming more committed, there is increasing stability in the industry. It is unlikely that another country could afford to, or would be willing to, have an industry develop as it has in the United States. It is hard to catch up and compete with this situation and Canada has scarcely started.

JAPAN

INTRODUCTION AND BUSINESS BASE

With a population of 120 million, Japan has a large domestic market for any technology. Of that population, 60 percent is concentrated in the Tokyo-to-Kyoto corridor with 15 million in the immediate Tokyo area. Transportation costs are comparatively low for this large concentrated market, especially when compared with Canada. Industry is very strong in Japan with the average market mix being 80 percent domestic and 20 percent export. This illustrates that Japan has a sufficiently large internal market to warrant the development of new products and does not have to rely on exports or a world market to justify product development.

This is in sharp contrast to Canada, where there is a small population spread across a large country which is very dependent on exports. Japan, with its unique language and culture, is racially homogeneous and the different sectors of the economy (government, industry and university) work together in harmony. Industry is largely Japanese-owned (pharmaceutical, 87 percent) and controlled, and can respond rapidly to government initiatives which are traditionally made in concert with industry. In contrast, the large companies in Canada are primarily owned by foreign-based multinationals and are usually not able to respond directly to government initiatives.

With its need to import most of its raw materials, Japan must sell manufactured products. This it does worldwide and it has become an experienced trading nation.

THE BIOTECHNOLOGY SEGMENT

Japan is particularly interested in biotechnology, a non-petroleum source of energy and chemicals, because biotechnology presents a very real possibility for solving the country's problem of lack of natural resources.

Japan began investing in the new biotechnology in 1980. The government has built a support structure for R&D, and for the establishment of government and industry collaborative projects. For the most part, this involves the large established Japanese companies in the pharmaceutical and chemical industries. These companies have extensive experience in bio-processing which provides them with significant competitive strength.

The first companies in Japan to enter the field of recombinant-DNA-produced pharmaceuticals were led by pioneering entrepreneurial managers.

BIOTECHNOLOGY R&D

In biotechnology, Japan (5 percent of GNP in 1980) is second only to the United States, and has declared this area one of national importance and eligible for priority treatment. Industry funds 75 percent of research in Japan and, by 1981, more than 61 percent of recombinant-DNA (rDNA) technology was funded by the private sector. A 10-year research program has been organized by the Ministry of International Trade and Industry (MITI) involving 14 established companies and with government support of over $130 million. This subsidy covers direct expenses only, not overhead, and any capital equipment purchased is government property. The program is administered by the Research Association for Biotechnology, which supports the member companies who conduct long-term research programs in the three areas of bioreactors, large-scale cell cultivation and rDNA. These programs are to run for a minimum of five years.

This illustrates how the national government is helping large Japanese companies build up their capabilities in fundamental areas of biotechnology research. Other agencies, such as the Ministry of Agriculture and Ministry of Health and Welfare, also fund research in biotechnology. In 1983, total funding amounted to over $80 million. A far greater portion of this goes to applied research than in the United States.

There is also a program to collaborate with foreign organizations to advance Japanese knowledge in areas of biotechnology where Japan is behind. Applied R&D programs are more common in Japanese industry with 80 percent of the work being done in pharmaceuticals, which is the area of highest added-value to the chemical raw material. Besides the strong industrial R&D base, there are several government laboratories, such as the Fermentation Research Institute, primarily devoted to applied biotechnology. While there is some work at universities that is pertinent and relevant, there seem to be much weaker links between universities and industry in Japan than in the United States or even Canada. MITI's regional development program -- Technopolis -- includes strengthening university/industry links. The patent information centre's (Japatic) on-line base of foreign and domestic patents is of great help in biotechnology.

APPLIED RESEARCH TO COMMERCIALIZATION

Japan has two devices designed specifically to strengthen small businesses:

* "Technical Development Subsidies to Medium and Small Enterprises", administered by the Small and Medium Enterprise Agency (SMEA) - encourages R&D in small and medium-sized enterprises (SMEs).

* "Financing of Small and Medium Enterprises' Industrialisation of the New Techniques", managed by the Small Business Finance Corporation -- loans for modernizing.

Funds are also allocated to national laboratories to carry out research and development of techniques appropriate to SMEs. There are tax deductions for incremental R&D, for foreign sale of technology and for SMEs.

The "Center for the Development of R&D-oriented Enterprises" guarantees debts and bank loans with respect to innovative activities. The centre is funded by both government and industry.

There are some 200 regional public research laboratories which are required to co-operate with SMEs. An automated information network has been set up for SMEs, going beyond purely technical information and covering commerce, finance, technology imports and so on.

COMMERCIALIZATION

In Japan there is a large pool of funds in savings accounts available to Japanese corporations for debt financing. Of great importance in the development of biotechnology has been the availability of sizable personal loans, as "venture capital", from wealthy individuals who are managers of Japanese companies. The government has not been a major source of financing for Japanese companies developing biotechnology.

Government support for R&D in biotechnology has been primarily directed to large existing firms (e.g., MITI program). In such production firms, involved in biotechnology, it is often easier and less costly to commercialize a new process since frequently equipment already on hand may be used. However, there are programs to help small and new firms to enter this area.

The phenomenon of new biotechnology firms (NBFs), which is a major part of the biotechnology R&D conducted in the United States, has not occurred in Japan. For small and medium-sized enterprises, Japan does have a Credit Guarantee System that helps small businesses financially. The Small Business Credit Insurance Corporation, financed by the national government, lends money to the Credit Guarantee Corporations which guarantee contracts with financial institutions. With the debt of the small business insured in this manner, the equity requirements are not the same as in North America where more equity is required for the same amount of debt. This is a major aid for small business in Japan that should be considered for use in Canada.

Authorized conversion of a business to a newly appearing growth area receives favourable taxation and financing from the Law of Extra-ordinary Measures for Business Conversion of Small and Medium Enterprises.

Subcontracting is widely practised in Japan between large and small firms -- but much less so in the biotechnology area. This is encouraged by low interest loans to purchase equipment and by modest tax treatment.

DISCUSSION

While the importance of government funding of applied research should not be minimized, of greater importance is the government's success in encouraging industry's involvement in, and long-term commitment to, biotechnology. The government has emphasized sensible development of mutually-agreed-upon research strategies, horizontal organization and co-ordination within the private sector, and timely funding of the necessary high technologies.

Because of the lack of venture capital structure similar to the U.S., Japan does not have a large group of NBFs. The government is introducing initiatives to change this and make it easier for enterprising small and medium-sized firms that lack business experience to raise funds in the finance market. The independence of SMEs is encouraged.

While relations between university and industry and the transfer of information are generally good, basic science departments of the universities do not communicate with industry, and the government is introducing programs to break down this barrier. There is also extreme secrecy between companies and, with little movement of personnel between companies, informal domestic technology transfer is limited. Formal technology transfer is also limited due to the small amount of sub-contracting in the field of biotechnology.

Japanese companies are actively importing technology from the US and other countries through joint R&D ventures and licensing agreements. In the US, NBFs accept research contracts from Japanese companies. The Japanese are acquiring foreign companies to gain access to their technology, markets and distribution networks.

Japanese industry has had a long and deep involvement with fermentation processes. It has developed this technology in recent years to be the major world producer and supplier of amino acids, supplying 90 percent of the world's needs. With this strong industrial base in fermentation technology, Japan is in a good position to commercialize the new biotechnology techniques and the procedures which use fermentation as one of the major manufacturing steps. While Japanese industry has not done the basic research in biotechnology, it has acquired technology with potential from the U.S. It has then set about working diligently to apply that knowledge to its own use. In doing so, it has developed new technology which is being used in Japan and may be licensed outside Japan.

This is, perhaps, one approach that Canada can consider as a way of trying to catch up in the most efficient manner. That is, Canadian industry can license existing Japanese fermentation processes and build on this base to produce the new products of biotechnology. It is important for Canada that any such licensing is not just an end in itself, but a means to developing new products and processes, or else Canada will be in the same position as it has been with regard to the United States -- just a licensee of technology.

Since the bulk of its research is done in industry, Japan does not have a domestic technology transfer problem. However, due to the few NBFs and lack of subcontracting in biotechnology, the amount of domestic biotechnology transfer cannot be compared to that which occurs in the U.S. The acquisition and transfer of foreign technology is carried out by the hundreds of commercial and scientific personnel from industry working around the world, as well as by such trading companies as Mitsui & Co. Ltd. whose Technical Development Division has a staff of over 100 with 20 percent foreign-based. They are responsible for technology transfer, both in and out, investments and sales. The Biotechnology section has 12 people in Japan as well as staff stationed in New York, San Francisco, London, Dusseldorf, Paris, Milan and Madrid.

The success of the Japanese government in co-ordinating the biotechnology effort is credited to the high degree of domestic control of industry and to the Japanese culture.

UNITED KINGDOM

INTRODUCTION AND BUSINESS BASE

For centuries the United Kingdom has been a trading nation. From around the world it has imported raw materials and used them to develop a strong, integrated and extensive manufacturing industry. Through so many years of experience, it has developed worldwide expertise in marketing.

Among the well-developed industries which will use biotechnology extensively are:

* the pharmaceutical industry, international and successful, including at least seven British-owned research-based companies, with a trade surplus greater than any country except the U.S.;
* the chemical industry which, with sales of more than $22 billion, exports 40% of its production;
* the food processing industry with sales of over $40 billion. Of the 25 largest food companies in Europe, 17 are British;
* the fermentation industry representing 4.5 percent of the total manufacturing sector.

The universities in the U.K. are among the oldest in the world, and are renowned for their scholarship and research. Many of their scientists have won Nobel prizes.

THE BIOTECHNOLOGY SEGMENT

Of the established firms the following are known to be active in biotechnology:

Albright & Wilson	Allied Breweries
Beecham Pharmaceutical Co. Ltd.	Boots
British Petroleum	*Cyanamid GB Ltd.
Dunlop	Glaxo Holdings, Ltd.
Imperial Chemical Industries	John Brown Engineers
*Lilly Industries Ltd. (U.K.)	*Pfizer Group Ltd.
*Proctor and Gamble	Prutec Ltd.
Rank Hovis McDougal	*Roche Products Ltd.
*G.D. Searle & Co Ltd. (U.K.)	*Shell Chemical
Simon-Hartley	John & E Sturge
Tate and Lyle, Ltd.	Unilever
Unigate	Wellcome Foundation Ltd.

*foreign-owned multinational

At least 10 other companies have chosen to set up separate companies for their efforts in biotechnology. But not all firms which could use and benefit from biotechnology have as yet done so. Many new organizations have been formed to exploit this new area. By 1984, 27 independent new biotechnology firms (NBFs) had been established. In addition, 12 biotechnology ventures had been created by university staff.

On a per capita basis, these may represent less than half the number established in the United States. This reflects the conservatism of British industry compared to the aggressive entrepreneural efforts in the U.S.

BIOTECHNOLOGY R&D

In 1972, the government adopted a rigorous customer-contractor principle for all applied R&D funded by government, which now appears counter-productive for biotechnology development. The Spinks report emphasized that biotechnology was the marriage of a diverse set of disciplines, and that there were neither established university departments to promote it nor well-developed industries to provide a market pull. Therefore, in a mixed economy, the full potential of biotechnology could not be realized by the private sector alone.

Nor was the structure of public and private support for R&D suited to the development of a subject like biotechnology. The scientists in universities and research councils needed to become more aware of the industrial applications of their work. Much better communication was required between those who are primarily market-oriented, and those who are primarily science- or technology-oriented. Universities and industry would have to provide an infrastructure for biotechnology which is process-oriented rather than solely product-oriented. Spinks recommended national priorities for research in biotechnology:

- genetic manipulation
- enzymes and enzyme systems
- monoclonal antibodies and immunoglobulins
- waste treatment (detoxification, by-product utilization)
- plant cell culture and single-cell protein
- production of fuels from biomass.

The University Grants Committee (UGC) of the Education Department provides funds to build the teaching and research base. Universities also receive support from endowment funds and other external sources -- student fees, research councils, charitable foundations and research contracts.

In 1982, the UGC provided special measures to protect biotechnology, increase research monies, increase contact between UGC and the Department of Trade and Industry (DTI), and end the British Technology Group's (BTG) monopoly rights over results of publicly funded research.

Recently, more emphasis was placed by the Science and Engineering Research Council (SERC) and UGC on grants to universities with strong bioscience departments. Special funds are provided for specific purposes. For example, in 1982, $1.27 million per year for three years was set aside to encourage links between process engineering and molecular biology.

Currently, the research councils are funding research in:

- biological control of agricultural diseases and pests
- biomass
- cell culture
- cloning (vegetative propagation)
- culture collection
- diagnostics, prophylactics and therapeutics
- enzyme and protein technology
- fermentation
- monoclonal antibodies
- recombinant DNA technology
- waste treatment and biodegradation.

As many as 22 British universities are considered to have the multidisciplinary expertise suitable to develop centres of excellence in biotechnology. Indeed a number of Centres (or Institutes) for Biotechnology have been established.

The NBFs, already formed, were essentially started as research companies. In most cases, research still is the principal activity of these organizations. In the research departments of the larger, long-established companies, groups have been formed to work in various areas of biotechnology.

The early and intimate involvement of Imperial Chemical Industries (ICI) in biotechnology resulted in the development of a single-cell protein for fodder. This is an exception to the often repeated rule that only small start-up companies can pioneer in the early stages of commercialization.

The British market is entirely open to investment from overseas. American companies, in particular, have found Britain an admirable place for biological research. One by one, the American drug companies are establishing research facilities in Britain. Likewise, the major British multinationals in biotechnology all have extensive research facilities in the United States.

APPLIED RESEARCH TO COMMERCIALIZATION

Realizing that success in biotechnology depends on capitalizing upon non-industrial research, the government has introduced support programs. These involve direct funding of R&D, partial funding of commercial ventures, and promotion of joint ventures between academia and private firms. Two groups have specific and exclusive responsibility for fostering biotechnology -- the Science and Engineering Research Council's (SERC) Biotechnology Directorate (BTD) and the Department of Trade and Industry's (DTI) Biotechnology Unit (BTU).

Three Councils

Three councils support biotechnology extensively. They are:

1) Science and Engineering Research Council (SERC) -- SERC funding is solely to universities. It is the only council which requires industry input to be certain that supported programs are likely to be useful to industry, thus assuring that industry/university links are formed. Where a perceived national need exists, SERC has implemented the Directorate Scheme.

These directorates are transitory and their programs are developed with inputs from the customers. The present budget of the BTD is $4.8 million with a planned growth to $6 million.

With seven areas of priority, the BTD has many programs of which the following are of most importance to technology transfer:

* Co-operative Grants Scheme -- in university with industrial partners paying at least one-third;
* Co-operative Awards in Science and Engineering (CASE) scheme -- up to 90 co-op students are working in industry at a time;
* Collaborative Training Awards Scheme -- short-term training projects in small firms;
* Integrated Graduate Development Scheme -- joint university/industry induction training of new graduates;
* Teaching Company Scheme -- promotes partnerships between industry and university/polytechnics, makes use of new technology and trains or retrains staff;
* a number of schemes to support international collaboration in biotechnology studies.

To assist in promoting these programs, particularly with small and medium-sized companies, SERC has appointed regional brokers. SERC also provides capital equipment grants.

In its efforts to further encourage an intimate relationship between industry and university, SERC has established:

- its own board of directors with half from industry and half from university or other councils;
- joint boards on programs;
- councils (or boards) on specific topics to discuss areas of technology
- joint boards with the five councils: SERC, MRC, NERC, AFRC and ESRC
- clubs and networks (e.g., BIOSET);

- student exchanges with many countries (except the United States);
- the Protein Engineering Club (SERC plus six firms which contribute $45 000 per year each)
- the Leicester Club (five non-chemical firms have put up $1.5 million to build a biotechnology centre). SERC has promised a capital equipment grant of $270 000 with additional support coming from AFRC and DTI. The next club will be on separation processes.

Independently of SERC some universities are establishing:

- new teaching facilities
- new professorships and lectureships
- new centres of biotechnology
- short courses for post-experience students

2) Agriculture and Food Research Council (AFRC) -- The bulk of AFRC funding goes to its own institutes with a small amount going to universities. AFRC has 30 laboratories with a staff of 1500 including 550 graduates. It supports research but not applications work. In 1982, this amounted to $7.6 million in the biotechnology area.

3) Medical Research Council (MRC) -- The MRC directs 60 percent of its funding in research to its own institutes and 40 percent to universities. Spending for biotechnology-related research in MRC laboratories for 1981 was over $5 million. There are a number of MRC research institutes funded by both MRC and industry.

Other Government Funding

The Department of Trade and Industry (DTI) has established a Biotechnology Unit (BTU) staffed by three experienced industrialists.

In 1982, DTI projected grant support of $24 million for three years and now projects grants of $48 million over the next three years, for basic research, feasibility studies and pilot plants. It now supports 40 projects. In 1983, DTI grants exceeded $4.5 million per year, while the present commitment is over $20 million.

DTI has undertaken a number of initiatives to encourage NBFs:

* strategic consultancies -- feasibility studies for a firm to enter a new market area;
* feasibility studies -- 70 percent of costs of consultant to evaluate project;
* industrial innovation -- R&D project grants up to one-third of cost, grant to be repaid if production goes outside Britain. BTU works with universities and institutes to develop patent positions for licensing purposes. University research may be funded indirectly by subcontract from industry;
* a directory of British technology which lists interests of researchers and companies, names of contacts and sources of funds for development. This has been very well received;
* sponsored the establishment of such club projects as Leicester Biocentre, Bioset, etc.;
* launched Agricultural Genetics Co.;
* DTI, along with AFRC and SERC, agreed to co-operate with firms to co-ordinate public funding of R&D in plant biotechnology;
* Research Requirement Boards (RRB) Grants, 25 percent grants in support of projects in industry;
* Product and Process Development Scheme (PPDS) which supports projects which have been demonstrated to be viable but would not go ahead without government assistance. This program has been criticized for its strict criteria of eligibility.

BTU provides limited grant funding of all aspects of commercialization. It seeks opportunities and holds the hand of the entrepreneur when necessary. BTU funding is increasing, but a major problem is the lack of awareness in both university and industry of problems and opportunities in biotechnology. BTU is considering spending additional funds to promote, by using experienced people, co-operation in this area. It finds that most firms are too inward-looking and are not run by scientists or engineers.

Through the Industry Act, financial investment assistance is available for new developments which relate to regional assistance. Over $22 million has been given to major biotechnology developments.

The Centre for Applied Microbiology and Research (CAMR) is financed by Department of Health and Social Services (DHSS), with further support from DTI and MRC. It sells its products and performs a good deal of contract research. It spends $3 million directly on applied biotechnology research and development with an additional $4.5 million going to underpinning research. The estimated government support of CAMR in 1982 was $1.8 million. DTI will provide $6 million for new expanded pilot plant facilities.

A number of commercial firms support people seconded to CAMR for training purposes or short-term problem solving. A two-way flow of information is a requirement.

CAMR works with European research institutes. Of its industrial contacts, 80 percent are foreign while university contacts are 35 percent foreign.

The British Technology Group (BTG) was formed by the fusion of the National Enterprise Board (NEB) and the National Research Development Corporation (NRDC). It operates as a catalyst for the development and exploitation of new technology.

BTG promotes the transfer of technology from the public sector to British industry. It is not a granting body but approaches each transaction on a commercial basis. It provides financing for researchers or institutions who want to set up a new company to commercialize their novel technology -- "Campus Investments" and "Academic Enterprise Competition".

BTG's normal method of investment is through joint-venture finance -- up to 50 percent -- and expects to recover its investment by means of a percentage levy on sales of the resulting products. Financing can include development work, production equipment, working capital and initial marketing. BTG recovers its investment and gets out of each venture as soon as possible after it is profitable.

Its activities may be subdivided into three areas:

* technology transfer -- eight people are active in this area. It sponsors relevant research in universities (40 projects), government and other laboratories;
* small companies -- "minimum fuss funding" of up to $90 000 is provided. It takes a 50 percent share in the early stages and recovers its investment as the company becomes profitable;
* investments -- catalytic investments are made with other financial and industrial partners. It finances all sizes of companies, including subsidiaries of foreign-owned companies, in amounts from $7 000 to $7 000 000.

BTG is staffed to patent, identify licensees, negotiate licence agreements, support development work and marketing, assess potential, and finance start-up companies.

The BTG strategy for further investment in biotechnology is to:

* seek out and promote opportunities in down-stream applications of genetic engineering and cell fusion (low-volume, high-margin products in health care, food production and fine chemicals);

* resond positively to technology transfer opportunities from universities and public sector laboratories (back a lot of starters, involve potential industrial partners as early as possible) and to opportunities for industrial investment in biotechnology infrastructure (equipment and hardware);
* avoid early investments in "big biotechnology" projects (heavy organic chemicals, bio-energy and waste recovery).

BTG funding, mainly from licensing, is re-invested in commercially attractive projects resulting from university or institutional research. Both BTU and BTG support can be used on the same project to achieve up to 67.5 percent. Estimated spending is over $8 million. In 1984, the total funds committed were some $20 million. This program of extensive support and encouragement promises to have a positive impact on commercialization.

Criticism of BTG includes lack of expertise in certain high technology areas, lack of marketing knowledge, poor marketing and lack of aggressiveness.

<u>Other Government Support Programs for the Entrepreneur</u>

- Small Firms Service -- advice, tax incentives;
- Council for Small Industries in Local Areas (COSILA) -- small loans, technical, financial and commercial advice;
- Development Agencies -- Scottish (SDA), Welsh, Northern Ireland, Industrial Development Board, London Enterprise Agency, Greater London Enterprise Board.

Government spending on applied research in biotechnology is of the order of $37 million to $45 million. The amount is much larger if basic work is included.

Additional Assistance

In varying amounts, additional assistance is given to support the exploitation of technology by the Royal Society, industry and research associations and charitable foundations. Wolfson Cambridge Industrial Unit (WCIU) is an example of one kind of assistance a charitable foundation gives to the commercialization of university expertise. Established to provide a link between the university researcher and industry, WCIU has developed an inventory of university expertise to meet requests from industry, charitable foundations, also support research programs and equipment and building acquisition.

Industry Involvement

As the interest in high technology heightens, industry is investing increasingly in university centres of excellence. Often a venture capital fund is formed with financing from industry, university and a foundation. Also, there is a growing investment by many industries in basic research at universities. For example, Tate and Lyle supports 30 projects in universities.

The increasing industrial support of biotechnology centres is carried out mainly through research contracts. British university science parks and innovation centres are growing rapidly. Thirteen are operational and another fifteen are on the way. Funding for these parks came from regional development agencies (2), local government (5), universities (8), banks (2), property developers (3) and private firms (1).

Industries support their own scientists at the University of Leicester Biocentre. Industries also use the centre as a window on worldwide developments in molecular biology. They see the need for personnel interchange in technology transfer. The Leicester science park is now looking to attract American firms as Cambridge has done.

The Agricultural Genetics Co. (AGC) was established (by BTG and five private investors) to exploit the technology being developed in the AFRC laboratories. It now has first rights to the work of six AFRC labs (30 percent of AFRC research). It has identified 26 promising work areas including biological control agents, micropropagation and straw degradation. It also offers management of contract research services and contract research. AGC has three foreign investors but was limited to 40 percent foreign investment (now 25 percent).

AGC identifies projects in universities and institutes (research council laboratories), puts together a proposal for development, then contracts back into the university/institute or private laboratory to do the work under AGC direction. It often uses scientists seconded from industry to work on projects in the institutes. Industry is very critical of the arrangements that AGC has been able to make with AFRC. On the other hand, AFRC believes that the sort of arrangement they have with AGC is the most effective way to transfer new agricultural technology to industry.

Innotech, a capital investment company, works with smaller firms and at an earlier stage than SDA and BTG. By actively supporting research and nurturing a growing personal relationship with the research team and the institute, Innotech helps to develop the proper attitude on the part of the team involved. These teams also are used to keep abreast of world technology.

Plant Resources Ltd. bought Tate and Lyle's biological pesticide interests and expects to be profitable in three years. The company is looking at a segment of the $20 billion worldwide pesticide market.

Celltech was established (by BTG and private investors) to commercialize the research of the MRC laboratories. (This is a privatized approach to commercializing research in the health sciences, a supplement to CAMR which has a higher research involvement.) A member of MRC is on Celltech's scientific board. It will be supporting a professor and a student for one year in an MRC laboratory.

Celltech has collaborative research with Oxford, Edinburgh and University College (London), and technical agreements with Sankyo, Sumitomo Serono Laboratories, etc., and joint ventures with Boots and Air Products. Its identified business areas are: health care, diagnostics, culture products and industrial microbiology. Four monoclonal antibodies are now being marketed. Celltech is involved in many information networks. Support for its research work is obtained from SERC, BTU and BTG.

There are no general rules for consultancies. Arrangements are left to the institution and the individual. Foreign firms are making more use of British biotechnology experts than are British firms.

COMMERCIALIZATION

There have been few governmental impediments to commercialization in biotechnology. The U.K. controls the export of goods but no biotechnology product is listed as a controlled commodity. The Genetic Manipulation Group (GMAG) was set up to oversee genetic engineering and control it where necessary. The Department of Health and Social Services (DHSS) administers the Medicines Act. Since it is effectively a monopoly buyer of the products of the pharmaceutical industry, DHSS consequently controls the industry's profits. The Ministry of Agriculture, Fisheries and Food (MAFF) regulates licenses for feedstock and food, albeit a little slowly. By controlling raw material prices within the common market the EEC, at times, makes the production of some products uneconomical due to the high controlled price of certain raw materials.

The export of technical information is not restricted. International technology transfer, inasmuch as it represents the loss of trained scientists to foreign biotechnology companies because of limited opportunities in Britain, is a situation which the government is taking steps to correct.

The government is making major efforts to improve the domestic situation with regard to the development of biotechnology and domestic biotechnology transfer. The brain drain is seen by many to hinder the rapid advance of British biotechnology.

In the exploitation of biotechnology in the United Kingdom, it was suggested that one should:

- identify opportunities (market pull)
- use academic consultants for short-term objectives
- use CASE, SERC awards, etc., for medium-term objectives
- utilize Science Clubs for long-term objectives
- always use other companies (for hardware and expertise, markets, etc.).

Government assistance to small business includes:

* Business Start-up Scheme -- offers tax relief at the top marginal rate for investors (funds) to make equity investment in start-up firms, thus diverting private-sector savings into productive industry. A number of professionally managed funds have been formed. Cambridge Life Science, the first British biotechnology firm to go public, benefitted from this scheme.
* Loan Guarantee Scheme -- guarantees financial institution loans of up to $112 000 for qualifying projects not backed by personal security. The effect of this widely-used scheme is that one no longer needs substantial personal means to set up a business.
* Special project funds are also available (for Celltech, the government put up half of $33 million and four companies provided the rest).

Problems encountered in starting a business include a banking system that is not geared to handle venture capital requirements. One efficient investment house has set up a list of areas of interest in biotechnology along with a list of areas of no interest.

While the legal profession seems to discourage small business starts, legal problems are more easily handled than in the United States.

A number of joint ventures have been put together, many with universities. The government provides funds for research while the private firms cover operating costs and market any products developed.

In establishing Imperial Biotechnology Ltd., Imperial College has retained a 25 percent to 30 percent interest and uses the facility one-third of the time for teaching and research. The staff is seconded from industry using regular students on projects as well as CASE students. They will license-in processes for their own production and have first refusal of new technology from Imperial College and the Centre for Biotechnology. Indirectly, they receive support from DTI grants. The areas in which they have most interest are:

- applied microbiological and biochemical research
- specialty enzyme products
- development of fermentation (enzymes, bio-polymers, therapeutic substances) and extraction processes
- production of novel materials for evaluation
- contract manufacture of specialty products.

PA Technology, which is probably the largest firm involved in the business of technology transfer and exploitation, has been eminently successful and has expanded its operations considerably.

A small number of NBFs have been established but, being perceived as a risk, do not receive the strong support from private investors enjoyed by NBFs in the U.S. The large, established chemical and pharmaceutical companies, which appear to be investing large sums in biotechnology R&D and have the experience and capital for large-scale production and marketing, are expected to take a leading role in the commercialization of biotechnology.

To date, products on the market are comparatively few, mainly in health care (monoclonal antibodies, diagnostics and pharmaceuticals).

To review, only two groups have the specific and exclusive responsibility of fostering biotechnology -- SERC's BTD and DTI's BTU. Many others play significant roles in supporting basic research (MRC, AFRC), in funding applied research (BTG, some investment houses, some interface companies) and in establishing companies (venture capital institutions, interface organizations such as SDA, PA Technology, Innotech).

DISCUSSION

Britain has a number of strengths in biotechnology. Its research base in the universities is superb with a large number of first-class universities strong in a sufficient number of disciplines to meet the needs for biotechnology. Its contributions have been outstanding. The quality of its work is such that its scientists have received a disproportionately large number of Nobel prizes. Its industrial base is excellent; the manufacturing, pharmaceutical, agriculture and food processing sectors are strong with large exports and a good export marketing capability. Capital is in good supply but U.S.-type venture capital is less obtainable. It has available to it a large domestic market -- the European Economic Community. Recently, comprehensive programs to bring all sectors together to foster the development of the biotechnology industries have been implemented and appear to be effective.

While its industry has been strong and international, the U.K. has had difficulty modernizing due to low profits in recent years and hence a shortage of cash for capital expenditures. It has also been reluctant to expand its research and development efforts into the new biotechnology.

A few larger firms have initiated programs. Interest is increasing, and now the pharmaceutical industry in general is involved. However, Celltech and AGC both lament the fact that British drug, chemical and food companies have shown little commercial interest in their work. While from its experience, BTG suggests that the universities' expectations in licensing are too high.

Discussion at the Biotechnology Centre, University of Cambridge, suggested that British industry was unreceptive to new technology due to the tax laws and culture. The centre prefers to work with British firms but will work with anyone who provides a suitable match. The need was stressed for a data bank of all know-how, patents, research, production, etc., in biotechnology available to all industry on a suitable basis.

As one respondent stated, "A committee is good for information gathering but personal contact is best for technology transfer. Informal discussion is needed between investor and scientist. People are the key to successful new ventures."

As the following comments reveal, the perception of the tax climate varies widely:

> "In the U.K. there are no tax breaks or R&D tax partnerships. Only U.S. or other foreign firms are attracted on a long-term basis due to the tax structure."

> "Venture capital is largely inappropriate in biotechnology. There are investors interested but lacking the tax incentive in the U.K., they can concentrate on building businesses in the U.S."

> "The U.K. grant aid and tax aid make it one of the best tax havens in the world."

> "It is the tax structure which prevents entrepreneurial activity and militates against established firms looking at new or advanced technologies."

In spite of their scientific contributions, which could be of benefit to humanity, the universities have been largely talking to themselves. They are not customer- or user-oriented nor are they product- or process-oriented. They do not speak the language of the financial community. Communication with industry is low on their priority list. When they do get involved with industry, their perception of the commercialization process leads to unrealizable demands and unattainable expectations. Even university/industry liaison offices now are vague about their role or mandate. Universities must be awakened to industrial needs and opportunities. Even though large companies conduct their own R&D, they also need universities; small companies must be involved with universities.

Two major problems have been the lack of entrepreneurs and the university/industry interface. Entrepreneurs have not been developed by the culture as they have in the U.S., nor have they been attracted or encouraged by the economic climate. Avalaible venture capital has been invested in Europe, North America or elsewhere. The financial community has not spoken the language of biotechnology and so there has been little communication. The few entrepreneurs in universities, who have attempted to establish NBFs, have not spoken the language of the venture capitalists, nor have they appreciated the marketing problem and the cost of getting from research to production.

Biotechnology transfer requires the ability to communicate intelligently, and willingly, with people of many disciplines. It is thought that the ability of the U.K. to compete internationally will be determined by the success of domestic technology transfer.

For technology transfer, an international base is important because there is an international occurrence of ideas which can be applied internationally. The British are especially good at basic research but do only 5 percent of world research. With this share declining, they must build so that they can understand and exploit the ideas of others. They have tended to concentrate high-level skills in the basic research but these skills are needed in other areas as well. There must be a movement of people from research to commercial activity.

The Scottish Development Agency (SDA) and like organizations are becoming increasingly capable of guiding and assisting the innovation process. They are using the following vehicles to improve the university/industry interface and hasten technology transfer:

- awareness programs (conferences, clubs, exhibitions)
- development projects to make commercial judgment
- enabling units (departmental structures, institutes)
- consultancies (technical, financial, marketing)
- teaching (technical upgrade, marketing, teaching companies).

By providing a focus for technology transfer mechanisms, these agencies can organize the entire process for commercial exploitation. They suggest the following routes for technology transfer:

* inward investment -- companies setting up subsidiaries or branch plants, either domestic or foreign;
* inward licensing -- companies must have the skills to successfully exploit acquired technology;
* university into industry;
* employee new starts -- new company spin-offs either from larger companies or universities;
* job-shop -- the buyer can lend or put people into the contractee company. Sometimes the job is done by small companies for major companies which may be persuaded to get into the business. This forces technology transfer.

Unilever treats biotechnology as any other technical area -- from basic research the project goes to business groups and then small companies are formed. People from Unilever are put into university departments to help identify research areas of interest to industry. Interaction is needed to stimulate the researcher.

At Imperial Biocentre, the movement of people is emphasized. They "scurry around meeting people, putting people together, being listening posts and going on the road encouraging universities industry, venture capitalists, etc."

Barriers that have slowed the movement of people and, thus, the transfer of technology are careers, pensions and attitudes, but mobility is increasing and attitudes are changing.

Financial investment firms must be staffed by people with appropriate skills. They must learn the language of the scientist and engineer so that they can understand the situation clearly. The skills of exploitation should be taught in schools. Industry, repeatedly confirms that a product champion is needed for successful innovation. Partnerships are a means of exploitation that is not being used to its potential.

While there was no indication of any policy on government procurement of the products of research, it was suggested that government buy-in, support more basic research, and make available more start-up funding.

The last few years have seen the government establish many initiatives to bridge the gap between university and industry. These programs are extremely comprehensive and cover the whole range of activities from support for applied research and development to partnerships in NBFs. The government has tackled the principal problem of the university/industry interface and, if the planned additional effort is put into this area, progress will likely accelerate.

Results from these initiatives are beginning to show. Universities are establishing biotechnology centres, research parks, joint ventures and even their own companies to exploit biotechnology. New companies are being formed to act at the interface and to contract research into universities and institutes until the technology is put into a company laboratory. There is excellent rapport among the government and promotors of biotechnology.

The established companies are becoming involved in biotechnology. They are being moved to action by market pull, seeing what their competitors are doing, and what is going on around the world. Since many are looking for a quicker return than is possible in biotechnology, any action taken in this area is based on a concern for company survival. Pharmaceutical companies, which are largely international, have programs in the U.K. and elsewhere and are making agreements with foreign firms.

The universities are still not happy with the lack of interest shown by the domestic firms and are increasingly willing to work with foreign firms in biotechnology. The agencies that operate the various schemes available, are not satisfied completely with the results to date and propose spending more effort bringing people together and working with them to improve communications.

To some extent, this accounts for the apparent success enjoyed by companies formed to operate at the interface. They spend a great deal of time developing intimate relationships with the researcher and assessing the research in biotechnology at the universities. Having decided on a particular program for exploitation, they sponsor ongoing applied research in universities or institutes to ensure that the various areas required for successful commercialization are covered. With this more complete package, and with the ability to speak the researcher's language, they are able to arrange for the venture capital necessary for successful commercialization.

BTU, BTG and the interface companies have a good deal in common in their approach to developing the biotechnology industry. BTU uses grants; the others use equity capital as well as BTU grants and/or BTG support. The interface firms meet slightly different needs and their success will depend on their expertise and aggressiveness.

With the many progams introduced during the past few years to support the transfer of biotechnology as well as its development in the United Kingdom, the mechanisms seem complete. The basic research base is still superb but is threatened by reduced government support. The interface between universities and industry is receiving a lot of attention and people and organizations are dedicated to improving it. The financial climate is slowly changing. There is a good deal of risk money available but there is still a substantial language barrier between scientist and financier. The ultimate impediment to exploitation of this resource is the national culture. Financial inducements may have to be increased to lessen the effect of this cultural bias against the drive to be entrepreneurial. Many in Britain expressed concern that the United States and Japan were moving ahead with their own biotechnology as well as taking advantage of British-developed technology. This may spur on U.K. companies. But it may also make them attempt to restrict access to and communication with the British scientific community which could do serious damage to the U.K. cause in the long run.

The biotechnology industry is likely to grow slowly and solidly with much less volatility and financial disappointment than has characterized growth in the U.S.

CANADA

INTRODUCTION AND BUSINESS BASE

Canada's economy has always been dominated by its resources, both renewable and non-renewable. Agriculture, forests, mining and fisheries have been the source of most export sales. Multinationals have played a part in this development. Of late, these industries have had a declining share of world markets. They should be major recipients of the benefits of biotechnology.

Canada is less well-developed industrially than the countries already considered. Many of the nation's raw materials are converted into useful products in other countries and imports of these finished products are substantial. With few exceptions, Canada's industries -- resource and manufacturing -- are ill-equipped to receive and commercialize transferred biotechnology. They are not staffed with scientists and engineers competent to communicate with the developers of the new biotechnology.

Canada's industrial structure is dominated by the multinationals, principally from the United States. As a result, research activity, which is so important in the development of biotechnology, is largely in the hands of the government through its laboratories and those of the universities.

The pharmaceutical/health care industry is probably over 75 percent foreign owned with imports amounting to 50 percent of the domestic market. Enforced licensing of pharmaceutical products has resulted in research activity being reduced to near zero. The agriculture and food products industry is largely a producer of raw materials with substantial exports. There is well-developed fermentation expertise in the beverage industry. The chemical industry comprises mostly heavy chemicals and few fine chemicals. Here again, the industry is effectively controlled by the multinationals.

The Canadian economy is based on selling resources which people are learning to avoid using. There is not a sufficient technology base, infrastructure or venture capital base to introduce the new processes of biotechnology at an attractive rate. The problem is further compounded by the size of the available market.

THE BIOTECHNOLOGY SEGMENT

In 1980, a government task force was established to evaluate opportunities for Canada in biotechnology. It made several recommendations which were not acted upon until 1983. Canada has yet to commercialize any particular area of biotechnology which could be competitive internationally. In reviewing Canadian activity in biotechnology in 1980 and today, it is apparent that domestic development of biotechnology is still in its early stages compared with the United States, Japan and the United Kingdom. (It may even have declined in relative terms.) While a number of companies have indicated activity in biotechnology, in most cases it is minimal, or in the established areas or is simply an interest. Programs have been established in a few firms such as Connaught Laboratories and Syntex and venture-capital-funded firms like Allelix, Bio Logicals, Iotech and Philom Bios.

BIOTECHNOLOGY R&D

Support for basic biotechnology research in universities is provided by the Natural Sciences and Engineering Research Council (NSERC) -- currently about $11 million per year -- and the Medical Research Council (MRC) -- about $20 million. There is, as yet, little other support. Research is carried out in most universities across the country and recognizes regional needs. In most cases, there will be no potential-user contact with the researcher. Programs are reviewed by peer groups with little or no industrial input.

It would be difficult for Canada to compete in the first commercial applications of biotechnology now taking place in the pharmaceutical industry. The human drug licensing law implemented in 1969 resulted in the closing of all research operations by multinational pharmaceutical companies in Canada.

Major areas of research in biotechnology which have been selected to receive the support of the federal government are:

- nitrogen fixation
- plant strain development
- cellulose utilization
- mineral leaching and metal recovery
- animal and human health care products.

Steps are being taken to establish and develop research networks in the selected target areas for biotechnology research, to encourage investment by industry in university research, and to promote interaction between federal departments, universities and industry. In addition to supporting biotechnology research in industry, the National Research Council sponsors three centres of expertise in biotechnology -- a new institute in Montréal, the Plant Biotechnology Institute in Saskatoon, and its Biological Sciences Division in Ottawa -- for a present annual commitment of about $73 million.

APPLIED RESEARCH TO COMMERCIALIZATION

Active federal support has been supplied for the innovation process through applied research and development, technology transfer and product and process establishment. The National Research Council (NRC) has its Industrial Research Assistance Program (IRAP), and the Department of Regional Industrial Expansion (DRIE) has the Industrial and Regional Development Program (IRDP) which has not realized its potential for innovation. Tax incentives for industrial R&D include 100 percent write-off plus investment tax credit for R&D expenditures.

More recently, the federal government has introduced the scientific research tax credit (SRTC) which industry, especially the small and medium-sized enterprises (SMEs), had long sought. In some instances, it has been of great assistance in biotechnology. Unfortunately, a legal loophole was discovered by the financial community which resulted in an abuse of the intent of the program. Much more revenue than budgeted has been foregone by the federal government without a corresponding increase in R&D. The regulations must be changed to prevent this abuse (the "quick flip") but it would be a tragedy to have established this incentive without having accomplished its intent.

In an effort to direct more government spending to SMEs, the federal Department of Supply and Services (DSS) is reviewing its purchasing policies. The federal Small Businesses Loans Act (SBLA) guarantees loans obtained from the private sector. The Federal Business Development Bank (FBDB) has operated for many years providing management services as well as loans, loan guarantees and risk capital to SMEs.

Quebec has over 100 programs to assist SMEs. Manitoba will team up with private investors to form venture capital corporations and hold up to 49 percent interest in them. It has a number of additional programs to help SMEs. The Ontario Development Corporation assists start-ups and expansions with term loans, guarantees to borrowers from private sources, as well as exports with a revolving line of credit (primarily for secondary industry). Alberta has a number of programs to assist SMEs such as the Small Business Equity Corp.(SBEC), Vencap Equities Alberta Ltd., Alberta Opportunities Co. and Calgary Research and Development Authority. Saskatchewan, British Columbia, New Brunswick, Nova Scotia, Prince Edward Island and Newfoundland also have in place, or are upgrading, programs to help establish SMEs.

Many have "incubation" programs which include building space.

British Columbia, through its Discovery Parks program, has one of the most complete packages to assist the SME. It most closely resembles the SDA and BTG in Britain. In spite of the success of this program in other areas (electronics, computer software, etc.), progress in biotechnology has been very slow, due largely to communications problems between scientist and financier and the financial condition of the province's industries. The market pull has not been there. Eventual use of biotechnology in B.C. will be mainly in the resource industries -- forest, fisheries and minerals.

All of the provinces have shown interest in commercial opportunities in biotechnology. Ontario, the Canadian Development Corporation and John Labatt Ltd. have invested in Allelix Corporation, which was established specifically to develop new biotechnology. Quebec strongly supports biotechnology and has invested in such organisations as BioEndo, Biopreserv, Biomega and l'Institut Armand-Frappier. There is some activity in most provincial research councils. The Alberta Research Council, which is just completing a new laboratory for biotechnology (fermentation), has R&D contracts with a number of companies which should help it toward the leading edge.

Research in the universities is scattered across the country with little focus and few connections with the marketplace. In some instances the universities have set up institutes to assist with multidisciplinary research and provide possibilities for industrial liaison (e.g., Guelph-Waterloo, McGill, Dalhousie). Many other universities are planning to form institutes but progress is slow without the focus an industrial infrastructure would provide.

A number of small research firms have established themselves near the universities. In most cases they suffer from lack of good market information, market access and, after a time, from lack of expansion funding (e.g., Quadra Logics, Gemini Biochemical, Pacific Isotopes). These will surely be surpassed by others with better connections to the markets (e.g., ABI Technology, PM Mineral Leaching Technologies, Biotechnica Canada, Chembiomed) provided financing is adequate when needed.

Provincial commitments to biotechnology in 1983-84 amounted to some $70 million. The private sector spent about $110 million in the same period.

Most established firms have not become involved in new biotechnology although tax laws favour investment in biotechnology R&D. Canada, like the United Kingdom, loses many of its trained personnel, of whom there are already too few, to other countries offering better opportunities. This will be a major factor in the success of the programs now being implemented to commercialize biotechnology.

A first step has been taken toward improved co-operation in biotechnology between industry, university and government by the establishment of biotechnology networks.

COMMERCIALIZATION

Frequent contact with foreign markets and technology draws attention to possible applications of newer technologies in domestic industry. One such example is the acquisition of Italian lysozyme extraction technology by an established firm, Export Packers Co. Ltd. of Winnipeg (Appendix III). In attempts to strengthen their position and speed up commercialization of new products, both Connaught and Allelix have sought and made agreements with foreign biotechnology firms. However, agreements with foreign companies are becoming increasingly difficult for several reasons.

Canada has little biotechnology expertise to share with a partner. Marketing arrangements are made on a regional rather than national basis so that Canada is included in marketing rights given to an American company. There is some evidence that, in many instances, a single production unit could satisfy the worldwide market for a product so production would be reserved for the inventing company.

DISCUSSION

Canada has little biotechnology to transfer since it has done so little research and development. There are a few universities working with groups on specific projects, principally in the U.S. Canadian firms traditionally do not work with other Canadian firms, particularly in new areas. This is probably due to the degree of foreign ownership.

Canada's greatest strength is probably its research base in the universities. A secondary research base is being expanded within the National Research Council framework. Canada, also, has a supply of capital -- largely untapped by biotechnology -- partly unavailable due to government regulation (limited risk funding by banks), partly diverted to other industries (mining and real estate) and often to other countries (U.S.). It also has a good supply of unsophisticated entrepreneurs usually involved in low technology industries.

Canada's weaknesses include a small domestic market, a very poor university/industry interface, lack of incentives for entrepreneurs in high technology and poor communications with the venture capital market. It has virtually no indigenous industrial research in biotechnology and little infrastructure to which it could transfer biotechnology for commercialization.

In spite of the considerable efforts, federal and provincial initiatives for biotechnology (advisory and study groups, institutes, crown corporations, etc.) have served only to increase the disproportionate amount of biotechnology done in government and universities but the activity must be in industry.

Comparatively little progress has been made towards establishing biotechnology in Canada. Industry still does not have the expertise to talk to the experts in biotechnology at the universities, nor has it shown an interest in acquiring it. The real impediments to the creation of new biotechnology firms (NBFs) or the upgrading of established firms to include biotechnology processing have not been alleviated. The importance of biotechnology to the future of Canada's industries suggests that it requires special attention.

The Canadian culture more nearly resembles that of Britain where there are fewer entrepreneurs and less risk-taking. The universities have tended to keep to themselves and follow their own research interests. There has been no attempt by much of industry to get involved with the university research base since its principal research was with the foreign parent. The role of the university has been described as:

- educating specialists
- helping to disseminate knowledge among potential users
- contributing to discoveries
- applying new knowledge.

Canadian universities have not given high priority to disseminating their knowledge to potential industrial users or applying this new knowledge for the benefit of humanity. Even though appropriate technology may have been developed in some universities, little has been transferred because of lack of Canadian market pull. Indeed, the pull has been such that some universities have made agreements with foreign firms.

There is recent activity on the part of most universities to move technology out by creating industrial liaison offices and "innovation centres". These have had limited success especially in biotechnology.

An interesting development is the creation of a "technology transfer office" at the University of Calgary staffed by a number of experts with plans to operate outside of the university administration but reporting to the Board of Governors. Time will show whether it can be successful in transferring biotechnology.

Lack of sufficient financial incentive has reduced the availability of venture capital and sent entrepreneurs elsewhere. In fact, Canadian firms have invested in biotechnology ventures in the U.S. rather than Canada.

DISCUSSION

GENERAL

It is evident that the United States has a clear lead in just about every aspect of biotechnology. It has an excellent research base, an entrepreneurial culture, a good supply of venture capital and a large domestic market. The establishment of a large number of NBFs was made possible by research contracts from government agencies. There is no problem with technology transfer in the U.S. The market pulls, after basic research has made the necessary discoveries.

The Japanese have observed the American situation and are trying to close the gaps in their country. They are increasing their basic research, building on their expertise in fermentation technology and making agreements with foreign firms to acquire or share technologies and markets. The government has been instrumental in providing leadership, co-ordination and financing. While communications between university and industry are not the best, there do not appear to be any serious problems in technology transfer in Japan. In addition, the Japanese have sufficient resources in the technology to bargain from a position of strength in international technology transfer.

The United Kingdom has a splendid research base but has lacked the entrepreneurship of the U.S. Financing has been available but, without the entrepreneur, the scientist and the financier have spoken different languages and so have not understood each other. The government has now put programs together to bridge this university/industry gap. These programs are comprehensive and will improve tremendously the transfer of and exploitation of technology. International transfer of biotechnology does not appear to be a problem. Britain has available to it the EEC market which is as large as that of the U.S.

Everyone recognizes the importance of people in transferring technology. In 1983 in the U.S., the National Institute of Health (NIH) had 800 visiting scientists. China has sent more than 9000 scientists to study in the U.S. in the last five-and-a-half years, and Japanese scientists are everywhere.

The earlier chapters of this report are replete with comments and examples of support for building strengths within, and strengthening collaboration between industry and university. This is the substance of technology transfer.

CANADA

UNIVERSITIES

Multidisciplinary and Interface Problems

One of the principal features of biotechnology is that it requires the contributions and the co-operation of a multitude of disciplines. As now organized, Canadian universities do not facilitate interdisciplinary research. If they are to become effective in biotechnology they must remove the barriers to people working with people in other departments -- in fact, they must insist on it.

The requirement for a multidisciplinary research group also poses a problem for the NBFs and SMEs. They are not large enough to support a complete group in-house and must use suitable outside resources such as universities. There are, then, two problems -- the multidisciplinary one and the university/industry interface. It is exceedingly important that appropriate university/industry relationships be established so that NBFs can get the help required.

In the U.S. and U.K., biotechnology has been the direct outcome of public funding of academic biomedical research. Because of the close relationship between academic and applied research, the universities have been forced to play major roles in the spawning and development of the industry.

One function of the university is to provide a world-class research base from which industrial laboratories can draw technical experts and technology which can be developed to create marketable products. The government must insist on maintaining excellence.

The university must become aggressive in determining the potential usefulness of its research. It should engage private sector expertise in market research and project evaluation. It must persuade someone to further develop and commercialize its research. It should use existing outside entrepreneurs who need funding support; such support could be made available through SBIRs or NRC or RDLPs. Failing this, the university must itself become entrepreneurial and gather together what is required to commercialize the technology. It must encourage those on its staff who are entrepreneurial to step out of the academic environment and contribute their talents to the outside world of biotechnology.

Much more drastic action must be taken if Canada is to benefit from the new products and processes of biotechnology. The university/industry relationship must be vastly improved so that confidence and trust are present on both sides.

There may be biotechnology in Canadian universities with excellent commercial potential, but the universities are not product- and process-oriented nor do they seem to want to communicate with industry except on their own terms. They seem to wish to develop some relationship with industry, in fact they accept money from the government to set up offices which purport to do this, but the process is controlled by the university and, frequently, does not meet industry even half-way.

Industry, not knowing that the university has anything to offer or being frustrated at previous attempts to communicate, no longer goes out of its way to spend its valuable time trying to relate to the university. It will take a substantial, concerted effort to eliminate the university/industry interface problem.

There must be some incentive, some reward for establishing adequate university/industry relationships. Certainly the NBF can not guarantee any reward, nor can the SME. Interface companies are required to work in this area.

NSERC can help in this university/industry interface area in biotechnology, especially for NBFs and SMEs, by amending the regulations of the undergraduate industrial fellowship program so that students can work for an industry in a university or government laboratory. In this manner, a company can assess the value of the technology being pursued as well as the people pursuing it. Many initiatives, which have been taken by SERC (U.K.) are applicable in Canada and should be used to bring industry and university together. (Many actions for improving the university/industry interface are suggested in Appendices I and II.)

INDUSTRY AND NBFs

Canada's most pressing problem is its lack of a biotechnology industry infrastructure. Such an infrastructure includes a sufficient number of firms with the capability of understanding researchers and engineers in biotechnology, production equipment which relates to the new bio-processes, access to the markets for the resultant products and management eager to exploit new technologies. This lack can be alleviated most readily by adopting sufficient incentives for entrepreneurs to commercialize technology acquired from foreign countries. Japan is the most likely source. On the receiving end of technology transfer, Canada must employ many more highly qualified scientists and engineers in the appropriate industries to ensure early success.

Canada must forget its past attitude that it will manufacture products only for the Canadian market. It must do as the Scandinavian and most other countries do, look at the world as a market opportunity and accept that the domestic market is only a small percentage of the total sales goal. It must also look at the availability of venture capital on a world basis.

There is no reason that capital should not be sought from the money markets of New York or London. The government should be working to aid both areas by seeking the admittance of Canadian produced goods, on a fair basis, to all countries to ensure that the market size, realistically available to Canadian producers, is equal to that of their competition.

Small entrepreneurs can only acquire biotechnology and commercialize it if they have some assured ability to market the product. This is very difficult in the pharmaceutical field, but might be a little more easily arranged in the health care/diagnostic field. It would be much easier to commercialize biotechnology in plant agriculture or food processing. However, products for these markets are farther removed.

Many of the NBFs in the U.S. were initially funded almost 100 percent by the government through NSF, NIH, DOD or DOE research contracts. Today most of the smaller NBFs and many of the larger are still recipients of these contracts. Funding through SBIRs has also been very useful and the R&D limited partnerships have been not only popular but have aided the establishment and considerable expansion of many NBFs. In the early stages of the expansion boom, much risk capital was ploughed into the industry with unrealistic expectations of reward. This situation must be watched very carefully in the non-entrepreneurial climate prevailing in Canada. Unfulfilled promises could ruin the entrepreneurial climate for biotechnology for years to come.

There seems to be a great deal of risk money available in Canada but it has gone mainly into the mining industry -- or into the U.S. Means must be found to control the money invested in SRTCs and ensure that its use yields results similar to the RDLPs in the U.S. Much persuasion, including government incentives, will be required to direct this money into the biotechnology industry. But unless this is done, the Canadian biotechnology industry will continue to fall behind those of other developed countries.

THE FOREIGN CONTROL PROBLEM

Canada has a problem which seriously affects the establishment and updating of industries in the new techniques of biotechnology. A large segment of Canadian industry is controlled by foreign-based multinationals which tend to have their principal, and usually only, research organizations in their home countries.

Accordingly, new processes and products are produced domestically as well. Foreign subsidiaries will adopt biotechnology in their Canadian operations only if there is a need for more than one unit in the world or if there are raw material or marketing advantages to production in Canada which overcome tariff and non-tariff barriers to the markets.

In Canada, these companies are market driven and little influenced by Canadian government R&D programs and incentives. Their policies are at the discretion of current foreign management. Once they have decided on an avenue to pursue, though, they will use any government monies for which they are eligible. Government policy has little or no effect on the foreign multinational's program in Canada. Any monies, taken by these companies, reduce the amount available for companies responsive to Canadian goals.

The large Canadian firm is usually locked into an indigenous raw material, using a well-established technology, and has no apparent reason to broaden its horizon. The foreign-controlled multinational will produce in its home market unless there is a distinct raw material or other advantage in Canada. At the moment, in biotechnology there appear to be few raw material situations which would give Canada an advantage. Since for many biotechnology processes one plant could meet world requirements, the possibility of a foreign-controlled company establishing a plant in Canada is rather remote. Canada, therefore, has few prospects unless the climate for the entrepreneur is made so attractive that he will step in, find processes, arrange licenses and suitable marketing, and proceed to commercialize.

It is imperative that, in the biotechnology area, organizations be established and supported which are Canadian-controlled, will market internationally and may become Canadian-controlled multinationals.

GOVERNMENT INITIATIVES

A national policy for biotechnology was proclaimed several years ago but its implementation has been only partial and very slow. Support for this sector includes the IRAP program of the NRC, which funds 50 percent of applied research costs, and the DRIE program to support innovation in industry. Neither program appears to have met the need in Canada for a greatly enhanced activity in biotechnology.

Support has also been given to the establishment of "innovation centres" at various universities. So far these have done little to resolve the university/industry interface problem. The climate for entrepreneurs has improved only slightly. Several large Canadian industries have invested in biotechnology projects in the U.S. One medium-sized firm has been established in Ontario with provincial and federal government assistance.

The National Research Council has been making notable efforts for some years to bridge the gap between government laboratories and industry. Many people from industry have been involved on its council, boards and committees. It has provided industrial research support through its IRAP program. It has attempted to commercialize research undertaken in government laboratories through the PILP program. It has had some measure of success although the presence of so many foreign-controlled companies has made its job very difficult. Even so, the barrier between government laboratory and industry, while not nearly as strong as that between university and industry, has not been removed as much as it should be.

The technology push can accomplish only so much and the market pull has not been there. Canadian-controlled industry has neither the capital nor the incentive to invest in new technology to the extent required to keep it competitive for the long term. It may be that the NRC should become even more aggressive in removing the barrier -- by having the scientists spend more time, not only with the scientific but also with companies' operating and management staffs. Enough time has been lost already by not removing these barriers to effective communication and co-operation between industry and government laboratories and universities.

The NRC has designated its laboratory in Saskatoon as the Plant Biotechnology Institute. This institute has a lot of technical strength and, provided its programs are tied closely enough to agricultural needs, should be very productive. A second Biotechnology Institute has been created in Montréal.

For this laboratory to fill the need for which it was created it must have good communications and close ties to industry. It will require current information on the commercializaton of biotechnology around the world. It should have access to information concerning the markets, and their availablilty, for products which are or could be made by biotechnology. If it is to strengthen industry and perform applied research and development, it must be more closely aligned to industry than it is to government. While it should have some commercial expertise in-house, it should contract out its requirements for market volume, location and availability and project evaluations to ensure that it has the best available competitive information about the world situation. Bio-networks will probably be of great value at this stage of development. Formation of bio-clubs by the universities should be even more valuable.

Two programs, adopted in foreign countries, look particularly attractive in the Canadian context. The Japanese Small Business Credit Insurance Corp. guarantees financial lending to small companies through the Credit Guarantee Corporations, as does the Loan Guarantee Scheme in Britain. This decreases the need for additional equity capital to maintain traditional debt to equity ratios. The Small Business Innovation Research (SBIR) program is operated in the U.S. by the National Science Foundation. In two phases, it supports NBFs up to US$240 000. Its use in Canada would not only provide considerable assistance to NBFs, but would avoid unfair trade practice criticism from the U.S. government.

The programs and performance of SERC (U.K.) and SDA (U.K.) are particularly good and much could be adopted from them for the Canadian situation.

The government support system in Canada consists of:

* The NSERC funds basic research in the universities. It is in a prime position to improve the industry/university interface by supporting research which could have an impact on industry, and by using many of the initiatives which SERC (U.K.) has put into place.

* The NRC, in addition to its own program of research in biotechnology, supports applied R&D in industry. It should increase its IRAP program to generate an expansion of the biotechnology industry similar to the NIH and NSF (U.S.) programs. It should co-operate in the creation and maintenance of NBFs especially new research companies and interface companies.

* DRIE supports the scale-up or commercialization of processes in industry. This agency has the most important role to play in the creation and development of NBFs and SMEs.

It must take a pro-active role in establishing NBFs, including interface and research firms, funding them when necessary, to ensure that the needed infrastructure is developed quickly. It must also fund the creation of a biotechnology data and market base, and the search for foreign technology and markets by the NBFs and SMEs.

* Other government departments contribute to the climate for business and entrepreneurial activity in Canada. Such a climate must be sufficiently attractive to result in the needed development of a biotechnology industry infrastructure. This requires the planning and program implementation by many government departments. Federal/provincial co-ordination would result in greater overall productivity and expedite attainment of the goals.

Biotechnology requires a long-term commitment. Canada has a major problem in enticing industry to participate because government policies have earned a reputation for being transitory.

RECOMMENDATIONS

Primarily as a result of the extensive discussions the authors have had with people in the industry, university and government sectors in the various countries (see Appendix IV), the following recommendations are made:

1) Government should declare biotechnology processing a top priority item.

MARKETS

2) Expansion of markets available to Canadian biotechnology processors should be negoatiated.

NEW BIOTECHNOLOGY FIRMS

3) DRIE should establish a vigorous program to assist the private sector in forming NBFs and commercializing biotechnology from foreign sources.

4) Programs should be established to bring Canadian biotechnology to commercialization. An entrepreneurial climate is required which would include such programs as loan guarantees, SBIR (U.S.), RDLP (U.S.), expanded government research contracting, agencies such as SDA (U.K.).

5) Export marketing efforts of NBFs and SMEs as well as exploratory missions for technology and markets should be supported.

UNIVERSITY/INDUSTRY INTERFACE

6) Private sector organizations to strengthen the university/industry interface should be supported.

7) Success or progress in improving the relationship as demonstrated by the establishment of biotechnology clubs, consultancies, technical agreements, temporary exchange of scientists, etc., should be rewarded.

8) NSERC should amend undergraduate industrial fellowship guidelines to encourage companies to have students work in university or government laboratories as well as in company laboratories. Implement many initiatives of SERC (U.K.).

INTELLIGENCE

9) The gathering of market information for NBFs should be encouraged.

10) An industry data base of research, technology and marketing should be established in the private sector.

11) In view of its success in biotechnology and other technology areas, it should be determined, in detail, why the SDA (U.K.) is so much more effective than Canadian federal or provincial organizations in creating NBFs.

APPENDICES

APPENDIX I

Areas of Collaboration Between Universities and Industry in the United Kingdom.

1) Personal assistance from industry with university activities:

- Lectures by industrialists at universities
- Industrialists serving on university and faculty committees, etc.
- Industrial advice on, and provision of problems for, research
- University staff and students visiting industry
- Industrial advice on curricula
- Use of industrial laboratories for higher degree work
- Secondment of industrial staff to work at universities
- Technical advice or assistance
- Use of equipment or facilities in industry
- Instrument development.

2) Use of university staff and facilities:

- Industry using more consultants
- Industry sponsoring research at universities
- Provision of special advisory or consultancy services
- Secondment of university staff to work in industry
- Refresher or retraining courses
- Industry sponsoring sandwich-course students and providing suitable training
- An increase in multidisciplinary projects
- Use of facilities or equipment at universities by industry.

3) Joint activities:

- Joint research programs with work at university and in industry
- Interchange of staff
- Joint supervision of students
- Local "science-based" industry developing from university departments
- Joint meetings or colloquia
- Joint appointments.

4) Positive role of "third parties":

- Industrial liaison centres run by universities
- Science Research Council schemes for improving contacts:
  a) Co-operative Awards in Pure Science (CAPS)
  b) Industrial studentships and fellowships
  c) Awards for Science, Industry and School Teaching (ASSIST)
  d) "Instant" awards
  e) Graduate schools
  f) Support for collaborative research grants
- Research associations translate research into technology for smaller firms and feed back to universities
- Ministry of Technology industrial units
- University grants committee "pump-priming" support for schemes of assistance to industry
- Professional institutions encourage joint activities and influence curricula by professional requirements
- Mininistry of Technology industrial liaison officers encourage university-industry links.

5) Financial (or similar) support from industry for university activities.

- Grants for research without a fixed timescale or agreed program
- Grants for studentships, fellowships, etc.
- Loans or gifts of equipment
- Endowment of a chair or university post.

Source: CBI, Industry, Science and Universities, 1970, Table 64.

ref: OECD: The Future of University Research 1981.

Appendix I lists a multitude of ways in which universities and industries can co-operate. These, of course, are all mechanisms for technology transfer.

APPENDIX II

There are many actions which can be taken by university, industry and all levels of government to improve the university/industry interface and thus use more fully and efficiently Canadian knowledge and people resources. Among these are:

Universities and Institutes

- Maintain high standards, strive for a world quality research base
- Remove organizational and other impediments to interdisciplinary co-operation
- Promote multidisciplinary research
- Seek to dispel the mistrust that academia has for business
- Promote co-operation with industry
- Give entrepreneurs more freedom in relations with industry
- Support staff visits to industry
- Encourage entrepreneurial staff to become involved in NBFs even on a full-time basis
- Establish biotechnology clubs
- Encourage the creation of independent research foundations and institutes by staff.

Appendix I lists a multitude of ways in which universities and industries can cooperate. These, of course, are all mechanisms for technology transfer.

Industry

- Develop worldwide marketing capabilities
- Acquire worldwide marketing research know-how
- Have an understanding of the biotechnology now in use and the areas of current research which will likely lead to new products and processes
- Learn how to establish joint ventures, both nationally and internationally, which will strengthen marketing and production capabilities
- Be a part of a biotechnology industry association
- Have access to or have in-house a high-quality research group
- Have good consultants
- Establish a scientific advisory board
- Have scientists trained in other more advanced laboratories, universities or industry
- If necessary, upgrade scientists continually through courses, seminars, conferences, personal visits, university courses
- Maintain the entrepreneurial spirit as long as possible both in industry and university
- Maintain an applied research program, both exploratory and market-directed
- Use public knowledge and licensed technology wherever it exists -- do not re-invent the wheel
- Participate in biotechnology clubs.

Government

Corporate activity should be based on market pull or need. With this in mind, after having been established, all proposed incentives should be reviewed regularly and maintained only for as long as they are doing effectively what they are supposed to do.

i) Federal

- establish a financial package (loans, tax relief, grants, etc.) to make it more attractive for entrepreneurial companies to become established and possible for them to survive;

- Assist universities in establishing working relationships with Canadian companies to speed the transfer of useful technology to the marketplace as quickly as possible;

- Give more incentive to industry to sell worldwide;

- Until it is established within industry itself, assist in detailed studies of world markets. This is especially important for the small firms with neither money nor expertise to do this most necessary job;

- Increase the incentive for firms to support research either in-house, or in other firms, institutes or universities;

- Increase the incentive for firms to maintain an adequate complement of engineers and scientists on staff to maintain technical competence and efficiency;

- Encourage firms to bring in outside experts to give seminars to their scientific staff on a monthly, or more frequent, basis;

- Devise a program to ensure that high technology firms are current in worldwide technology and in its applications;

- Establish an aggressive program for bringing together Canadian entrepreneurs and foreign opportunities in biotechnology on a worldwide basis. This assumes an adequate worldwide technical awareness capability supported at first by government but, hopefully, later by industry associations or companies themselves;

- Maintain the university research base by supporting excellence;

- Support the continual modernizing of research equipment;

- Encourage joint industry-university entrepreneurship;

- Devise schemes to establish and support SMEs and NBFs such as are available in Japan and the U.S.;

- Establish agencies, such as the Scottish Development Agency (SDA), to provide more complete assistance to the establishment of high-technology firms;

- Support the establishment of a comprehensive data bank in biotechnology, technical and commercial, in the private sector for the use of government, university and industry on an appropriate basis.

ii) Provincial

- Provide good basic training in the sciences for all students and high-quality training opportunities for scientists and engineers;

- Provide financial and tax incentives for small firms to encourage the start-up and help the survival of new businesses in biotechnology;

- Support, both financially and with market assistance, small firms in the new technologies.

iii) Municipal

- Establish offices to keep local industry aware of technological developments; to identify the new technology relating to companies already in the municipality so that these companies might expand, form joint ventures, or so that new attractive industries might be established in the locality;

- Devise a financial and tax incentive program for the municipality which will assist new entrepreneurial companies to become established;

- Encourage education in the basic sciences for all students in the municipality.

APPENDIX III

Two Recent Transfers of Foreign Technology to SMEs in Canada

Enzyme Technology

A Canadian company, Export Packer Co. Ltd., on a business mission to Denmark to buy egg breaking equipment, observed the production of lysozyme.

Lysozyme, present in egg white in concentrations of 0.5 percent, has inhibiting and lytic properties over certain bacteria. It is an effective immunological agent and is widely used in human therapy for treatment of viral and bacterial infections. The well-established market in Europe and Japan for pharmaceutical use is worth about $40 million. In the food industry, it is used by the Japanese as a preservative for fresh vegetables, meat, fish, fruit and sake as well as in several cosmetic and pharmaceutical preparations. The potential market for food preservation is not known.

Lysozyme is extracted by an ion-exchange chromatographic process followed by differential precipitation. The process is patented by an Italian company and is in commercial use in Italy, the Netherlands, Germany and Denmark.

With an adequate raw material position (70 percent of the egg breaking market) and marketing channels in place, Export Packers undertook to transfer and commercialize this technology in Canada. Lysozyme must be marketed outside Canada and the U.S. since in neither country has its use been approved for pharmaceutical or food preparations.

After one year of negotiations with the Italian company and Canadian regulatory authorities and after the approval of financial support from the Enterprise Development Program of the former Department of Industry, Trade and Commerce, construction of the pilot plant in Canada started in March 1982. Pilot scale experiments commenced in August and production started in March, 1983.

From material which was previously destroyed, a commercially valuable, high-quality enzyme is being produced. The product is all exported to Japan and Europe. The company is now in a position, technologically, to meet the needs of the North American market when one becomes available.

Processing Technology

A small Canadian processor and marketer of milk products, Nelson's Dairy Ltd. of Weston, Ontario, learned of the development of a process in the United States which could be used for the production of shelf-stable pasteurized milk with no objectionable off-flavours. A sample of this product had been evaluated at the University of Guelph but no initiatives were taken by the larger companies.

DASI Industries Inc. of Maryland had acquired the rights to a Free Falling Film process and studied its applications over a period of years. Samples of the processed milk first became available in 1978. Nelson's was interested in the product but did not have sufficient resources of its own to commercialize the process. Suitable processing equipment was not commercially available.

It required the assistance of an knowledgeable entrepreneur, Gelda Scientific, to arrange for the development and production of suitable equipment by Tri-Canada Inc., a leading food equipment manufacturer, and to assist in obtaining financial support through the Enterprise Development Program of the former Department of Industry, Trade and Commerce.

After two-and-a-half years of devlopment work, a commercial totally automated system was installed in 1983. It has since been evaluated in a number of other related products. Evaluation of the product by the trade has been favourable and market acceptance is growing.

A recent study predicts that an aseptic milk could achieve a 2 percent share of the North American market in five years. With the shelf life extended to six to eight weeks in a conventional package the market share will be much higher. Two complete systems have already been sold to Menken Dairy in Holland. Other European dairy experts are evaluating the system and exports are expected to grow. The domestic market for the system is also expected to grow but more slowly.

APPENDIX IV

Visits Made by Frank Maine Consulting Ltd. to the Following:

United States

Agouron Institute
Arco Plant Research Institute
Biogenex Laboratories
Bioresponse Inc.
Calgene, Davis
California Institute of Technology, Biology Department
California Institute of Technology, Biochemical Engineering Group
Cetus Corp.
Chiron Corp.
Engenics Inc.
Genentech, Inc.
Helicon Foundation
Hybritech, Inc.
Ingene
Microbial Products, Inc.
Phytogen
Plant Genetics, Inc.
Salk Institute for Biotechnology Industrial Associates Inc.
Salk Institute for Biological Studies
Stanford University School of Medicine
Syntro Corporation
University of California/San Diego, Biology Department
University of California/Los Angeles, Biomedical Group
University of California/Los Angeles, Department of Biology

Japan

Calpis Food Laboratory Co. Ltd.
Délégation du Gouvernement du Québec
Eurogestion
Japan Industrial Technology Association (JITA)
Kirin Brewery Co. Ltd.
Kyowa Hakko Kogyo Co. Ltd.
Mitsubishi Chemical Industries Ltd.
Mitsubishi Petrochemical Co. Ltd.
Mitsui & Co. Ltd.
Mochida Pharmaceutical Co. Ltd.
Nagase & Co. Ltd.
Nitto Boseki Co. Ltd.
Research Association for Biotechnology
Research Development Corporation of Japan (JRDC)
Shionogi & Co. Ltd.
Takeda Pharmaceutical,
Takii & Co. Ltd.
Technology Transfer Institute

United Kingdom

Agricultural Genetics Co.
Axon Healthcare
Biotechnology Unit (Government Laboratory), Department of Trade and Industry
British Technology Group
Cambridge University Biotechnology Centre
Celltech
Centre for Applied Microbiology and Research (CAMR)
Centre for Biotechnology, Imperial College, University of London
Innotech Investments
PA Technology
Science and Engineering Research Council (SERC)
Scottish Development Agency
Tate & Lyle
University of Leicester Biocentre
Wolfson Cambridge Industrial Unit

Canada

Alberta Research Council
Allelix Inc.
Calgary Research and Development Authority
Canadian Hunter Explorations Ltd. (Biotechnica Canada)
C.I.L. Inc.
Chembiomed Ltd.
Cominco Ltd.
Corby Distilleries Limited
Discovery Parks Inc.
Du Pont Canada
Gemini Biochemical Research Ltd.
Government of Alberta, Office of Science and Technology
Government of British Columbia, Ministry of Industry - Ministry of Universities, Science and Communications
Government of Manitoba, Industry, Trade and Technology
Guelph-Waterloo Institute for Biotechnology
Joseph E. Seagram & Sons Limited
Labatt Brewing Company Limited
Medical Research Council
Ministry of State for Science and Technology
Molson Industries Limited
National Research Council
Natural Sciences and Engineering Research Council
PGE Technology
Plant Biotechnology Institute
PM Mineral Leaching Technologies Inc.
Quadra Logic Technologies Inc.
RE Tech (Capital Applied Research & Technology Ltd.)
Saskatchewan Research Council
Science Council of Canada
The Winnipeg Rh Institute Inc.
University of Alberta
University of Calgary
University of Guelph
University of Saskatchewan

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(3) ibid p. B57ff
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(5) ibid p. B74ff, B105
(6) ibid p. B71ff
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