National Biotechnology Advisory Committee

1985 Survey of Canadian Fermentation Industry and Facilities for Scale Up and Process Development

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> 1985 Survey of Canadian Fermentation Industry and Facilities for Scale Up and Process Development

Prepared for the National Biotechnology Advisory Committee by:



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INTRODUCTION

In Vancouver in March 1984, a report entitled "Survey of Canadian Fermentation Industry and Facilities for Scale Up and Process Development" was presented at the National Biotechnology Advisory Committee workshop on Engineering and Fermentation Aspects of Industrial Biotechnology. The present report is intended as a follow up study to the original report, and provides an updated assessment of biotechnological activity in the industrial, university and government sectors. The information contained in this report was collected through limited telephone, personal and site contacts, and is felt to provide a reasonably accurate assessment of the Canadian situation.

The report concentrates on three main topics: the identification of organizations involved in the industrial scale exploitation of biotechnological methods, the existence of pilot scale fermentation equipment in Canada and private/public sector and university R & D interests related to fermentation engineering and scale up.

As is the case with all surveys of this kind, it is very difficult to ensure that it is complete. Should the reader have any suggestions, additions or corrections to what is presented, please contact Andris Ortmanis of Diversified Research Laboratories, 1047 Yonge Street, Toronto, Ontario M4W 2L2. Information received will be recorded and used as a contribution for future updates of the report.

This report was prepared for the National Biotechnology Advisory Committee, as part of its continuing responsibility to assess biotechnological development in Canada, and to promote commercial biotechnology. For further information on the committee and its activities, please contact the secretary, Dr. David B. Shindler, 235 Queen Street, 8th Floor West, Ottawa, Ontario, KIA 1A1. (613) 990-6322 An inventory of industrial fermentation activity in Canada has been made, and the results are compiled in Table A.1 of Section A. Several different types of industrial scale fermentations exist, and not all are included in this list. For example, while it is recognized that the wastewater treatment industry represents by far the greatest application of biological processing on a large scale, the types of technology employed are quite different from those used in the production industries, and therefore excluded from the listing. However, processes which utilize a specific industrial effluent as a feedstock for the fermentation of a specific valuable product, such as that used by Ontario Paper Co., are included.

A secondary category of fermentation technology which does not appear in this compilation, involves fermentations carried out by breweries, alcoholic beverage distillers, wineries and dairy product manufacturers. These are well established industries in Canada, and for the most part, do not yet rely on highly technical, innovative fermentation processes. However for the sake of completeness, separate diagrams which document the distribution of these industries across Canada appear in Figures A.1 - A.4 of Section A. These diagrams are reprinted as they appeared in the previous 1984 report, as significant changes have not occurred in these industries in the past 18 months, except for the introduction of microbreweries, small scale privately financed brewing companies, in several provinces.

The listing compiled in Table A.1 is very similar to that presented 18 months ago, in that very few additions have been made. Thus, it consists primarily of fermentation industries producing yeast, fuel alcohol, alcohol for vinegar production, vinegar and dextran products. Two additions to this category are a vinegar manufacturer and a producer of alcohol destined for vinegar production.

Two major vaccine and fine biochemical compound producers in Canada are Connaught Laboratories and the Institute Armand Frappier. However, this listing includes an increasing number of small manufacturers producing a specific or limited range of products. This is demonstrated by the addition of Helix Biotech Ltd. and ABI Biotechnology to the list of companies such as Langford Laboratories, Research Foods, Rhizotech Laboratories, and Vetrepharm, which produce high value medicinal, veterinary, agricultural or diagnostic compounds.

INVENTORY OF THE CANADIAN FERMENTATION INDUSTRY (cont'd)

Three plants utilizing large scale immobilized enzyme/whole cell technology are currently operating in Ontario, producing high fructose syrup. Located in Port Colborne, London and Cardinal, they are a joint venture between John Labatt Limited and Canada Starch Company Limited and are operated under the name of CASCO Inc.

INVENTORY OF PILOT SCALE FERMENTATION FACILITIES

In establishing criteria for an inventory of Canadian fermentation pilot scale facilities, it has been assumed that the facility should be capable of providing an intermediate process capacity for the evaluation of technical and economic feasibility. Based on this premise, a minimum fermentation capacity of 100 L was used in the previous report, and has been accepted as a reasonable capacity for this follow up survey. The compilation of scale up facilities is presented in Table B.1 in Section B of this report. Additional information on the nature of the facilities was collected and is also presented. Both upstream and downstream processing capabilities of the facilities are indicated whenever this information was available, and a list of current/past projects, staffing and present status of the facilities is briefly summarized. It is often the case, especially in the fermentation of high value biomolecules, that a production facility may be the same scale or smaller than a 100 L facility. Thus, many "pilot scale" facilities serve as production facilities some fraction of the time, but to have redefined the scale of a pilot facility to below 100 L, would have resulted in a listing containing predominantly lab scale equipment.

R & D ACTIVITY RELATED TO FERMENTATION ENGINEERING

Table C.1 in Section C provides an indication of private sector and government activity in the area of fermentation engineering, while highlights of university projects which involve fermentation are summarized in Table C.2. The breadth of activity which has emerged over the past few years, indicates the rapid evolution of many R & D programs adopting the new technology. Section A. Canadian Industrial Fermentation Activity

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Table A.1 Industrial Fermentation Activity in Canada

FACILITY/LOCATION PRODUCTION INTERESTS ABI Biotechnology Produce high value medicinal products Winnipeg, Manitoba by fermentative processes for domestic/ export markets. Produce vinegar using packed generators Canvin Products Ltd. Wolfeville, N.S. and submerged process licenced from Frings, Germany. Toronto, Ont. Chatham, Ont. Saskatoon, Sask. Produce vaccines for domestic and Connaught export markets. Products include Laboratories tetanus, diphtheria, pertussis and Willowdale Ont. acellular pertussis vaccines prepared in 20 L - 1500 L batches. In-house R & D program with pilot plant scale up/production facilities. Dextran Products Ltd. Produce dextran, approximately 35 tonnes anually, in two 10,000 L Div. of Polydex fermentation vessels. Perform in-house Pharma Ltd. R & D to develop process and products. Scarborough, Ont. Produce yeast. R & D, product and Fleischmann Ltd. process development done either Montreal, Que. Calgary, Alberta in-house, or by parent company, Nabisco Brands Limited. Produce vinegar using classical packed Heinz Company Ltd. Leamington, Ont. generators and submerged process licenced from Frings, Germany, in 6000 gallon batches. Do in-house R & D on developing strain tolerance to vinegar, ability to use alternate substrates and faster fermentation time. Small scale producer of veterinary Helix Biotech Ltd. products and clinical diagnostic kits, Richmond, B.C. although not exclusively by fermentative techniques. The Institute Armand Frappier produces Institute Armand vaccines in 150 L - 190 L batches for Frappier domestic and export markets. In-house Laval, Quebec R & D program to develop fermentative transformation/synthesis capabilities.

Lallemand	Ltd.	The production of yeast for breweries,
Montreal,	Que.	bakeries, wineries and distilleries
		performed in 60000 L - 80000 L stirred tank fermentors. The addition of a
		150000 L vessel and two 2000 L vessels,
		has recently expanded both production
		and in-house R & D capabilities.
		Research centres on the development of
		wine yeasts, distillers yeasts and
		resistance of yeasts to cryogenic
		processing and ethanol.
Langford	Laboratories	Produce bactering and vaccines for

Langrord Laboratories Produce bacterins and vaccines for Guelph, Ontario veterinary applications. Products include rabies and distemper vaccines, which are batch fermented in new 250 L facility. Active R & D work in area of tissue culture.

Mohawk Oil Ltd. Minnedosa, Man. Converted old distillery to produce fuel alcohol using standard yeast fermentation technology. Produce 21000 L alcohol daily with ten 14000 L fermentors. R & D work centres on lignocellulytic technology development, upon which the alcohol process is based.

Northwest Food and Produce alcohol using standard yeast Fuels. Kerrobert, Echnology from distillers dry grains Sask. at 600 gal/day, primarily as feedstock for vinegar manufacturers. Will expand production capability in fall 1985 with addition of 7000 gallon fermentor. R & D work centres on process development with Saskatchewan type grains and reducing the fermentation times to increase productivity.

Ontario Paper Co. Fermentation facility producing 5000m³ Ltd. St. Catherines, alcohol annually from spent sulfite Ontario liquor of paper manufacturing process. Alcohol process operates at a loss, but is beneficial to downstream vanillin productions. Little R & D work on alcohol process - emphasis on paper production. Reinhart Vinegar Ltd. Produce vinegar using submerged process Stayner, Ont. licenced from Frings in Germany. R & D Ohambly, Que. work is carried out in-house, but also rely on process developments by group in Germany. Research Foods Small scale production of vomitoxin bownsview, Ontario standards with technology developed by

Rhizotech Laboratories Inc. St. Jean Crysostome, Quebec Produce <u>Rhizobium</u> for use as fertilizer on 2 L scale. Producer of "Frankia" bacteria used for nitrogen fixation in shrubs and land reclaimation operations. Involved in plant tissue culture for forestry service and developing production methods for microbial insecticide.

Agriculture Canada.

Rosell Institute Produce bacteria for dairy, food, St. Laurent, Que. hygenic and therapeutic uses. Also involved in R & D work on nitrogen fixing bacteria. Production and R & D fermentors include aerobic 2000 L and 1500 L vessels while have anaerobic 300 L vessel. Plans to supplement these with 1500 L vessel exist.

Schwartz Inc.Produce vinegar using packed generatorHalifax, N.Slicenced from Frings, Germany.Candiac, Que.

St. Lawrence Starch Produce 15000 USG/day potable alcohol Co. (97%) using standard yeast fermentation Mississauga, Ont. of starch/hemicellulose. Also involved in the sale of reactors for production of fermentable sugars, glucose and corn syrups.

Vetrepharm Inc. Produce bacterins and nutritional London, Ont. pharmaceutical hormone and vaccine preparations for veterinary use. Production runs are in small scale fermentation equipment, up to 10 L, and R & D work concentrates on development of commercial products as needs of veterinary care change.



FIGURE Al.1: Distribution of breveries by provinces



FIGURE A1.2: Distribution of wineries by provinces

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FIGURE Al.3: Distribution of potable alcohol distilleries by provinces.

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Section B. Pilot Scale Fermentation Facilities

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Table B.1 Existing Fermentation Pilot Scale Facilities

FACILITY/LOCATION/CONTACT	FERMENTATION EQUIPMENT	ASSOCIATED FACILITIES	COMMENTS
Alberta Environmental Centre Vegreville, Alberta A. Van Roodselaar	250 L instrumented fermentor with smaller support vessels. The batch vessel has micro- processor control capabilities.	DOWNSTREAM processing equip- ment includes electrical in- cineration of fermentor gaseous effluent, a filter press, centrifuge and a hammer mill.	Primarily a support facility for lab scale R & D work. Staffed by 3 biochemists, 2 technologists and a mech- anical engineer. Unavailable for private sector contract research under present admin- istrative arrangement.
Alberta Research Council Edmonton, Alberta M. Kole	Fully instrumented 1500 L batch stirred tank/airlift fermentor with instrumented 250 L and 150 L batch stirred tank fermentors. A 250 L airlift and two 150 L stirred tank fermentors will be on stream in the near future. Support fermentors (10) in 15- 28 L range now operating or in planning stages. Interface of major fermentors to VAX computer system for data-logging/process control.	UPSTREAM processing facil- ities consist of storage vessels (375-1000 L). DOWNSTREAM equipment in- cludes continuous centri- fuges, spray drier, lyoph- ilization unit and pilot scale gel filtration column capability.	The pilot facility has been constructed to maximize flexibility vital for con- tractual research and consul- ting services. A full ana- lytical laboratory services the unit. Current work centres on the development of ice inducing bacteria.
Bio-hol Developments Weston Research Centre Downsview, Ontario G.R. Lawford	Fully instrumented micro- processor control based 250 L, 400 L and 500 L stirred tank fermentors for batch and cont- inuous fermentations. Media sterilization/holding vessels with 1000 L and 3000 L capacities are convertible to fermentors.	UPSTREAM processing equip- ment include a biomass hy- drolysis extrusion system with centrifugal separation and purification equipment, filter press and evaporator. DOWNSTREAM processing con- sists of continuous centri- fugation, filter pressing, evaporation, ultrafiltration and reverse osmosis unit operations.	Pilot plant manned by Biotech- nology Department staff as required. Full lab scale R & D and analytical back-up facil- ities. Plant formerly used to demonstrate the production of fuel alcohol from biomass residues, but currently oper- ates intermittantly on in-house R & D projects. Contractual R & D pilot scale projects sought.

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FACILITY/LOCATION/CONTACT	FERMENTATION EQUIPMENT	ASSOCIATED FACILITIES	COMMENTS
Connaught Laboratories Ltd. Willowdale, Ontario K. Phillips	Several fully instrumented 150 L and 100 L stirred tank fermentation vessels.	UPSTREAM processing equip- ment consists of media prep- aration facilities, medium filter and autoclavable 400 L medium storage tanks. DOWNSTREAM processing equip- ment includes ultrafil- tration membrane facilities, continuous Dynamill for cell breakage, continuous centri- fuges and large scale column chromatography for protein separation/preparation.	Since the pilot facility is housed in the same area as the production facility, a containment area licensed for the production of bio- logical compounds for clinical trials limits the nature of pilot plant work in some cases. The unit is used exclusively as a testing facility for in-house R & D projects.
Envirocon Limited Vancouver, B.C. R. MacDonald	Fully controlled 1000 L and 10,000 L fermentors operable in batch or continuous mode. Specifically designed for both stirred tank and airlift fermentation modes.	UPSTREAM processing equip- ment consists of screening and continuous sterilization equipment while DOWNSTREAM processing equipment in- cludes rotating drum filter and rotating drum drier.	Equipment specifically designed for pilot scale evaluation of fungal SCP production from pulp mill sludge (cellulose), to provide product for feeding trials. Presently unused, it is available for contract research work.
Institute Armand Frappier Montreal, Quebec G. Vezina	Two 50 gallon (190 L) and one 150 L stirred tank fer- mentation vessels. These are fully instrumented reactors.	UPSTREAM processing facil- ities are limited to culture medium preparation equip- ment, but DOWNSTREAM pro- cessing has biomass separ- ation facilities.	Since the facility serves as both an R & D and production tool, strict security limit- ations imposed by the federal government on process equip- ment used to produce vaccines limits the use of the equip- ment. Available on contract with experienced operating personnel.
Iotech Corp. Ottawa, Ontario S. McGuire	Computer interfaced 2000 L and 200 L stirred batch fer- mentors.	UPSTREAM processing consists of lignocellulose degradation equipment. DOWNSTREAM sep- aration operations.	In-house R & D on production of sugars, alcohol and other chemicals from lignocellulosic feedstocks.
National Research Council Halifax, N.S. A. Taylor	250 L instrumented computer controlled stirred tank.	DOWNSTREAM processing equip- ment consists of filtration and extraction facilities, specifically designed for mycotoxin handling.	Facility used for vomitoxin standard production and for R & D in products for the agriculture industry.

FACILITY/LOCATION/CONTACT

National Research Council Ottawa, Ontario D. Armstrong

National Research Council Saskatoon, Saskatchewan J. Grootwassink

POS Saskatoon, Sask. D. Hrytzak 2600 L custom made stirred tank reactor with pH and temperature control with capability of aseptic operation.

FERMENTATION EQUIPMENT

batch fermentor with incipient

processor for central and data-

130 L batch/continuous instru-

plans to interface to micro-

Fully instrumented 250 L

logging operations.

mented fermentor.

ASSOCIATED FACILITIES

DOWNSTREAM processing capabilities include biomass harvest by continuous centrifugation, ultrafiltration apparatus and facilities for low temperature trapping of volatile components of the fermentation broth.

UPSTREAM processing equipment consists of wet and dry milling equipment and sieving equipment for grain preparation. DOWNSTREAM equipment consists of batch/ continuous centrifuges, UF filtration apparatus, spray drier, multiple effect plate evaporator, drum drier, homogenizer, pilot scale lyophilization apparatus and pilot scale pressure cooker.

UPSTREAM equipment consists of 6-8 wet mills for grain processing. The DOWNSTREAM equipment consists of 3 continuous centrifuges, filter press, spray, flash, microwave and tunnel driers, and lyophilization apparatus.

COMMENTS

The facility is used exclusively for collaberative projects on topics such as utilization of low alcohol waste streams and fermentation of fine biological products.

The centre's activity focuses on plant biotechnology, and the equipment is used for ongoing projects. The facility is manned by 2 Ph.D's and 4 technical staff, and is available to external users on a contractual basis.

This pilot scale research facility is provided to the client to aid scale up and production viability testing of processes. Although currently has limited fermentation capabilities, the acquisition of additional fermentation equipment is being considered. Facility operates at 100% capacity on contractual basis.

FACILITY/LOCATION/CONTACT	FERMENTATION EQUIPMENT	ASSOCIATED FACILITIES	COMMENTS
St. Lawrence Starch Co. Mississauga, Ontario P. Assarsson	Designed a 240 gal (900 L) batch reactor for yeast alcohol fermentation. Low instrument- ation. Smaller vessels for solid state fermentation.	UPSTREAM processing equipment consists of hydrolyzation unit. DOWNSTREAM equipment consists of screens, filter press and belt press.	Facility in 100% usage by in-house and contract R & D projects. Engineering/ microbiology consulting staff concerned with the hyrolysis of starchy sub- strates, pectin, hemicellu- lose and cellulose for ferm- entation to potable alcohol (St. Lawrence Starch) pro- duction. Have collaborated with POS on alcohol projects.
University of Alberta Dept. of Biochemistry Ecomonton, Alberta K. Iwonika	Instrumented 450 L batch fermentor.	DOWNSTREAM processing con- sists of a continuous cent- rifuge.	The facility is operated to produce approximately 40 batches/year of Escherichia <u>coli</u> for enzyme and other biomolecule isolation.
University of British Columbia Dept. of Microbiology Vancouver, B.C. D. Kilburn	Microprocessor controlled 150 L batch stirred tank fermentor.	DOWNSTREAM processing equip- ment consists of continuous centrifuge and ultrafil- tration units.	Activity in animal cell culture to produce lympho- kines and interferon. Work with cellulolytic organisms as well. NSERC Infrastruct- ure grant sought to provide full time staffing.

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FACILITY/LOCATION/CONTACT

University of British Columbia Dept. of Chemical Engineering Vancouver, B.C. R. Branion

University of Calgary Faculty of Science Calcary, Alberta M. Gaucher

University of Laval Dept. of Chemical Eng. Laval, Ouebec A. LeDuy

University of Ottawa Dept. of Biochemistry Ottawa, Ontario I. Altosaar

Universite du Ouebec a Trois Rivieres Trois Rivieres, Quebec M. Lapointe

FERMENTATION EQUIPMENT

Small aseptic (60 L) batch stirred tank/airlift fermentation vessel. Also open 150 gal (570 L) and three 35 gal (130 L) temperature controlled agitated fermentation tanks.

Instrumented 500 L batch stirred tank and microprocessor interfaced with instrumented 150 L vest by continuous centribatch/continuous fermentor with conversion to airlift capability. Smaller fermentor and support vessel facilities as well.

Two 1500 L batch stirred tanks with limited instrumentation. Not operated aseptically.

150 L batch/continuous instrumented stirred tank fermentor.

Open air 2200 L plastic stirred tank fermentor operating as activated sludge system, with associated control facilities. Both batch and continuous operation possible.

ASSOCIATED FACILITIES

DOWNSTREAM processing includes membrane filtration. flash evaporation and drum drier equipment.

DOWNSTREAM processing capabilities include cell harfugation, UF membrane filtration and cell disruption in homogenizer.

COMMENTS

Work has included high temperature agricultural waste treatment and lactic acid fermentation.

The larger fermentor used to produce cell batches. The 150 L vessel used in immobilized cell work and continuous penicillin production studies. Computer control studies in progress by L. Behie of Chemical Engineering Department. Equipment available on contractual basis to interested parties.

Developing non-aseptic fermentation processes with little upstream or downstream biomass processing.

Presently seeing little use. Formerly used by industrial clients but currently available on a contractual basis. Staffed by members of Biotechnology unit.

The facility is involved with spent sulphite liquor conversion to SCP, but seeks contractual R & D engagements.

centrifuge and pilot scale protein separation/purification unit.

DOWNSTREAM processing equip-

ment consists of continuous

UPSTREAM processing equipment consists of continuous sterilizer and DOWNSTREAM capabilities include continuous centrifugation and spray drying.

FACILITY/LOCATION/CONTACT

University of Toronto Dept. of Biochemistry Toronto, Ontario H. Lawford

University of Toronto Faculty of Medicine Toronto, Ontario M. Paull

University of Waterloo Institute for Biotech Res. Waterloo, Ontario M. Moo-Young

FERMENTATION EQUIPMENT

250 L stirred tank fermentor with basic control systems.

250 L stirred tank fermentor with basic control systems.

1200 L computer coupled airlift fermentor.

ASSOCIATED FACILITIES

DOWNSTREAM processing consists of continuous centrifuge.

UPSTREAM processing consists of a 200 L medium supply tank, and DOWNSTREAM processing consists of a continuous centrifuge.

UPSTREAM equipment consists of continuous sterilizer, feed preparation, holding and pretreatment tanks. DOWNSTREAM equipment consists of continuous centrifuge and drier.

COMMENTS

Fermentor used to grow cell batches as required by departmental staff and research associates.

Fermentation facility used to provide batches of organisms. One technician involved in this process.

Current work includes development of fungal SCP production from pulp mill sludge in cooperation with Envirocon. Facility operates at 50-60% usage and is staffed by fermentation and computer technicians and academic staff. Used as teaching facility within university, but available for contract use.

University of Western Ont. Faculty of Engineering Science London, Ontario A. Margaritis Two 1000 L batch/continuous stirred fermentors. Plans to scale up existing 26 L airlift vessel to 250 L or 1000 L are possible. UPSTREAM processing equipment includes mill for cellulosic material degradation. DOWNSTREAM equipment consists of continuous centrifuge, ultrafiltration units and homogenizer. Intermittent work on the continuous fermentation of ethanol by immobilized yeast. Production of biosurfactants studied. Cyclosporin A fermentations conducted in airlift fermentation equipment. Available for use on contractual basis.

Equipment originally at the Technical University of Nova Scotia where the yeast production of fuel alcohol from waste potato starch was investigated. Currently seeking commercialization opportunities.

Woodside, R. Halifax, N.S. Custom built 125 L airlift fermentor with basic instrumentation.

PROPOSED PILOT SCALE FERMENTATION FACILITIES

ORGANIZATION/LOCATION	PROPOSED FACILITY
ABI Biotechnology Winnipeg, Manitoba	Plan 6000 ft ² facility with 10 L, 20 L, 150 L and 500 L fermentation vessels. Down- stream processing would con- centrate on pilot scale protein purification facilities - column chromatography. Fermentation on line in Fall 1986.
Agriculture Canada Ottawa, Ontario	Intended to provide industrial clients with an opportunity to draw on expertise and facil- ities of planned Food Research Institute in Ste. Hyacinthe, Quebec. Will have 1500 L, 200L, 150 L and 20 L computer controlled fermentation appara- tus with upstream UHT process- ing and 600 L media storage facilities. Proposed down- stream facilities would include continuous centrifuge, homo- genizers and protein separation columns.
Allelix Inc. Mississauga, Ontario	Currently writing specifi- cations for pilot facility which is to include 200 L airlift and 1000 L tank fer- mentor. These facilities will be designed to meet the production requirements of specific compounds.
Cangene Corp. Mississauga, Ontario	Plan to acquire a fully instrumented 120 L fermentor which would support on-going research projects.
Fermtech R&D Inc. Mississauga, Ontario	Plan to occupy 4000 ft ² pilot/ testing/production facility with instrumented 500 L stirred tank fermentor, for probiotic production.

Forintek Canada Corp.Plan to supplement facilitiesOttawa, Ontariowith a 100 L fermentation pilotplant.Upstream processing toinclude steam explosion gun.

PROPOSED PILOT SCALE FERMENTATION FACILITIES

ORGANIZATION/LOCATION

National Research Council Montreal, Quebec

PROPOSED FACILITY

The Biotechnology Research Institute is in the process of selecting and designing equipment for its pilot plant. Will have 1500 L stirred tank fermentor and several fementors in range of 100 L - 1000 L. Planned upstream processing facilities include grinders, mixers and continuous sterilizers while downstream equipment to consist of continuous centifuges, filters, UF/RO membrane filters and driers.

Pulp and Paper Research Institute of Canada Pointe Claire, Quebec

University of British Columbia Vancouver, B.C.

University of Western Ontario London, Ontario The PPRIC plans to develop facility to complement lab scale facility. Investigating 75-100 L scale vessels with undetermined schedule to acquire 250 L fermentation capacity.

The Campus of the University of British Columbia is the site for the construction of a \$31 million biotechnology facility, \$8 million of which is slated for pilot plant construction. Unit will be designed for medicinal product synthesis i.e. lymphokines, interferon.

The University of Western Ontario has plans to construct 250 L or 1000 L airlift fermentor for scale up studies.

Section C. Government Organizations and Private Sector Companies Involved in Fermentation R & D Activity

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Table C.1Private/Government Biotechnological andFermentation Activities

COMPANY/LOCATION

BIOTECHNOLOGICAL INTERESTS

- ABI Limited A new biotechnology company currently Winnipeg, Manitoba involved in the fermentation and purification of biological molecules such as Interleukan-2. Also produce human blood clot factor-VIII. Have in-house fermentation R & D program, and accept contract research work. A fermentation pilot facility is planned.
- Agriculture Canada Involved in a wide range of agricul-Ottawa, Ontario tural biotechnology. Research and Ste. Foy, Que. development interests include waste Ste. Hyacinthe, utilization to produce ethanol, Que. flavours and other metabolites, membrane process for nitrogen fixation, plant breeding, the development of gene transfer techniques, plant cell culture to produce flavours and enzymes and mycotoxin and SCP production. Also interested in fermentation of lactic acid, specific enzymes and fermented food products. Pilot plant facilities are under construction in Ste. Hyacinthe, by the Food Research Institute.
- Alberta Environmental The Alberta Environmental Centre Centre conducts research for the Alberta Vegreville, Albta. provincial government and ARC. Now 5 years old, it currently concentrates on wastewater technology, involved primarily in decolourization and deodorization of municipal and pulp mill effluent. The microbiology of fungal processes is also investigated. They have a pilot scale fermentation support facility in-house.

Alberta Research Council Edmonton, Alberta The Alberta Research Council undertakes work in three broad areas; fermentation technology and scale up, plant cell culture and crop cold hardiness improvement and genetic engineering. The first fermentation scale up project in a new pilot plant facility is the production of an ice inducing bacteria. Crop frost tolerance work is being conducted on wheat and alfalfa plants using tissue culture techniques. The genetic engineering work to date has been a joint project with Biologicals, and involves the synthesis of vectors for gene transfer in yeast and bacteria. Some gene cloning work is also on-going.

Allelix Inc. Mississauga, Ont. Active in the development of diagnostic reagent kits, plant and animal cell culture research, and the development of fermentative processes to produce high value biochemical compounds. Currently operating on lab scale capacity with computer interfaced equipment, but plan to scale up to pilot scale production in in-house facility.

B.C. Research Biotechnological interests span Vancouver, B.C. several areas of application. Have over 30 years of experience in biohydrometallurgy and biological leaching of ores. These projects involve industrial research contract Also involved in production of work. biological polymers for tertiary oil recovery, methanation of residual hydrocarbons in spent oil reservoirs and production of biopolymers from methanol. Produce test kits for aquaculture and produce carotinoid containing yeasts as aquaculture feed. Also involved in microbial treatment of leachate, pulp and paper industry wastewater and oil refinery effluent.

Cangene Corp. Mississauga, Ont. Cangene conducts contractual development of proprietary, product independent expression systems using recombinant DNA, genetic engineering and applied and industrial microbiological techniques. Work relates to products in the food and medicinal areas, the latter being composed of enzyme, antigen and secondary metabolite production. Small scale in-house fermentation system is planned to be supplemented with 120 L batch/continuous facility.

Centre de recherche The Centre de recherche industrial du industrielle du Quebec has an in-house R & D program Quebec investigating the fermentative production of biofungicides, biopesticides Ste. Foy, Que. and polyols. Involved in fermentor and immobilized fermentor design and development. Additional on-site projects include the production of methane from animal wastes as well as anaerobic digestion systems and materials.

ConnaughtInvolved in the production of
vaccines for the domestic and exportLaboratoriesmarkets. Research work centresWillowdale, Ont.on the development of production
systems for human insulin and carrier
hapten vaccines. Have R & D
fermentation facilities as well as
production facilities.

Forintek Canada Corp. Centres on the conversion of ligno-Ottawa, Ont. Cellulosic material into solvents and fuels such as butanol, butanediol, acetone and ethanol. Future plans include the possibility of complementing existing laboratory fermentation facilities with pilot scale equipment for economic and technical feasibility studies. Institute Armand Frappier Montreal, Que. The Institute Armand Frappier conduct research into the production of microbial enzyme complexes. They have a pilot scale facility to complement their R & D fermentation lab scale work. Currently involved in a wood to ethanol bioconversion project. Accept research contracts to conduct basic R & D projects or feasibility studies for external clients.

Iotech Corp. Conduct in-house R & D work on the con-Ottawa, Ont. version of lignocellulosic material to fermentable sugars, alcohol and other chemicals. Have pilot scale fermentation capabilities.

John Labatt Ltd. R & D work centres on genetic manipul-London, Ont. R & D work centres on genetic manipulation of brewing yeasts, to develop alcohol tolerance and temperature resistance characteristics. Yeasts with alternate substrate specificities and increased amylase levels are also investigated. Scale up of brewing processes possible in specialized in-house pilot facility.

Lallemand Inc. Montreal, Que. Conduct applied R & D program in-house aimed at the production and development of yeast strains for both domestic and foreign breweries, wineries, distilleries and bakeries. Investigate yeast resistance to freezing and tolerance to ethanol among other projects. Have pilot facility in which to study different fermentation control strategies before implementing these on production lines.

National Research The National Research Council is Council involved in R & D work centring on Halifax, N.S. vomitoxin and its derivatives and the study of isocyanide metabolites in fungi. Pilot plant facilities complement the lab scale fermentation work. National Research Council Ottawa, Ontario The National Research Council conducts work in various areas, including nitrogen fixation and anaerobic waste digestion. Current work centres on the conversion of low alcohol waste streams into higher value ester and aldehyde solvents, and the fermentation of high value biological compounds.

National Research Council Montreal, Que. The National Biotechnology Institute have formed a bioprocess engineering group, and will be equipping themselves with state of the art fermentation facilities.

National Research The Plant Biotechnology Institute, Council has a diverse research program in Saskatoon, Sask. several areas of herbarian studies. The Plant Product Technology group has three major interests, alkaloids from cell culture, crop quality improvement and enzyme technology such as yeast lytic enzymes, inulase, lactase and oxoprolinase. The genetics, physiology and fermentation of alkaloid containing plants such as Catarantus roseus (Periwinkle) have been investigated, as has enzyme production, by employing plant suspension tissue culture.

Nova Husky Research Involved in petroleum microbiology. Corp. Calgary, Research interests include Alberta biodegradation, bacterial corrosion of metals and biological in situ agents for enhanced oil recovery. Plan to develop extensive fermentation program with methanol feedstocks.

Ontario Research The Ontario Research Foundation was set Foundation Up to perform lab scale contract Mississauga, Ont. The ontario Research Foundation was set up to perform lab scale contract research work. Expertise lies in alternate fuels from biomass, the production of fermentable substrates from wastes by wet oxidation, the recovery of fermented products from fermentation broths and the microbial leaching of ores.

Pulp and Paper Research Institute of Canada Pointe Claire, Que.	The Pulp and Paper Research Insitiute of Canada has recently constructed an addition onto its existing facilities, specifically for the Biotechnology Group. In-house R & D concentrates on the enzymology of lignin degradation and enzymatic means to increase the strength of mechanical pulps. Some recombinant DNA work done in-house. Plans for a 250 L pilot fermentation facility are in progress.
Roselle Institute Montreal, Que.	The Roselle Institute under Rougier Inc. conduct in house R & D on bacterial strain development. Recently involved in nitrogen fixing bacterial studies. Have pilot/production scale facilities for lab work scale up.
St. Lawrence Starch Co. Mississauga, Ont.	Conduct in-house research centred on the yeast digestion of starch and hemicellulose and the production of potable alcohol. Operate a versatile 250 L batch fermentor and pilot facility as integral part of this R & D commitment.
Wastewater Technology Centre Environment Canada Burlington, Ontario	Work centres on anaerobic digestion of high strength, high temperature industrial effluent. In-house evaluation of effluents performed before design of "in situ" treatment facilities.
Weston Research Centre Div. of George Weston (Diversified Research) Toronto, Ontario	Conduct biotechnological R & D program concentrating on food, pulp and paper and energy industry applications. Current work involves microbial exo- polysaccharide and microbial lipid fermentation and the conversion of waste streams to higher value biological products. Formerly involved in the Bio-hol demonstration of fuel alcohol production from biomass residues. Full pilot plant facilities available.

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Table C.2Highlights of University Biotechnology R & DActivities Which Involve Fermentation Engineering

McGill University A multidisciplinary biotechnology group Montreal, Que. has been set up within the University. The Department of Chemical Engineering (B. Volesky, R.J. Neufeld, D.G. Cooper, W.I. Patterson) are engaged in the development of the acetone butanol ethanol (ABE) fermentaion, the production of microbial surfactants, the development of immobilized enzyme reactors and the development of biosorbants. Dr. T.M.S Chang of the Department of Artificial Cells and Organs is actively involved with enzyme immobilization systems, particularly encapsulation in artificial membranes. Dr. D.P Verma of the Department of Biology works on symbiotic nitrogen fixation and the molecular genetics of both the host plant and the bacterial component.

> The Department of Chemical Engineering, (A. Daugulis, D. Bone, M.F.A. Goosen, R.H. Clark) is involved in research work covering the following topics: design and scale up of immobilized whole cell reactors, enzyme and solvent production by multistage fermentation, extractive fermentation, fermentation of DNA recombinants, and the encapsulation of animal cells. Fermentation work is generally performed on a laboratory scale, but 70 L fermentation capability exists. The Department of Microbiology, (A.M.B. Kropinski) is involved in strain and fermentation medium development for the ABE (acetone, butanol, ethanol) fermentation.

Queens University Kingston, Ont.

University of British Columbia Vancouver, B.C.	The University of British Columbia has significant involvement in biotechnololgical R & D work. The Department of Microbiology (D.Kilburn) does work in animal cell culture to produce interferon and lymphonkines, and conducts genetic engineering on cellulolytic organisims. R. Branian of the Department of Chemical Engineering is involved with high temperature agricultural waste digestion and plant cell culture. The Department of Chemistry (J. Kutney) is involved in plant tissue culture for anti-cancer agents, fungal fermentation of pulp and paper wastes to produce oral contraceptive ingredients and research into biobasin development (environ- mental technology). A \$31 million complex including a pilot fermentation facility will be built on campus for medicinal bioproduct R & D.
University of Calgary, Calgary, Alberta	The Department of Biochemistry (M. Gaucher) and Chemical Engineering (L. Behie) conduct research into the production of monoclonal antibodies and the continuous production of penicillin as well as the computer control of these operations. They have also recently run immobilized cell systems in their pilot scale fermentation facility.
University of Laval Quebec, Que.	Production of algae in photobioreactors and anaerobic digestion of algae to biomass are the R & D interests of A. Leduy. Work also centers on cellulase production.

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University of Toronto H.G. Lawford of the Biochemistry

Toronto, Ontario

Department is involved in small scale continuous culture research under contract to the food industry. The Plant Biotechnology Centre of the Botany Department (N. Straus, F. Dicosmo) are involved in small scale plant tissue culture, extracting secondary metabolites with medicinal value. The Department of Chemical Engineering (M. Wayman) is involved in the fermentation of lignocellulosic wastes to fuels.

Universite de Quebec a Trois Riveres Trois Riveres, Quebec

University of Waterloo, Waterloo, Ontario biomass production from spent sulfite liquor in their own 2200 L open stirred tank reactor. The Institute for Biotechnological

The Pulp and Paper Research Centre (M. Lapointe) has long been involved with

Research (M. Moo-Young) conducts research in fermentation and enzyme technologies, with a pilot plant support facility. Work is done to develop new biological processes with regard to waste management.

University of Western Ontario London, Ontario The Department of Chemical and Biochemical Engineering (A. Margaritis, N. Kosaric) has research interests in fuel ethanol, cyclosporin A and hydrogen production. Other R & D interests include immobilized cell technology, bioreactor design, thermostable cellulases and wastewater treatment. Pilot plant facilities. Section D: List of Organizations Contacted

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