AGRI-FOOD INDUSTRIAL BIOTECHNOLOGY IN CANADA

AN OVERVIEW

FOOD PRODUCTS DIRECTORATE

TECHNOLOGY WORKING SERIES NO. 4

Industry, Science and Technology Canada
Industrie, Sciences et Technologie Canada

Canada

AGRI-FOOD INDUSTRIAL BIOTECHNOLOGY IN CANADA

AN OVERVIEW

FOOD PRODUCTS DIRECTORATE

TECHNOLOGY WORKING SERIES NO. 4

Prepared by:
Food Products Directorate
Service Industries and
Consumer Goods Branch
Industry, Science and
Technology Canada
Ottawa, Ontario
K1A 0H5

June 1989

Author: G. Ingham
Tel.: 954-3092

AGRI-FOOD INDUSTRIAL BIOTECHNOLOGY IN CANADA

FOREWORD

Biotechnology, or the application of biological sciences to commercial products and processes, is not a new field because, for many years, enzymes and living microbes such as yeasts and bacteria have been employed in the production of foods, beverages, pharmaceuticals and chemicals. However, the full potential value of microorganisms did not become apparent until advanced recombinant DNA methodology was developed in the early 1970s. This technique involves the combination of genetic material from two distinct sources and makes possible the construction of new life forms capable of performing functions significant to several industries. In addition, the techniques of cell culture, cell fusion and enzyme systems have also expanded the opportunities for applications in human and animal health care, resource processing, agriculture and energy systems.

This report will examine the biotechnology activities in Canada which are focused on commercial applications in the agri-food sector. The agri-food sector includes primary agricultural operations, food and beverage processing, and products which modify food properties or contribute to the efficiency of plant and animal production. The industry classification, agri-food, is used to recognize the increasing convergence of agriculture and industrial practices, creating a reorientation in relationships between and among agro-suppliers, farmers and the food processing industry. This relationship is expressed in the formation of new science-based agricultural companies or the establishment of new divisions within existing companies, created to exploit the techniques of biotechnology through products designed for a variety of agri-food markets.

Estimates of potential markets for biotechnology based products in the agri-food industries vary widely but it is generally recognized the potential for Canadian and world markets is very large. This potential for commercial products and services has stimulated rapid expansion in the number of companies which have initiated agri-food biotechnology development activities. In recognition of these new developments, this report has been prepared to provide an overview of applicable biotechnology techniques in the agri-food sector, current developments and the areas of greatest opportunity and interest. The report also provides a brief review of the major factors that influence the application of biotechnology in the sector as well as possible strategic directions. An Appendix contains a representative list of Canadian companies active in the sector.

TABLE OF CONTENTS

INTRODUCTION AND OVERVIEW

In the later half of the 1970s and early 1980s, international interest in biotechnology developed rapidly and resulted in the formation of many small entrepreneurial firms and the expansion of research and development programs by large established companies in the major industrial countries. Many of the new research oriented firms were set up through affiliations between venture capitalists and university professors with expertise in the scientific techniques of biotechnology. The leading country in establishing new enterprises and in expanding the R&D activities of major corporations was the United States. Canadian activity has expanded at a slower pace but approximately two hundred commercial organizations are now active in a range of research, development and new commercial applications of biotechnology.

The initial enthusiasm that biotechnology developments generated in the industrial countries was primarily centred on products and processes for the health care industry. High value products, which could not be produced by the processes commonly used by the pharmaceutical and chemical industries, could be prepared in sufficient quantity for evaluation in potential health care applications using the new techniques of biotechnology. For example, interferon, which occurs in minute quantities in the human biological system, has been prepared by new processes and has been the focus of intense investigation as a cure for several types of cancer. Other products for treating blood clots and many diagnostics have reached the marketing stage. Many biotechnology firms which were primarily focussed on research are now concentrating on developing commercial products for market and are diversifying their programs to cover a broader range of industries including agriculture, food and beverage. New companies, primarily in North America, are being established to focus on the opportunities in the agri-food sector. These latter areas, which were passed over at first, appear to have eventual biotechnology applications much greater in terms of dollars than health care.

THE AGRI-FOOD SECTOR

The economic activities which comprise the agri-food sector, agricultural operations and food and beverage manufacturing, are closely linked in contributing to Canada's industrial output and international market competitiveness. Efficient agricultural operations are essential to the consistent supply of commodity materials for food processing. Measured by farm cash receipts, agricultural output was $21 billion in 1986. In the same year, the value of shipments by the food processing industries was $40 billion comprised of beverage shipments of $5 billion and food at $35 billion.

Output of the sector has expanded steadily although at a somewhat slower pace than the total manufacturing sector. In the ten-year period from 1976 to 1986 food, beverage and agricultural products doubled in annual value. Growth has resulted from population increases, increasing demand for more sophisticated or intensely processed (value added) products and increased consumption or trade of certain items. Among these growth factors, population increase is of declining influence in the total value of shipments by the agri-food sector.

The agri-food sector is a major contributor to the production of goods and services in Canada. It also has an important regional impact across the country. Export-import balance of trade in 1986 provided a net contribution of $3 billion to Canada's balance of payments. The processing industry is also becoming more international through multi-national corporate ownership, trade flows and linkages with international partners. There has been significant consolidation and rationalization of food and beverage companies during the past 10 years.

Agri-food is not a high-tech sector when measured by the amount of industry-sponsored R&D expressed as a percentage of sales. The figure for the Canadian food industry is only approximately 0.5 per cent. However, there appears to have been an increase in the number of small and medium size companies which conduct R&D activities. Also, the research conducted by supportive institutions in government and universities in agri-food is at a higher level than for other industries which have a greater direct research expenditure relative to sales.

A special feature of this industry in the industrially developed countries is the extensive application of technologies developed in other industries. The agri-food industry is a large user of technology developed in the machinery, chemical and packaging industries. In the food processing sectors, studies in the United States have shown that approximately half of research and development technology originates in other industries. For the Canadian agri-food industry, the patterns of technology applications appear to indicate that an even higher proportion of inter-industry technology transfer occurs than in the U.S. agri-food sector.

Agri-Food Biotechnology Applications

The agri-food areas where potential for biotechnology applications is most evident involve very large markets which are served by relatively low-priced high-volume products. Entry into these markets will demand a high level of process efficiency or a substantial improvement in product quality to provide the necessary advantage over existing products or processes. For example, proteins

manufactured from plant biomass or chemicals can compete in the marketplace with natural protein products only if lower production costs result from the use of efficient fermentation or microbial processes.

Biotechnology is also applied to meet food and beverage market demands generated by changing consumer product preferences. The current trend towards a more healthy life style has encouraged increased emphasis on low calorie foods and natural products. Market demands in North America have led to the introduction of low alcohol content beverages, the manufacture on a large scale of low fat dairy products such as yogurt, and the development of foods and beverages which use the sweetener aspartame in place of sugar. All of these new products involved biotechnology developments.

At the same time, advances in agronomic technologies to improve the quality of food raw material and the efficiency of agricultural operations are proceeding but are subject to the relatively long development period characteristic of this type of change. Biotechnology techniques will be of value in improving crop productivity by speeding up the process of developing improved cultivars or by extending the range of genetic variability available to a particular crop for manipulation and selection under traditional breeding approaches. The effects on agriculture of the new wave of biotechnology are likely to be evolutionary rather than revolutionary.

Agri-Food Biotechnology: Special Characteristics

Two major factors have encouraged the agi-food sector to harness advances in biotechnology: government policies and market demand. An example of a market driven application is the production of rennin by a new biotechnology process to augment the supply of natural rennin used in large quantities for the manufacture of cheese. Government policies have been a major consideration in the use of agricultural raw materials for the production of alcohol. The key factor in the displacement of one third of the sugar market in the United States by high fructose syrup was the government policy of setting artificially high prices to protect the domestic sugar cane industry. This policy made it economically attractive to develop and install large corn starch conversion operations in the United States which established the high volume, commodity-based technology which was subsequently applied in Canadian and Japanese plants. Likewise, the high volumes of fuel alcohol produced in Brazil and the United States, using field crops as raw materials for fermentation, resulted from government taxation policies in the U.S. and both taxation and regulations on automotive fuel in Brazil.

Biotechnology developments are of special interest for regional development in Canada. The

agri-food sector, which is established in all regions, offers a market pull for applications in new products and processes. This special characteristic of the industry is complementary to government policies and programs designed to foster industrial growth on a national basis.

Biotechnology: A Strategic Technology

Assessments of the impact of technology on the agri-food sector in the EEC and the United States over the next 10 years have placed biotechnology among the five most critical technologies. The importance of the agri-food industry in the Canadian economy and the continuing need to be fully competitive in world markets support the identification of biotechnology as a strategic technology for Canada.

Process efficiency and response to market shifts are crucial competitive factors for agri-food companies and should provide them with a strong impetus to conduct commercial biotechnology development activities or to establish sources of expertise from other Canadian or foreign enterprises.

APPLICABLE BIOTECHNOLOGY TECHNIQUES

Biotechnology is often misused as a synonym for genetic engineering or recombinant DNA. In actuality, these latter two terms are interchangeable and comprise one of several technologies which are combined under the "umbrella" term of biotechnology. Hybridoma cloning, cell fusion, enzyme technology, embryo transplantation, embryo pre-selection, plant tissue culturing and various fermentation processes are other advancing techniques commonly classified in the biotechnology field and generally applicable in the agri-food sector. These will be explained individually below.

Fermentation

Fermentation is the critical process by which living organisms are used to manufacture commercial products. The typical process is performed in a large tank which contains a liquid medium composed of nutrients and other ingredients needed to propagate producing organisms. The large alcoholic beverages industry is based on the conversion of sugars and starches to wine, beer and alcoholic liquids used in the manufacture of distilled spirits. Bread and cheese are also products of fermentation.

Process methods for the production of beer, wine, bread and cheese, all products of microbial fermentation, have evolved over a period of several millennia. New products, including food and beverage additives such as enzymes, flavours, and colourants, have resulted from the more recent scientific advances in biotechnology. These products have a relatively high market value which results from complex

or unique processes used in manufacturing operations. In contrast, the production of commodity type products, which compete in the market place with relatively low value animal feeds or human foods, depend upon the efficiency of the fermentation process to achieve low-cost, high-volume processing. An example of biotechnology applications for large tonnnage agri-food products is the new fermentation processes which have recently been applied to permit mass cultivation of microbes ("single-cell protein") to supplement animal feeds derived from field crops and for specialty human foods. World production of single cell protein, primarily in "Eastern Block" countries, is estimated to be in excess of 500,000 tons annually.

Continuing improvements in fermentation are critical to the commercial development of new products for the agri-food industry. Significant research efforts are now being devoted to designing fermentation systems capable of utilizing microorganisms on a large scale. The production of specialized yeasts using molasses as the substrate (raw material) is an example of a product and process development involving an improved fermentation processes. Improvements to processing equipment, utilizing computerized control or changes to fermentation tank design, have been identified and pilot plant scale units are being evaluated. Specialized systems will be required to harness genetically-modified organisms, as they emerge from the research laboratories, to applications in commercial process operations.

Enzyme Technology

Enzymes are organic catalysts which accelerate the conversion of the basic raw materials to products of higher value or modified properties. Enzyme technology is fundamental to many biological conversions. In food and beverage processes, enzymes are the essential material for defining conversion efficiency and product taste characteristics. Brewing and the extraction of fruit and vegetable juices are two processes which utilize large volumes of enzymes.

An efficient system for converting the lactose in dairy products to sugars which are more easily digested, resulted from the application of immobilized enzymes in a continuous system. In this technique, enzymes or living cells containing enzymes are bound to inorganic materials such as glass particles. This confinement results in a high local concentration of the catalytic substance which can be applied to a continuous flow fermentation system to yield various commercial products.

Advances in recombinant DNA technology have made possible the creation of genetically-altered microorganisms capable of producing catalytic enzymes in a more efficient manner. Specific properties can be "engineered" into the enzymes and costs can be reduced by increasing product

concentration per unit volume. Cost reductions in the production of enzymes and in the processes which utilize these catalysts will be a major factor in the choice between using chemical or biotechnology processes for food and food additives manufacture. For example, a genetically altered microorganism has improved the process and reduced the operating costs of producing cellulase, the enzyme used to covert cellulose to sugars.

Recombinant DNA (Genetic Engineering)

The most basic technique of biotechnology, recombinant DNA technology or gene-splicing, refers to a method by which genetic material from two distinct life forms are combined to create a modified organism which produces a desirable product or performs an important function. Since the discovery of gene-splicing techniques in 1973, there has been a tremendous increase in the scientific investigations to modify life forms as the basis for new products or processes in several industry sectors. Modified bacteria have been developed which produce useful quantities of important substances such as amino acids, enzymes, vaccines and pharmaceutical products. While recombinant DNA technology has been applied on a limited commercial scale to manufacture high value animal vaccines, the adaptability of this technique to low cost, mass production of the kind needed to achieve commercial success in the processed food sector remains in question.

Cell Fusion

Cell fusion is a technique in which basic plant life forms or protoplasts from two different plants are separated and blended together to form a new cell which contains genetic material from both the original donors. The recombinant protoplast can be induced to proliferate and regenerate entirely new hybrid plants. Essentially, this method arrives at the same result as recombinant DNA and results in the creation of modified plant forms capable of generating desired basic agri-food products such as herbicide resistant field crops, disease resistant plants or plants which grow more rapidly than existing varieties.

Hybridoma Cloning

Hybridomas are formed by the fusion of a normal cell with a high growth cell to produce a hybrid capable of rapid growth. The hybridoma may then be used for the production of high purity antibodies - the biological proteins which protect plants and animals against invading diseases. These antibodies can be formed to target a specific type of antigen (an invader which can destroy living organisms in plants, animals and humans). As a result of the highly specific nature of hybridoma antibodies, drugs for animals can be directed to the diseased tissue or tests can be developed to detect specific diseases. Food purification by screening out

harmful microorganisms is also possible. Quality control procedures based on the detection of toxins by monoclonal antibodies can be developed to monitor and improve the safety of food processes.

Plant Tissue Culturing

In this technique, a small piece of tissue is cut from a seedling shoot or other appropriate plant part and placed in a growth medium containing plant hormones and nutrients. The cells of the tissue grow and divide forming a fibrous mass comprised of a clustering of plant cells. Single plant cells are separated and left to regenerate clones of the original plant or are modified by a technique such as fusion to create a genetically altered plant form.

Plant tissue culture offers significant production improvements in the agricultural and horticultural industries. By isolating plant cells with superior traits or genetically modifying them to achieve the same results, it is possible to develop new plant breeds that have commercial advantage over natural varieties. Some of these advantages are the development of food and food crops with improved yields and the creation of plant varieties able to grow under adverse conditions such as drought. Since thousands of plants can be regenerated from one piece of tissue, cell culture offers a means of cloning far more plants in less time than is possible using conventional methods of propagation.

Embryo Transplantation

Embryo transplantation is a technique of biotechnology whereby large numbers of quality livestock can be bred from a small number of superior animals. For example, a cow with superior genetic characteristics is treated with special fertility hormones which cause the animals ovaries to release as many as twelve or more eggs during ovulation. These eggs are then fertilized through artificial insemination and incubated inside the mother for a week to ten days. After the incubation period the embryos are removed and stored by freezing or are immediately transplanted to other female animals which are genetically inferior or of less value than the natural mother. Following the normal gestation period, the recipient mother bears the offspring which possess the characteristics of the superior animal. In this way, a single superior cow can produce up to twelve calves in a single season improving herd quality more rapidly than by normal reproduction. The efficiency of the techniques has led to widespread use in Canada and facilitated exports of embryos to herd owners in the United States, South American countries, Europe and the U.S.S.R. Embryo export can be undertaken where shipment of live breeding cattle could pose health problems for the animals or be otherwise difficult and uneconomic.

Further advances in embryo transplantation have recently

been made by the subdivision of the fertilized eggs prior to implantation in surrogate mothers. These techiques, along with new methods of identifying the sex of the embryo, have greatly enhanced cattle reproduction productivity and herd quality.

AGRIFOOD: CURRENT CANADIAN BIOTECHNOLOGY DEVELOPMENTS AND APPLICATIONS

The two sectors which have drawn most of the attention in biotechnology developments are health care and agri-food. Canada's well developed agricultural and food processing industries provide a strong economic and market base for the application of biotechnology in improving the efficiency of agriculture and in developing modified foods or new food processes. The breadth and size of these economic sectors also provides an opportunity for developments in related sectors, such as food additives and aquaculture. In Canada, the number of companies engaged in biotechnology developments in the agri-food sector approximately equals the number in the health care sector.

The following table summarizes typical industrial agri-food biotechnology developments and activities by product or sector.

TYPICAL INDUSTRIAL AGRI-FOOD BIOTECHNOLOGY DEVELOPMENTS

Product or Sector	Number of Canadian Enterprises Reporting Activities	Typical Developments - and applications
1. Aquaculture	12	Fish vaccines. Special seafood systems. Sea plants.
2. Animal Production	13	Milk production enhancement. Control of animal quality & sex by embryo transplants. Growth stimulants. Animal vaccines special feedstocks-single cell protein and modified cellulose feeds. Diagnostics-monoclonal antibodies for animal health.
3.Alcohol alcoholic beverages	9	Ethanol processes based on field crops or food processing by-products. New wine yeasts. New brewing yeasts. Yeast strains development.
4. Baking and pasta	2	Fast rising dough. Hydrolylic enzymes. Baking processes. New process for bakers yeast.
5. Beverages	5	Process for clarification of fruit juices and wine using enzymes. Enzymatic process for juice extraction. New wine processes.

Product or Sector	Number of Canadian Enterprises Reporting Activities	Typical Developments and applications
6. Dairy Products	4	Cheese additives. Lactose free milk. Modified lactic acid bacteria. Immobilization of lactic acid bacteria. Special bacterial additives for yogurt.
7. Enzymes	5	Encapsulated enzyme processes. Enzymes for food processes. Oilseed processing.
8. Field Crops	10	Herbicide resistant crops. Seeds to modify components of crops. Seed treatment for disease resistance. Crops resistant to insect attack. Diagnostics to detect crop diseases. New crop varieties i.e. barley.
9. Field Crop additives	15	Bio fertilizers. Bio herbicides. Bio fungicides. Bacterial growth promotors. Special microganisms i.e. Nitrogen fixation. Algae products to improve soil fertility. Bioinsecticides.
10. Food Additives	5	Flavours aromas colorants. Texture modifications and suspending agents. Biosurfactants.

Product or Sector	Number of Canadian Enterprises Reporting Activities	Typical Developments and applications
11. Food Processing	14	Diagnostic test systems. Protein and enzyme extracts. Biosensors and probes for testing conditions. Enzymatic conversion processes. Preservatives for fruits and vegetables.
12. Horticulture and special plants	4	Plant cell culture processes. Specialty decorative plants.
13. Plant Foods	4	Mushroom processes. Soya bean hydrolysates. Sprouts.
14. Sweeteners	3	Low calorie sweetners. High fructose syrups. Conversion of by-product milk lactose.
15. Reactor Development for BioProcesses	3	Alcohol process development. Special fermentation reactors.
16. Waste products conversion and treatment	9	Food processing treatment. Conversion of waste products. Special biological treatment systems.

OPPORTUNITY AREAS IN AGRI/FOOD BIOTECHNOLOGY

The agri-food sector tends to respond to major technology advances, including biotechnology, at a slower pace than more research intensive industries. However, within the confines which guide the application of new technology to the food and agricultural industries, there are many opportunities for applications of biotechnology as the basis for new products and more efficient production systems. The commercial applications of biotechnology which appear to have the greatest promise for development or commercial exploitation by Canadian enterprises are summarized below.

A. Agricultural Applications

1. Modification of Field Crops

Manipulation of plant genes can modify seeds to contain different amounts of components which are in demand to meet industrial processing and food nutritional needs. Using this biotechnology technique, modification of the fatty acid composition of canola, a major cash crop in Canada, is being examined in research projects. The market base for flaxseed could be expanded if plant varieties can be developed that produce flaxseed oil suitable for human consumption. The creation of herbicide-tolerant field crops by similar techniques is also of great interest to seed companies, chemical manufacturers, and farmers. By planting herbicide resistant crops, farmers might have the flexibility to select a herbicide on the basis of its efficiency against a particular weed species rather than according to its toxicity to the crop species. In addition, herbicide-resistant plants may lead to reduced production costs (reduced crop loss) and less tillage time in certain cases. In Canada, annual losses to the canola crop from weeds and fungal diseases have been estimated at $70-80 million in an annual market worth $800 million.

2. Field Crop Production Enhancers

A promising new market for the products of biotechnology lies in the application of soil amendments such as fungi (which promote nutrient uptake in plants), growth promoting rhizobacteria, nitrogen-fixing rhizobium and an assortment of microbes that enhance the growing region around the roots of plants. Microbial growth promotion products have a favorable potential for applications focussed on legumes and canola plants. Based on a large domestic market for these products and the current involvement of companies with a high level of scientific and technological expertise and excellent public support research facilties, Canada may have the potential to become a world

leader in this area of agri-food products.

3. Field Crop Protection

Opportunities exist in pest control, plant disease diagnosis, special preservatives and herbicides. The general outlook for these products is for applications in narrow market niches for which specific evaluations and effective marketing are necessary. Such niche markets may be identified where regulation precludes the use of existing chemical products. However, regulatory issues may also limit the use of microbial pesticides and some bio-herbicides.

4. Animal Health Care

Several animal health care products developed via biotechnology are already on the market and more are under development. The number of animal vaccines continues to expand and veterinary diagnostics offer many market opportunities. The treatment of diseases with monoclonal antibodies, interleukin and interferon are also promising applications.

5. Animal Production Enhancers

Products which will have an impact on the animal feed business include: amino acids and vitamins produced using fermentation methods, silage innoculants containing enzymes or microbial agents, and single cell protein. Silage innoculants, added to corn prior to its fermentation and conversion to silage, facilitate fermentation and increase the feeding efficiency of cattle. Single cell protein could become a large volume commodity product if there is a significant and sustained increase in the prices for feed grains.

Growth hormones or hormone release factors are being evaluated for increasing feeding efficiency of poultry, swine, and cattle. Bovine growth hormone can increase milk production without an equivalent increase in feed intake.

6. Specialty Plants and Horticulture

Applications of large scale plant micropropagation could play a role in the horticultural and ornamental products industries within the next few years. Current methods of propagation are difficult to automate and require a high input of hand labour. Specialty plants and seeds from micropropagated plants appear to offer the best opportunity for the application of these complex biotechnology systems.

B. New Food Products and Processes

1. New Food Processing Systems

Enzyme applications are central to the development of new processes in the food industry. Growing markets for enzymes are for use in the clarification of fruit juices and the extraction of apple juice from the raw

fruit. Other processes are the accelerated maturing of cheese and the fast baking system using enzymes in bread processing. Lactose free milk can be produced by a new process using enzymes which remove the lactose by enzymatic action. This application of enzyme processing could open up huge oriental and other lactose-sensitive markets to milk products. There is an excellent potential to develop highly efficient processes and to lower process costs through the use of immobilized enzyme systems which greatly reduce costly enzyme consumption. The efficiency of yeast production systems will be improved with the development of computer controlled fermentation systems. Biosensors and diagnostic test systems will also contribute to improved reliability and safety of food processing systems.

2. Foods and Food Additives

Biotechnology has been applied in the food industries to either add nutrition, improve flavour of the final products, or to perform certain functions in processing operations by utilizing the catalytic properties of enzymes. The application of these techniques will be extended by the development of genetic engineering (recombinant DNA), immobilized enzymes and protein engineering. Plant cell culture is also being intensively evaluated for the production of many special products including food enhancers such as flavours and colours.

Several food product areas in which there are significant potential for the application of new or improved biotechnology are described in the following sections:

a) Sweeteners

The significant impact that biotechnology can have on the production of food ingredients is exemplified by the development of aspartame in the United States. This sweetener, which meets a market demand for reduced calorie content, is extensively used as an ingredient in food and beverages. Fermentation processes are used in some of the production stages. Research has been conducted in Canada on alternative process techniques for alternate sweeteners but commercial development has not yet been undertaken. As the low calorie sweetener market continues to grow, there may well be opportunities for new process developments by Canadian enterprises such as xylatol production from cellulose.

b) Alcohol and Yeasts

Yeasts, which are used in baking, beer, wine, distilled beverages, and for specialized feeds, are basic products of biotechnology. Yeast technology is closely linked to the production of ethyl alcohol (ethanol) and beverages which contain alcohol. The largest single market for yeast are the strains used for bakers yeast. New developments continue to be evaluated for specialized yeast applications such as the production of low alcohol beer,

wine fermentation and in the conversion of carbohydrates to ethyl alcohol. Agri-food materials which could be used in large quantities as raw materials as markets for ethanol grow include: starches from corn, wheat, barley and potatoes; sugars from beet and sorghum; and by-product carbohydrates from food processing.

c) Proteins

Single cell proteins may be used for human foods or as a component in animal feedstocks. Applications for human foods have to meet many regulatory requirements and food industry quality standards. In the case of animal feeds, production and marketing economics are of paramount importance. However, if production of single cell proteins is coupled to production of another material or to the utilization of by-products or "wastes", then the process could become more attractive in terms of economics and industrial production.

d) Dairy Products

Biotechnology is being applied to traditional dairy products processes by the development of improved starter cultures and the use of enzymes to modify cheese flavour more rapidly. New types of yogurt containing bifido bacteria are being marketed in other countries such as Japan and could be introduced to the Canadian market. Fermented milk drinks have also been developed in other countries, but as yet only relatively small volume Canadian markets have been established.

e) Fats and Oils

Oils, produced from biomass, could find applications in the replacement of vegetable oils and fats such as cocoa butter and palm oil. Other applications of biotechnology may be visualized in the production of food grade emulsifying and de-emulsifying agents and in the enzymatic extraction of fats and oilseeds to replace solvent extraction.

f) Food Additives and Special Functional Ingredients

Additives which modify or improve the taste, texture, appearance and nutritional qualities of food include: amino acids, vitamins, preservatives, polysaccharides, flavourants, fragrances, colourants, and antioxidants. These high value products may be produced by biotechnology processes. Products such as xanthan gum and vitamin C could be produced from low cost starch or other carbohydrates and may be economically viable options for production in Canada.

Established markets with good growth rates provide a market pull for new sources of food additives and ingredients. Process development for flavours, colourants and fragrances may require several years of research and commercial development before significant market penetration can occur from new biotechnology developments.

FACTORS INFLUENCING FUTURE COMMERCIAL AGRI-FOOD BIOTECHNOLOGY DEVELOPMENT IN CANADA

Canada's large and diversified agri-food sector can provide the market pull to stimulate and sustain the research, commercial development and investment required to convert the promise of biotechnology into commercial products and services.

Canada already has considerable strength in the traditional process applications of biotechnology by food and beverage companies. Total shipments of biotechnology based products are valued at approximately $3.5 billion annually, primarily as dairy and alcoholic beverage products. Manufacturing processes, except for a few systems based on "new" biotechnology, utilize processes which have evolved over many years (traditional biotechnology). However, a number of Canadian companies, both large and small are active in evaluating the technological and market opportunities which are evolving from new applications of biotechnology.

The importance of the agri-food market has been increasingly recognized by governments in the establishment of research and development facilities in several regions of Canada. Industrial interest has been somewhat slow to develop but there has been a recent increase in the number of enterprises active in new commercial biotechnology activities. However, further recruitment of major food processing firms would be a major step forward.

In agriculture, promising developments are occurring in plant crop improvements, animal production, seed development, and in products to improve the efficiency of agricultural operations. Canada has excellent research facilities, strong technological expertise in government, and university institutions which are supportive of developments in these areas. A major constraint to industrial exploitation of seeds development is the lack in Canada of plant breeders rights. In most western countries, plant breeders rights are protected under the International Convention for the Production of New Varieties of Plants, but Canada has not to date ratified the convention.

The relatively small size of the Canadian market may hinder the development of specialized food additive products such as flavourants and texture modifiers which have high unit value but limited volume applications. Trade factors such as non-tariff barriers and inter-country differences in food regulations will be critical factors in establishing new product sales in international markets. Changes in the environment for international trade will also

result from the Canada/U.S.A. Free Trade Agreement as well as the single European market to be formed by 1992.

In meeting the demands of the growing market for animal health care products, Canadian expertise has developed in specialized product areas such as biologicals and vaccines which have benefitted from supportive co-operation among governments, universities and private companies. On the other hand, the broader product areas such as antibiotics, vitamins and amino acids tend to be dominated by major chemical and pharmaceutical manufacturers based in other countries. Many of the biotechnology applications for new product development are being developed in R&D centers located in the home country of these enterprises. In addition, most of the large companies are strong financially, have effective technology development resources and already possess global marketing and distribution networks. Animal drug production is a diversification of their principal activities. In this product area, the restraints in Canada are therefore similar to those facing Canadian companies in the human pharmaceutical industry.

In addition to the developments which are occurring in Canada, Canadian enterprises have extensive and growing linkages with sources of new technology in other countries. Linkages are evident primarily in corporate ownership and trade activities both within the biotechnology sector and others from which technology is transferred. Missions of industry representatives to or from Japan, South Korea, France, West Germany and the United States have encouraged cooperation between Canadian and foreign enterprises in developing new products and services.

The relatively limited level of risk capital and funding for new technology developments in Canada may have deterred entrepreneurial enterprises from more active participation in biotechnology developments. Government incentive programs have been directed primarily at research rather than at commercial biotechnology developments. Recent initiatives by federal and provincial governments provide support specifically for biotechnology developments and should be a positive factor in accelerating investments in commercial developments. New initiatives will include the Strategic Technologies Program administered by Industry, Science and Technology Canada (ISTC) and the National Agricultural Biotechnology Initiative (NABI). The federal government and the four western provincial governments will provide up to $50 million for the funding of agricultural biotechnology developments under NABI.

INTERNATIONAL ASPECTS OF AGRI-FOOD BIOTECHNOLOGY DEVELOPMENT

Japan

Japan is regarded as the major world competitor to the United States in commercial applications of biotechnology. Its long history and usage of fermentation techniques has given extensive experience to large firms in established industries. The majority of Japanese firms involved in biotechnology are financially strong and many are involved in several industry sectors which combine expertise in food processing with specialty chemical technology. Firms such as Ajinomoto and Kyowa Hakko operate large food processing facilities supported by extensive technology development facilities. Trading companies have manufacturing subsidiaries and conduct extensive world searches for leading technology developments or investment opportunities. One highly diversified Japanese company has recently acquired a license from a Canadian technology development enterprise for a microbial product for use in specialty dairy foods.

United States

The U.S. is unique in having a large number of small, start-up firms involved in the commercialization of biotechnology developments in addition to the large, well established ones. Some of the larger process companies, such as Monsanto, focus on in-house developments but many companies have opted to invest in collaborative research with the highly specialized new enterprises. Consumer products companies have tended to pursue specific developments which will reduce the input cost of raw materials. The $6 billion seed market is one of the largest markets to which biotechnology is directed. Sweeteners produced by biotechnology based processes, comprise a market of similar value.

Europe

Leading countries in the application of biotechnology to the agri-food industry are the U.K., Denmark, France and West Germany. The U.K. appears to be the most advanced in commercial developments of commodity foodstuffs whereas France has several companies which concentrate on specialty food product development. Novo, a Danish company, is the world leader in the development of enzymes for a broad range of applications in the agri-food industry. West Germany's well organized research activity is now serving as the base for increased commercial activity by new enterprises within the large established process companies.

Governments in France and the United Kingdom have assigned a high priority to biotechnology developments in agri-food sector. In France, the utilization of biotechnology by the agri-food industries has been selected as

one of the two highest priorities of the Program Mobilisateur. As part of this major industrial development initiative, the intent of the agri-food research program is to generate cooperative industry/university research. In the U.K., government programs have given priority to biotechnology, particularly in new plant breeding techniques and in enzyme engineering with increased emphasis on food research.

STRATEGIC DIRECTIONS

Canada's huge agri-food industry offers numerous opportunities for the application of biotechnology in improving the efficiency and lowering unit costs of agricultural operations and in expanding and diversifying markets of food and beverage enterprises. The need to develop and exploit new technology is driven by intense competition in international markets for commodity agricultural products and for food and beverage processors to meet changing market demands for new or modified value-added food products. The regional, economic and trade importance of the agri-food sector offers opportunity to both the public and private sectors to jointly build an expanded technological capacity, responsive to market needs and leading to increased commercialization.

The lack of resources for commercial scale up, market access (especially in international markets), or for maintaining an effective intelligence on rapidly advancing new technologies are some constraints to commercial development faced by the private sector, particularly the smaller enterprises. Industrial organizations and governments in other countries have recognized that the formation of linkages between both large and small enterprises can overcome some of these constraints. In Canada, the pace of private sector activities is increasing, accompanied by the entry of numerous small and large companies into all stages of research, development and commercialization. The need for these linkages will increase and the formation of national and international strategic alliances should be encouraged.

National and international strategic alliances can be fostered by supporting forums at which companies and research organizations can meet to discuss mutual technology and commercial development objectives. Such forums could be held as workshops or seminars, possibly in conjunction with an industrial association such as the Industrial Biotechnology Association of Canada (IBAC). Technology missions to other countries and from other countries may also be organized to facilitate the formation of strategic alliances.

A focus should be maintained on attracting investment by national and international enterprises which have the necessary resources to develop and exploit

commodity products such as starch conversion products which must be manufactured on a large scale. Increased participation in large scale biotechnology developments by major enterprises will play a critical role both in agriculture and the processing sectors.

Governments can play an effective role in facilitating commercial biotechnology developments and strategic alliances by augmenting and strengthening the flow of information to the private sector, by using existing technology development and transfer facilities in Agriculture Canada, the National Research Council and other agencies, and by ensuring a regulatory environment which is sensitive to these developments. As well, a bill to establish plant breeders rights is currently before parliament. This would place companies which are developing improved seeds or plant varieties in a commercially competitive position equivalent to similar development companies in other western countries. A continuing assessment and review of worldwide developments as well as Canada's relative strength in biotechnology as applied in the major industrial sectors could be an effective activity as part of the intelligence role of Industry Science and Technology Canada.

Within Industry, Science and Technology Canada, the Biotechnology and Health Care Products Directorate of the Resource Processing Industries Branch has overall responsibility for biotechnology activities and policy. This branch also has the responsibility for three industrial sectors in which biotechnology has a major economic and commercial potential; Health Care, Chemicals and Pulp and Paper. The Food Products Directorate in the Service Industries and Consumer Products Branch has the lead role for agri-food biotechnology activities. Regional offices maintain a detailed intelligence on company developments and provide departmental assistance to all the industry sectors in which biotechnology can be applied for the production of goods and services.

APPENDIX I

TYPICAL INDUSTRIAL COMPANIES OR LABORATORIES WITH ACTIVITIES IN AGRI-FOOD BIOTECHNOLOGY DEVELOPMENT *

Company	Activity
Allelix Agriculture Toronto, Ontario	Growth Promoters Field Crop Seeds with Modified Genetics
Agropur Coopérative Grandy, Quebec	Proteases for Cheese-Making Lactic Ferments
Advanced Biotechnology Ltd. Aldergrove, B.C.	Aquaculture, Mushroom Culture Financing Biotechnology Companies
Les Aliments Carrière Saint-Denis sur Richelieu, Quebec	Lactic Fermentation of Vegetables
Alta Genetics Inc. Calgary, Alberta	Embryo Sexing and Genetic Engineering Cloning of Cattle Embryo
Aqua Health Ltd. Charlottetown, P.E.I.	Fish Vaccines and Other Veterinary Bacterins
B2 Enterprises Ltd. Choiceland, Saskatchewan	Growth Regulators for Crops
Bay D'Espoir Salmon Hatchery Ltd. St. Alban's, Newfoundland	Salmonid Aquaculture Chromosome Set Manipulation
IAF Biochem International Inc. Laval, Quebec	Health Care Products for Animals
Bio Field Technologies Research Inc. Ottawa, Ontario	Algae Strain Modification and Effect on Soil Properties
Bio-Hol Developments Toronto, Ontario	Zymomonas Fermentation Technology Pilot Plant Alcohol Process Studies
Bionov CNP Inc. Quebec, Quebec	Production of Biomass for Processing into Food

Company	Activity
Bioprotein Canada Inc. Hamilton, Ontario	Immobilized Proteolytic Enzymes for Cheddar Cheese Production Immobilized Bacteria for Waste Water Treatment
Bio-Research Laboratories Senneville, Montreal	Toxicity Testing of New Biotechnology Products
Bio-Response Systems Ltd. Halifax, Nova Scotia	Toxicity Testing Systems Using Genetically Engineered Bacteria
Biorex Groupe Conseil Inc. St. Foy,Quebec	Aquaculture - Sterile or Hybrid Stocks of Salmonidae
Biostar Inc. Saskatoon, Saskatchewan	Development and Testing of Animal Health-Care Products, Vaccines, Monoclonal Antibodies
Biosystech Consulting Inc. Mississauga, Ontario	Enzyme and Microbial Process for Foods
Biotechnica Canada Inc. Calgary, Alberta	Plant Breeding R&D in Oil Seeds, Cereals, Forages and Horticulture
Blueberry Acres Ltd. Centreville, Nova Scotia	Plant Tissue Culture for Ornamental and Fruit Plants
Brookside Farms Inc. Abbotsford, B.C.	Extraction of Enzymes and Biochemicals from Food Processing
Canadian Seed Coaters Ltd. Brampton, Ontario	Growth Promoting Regulators, Enzymes, Rhizobium Products
Canpolar Inc. Toronto, Ontario St. John's, Newfoundland	Biosensors for Food Processing Applications
Canpro Laboratories Downsview, Ontario	Pesticides and Herbicides for Agriculture
Casco Inc. Etobicoke, Ontario	Enzyme Process Development Conversion of Starch to Sweetners

Company	Activity
Champlain Industries Ltd. Mississauga, Ontario	Enzyme and Fermentation Process Yeast Extracts
Chateau Des Charmes Wines St. Davids, Ontario	Viticulture and Wine Process Development
Ciba-Geigy Canada Ltd. Mississauga, Ontario	Animal Health Care, Plant Protection, Seeds
C-I-L Inc. Toronto, Ontario	Microbial Pesticides, Forage Innoculants
Les Clay & Son Ltd. Langley, B.C.	Tissue Culture Development of Ornamental and Horticultural Plants
CPS Foods Ltd. Winnipeg, Manitoba Saskatoon, Saskatchewan	Development of New Oil Seeds Crops
Cyanamid of Canada Ltd. Markham, Ontario	Animal Health Care Products
Dairyland Foods Burnaby, B.C.	Dairy Food Processes
Diversified Research Laboratories Ltd. Toronto, Ontario	Microbial Lipids, Biosurfactants Microbial Polysacharides
Elanco (Eli Lilly Canada Inc.) Toronto, Ontario	Animal Health Care Products
Elite Seed Potato Farm Alberton, P.E.I.	Tissue Culture Development of Disease-Free Potatoes
Endogro Systems Inc. Bedford, Nova Scotia	Agriculture Use of Specialized Fungi
Export Packers Company Ltd. Winnipeg, Manitoba	Extraction of Enzymes and Biochemicals from Food Processing
FMG Integrated Biotechnical Laboratores Ltd. Richmond, Ontrio	DNA Gene Probes and Polyclonal Antibodies
Gelda Scientific and Industrial Development Corporation Toronto, Ontario	Fermented Dairy Products Industrial Enzymes

Company	Activity
The Griffith Laboratories Ltd. Scarborough, Ontario	Fermentation Process in Baking Enzymology in Flavour Development
Iogen Corp. Ottawa, Ontario	Food Products from Biomass
Labatt Brewery Company Ltd. London, Ontario	Beverage Fermentation, Yeasts, Flavours
Lallemand Inc. Montreal, Quebec	Fermentation in Yeast Processing
Langford Inc. Guelph, ONtario	Animal Health Products Vaccines
A. Lassonde & Fils Inc. Rougemont, Quebec	Enzymatic Clarification of Fruit Juices
Marbicon Inc. Berwick, Nova Scotia	Plant Tissue Culture Development of Herbicide Resistant Plants
Microelite Plant Laboratories Inc. Kentville, Nova Scotia	Plant Micropropagation
Molson Breweries of Canada Ltd.	Genetic Engineering of Yeast
Nelson's Dairy Toronto, Ontario	Immobilized Lactase Enzyme Process Dairy Products
Palliser Animal Health Laboratores Ltd. Lethbridge, Alberta	Animal Virus Diagnostic Test Development
Philom Bios Inc. Saskatoon, Saskatchewan	Bioherbicides, Biofertilizers, Biofungicides
Premier Peat Moss Ltd. Riviére-du-Loup, Quebec	Biofertilizers
Proplant Garden Products Ltd. Port Coquitlam, B.aC.	Tissue-Cultured Tropical Foliage Plants
Purdel Cooperative & Agro-Alimentaire Comté de Rimouski, Quebec	Shrimp: Enzymes, Pigment Flavour Extraction
Rhizogen Corp. Saskatoon, Saskatchewan	Legume Growth Innoculants

Company	Activity
Les Laboratoires Rhizotec Inc. Saint-Jean Chrysostome, Quebec	Biofertilizers, Fungus Fermentation
Institut Rosell Inc. Montreal, Quebec	Micro Organisms for Food Processing
Joseph E. Seagram & Sons Limitée Montreal, Quebec	Fermentation Processes
Syndel Laboratories Ltd. Vancouver, Ba.C.	Aquaculture Products for Fish Health
Veterinary Infectious Disease Organization Saskatoon, Saskatchewan	Animal Health Care Products Vaccines, Diagnostics
Vetrepharm Inc. London, Ontario	Animal Health Care Products
Western Biologicals Ltd. Vancouver, Ba.C.	Plant Tissue Culture Mushroom Strain Development

* Source: - 1988 Canadian Biotechnology Industry Sourcebook