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# MOSST Background Paper

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BIOTECHNOLOGY IN CANADA

JUNE 1980



Ministry of State Science and Technology Canada

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#### INTRODUCTION

Recent advances in the study of cellular and molecular biology together with a broadening of appreciation of the unique capabilities of microorganisms have thrust the world onto the threshold of a new technological revolution. This biotechnology revolution, in providing a unique opportunity for the world to develop a more comprehensive understanding of its biological resources, will impact heavily upon many areas. Some of these areas include health, energy, food, mining, agriculture, industrial chemicals and the environment. New processes for the production of pharmaceuticals and diagnostic reagents, the production of alternate energy sources as well as more efficient exploitation of current reserves, new foodstuffs, modifications to traditional mining methods, new plant varieties, fertilizers and herbicides, alternate approaches to industrial chemicals and processes, and new techniques for waste treatment and pollution control: all of these developments and many more will be featured as the biotechnology revolution gathers momentum.

This background paper is part of a process to develop a federal policy for the promotion and development of biotechnology in Canada. As the first phase in this process this paper describes the present biotechnological activity in Canada, both in terms of its location and its areas of application. In addition some of the applications of biotechnology, which are amongst the many opportunities offered by this area of technology, are described in a Canadian context.

This paper presents a reasonably comprehensive listing of Canadian biotechnological activity but does not pretend to be exhaustive. In addition no attempt has been made to evaluate in terms of excellence, the activities described.

### DEFINITION

The term biotechnology has been accepted worldwide to mean the exploitation of microorganisms or their components to provide certain goods and services. Biotechnology is, in fact, an umbrella term which covers a range of technologies. These technologies, however, may be classified into three non-mutually exclusive areas: fermentation technology, enzyme technology, and genetic and cellular manipulative technology. It is, therefore, against this definition and/or description of biotechnology that Canadian research and development activity has been examined.

### BACKGROUND

The present attraction of biotechnology is two-fold. First, from an industrial process point of view, the basic feedstocks or substrates are renewable resources such as cellulose, sugar or starch. This means that biotechnological processes are less likely to be affected by the same cost spirals which currently plague conventional processes based upon non-renewable resources. Second, from an environmental stand-point, the by-products of biotechnological processes can represent a net benefit to the environment in the form of carbon dioxide, water and biologically acceptable nitrogen fertilizers. This is in sharp contrast to the toxic effluents of today's chemical processes.

Internationally an investment explosion is occuring as many see biotechnology as having as large, if not larger impact upon industry and society than the microelectronics revolution. Japan, for example, has a long tradition of success in exploiting microorganisms, and one which has led to a present level of industrial activity which earns over \$15 billion per year or nearly 5 per cent of its gross national product. In France, a recently released report, "Science de la vie et société", has indicated that biotechnology will produce 30,000 new jobs in France over the next decade, including 6,000 research positions. In Brazil the highly publicized gasohol program is well underway and diversification is now being planned to supplant their petroleum based chemicals industry with one based upon alcohol produced via fermentation.

In the U.S., in addition to the Government's proposed \$3 billion - 10 year program of loans and loan guarantees for the production of alcohol fuels, large industrial concerns in the chemical, petroleum, pharmaceutical and food sectors are actively engaged in developing or expanding in-house biotechnological capabilities. Most of the publicity in the genetic manipulative area has been generated by three new firms: Cetus, Genentech and Genex. Cetus is owned jointly by Socal (Chevron), Standard Oil of Indiana and National Distillers and has a net worth of approximately \$100 million. Genentech is owned by Inco, Kleiner and Perkins, Monsanto, the Hillman Company of Pittsburgh, the Mayfield Fund of San Francisco, Soffinova and Lubrizol Corporation and has a net worth of \$65 million. the smallest of the three, is owned by Emerson Electric and the Koppers Company with a net worth of \$9 million.

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The European Economic Community has recently received and given preliminary approval to expenditures of \$50 million on biotechnology over the next five years. The program is designed to build-up capability in a number of key biotechnological areas and has been unanimously approved by European industry. In the UK a major report of the Royal Society, the Advisory Board for the Research Councils and the Advisory Committee for Applied Research and Development has called for a \$10 million annual expenditure on biotechnology, over and above existing allocations, to be coordinated by a Joint Committee for Biotechnology. Within Europe, West Germany is generally considered to be the leader: government spending on the basic problems of biotechnology is about ten times that in France or the UK. All together, between 1972-78, West Germany invested \$100 million in biotechnological R&D.

# BIOTECHNOLOGICAL ACTIVITY IN CANADA

Annex I of this report provides a directory of biotechnological activity in Canada by individual sector. In the government sector, the National Research Council of Canada and Agriculture Canada represent the major federal centres of activity whereas provincially the Research Councils of Alberta, Saskatchewan and Manitoba are presently involved in varying levels of biotechnological activity. In the industrial sector, thirty-three firms

have been identified as pursuing aspects of biotechnology ranging from basic research to process and equipment design. In the universities, the research activities of ninety-seven scientists distributed amongst twenty-two such institutions are highlighted.

Annex II of this report provides a classification of the activities described in Annex I, by areas of application. In terms of the number of performers the area of application identified as biomedical product development would appear to have the greatest attraction for current Canadian biotechnological activity across all three sectors.

# SOME OF THE BIOTECHNOLOGICAL OPPORTUNITIES TO CONSIDER IN A CANADIAN CONTEXT

The purpose of this section is to describe a few of the currently envisioned applications of biotechnology and how these might be considered, from a Canadian perspective, in relation to industrial development.

First it should be remembered that irrespective of how the fermentation technologies, the enzyme technologies or the genetic and cellular manipulative technologies are to be applied, most of the processes developed will, at some stage, depend upon the availability of carbohydrate. Carbohydrate is, however, derived from a renewable resource, biomass. Canada, because of its large biomass resources is therefore richly endowed with the basic "feedstock" for practically every conceivable biotechnological process.

One way one might consider the opportunities offered by biotechnology to Canada's industrial development is in relation to the resource sectors. A large portion of our economy is resource based: energy, forestry, food/agriculture and mining. While in the past one might argue that Canada has failed to take fullest advantage of its natural wealth, biotechnology would seem to offer the opportunity to exploit our resources more efficiently, while at the same time developing our potential to be world leaders in resource management.

To illustrate possible opportunities, each of these four resource sectors is discussed below, with comments on where applications of biotechnology might have considerable potential for Canada.

# Energy

The production of alcohols via fermentation offers an additional source of liquid fuels to meet our growing energy demands. A great deal has been written, discussed and analyzed concerning the use of alcohols as alternate liquid fuels and it seems clear that alcohol will form one part of Canada's future energy puzzle. From a scientific and technical point of view, the fermentation of alcohol is well understood. While future studies will focus on efficiencies, namely microorganism selection, substrate modification and process engineering, it is reasonable to expect that at least certain regions of the country could develop alcohol production capabilities within a fairly short period of time. The large agricultural sector in Canada provides an excellent source of the basic substrates for the commercial production of alcohol and therefore an alcohol fuels initiative is an opportunity worth considering.

Another possible opportunity is in the area of methane production. Methane can be generated biologically from the anaerobic fermentation of industrial, domestic and agricultural wastes. Methane thus derived could be introduced directly into existing natural gas pipelines for domestic use or export. Another possible avenue for methane is its subsequent hydration to methanol, providing an alternate source of liquid fuel. One side product of this fermentation is a residue rich in nitrogen and minerals. This residue could become an excellent source of natural, environmentally acceptable fertilizers.

The opportunities for Canada which might arise from efforts directed towards methane production are: (1) increased sources of natural gas; (2) Canada becomes a developer of new aspects of waste treatment and pollution control technologies; (3) effective capitalization upon existing activities in Canada; (4) reduction of costs to industry of waste treatment and disposal; (5) production of environmentally acceptable fertilizers thereby further reducing demands upon petroleum based fertilizers.

Biotechnology might also be explored in connection with Canada's petroleum reserves. One specific area which may present an opportunity is petroleum recovery. Canada has vast reserves of petroleum locked within the tar sands of Alberta and Saskatchewan. The current processes for petroleum recovery from these areas are expensive, energy intensive and inefficient. One major problem which accounts for a major portion of these ills is the difficulty in bitumen separation. Microbial methods for the separation of bitumen are currently being investigated in Canada with encouraging results. A greater emphasis on this application of biotechnology could impact considerably upon the effective recovery of this resource.

Another problem of oil recovery, generally, is complete tertiary oil recovery, that is, recovery of oil which has seeped from major basins and is dispersed throughout a variety of geological formations. Microbial exopolysaccharides are polymers produced by microorganisms possessing a range of characteristics. One of these characteristics is their ability to alter the rheological properties of aqueous solutions, either through gelling or through the alteration of their flow characteristics. The polymers can therefore be used to improve water-flooding techniques in which the aqueous solution of polymer gives an increased efficiency of contact with, and displacement of oil.

While this biotechnological method of oil recovery is being examined in other countries, little activity is noticeable in Canada. The justification for Canada to consider developing its own technological expertise in this area, as opposed to purchasing it from abroad, lies in the fact that no two oil fields are similar. Canada's oil fields have distinct differences in salinity, pH and temperature as compared with fields in the North Sea or Persian Gulf, for instance.

An added potential spin-off from the investigation of microbial polysaccharides activity is the utilization of these polymers in the detergent - laundry, textile, paper, paint, food and pharmaceutical - cosmetic industries.

Thus within the energy area, alcohol and methane generation, bitumen degradation and microbial exopolysaccharide utilization are seen as a few of the opportunity areas to be considered for Canada.

# **Forestry**

A major concern of both federal and provincial governments is how to achieve the effective management and utilization of Canada's forestry resource. Through two not unrelated applications of biotechnologies, opportunities can be envisioned for the improved efficiency of exploitation of this resource.

In some of the processes employed for the production of pulp and paper spent sulfite liquors form a major waste problem. These liquors contain, in addition to carbohydrates, many toxic compounds such as resin acids, chlorinated resin acids and chlorinated unsaturated fatty acids. In principle, the discharge of such industrial wastes is subject to ever increasing regulations, with the result that firms now pay enormous costs for waste treatment or sewage system utilization. It is now possible, however, to ferment at least a portion of this waste into a valuable feedstock for animals and human consumption; this feedstock is known as single-cell protein (SCP) and will be discussed more fully in the section on food/ agriculture. Suffice to say biotechnology could conceivably offer the pulp and paper industry the opportunity of reduced costs in terms of waste treatment and increased revenue in terms of supplementary product production.

Approximately 37% of Canada's landmass is covered by forests. This is potentially an extremely large source of carbohydrate. The problem of trees as a carbohydrate source is that this carbohydrate is bound up in a complex package of lignin and various celluloses. In order to generate carbohydrate from a wood source one must degrade or extract the lignin and degrade the celluloses. Traditionally this has been done chemically with limited efficiency and resulted in a significant waste problem. Microbial degradation offers clear advantages here and could provide an opportunity for the utilization of the entire forestry resource. The resultant increased availability of carbohydrate could have implications

for many areas in which large quantities of carbohydrate substrate are required for fermentation.

Thus within the forestry area, waste treatment and utilization and carbohydrate generation are some of the applications of biotechnology which might offer significant opportunities to Canada.

# Food/Agriculture

The food/agriculture area might be considered, both in the short and long terms, as another resource area in which biotechnology could have opportunities for Canada.

In the short term, it is possible that single cell protein (SCP) production might become an important source of human and animal feedstuff. SCP is merely a microorganism whose protein content, on a dry weight basis, can range from 50-80% of total weight. The amount of protein is usually determined by the nature of the carbon source with the subsequent amino acid ratios controlled genetically. The techniques of mutant selection and genetic engineering could allow for control over the actual protein composition of SCP, making it possible for selective generation of highly specific dietary supplements. While the exploitation of SCP domestically as for example, animal feed, could free up for alternate fermentations other carbohydrate sources (corn)traditionally needed as feedstocks, Canada could also export a large quantity of SCP to underdeveloped countries.

A more long term possible opportunity is the application of biotechnology to the field of nitrogen fixation. types of plants generate their own nitrogen fertilizers by "fixing" nitrogen from the atmosphere via a bacteriallymediated system. Through cellular and genetic manipulative technologies research is being aimed at adapting both the bacterially-mediated system and the plants to create a greater variety of nitrogen-fixing crops. The possible advantage of this type of system being exploited more broadly would be the resultant lack of requirement for artificial nitrogen fertilizers thereby decreasing the environmental hazards posed by these unnatural elements. Since most commercial fertilizers are petrochemicals or petrochemicallybased, this type of system, if more widely applied, could reduce the demand for these increasingly costly fertilizers.

In addition to nitrogen fixation, biotechnological techniques such as plant cell culturing, cell fusion and genetic manipulations could, for example, provide new plant varieties more resistant to low temperatures and soil variability, higher yielding and tailored more specifically to requirements.

Pest management is another area where a biotechnological approach might be worth considering. Emphasis in this area has already settled on viral and bacterial pathogens as insect controls and could result in highly selective measures for the eradication of unwanted insects. Because of the diverse nature of the pest control problem in Canada a broad effort would be required which, if successful, could result in Canada becoming a world leader in insect control.

Thus within the food/agriculture area, SCP production nitrogen fixation, plant strain development and pest management are seen as some of the possible opportunity areas which might be considered for the application of biotechnology in Canada.

# Mining

One of the weakest areas of understanding concerning the application of biotechnology is in the area of mining. The economically significant interrelation of organisms and metals can be divided into two main areas: first, the extraction of metals from insoluble materials principally through leaching by acidophilic iron-oxidizing and sulphur-oxidizing bacteria, and second the recovery of metals from solution by organisms. It is in these two areas where biotechnology might be considered an opportunity for Canada, as a non-energy intensive, non-polluting means of efficiently realizing its mineral wealth.

From Canada's mineral resource perspective the bacterial leaching of copper, uranium, nickel, lead and zinc could be considered as possibilities. Internationally this method has been applied to low-grade ores with modest success. The microbial treatment of metal mixtures, mine tailings etc. might also offer considerable promise.

A more futuristic possible opportunity lies in the use of microorganisms as vehicles of metal recovery. It has been know for some time that certain bacteria have selective affinities for certain metals. Applications of these characteristics or even the genetic engineering of the organism to make it more selective could result in tools for trace metal recovery and water purification.

Thus within the mining area, consideration might be given to the applications of biotechnology in metal extraction and recovery.

# Health Care Products

While not considered one of the resource sectors, the area of health care products stands to benefit enormously from the applications of biotechnology. Because of Canada's lack of an established health care products industry, we suffer from a severe balance of payments deficit in this area as well as the lack of suitable industrial employment opportunities for research personnel trained in the health field.

The application of biotechnology to the production of hormones, vaccines, antibiotics and other pharmaceuticals, as well as the whole field of immuno-diagnostics are some of the industrial opportunities being discussed world wide.

Although, the information from Annex II would indicate that some biotechnological activity is apparent in all sectors in Canada in this area, it is not possible at this time, given the embryonic stage of these developments, to suggest more specifically the Canadian opportunities. It is evident, however, that this area may have considerable potential for Canada and therefore will need to be considered carefully.

#### Conclusions

Throughout the course of the consultations carried out in preparation of this paper a number of significant aspects of current Canadian biotechnological activity were noted. These are:

- 1. The current production of research-trained manpower from Canadian universities in disciplines such as biochemistry, biochemical engineering, applied microbiology and applied genetics is weak. Moreoever people presently being trained in genesplicing techniques required for DNA research are being actively recruited by American companies. Finally importation of skilled manpower from other countries will be hampered by the world-wide expansion of biotechnological activity and the subsequent high level of demand for this expertise.
- 2. Although the overall level of industrial biotechnological activity in Canada is low, programs such as PILP and IRAP have been successful in the further promotion of this industry.

- 3. There does not exist, in any Canadian university or technical college, a department of applied microbiology.
- 4. From a university perspective there are pockets of biotechnological expertise scattered across the country with little, if any, interconnection within institutions, let alone between institutions. The university scientists, even amongst the applied disciplines, lack the necessary marketing and financial support to determine the commercial potential of their work.
- 5. In order for Canada to develop an industrial biotechnological capability, it will not be possible to exploit all of the possible opportunities envisioned. Further in-depth analysis is necessary to identify that particular range of opportunities which are worth exploiting in a Canadian context.

### ANNEX I

# BIOTECHNOLOGICAL ACTIVITY IN CANADA - BY SECTOR

The activities described in Section I have been grouped according to three sectors, Government, Industry and University. Each listing contains the name and address of the firm, agency or institution, the individual to be referred to for further clarification and a description of the activity.

#### GOVERNMENT SECTOR

#### FEDERAL

### G-1 AGRICULTURE CANADA

General: E.J. Leroux

Assistant Deputy Minister

Research Branch

Sir John Carling Building

Carling Avenue Ottawa, K1A OC5 (613) 995-7084

(a) Chemistry and Biology Research Institute Ottawa, Ontario
J.G. Saha
(613) 995-3104

Development of means of fixing atmospheric nitrogen through the study of hosts, bacteria and the biological processes; also increase nitrogen fixation efficiency through hydrogen utilization.

Production of doubled haploids for breeding cereal and cruficer species, cell and protoplast cultures for mutant selection, parasexual hybridization, whole plant regeneration and interspecific gene transfer.

(b) Ste-Foy Research Station Ste-Foy, Quebec S.J. Bourget (514) 694-4814

> Development of means of fixing atmospheric nitrogen through the study of hosts, bacteria and the biological processes.

(c) Beaverlodge Research Station Beaverlodge, Alberta L.P. Spangelo (403) 354-2212

Assessment of nitrogen fixation potential of forage legumes, bacterial selection and improvements in innoculants and innoculation methods.

(d) Lethbridge Research Station Lethbridge, Alberta J.E. Andrews (403) 327-4561

Nitrogen fixation in wheat strains; transfer of specific traits to wheat.

(e) Swift Current Research Station Swift Current Saskatchewan A.W. Strachan (306) 773-4621

Methodology of assessing viability and effectiveness of inocula, nodulation and nitrogen fixation by non-leguminous shrubs; utilization of high nitrogen-fixation annual legumes as fertilizers.

(f) Brandon Research Station Brandon, Manitoba W.N. MacNaughton (204) 728-7234

Haploidy techniques in barley breeding.

(g) Vancouver Research Station Vancouver, British Columbia N. Weintraub (604) 224-4355

> Meristem tip cultures for the production of virusfree stocks; pathogen free cell lines.

(h) Saskatoon Research Station Saskatoon, Saskatchewan J.E.R. Greenshields (306) 343-8214

Haploids in rapeseed; protoplast fusion for Brassica hybrids.

(i) Morden Research Station Morden, Manitoba E.D. Putt (204) 822-4471

Tissue culture for disease free stocks and preservation of germplasm.

(j) Summerland Research Station Summerland, British Columbia J.C. Russell (604) 494-7711

Tissue culture for fruit tree propagation.

### G-2 ENERGY MINES AND RESOURCES

M. Silver
Canada Centre for Mineral and Energy Technology
Mineral Science Laboratories
Ore Processing Laboratory
555 Booth Street
Ottawa, KIA OG1
(613) 995-4706

Microbial leaching of uranium, composting efficiencies

# G-3 ENVIRONMENT CANADA

Inland Waters Directorate Canada Centre for Inland Waters National Water Research Institute Burlington, Ontario L7A 4A6 (416) 637-4303

(a) D. Liu

Biodegradation of petroleum via fermentation processes

#### G-4 HEALTH AND WELFARE CANADA

General: A.J. Clayton

Director General

Laboratory Centre for Disease Control

Health Protection Branch

Tunney's Pasture Ottawa K1A OL2 (613) 992-6385

(a) J. Konowalchuck and L. Perelmutter

 $\label{lem:continuous} \mbox{ Hybridoma techniques for selective immunoglobulin production}$ 

(b) J.R. Dillon

Molecular genetics of plasmids and transposable elements of medical importance

# G-5 NATIONAL RESEARCH COUNCIL OF CANADA

# Atlantic Regional Laboratory

General: F. Simpson

Director

1411 Oxford Street Halifax, Nova Scotia

(902) 429-6450

(a) J.P. Van der Meer

Genetics of algae culture, algae as a food source.

## G-6 NATIONAL RESEARCH COUNCIL OF CANADA

# Division of Biological Sciences

General: C. Bishop

Director

100 Sussex Drive Ottawa K1A OR6 (613) 995-6600

(a) S.M. Martin (613) 992-2367

Anaerobic microbiology, methanogenic bacteria, hydrogenases, continuous culture studies, enterotoxins, growth of pathogenic bacteria.

(b) M.B. Perry (613) 992-8995

Antigens of pathogenic bacteria, Neisseria species, chlamydia, pneumococcus, streptoccus; structure-function in polysaccharide antigens, use in vaccines and diagnostics; synthetic antigens; monoclonal antibodies from hybridomas.

(c) C.P. Lentz (613) 992-3310

Biogas fermentation, practical production of biogas from sewage sludge and food wastes.

(d) A.P. James (613) 992-6512

Cloning of genes in yeast and bacteria; transformation of yeast; studies on gene expression; synthesis of genes and of linker segments for plasmid linking; structure of chromatin; restriction enzymes; ribosome structure.

(e) K.R. Lynn (613) 992-6541

Protein biochemistry; isolation and characterization of eznymes - hydrogenases, protein kinases, sulfatases; immunoglobulins.

# G-7 NATIONAL RESEARCH COUNCIL OF CANADA

### Prairie Regional Laboratory

General: B. Craig
Director
110 Gymnasium Road, U. Campus
Saskatoon, Saskatchewan
(306) 665-4191

(a) C.G. Young

Protein, starch and sugar processing

(b) J. Groot Wassink

Enzyme recovery and utilization; inulase and lactase production by yeast cultures.

(c) N.G. Kurz

Plant cell culture; pharmaceuticals production

(d) F. Constabel

Plant cell culture; pharmaceuticals production

(e) R. Tyler

Enzyme isolation from plant seeds

(f) R. Reichart

Food process engineering

(g) J. Child

Immobilized cells, annucleated - utilization
in fermentations

(h) P.S.S. Dawson

Continuous phased culture as fermentation technology

#### PROVINCIAL

## G-8 ALBERTA RESEARCH COUNCIL

Frontier Sciences Division 11315-87th Avenue Edmonton, Alberta T6G 2C2 (403) 432-8019

(a) D. Currie

Heavy oil degradation by microorganisms Cold temperature microbes for petroleum degradation

Long Range Plan (Biotechnology)

- Low frost tolerance crop breeding
- Nitrogen fixation improvements for crops
- Exploitation of plant hormones

# G-9 MANITOBA RESEARCH COUNCIL

501-One Lakeview Square 155 Carlton Street Winnipeg, Manitoba R3C 3H8 (204) 944-3505

(a) B.F. Dodds Program Director

Recently opened Industrial Technology Centre will feature a life sciences section emphasizing fermentation, cellular and genetic manipulative capabilities for industrial support

### G-10 NOVA SCOTIA RESEARCH FOUNDATION CORPORATION

Biology Division 100 Fenwick Dartmouth, Nova Scotia B2Y 3Z7

(a) K. Hellenbrand

Industrial fermentation for polysaccharide production and utilization

# G-11 SASKATCHEWAN RESEARCH COUNCIL

Chemistry and Biology Division 30 Campus Drive Saskatoon, Saskatchewan S7N OX1 (306) 664-5400

# (a) D. Thompson

Lignocellulosic treatment to increase cellulose and hemi-cellulose availability for fermentation

Compaction of lignocellulosic materials

#### INDUSTRY SECTOR

#### I-1 AYERST LABORATORIES

1025 Laurentian Boulevard P.O. Box 6115 Montreal, Quebec H3C 3J1 (514) 755-6771

(a) G. Vezina

Antibiotic production, pilot plant capability for antibiotic fermentations

Protoplast fusion activity

Future recombinant DNA work for production of peptide hormones.

## I-2 B.C. RESEARCH COUNCIL

3650 Wesbrook Mall Vancouver, British Columbia V6S 2L2 (604) 224-4331

(a) C. Walden

Conversion of black liquor from pulp mills into a fermentable substrate; fermentation process for commercial production of alginic acid

(b) J. Mueller

Biohazards and studies of biotoxicity

(c) A. Brunesteyn

Microbial leaching of base metals

### I-3 THE BORDEN COMPANY LIMITED

1275 Lawrence Avenue East Don Mills, Ontario M3S 1C5 (416) 445-3131

(a) Tillsonburg, Ontario Laboratories

Immobilization of lactases for whey treatment-waste treatment process

### I-4 CAMBRIAN PROCESSES LIMITED

D.H. Lees Director Research and Development Division 2465 Cauthra Road Mississauga, Ontario L5A 3P2 (416) 272-1400

(a) Novel fermentor design and application to amylase production

## I-5 CANADA PACKERS

P. Ziegler Research Centre 2211 St. Clair Avenue West Toronto, Ontario N6N 1K4 (416) 766-4311

(a) Biochemicals from animal residues

# I-6 CEDARLANE LABORATORIES LTD

S. Abrahams President 493-A Wellington Road London, Ontario N6C 4R3 (519) 686-0415

(a) Antiserum production, monoclonal antibody production

### I-7 CHEMBIOMED LTD

R.U. Lemieux President University of Alberta W5-56 Chemistry Building Edmonton, Alberta T6G 2E1 (403) 432-3111

(a) Immunoadsorbents and artificial antigens for the improvement and development of blood typing reagents.

## I-8 CONNAUGHT LABORATORIES LIMITED

D.S. Layne Vice-President Research and Technology 1755 Steeles Avenue West Willowdale, Ontario M2N 5T8 (416) 667-2922

Connaught Research Institute being established will focus on:

- (a) Immunology to build upon existing strengths and promote development of monoclonal antibodies
- (b) Genetic Engineering establish recombinant DNA capability
- (c) Cell science development of cell lines
- (d) Bioengineering and technology medical device development such as artificial pancreas.

### I-9 ENS BIOLOGICALS INC

R. Bender President 20 Victoria Street Suite 405 Toronto, Ontario M5C 2N8 (416) 364-2371

(a) Three main divisions (Molecular Genetics, Nucleic Acids and Fermentation) which operate primarily from leased space within Canadian universities; also own a microbiology firm in California

# I-10 FRASER VALLEY MILK PRODUCERS ASSOCIATIONS

G.W. Park President 6800 Lougheed Highway P.O. Box 9100 Burnaby, British Columbia V6B 4G4 (604) 298-1373

(a) Treatment and utilization of whey

### I-11 GENERAL FOODS LIMITED

I.M. Saslaw Research and Development Department 2200 Yonge Street Toronto, Ontario M4S 2C6 (416) 481-4211

(a) D. Mercer (Coburg, Ontario)

Protein extraction and novel fermentation products

# I-12 GEORGE WESTON LIMITED

R. Lawford
Weston Research Centre
1047 Yonge Street
Toronto, Ontario
M4W 2L3
(416) 922-2500

(a) Fermentation products as foodstuffs

### I-13 INSTITUT ARMAND FRAPPIER

531, boulevard des Prairies C.P. 100 Laval-des-Rapides Québec (Québec) H7V 187 (514) 687-5010

(a) V. Portelance

Bacterial strain development for cellulose degradation

Genetically engineer sub-unitary viral vaccines

Production of restriction enzymes and monoclonal antibodies

#### I-14 IOTECH CORPORATION LTD

E.A. Delong 15 Milne Crescent Ottawa, Ontario K2K 1H7 (613) 592-5667

(a) Process development for cellulose and hemicellulose pretreatment to permit greater accessibility of carbohydrates in fermentation. Convert lignin to a chemically active, easily extractable form

# I-15 KERR-ADDISON MINES LIMITED

P.O. Box 91 Commerce Court West Toronto, Ontario M5L 1C7

(a) Processing of low-grade uranium ore microbiologically at Agnew Lake, Espinola, Ontario

# I-16 LABATTS BREWERIES OF CANADA LIMITED

B. Shelton Corporate Director Research and Development 150 Simcoe London, Ontario N6A 4M3 (519) 673-5050

- (a) High fructose syrup manufacture, food processing
- (b) G. Stewart (519) 673-5326

Physiology and genetics of yeasts; ethanol tolerance and production; application of recombinant DNA technology to yeasts

## I-17 LALLEMAND INCORPORATED

S. Lee 1620 Prefontaine Montreal, Quebec H1W 2N8 (514) 522-2133

(a) Yeast production, single cell protein production.

# I-18 L.J. McGUINNESS AND COMPANY LTD

2 Algoma Street Toronto, Ontario M8Y 1B9 (416) 259-3761

(a) Distillery waste utilization

# I-19 MARINE COLLOIDS

I.C. Welsh Head Cultivation Division 660 Portland P.O. Box 2610 Dartmouth, Nova Scotia B2W 2EO (902) 434-2840

(a) Marine plant cultivation for specialty chemicals

# I-20 MDS HEALTH GROUP LTD

J. Nixon Research Director 30 Meridian Road Rexdale, Ontario M9W 4Z9 (416) 675-7661

- (a) Development of diagnostic reagents based upon the antigenic properties of microorganisms, diagnostic system for gonorrhea
- (b) Enzyme linked immunochemical diagnostics
- (c) Development of antibodies to chlamydia
- (d) Future development of monoclonal antibodies to microorganisms

### I-21 MICROBIOS LIMITED

J.W. Costerton President 4828 Dalhousie Drive N.W. Calgary, Alberta T3A 1B2

- (a) Biocide development against corrosion causing bacteria
- (b) Biocide development against sulfur cycle bacteria affiliated with oil recovery

### I-22 MOLSON BREWERIES OF CANADA LIMITED

R.L. Weaver Director Research and Development Division 1555 Notre-Dame Street East Montreal, Quebec H2L 2R5 (514) 527-5151

(a) Fermentation genetics, rapid fermentations and product analysis

### I-23 MUTATECH

J. Heddle Department of Biology York University Downsview, Ontario M3J 1P3 (416) 667-2335

(a) Diagnosis of genetic defects

# I-24 NORTHERN PURIFICATION SERVICES LIMITED

139 Riverside North Vancouver, British Columbia V7H 1T6 (604) 929-1271

(a) Thermophilic conversion of wood waste into animal feed

#### I-25 ONTARIO RESEARCH FOUNDATION

Chairman W.R. Stadelman Sheridan Park Mississauga, Ontario L5K 1B3 (416) 822-4111

- (a) Application of wet air oxidation technology to preparation of fermentable substrates from biomass
- (b) Actively recruiting recombinant DNA expertise

#### I-26 PLASTISTARCH CORPORATION

J. Hughes President 2775, rue de Miniac Montreal, Quebec H49 1L9 (514) 332-2392

(a) Process development and equipment design for breakdown of starch into fermentable carbohydrate.

#### I-27 PULP AND PAPER RESEARCH INSTITUTE

570 St. John's Boulevard Pointe-Claire, Quebec H9R 3J9

(a) L. Jurasek
Biological Chemistry Group
(514) 697-4110

Biological degradation of lignin and modification of lignocellulosics

Enzymatic conversion of cellulosic residues into fermentable substrates; enzyme isolation, characterization; development of enzyme mimics

(b) Pollution abatement division

Microbial process for the separation of bark and wood

(c) Product development division

Wood seasoning - biological hydrolysis of wood extractives

#### I-28 REED LIMITED

J.V. Benko Director Lignin Products Division P.O. Box 2025 Quebec, Quebec G1K 7N1

(a) Utilization of spent sulfite liquor for single cell protein production

#### I-29 RUSH ENGINEERING SERVICES LIMITED

R.J. Rush Director Research and Development Rural Route 3 Listowel, Ontario N4W 3G7 (519) 887-9073

(a) Thermophilic anaerobic fermentation of animal waste for protein and methane production

## I-30 J.M. SCHNEIDER INC.

321 Courtland Ave East Kitchener, Ontario N2G 2X8 (519) 885-8100

(a) F. Murray

Waste utilization

#### I-31 SHELL CANADA LIMITED

T. McIvor 505 University Avenue Toronto, Ontario M5G 1X4 (416) 597-7622

(a) Considering fermentation facility in southwestern Ontario for antibiotic production

#### I-32 SILVERWOOD INDUSTRIES LTD

A. Sargent
Director
Research and Development
75 Bathurst
London, Ontario
N6B 1N8
(519) 672-9111

(a) Single cell protein production from whey, fermentation process development

## I-33 SYNTEX CORPORATION

J. Freed President Syntex Research 3401 Hillview Avenue Palo Alto, California 94304 (415) 855-5163

(a) Will establish basic research facility in Mississauga, Ontario in mid 1981. Research will focus on enzyme regulation with eventual lead into health care product development.

#### U-1 UNIVERSITY OF ALBERTA

Edmonton, Alberta T6G 2E1 (403) 432-3111

### Department of Biochemistry

- (a) V. Paetkau Lymphocyte proliferation, gene expression
- (b) L.B. Smillie Industrial enzymes

## Department of Chemical Engineering

(c) F. Otto - Food processing, systems development

### Department of Chemistry

(d) R.U. Lemieux - Immunochemistry, immunoadsorbents (Chembiomed Ltd.)

## Department of Immunology

(e) E. Diener - Immunoregulation, immunology and industrial applications

# Department of Microbiology

(f) D. Westlake - Microbial metabolism, antibiotic production

#### U-2 UNIVERSITY OF BRITISH COLUMBIA

2075 Wesbrook Place Vancouver, British Columbia V6T 1W5 (604) 228-2211

#### Department of Biochemistry

- (a) M. Smith Studies on nucleic acids, bacterial genetics
- (b) G. Tener Genetic controls, cloning

### Department of Chemical Engineering

- (c) R. Branion Fermentation parameters of single cell protein production
- (d) K.L. Pinder Waste treatment

## Department of Chemistry

(e) J.P. Kutney - Plant cell alkaloids as pharmaceutical agents

# Department of Medical Genetics

(f) R.C. Miller - Recombinant DNA and studies on bacterial genetics

# Department of Microbiology and Immunology

- (g) J. Levy Studies on monoclonal antibodies
- (h) R.A.J. Warren Recombinant DNA

#### U-3 UNIVERSITY OF CALGARY

2920-24 Ave. N.W. Calgary, Alberta T2N 1N4 (403) 284-5110

#### Department of Biology

- (a) R.B. Church Studies on gene expression, cloning
- (b) J.W. Costerton Microbiological antibiotic production against Pseudomonas
  - Vaccine production utilizing bacterial exopolysaccharides
- (c) Metering devices and methods to control bacterial fouling of industrial heat-exchange systems
- (d) G.M. Dixon Bacterial and mammalian genetic engineering
- (e) E. Layshley Microbial leaching of minerals

#### Department of Chemistry

(f) G.M. Gaucher - Fungal secondary metabolism and extracellular enzyme production

#### Faculty of Medicine

(g) L.M. Jerry - Medical applications of genetic manipulations, interferon and other immunology studies

## U-4 CARLETON UNIVERSITY

Ottawa, Ontario KlS 5B6 (613) 231-4321

## Department of Biology

- (a) B. Iyer Nitrogen fixation studies
   Application of recombinant DNA techniques
   to studies of bacterial genetics
- (b) G. Setterfield Plant cell culture, cell fusions to produce new plant strains
- (c) H. Yamazaki Genetic engineering, regulation of metabolite production

# U-5 DALHOUSIE UNIVERSITY

Halifax, Nova Scotia B3H 3J5 (902) 424-2211

# Department of Biochemistry

(a) W.F. Doolittle - Bacterial and algae genetics

# Department of Biology

(b) L.C. Vining - Antibiotic fermentations

#### U-6 UNIVERSITY OF GUELPH

Guelph, Ontario N1G 2W1 (519) 824-4120

### Department of Botany and Genetics

(a) R.L. Peterson - Crop improvement through plant cell and tissue culture

## Department of Chemistry

(b) B.E. Ellis - Secondary metabolites in plant cells, pharmaceutical applications

### Department of Microbiology

- (c) P. Dobos Viral control of insects, pancreatic necrosis virus and spruce budworn polyhedrosis virus
- (d) N.A. Epps Monitoring system for salmonella, structural barriers to microbial penetration
- (e) C.W. Forsberg Microbial activity of bovine rumen, feedstock degradation
- (f) K.F. Gregory Single cell protein from starchy substrates by thermotolerant fungi
  - Recombinant DNA application to bacterial amylase production
- (g) R.A. Johnson Diagnosis of bacterial and viral induced fish diseases
- (h) R.E. Smith Waste treatment and utilization by microbial conversion
- (i) Single cell protein production as animal feed
- (j) Biodegradation of cellulose and lignin
- (k) R.M.W. Stevenson Diagnostic techniques for microbial diseases in fish

# Ontario Agricultural College

# Department of Crop Science

- (1) K.J. Kasha Crop improvement through plant cell and tissue culture
- (m) D.T. Tomes Crop improvement through plant cell and tissue culture

# Department of Environmental Biology

- (n) D.L. Collins-Thompson Food microbiology
  Control of food-borne pathogens by
  inherent microflora in food and by
  antimicrobial food additives
- (o) C.T. Corke Microbial degradation of pesticides, soil microbiology
- (p) J.D. Cunningham Industrial microbiology, fermentations and industrial waste management

# U-7 UNIVERSITE LAVAL

Cité universitaire Québec, Québec GIK 7P4 (418) 656-2131

## Alimentation

(a) D.J. Goulet - Cheese whey fermentation; lactic acid production

# Génie Chimique

(b) A. LeDuy - Studies on yeast cultures, treatment of industrial effluents

### Faculté de Foresterie

(c) J. André Fortin - Studies on nitrogen fixing bacteria and their industrial inoculation

#### U-8 UNIVERSITY OF MANITOBA

Winnipeg, Manitoba R3T 2N2 (204) 474-8880

## Department of Immunology

(a) A. Sehon - Monoclonal antibody production

# Department of Physiology

(b) H. Friesen - Genetic engineering and endocrinology

### Department of Plant Science

- (c) W. Bushuk Energy from agricultural biomass (affiliation with Biomass Energy Institute)
- (d) H.M. Lapp Energy from agricultural biomass (affiliation with Biomass Energy Institute)

## Department of Zoology

(e) M. Samoiloff - Mutant bacterial strain development for commercial use

#### U-9 McGILL UNIVERSITY

P.O. Box 6070 Station A Montreal, Quebec H3C 3G1 (514) 392-4311

## Department of Agricultural Engineering

(a) P. Kok - In situ fermentation electrode calibrator

## Department of Biochemistry

(b) A. Graham - Gene cloning, recombinant DNA

## Department of Biology

- (c) A.H. Bussey Fundamental studies of yeasts
- (d) D. Verna Genetics of nitrogen fixation

## Department of Chemical Engineering

- (e) B. Volesky Biosorbent properties of microbial biomass
- (f) Industrial solvents from renewable resources via fermentation
- (g) Fermentation process optimization

### Department of Physiology

(h) T. Chang - Enzyme immobilization

## U-10 McMASTER UNIVERSITY

Hamilton, Ontario L8S 4L8 (416) 525-9140

### Department of Biochemistry

(a) W.W. Chan - Enzyme immobilization

## Department of Biology

(b) J.J. Miller - Yeast sporulation, physiology

### Department of Chemical Engineering

- (c) A. Benedek Waste treatment
- (d) K.L. Murphy Waste treatment; systems development

### Department of Medicine

(e) J. Bienenstock - Production of monoclonal antibodies to herpes viruses

### Department of Pathology

(f) W.E. Rawls - Studies virus replication, monoclonal antibody development

#### U-11 MEMORIAL UNIVERSITY OF NEWFOUNDLAND

Elizabeth Avenue St. John's, Newfoundland A1C 5S7 (709) 753-1200

### Department of Biochemistry

- (a) N.F. Haard seaweed polysaccharide degrading enzymes
  - animal feed from bogland, hay and fishery waste fermentations
- (b) B.H. Sells Bacterial genetics

## Department of Biology

(c) R.A. Nolan - Fungi as bioinsecticides

### Department of Pathology

(d) M. Laird - Vector pathology, isolation and applications of insect pathogens

# U-12 UNIVERSITÉ DE MONTRÉAL

Ecole Polytechnique Case Postale 6128 Montréal, Québec H3T 1J4 (514) 343-6111

# Génie chimique

- (a) A. Rollin Food processing, reactor design
- (b) D. Rouleau Bioreactor design
- (c) Utilization of immobilized enzymes for lactose hydrolysis

## U-13 UNIVERSITY OF OTTAWA

Ottawa, Ontario KlN 6N5 (613) 231-3311

# Department of Biochemistry

(a) I. Altosar - Xylitol dehydrogenases in chemostats

# U-14 UNIVERSITÉ DE QUÉBEC à TROIS-RIVIÈRES

335 boulevard des Forges Trois-Rivières, Québec G9A 5H7 (819) 376-5011

## <u>Génie</u>

(a) J.J. Garceau - Single cell protein production from sulfite liquors

## U-15 QUEEN'S UNIVERSITY

Kingston, Ontario
K7L 3N6
(613) 547-5511

## Department of Biochemistry

(a) J. Spencer - Studies of bacterial genetics, recombinant DNA

### Carbohydrate Research Institute

(b) W.A. Szarek - Development of sweetening agents

# Department of Chemical Engineering

(c) D.H. Bone - Microbial conversion of plant waste, single cell protein production

# Department of Chemistry

(d) S. Wolfe - Microbial transformations, microbial antibiotic production

## U-16 UNIVERSITY OF REGINA

Regina, Saskatchewan S4S OA2 (306) 584-4111

# Department of Microbiology

(a) D.R. Cullimore - Photosynthetic bacterial digestion of animal waste

#### U-17 UNIVERSITY OF SASKATCHEWAN

Saskatoon, Saskatchewan S7N 0W0 (306) 343-2100

### Department of Chemical Engineering

- (a) E. Davis Microbial waste treatment
- (b) D.A. MacDonald Sugar production from aspen cellulose
   Single cell protein production from biomass

### Department of Chemistry

(d) J.M. Pepper - Aspen lignin degradation by fungus

#### Department of Dairy and Food Science

- (e) W.M. Ingledew Single cell protein production and yeasts for food and feed
- (f) Alcohol production without substrate modification
- (g) High gravity fermentations and quality control methods
- (h) Studies on yeasts
- (i) G.A. Jones Degradation of aromatic compounds in anaerobic fermentations
- (j) In vitro digestibility procedures for unconventional forages
- (k) Rumen fermentations

## Department of Microbiology

- (1) G. Khachatourians Anucleated microbial cell, production and physiologies
- (m) Anucleated microbial cells in vaccine production
- (n) Fermentation processes using immobilized cells
- (o) Single cell protein and alcohol production from starch

# UNIVERSITY OF SASKATCHEWAN (cont'd)

- (q) I.A. Rainshaw Monoclonal antibody production

## Department of Veterinary Microbiology

(r) C.H. Bigland - Vaccine development for infectious diseases in food producing animals

## U-18 UNIVERSITY OF TORONTO

Toronto, Ontario M5S 1A1 (416) 928-2011

# Department of Chemical Engineering and Applied Chemistry

(a) M. Wayman - Alcohol production from wood

(b) - Autotrophic microbes for organic materials production

(c) - Single cell protein production

# U-19 UNIVERSITY OF VICTORIA

P.O. Box 1700 Victoria, British Columbia V8W 2Y2 (604) 447-6911

# Department of Biochemistry

(a) T. Pearson - Production of monoclonal antibodies to common antigenic components of trypanosomes

# U-20 UNIVERSITY OF WATERLOO

Waterloo, Ontario N2L 3G1 (519) 885-1211

# Department of Chemical Engineering

(a)	M. Moo-Young - Production of single cell protein from
	organic wastes
(b)	- Production of alcohols and methane from
	agricultural and municipal wastes by
	fermentation processes
(c)	
(0)	- Development of multi-phase contactors
	as bioreactors
(d)	K.F. O'Driscoll - Immobilized enzymes for biomedical
	applications
(e)	C.W. Robinson - Production of single cell protein from
•	organic wastes
(f)	- Production of alcohols and methane
( + )	
	from agricultural and municipal wastes
	by fermentation processes
(g)	<ul> <li>Food processing and rheology</li> </ul>
(h)	- Bioreactor development
(i)	J. M. Scharer - Single cell protein production via
	anaerobic digestion of cellulosic waste
(j)	- Production of alcohols and methane from
()/	
<i>(</i> 2. )	organic waste
	P. Silveston - Waste treatment
(1)	<ul> <li>Computerized design of bioreactors and</li> </ul>

processes

## U-21 UNIVERSITY OF WESTERN ONTARIO

London, Ontario N6A 3K7 (519) 679-2111

## Department of Bacteriology and Immunology

(a) R.G.E. Murray - Bacterial cytology

# Department of Biochemistry

(b) G. Mackie - Bacterial genetics

(c) B.D. Sanwal - Somatic cells and enzymology

#### Department of Plant Science

(d) R.B. Van Huystee - Secondary metabolites in plant cells, pharmaceutical applications

## Faculty of Engineering Science

(e) N. Kosaric - Industrial wastewater treatment

 (f) - Single cell protein and other foodstuff production from industrial and agricultural residues

(g) A. Margaritis

- Reactor development for biochemical processes

(h) - Bioenergy production of gaseous and liquid fuels by fermentation

(i) - Microbial separation of bitumen from tar sands, biosurfactants and bioemulsifiers

#### U-22 YORK UNIVERSITY

4700 Keele Street Downsview, Ontario M3J 1P3 (416) 667-2100

## Department of Biology

- (a) J. Friesen Gene cloning, recombinant DNA, yeast genetics and fermentations
- (b) J. Heddle Genetic defect diagnosis
- (c) R.E. Pearlman Biochemical and genetic analysis of nucleic acid metabolism

## Department of Chemistry

(d) C. Leznoff - Insect sex pheremones

#### ANNEX II

#### BIOTECHNOLOGICAL ACTIVITY IN CANADA - BY AREA OF APPLICATION

The three groupings of technologies (fermentation, enzyme, cellular and genetic manipulative) which comprise biotechnology are recognized to be applicable to a number of important areas. Those areas which can presently be identified include:

- <u>A</u> <u>Waste Treatment and Pollution Control</u> The treatment or reprocessing of industrial, agricultural and domestic waste, and the control of environmental pollutants.
- <u>B</u> Raw Material Extraction and Preprocessing The concentration and isolation of minerals and metals, petroleum recovery, and the pretreatment of potential fermentation feedstocks.
- <u>Biomedical Product Development</u> The preparation of pharmaceuticals, vaccines, and diagnostics as well as methods of toxicity evaluation.
- <u>Prood Production</u> The development of new animal and human feedstocks.
- <u>Agricultural Improvements</u> The creation of new plant strains, pesticides, fertilizers, and new fertilization methods.
- Fuels, Industrial Chemicals, Biochemicals and Catalysts The generation of alcohol and hydrogen fuels, new petrochemical sources as well as enzyme isolation and utilization.

<u>Process and Equipment Design</u> - The design of new fermentation reactors, alternate batch processes, monitoring devices, instrumentation and other aspects of process engineering.

In this section, some of the activities described in Section I have been classified according to the aforementioned seven areas where biotechnology is seen to apply. However, since not all of the Section I listings lent themselves to this classification, the number of identified activities in Section II is less than Section I. Moreover some duplication of assignment amongst the categories has been necessary to ensure a more complete representation of the activities of an individual or group.

The numbering in this Section coincides with that utilized in Section I. For example U - 3(b) refers to the University sector, entry number three (University of Calgary) and J. W. Costerton. The reader is then directed to Section I for more detailed information.

### A. Waste Treatment and Pollution Control

G-3(a), G-6(c), G-6(d), G-8(a)

I-2(a), I-3(a), I-10(a), I-18(a), I-24(a), I-27(b), I-28(a), I-29(a), I-30(a)

 $\begin{array}{l} U-2(d),\ U-6(g),\ U-6(o),\ U-6(p),\ U-7(b),\ U-10(c),\ U-10(d),\ U-11(a),\\ U-14(a),\ U-15(c),\ U-16(a),\ U-17(a),\ U-17(i),\ U-20(a),\\ U-20(e),\ U-20(i),\ U-20(k),\ U-21(e) \end{array}$ 

### B. Raw Material Extraction and Preprocessing

G-2(a), G-11(a)

I-2(a), I-2(c), I-14(a), I-15(a), I-21(a), I-21(b), I-25(a), I-27(a)

U-3(e), U-6(j), U-17(b), U-17(d), U-21(i)

## C. Biomedical Product Development

G-4(a), G-4(b), G-6(b), G-6(d), G-7(c), G-7(d)

I-1(a), I-2(b), I-6(a), I-7(a), I-8(a), I-8(b), I-8(c), I-8(d), I-13(a), I-20(a), I-20(b), I-20(c), I-20(d), I-23(a), I-31(a), I-33(a)

 $\begin{array}{l} U-1(d),\ U-1(e),\ U-1(f),\ U-2(e),\ U-3(b),\ U-3(g),\ U-5(b),\\ U-6(b),\ U-6(d),\ U-8(a),\ U-9(h),\ U-10(e),\ U-10(f),\ U-15(d),\\ U-17(m),\ U-17(q),\ U-17(r),\ U-19(a),\ U-20(d),\ U-21(d),\ U-22(b) \end{array}$ 

### D. Food Production

G-5(a), G-7(a)

I-10(a), I-11(a), I-12(a), I-16(a), I-17(a), I-24(a), I-28(a), I-29(a), I-32(a)

U-2(c), U-6(f), U-6(i), U-6(n), U-7(a), U-11(a), U-14(a), U-15(b), U-15(c), U-17(c), U-17(e), U-17(o), U-18(c), U-20(a), U-20(e), U-20(i), U-21(f)

## E. Agricultural Improvements

$$U-4(a)$$
,  $U-4(b)$ ,  $U-6(a)$ ,  $U-6(c)$ ,  $U-6(1)$ ,  $U-6(m)$ ,  $U-7(c)$ ,  $U-9(d)$ ,  $U-11(c)$ ,  $U-11(d)$ ,  $U-22(d)$ 

## F. Fuels, Industrial Chemicals, Biochemicals and Catalysts

$$G-6(a)$$
,  $G-6(c)$ ,  $G-6(e)$ ,  $G-7(b)$ ,  $G-7(e)$ 

$$I-5(a)$$
,  $I-16(b)$ ,  $I-19(a)$ ,  $I-27(a)$ ,  $I-29(a)$ 

$$U-1(b)$$
,  $U-8(c)$ ,  $U-8(d)$ ,  $U-8(e)$ ,  $U-9(f)$ ,  $U-10(a)$ ,  $U-12(c)$ ,  $U-13(a)$ ,  $U-17(f)$ ,  $U-17(1)$ ,  $U-18(a)$ ,  $U-18(b)$ ,  $U-20(b)$ ,  $U-20(f)$ ,  $U-20(j)$ ,  $U-21(h)$ 

#### G. Process and Equipment Design

G-3(a), G-7(f)

$$I-4(a)$$
,  $I-14(a)$ ,  $I-22(a)$ ,  $I-26(c)$ ,  $I-27(a)$ ,  $I-29(a)$ ,  $I-30(a)$ 

$$U-1(c)$$
,  $U-2(c)$ ,  $U-3(c)$ ,  $U-9(a)$ ,  $U-9(g)$ ,  $U-10(d)$ ,  $U-12(a)$ ,  $U-12(b)$ ,  $U-17(g)$ ,  $U-20(c)$ ,  $U-20(g)$ ,  $U-20(h)$ ,  $U-20(1)$ ,  $U-21(g)$ 

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