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A PROGRAM FOR THE
INDUSTRIAL PROMOTION
OF BIOTECHNOLOGY IN LATIN AMERICA

Report to UNIDO

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March, 1990

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INTRODUCTION

In line with the "Regional Cooperation Programme for the Industrial Recuperation of Latin America and the Caribbean" and following the general guidelines of the Operational Plan for the Promotion of Biotechnologies presented to GRULAC , a survey has been carried out into the current state of bio-industry in Latin America, its principal technological and mercadological strengths and weaknesses. This survey can be found in Annexes I and II.

The central part of the current document will be concerned with the presentation of a unified group of three action proposals. Given the variety of the weaknesses of bioindustrial development in the region our proposal aims to take into account four types of criteria:

- a) the objectives indicated in the "Regional Cooperation Programme" in paragraphs 7 and 9 , particularly those related to the need to increase international contacts with small and medium enterprises, entrepreneurial renovation, and association with foreign firms for industrial and technological renovation;
- b) the need to identify **specific niches** within this general context of multiple deficiencies which have a strong multiplying impact. In particular our aim is to **avoid the replication** of actions being undertaken by other international agencies whether in the field of scientific training, support for scientific and technological research, cofinancing of projects, incentives for the development of venture capital, and other initiatives which already count on some type of support;
- c) that the proposals should have the support of national institutions, particularly business associations committed to participate in the financing of initiatives;
- d) institutional support for the proposals should have an explicit cut-off date , by which time the activities should be self-sustaining.

Within the context of these four criteria therefore we propose three projects:

1. "Information and Support for Bioindustrial Investment".

2. "Training of Bioindustry Promoters".

3. "Industrial Extension of the Regional Biotechnology Programme".

The first project is entirely new and innovative as is the second which largely complements the initial project. The third project aims to provide a new orientation, that of industrial application, to the scientific and technological effort developed by the Regional Biotechnology Programme.

Finally we should note that , given the multisectoral character of biotechnologies, this proposal could establish an important interface with actions in other sectors, particularly agrofood.

PROJECT NO. I
INFORMATION AND SUPPORT FOR
BIOINDUSTRIAL INVESTMENT

A - CONTEXT

In the process of carrying out the information survey for the Report it became clear that a basic initial obstacle to the elaboration of an adequate diagnosis on the state of biotechnologies in Latin America is the lack of appropriate and up-dated information on the supply and demand for technology and products in the different countries of the region. This is a problem experienced both by would be investors, businessmen in the sector and those responsible for public promotion policies.

The existence of relevant information is a basic precondition for identifying the technological, industrial, and commercial needs and potential of the continent. We propose therefore the creation of Information and Promotion Centres which will function as continuously updated data banks, counting on specialised staff capable of providing the necessary support to technologists and entrepreneurs and linked on-line to other countries in the region and with the North, generating a system of intra- and intercontinental exchange.

The creation of Information and Support Centres for Biotechnology has the following objectives:

- 1) Generate a mechanism for the permanent supply and creation of opportunities without substituting for the investor or promoting artificial industrial projects.
- 2) Produce precise and up-dated information on technologies and products offered or required, including costs and commercial availability.
- 3) Place such information at the service of interested groups in each country and abroad.
- 4) Create an intra-Latinamerican information network.
- 5) Connect this network up to similar structures in the advanced countries.

The national data banks should be permanently updated so that the information has real commercial value, including aspects of relevance to potentially interested foreign investors, such as general investment climate, regulations on industrial property. It is fundamental therefore that the Information Centres should have a solid support infrastructure with qualified personnel to attend demands from abroad.

During the initial years of the system's implementation a broad information campaign should be mounted through the organisation of seminars with national and foreign business interests, and wide dissemination of the system's existence should be guaranteed

in the specialised Journals.

Once fully functioning the system should be self financing but not profit seeking, with payment for services ensuring its overheads.

B. PROJECT JUSTIFICATION

The formation of an intra and intercontinental information network will allow for the identification of investment opportunities and promote a vision of the regional market as a whole thereby permitting agreements on a subregional or even continental scale. The existence of Information and Support Centres would similarly permit the presence of small and medium foreign firms without the financial means to ensure the necessary information on the regions markets.

While this project aims to stimulate the modernisation of the continent's bioindustry, particularly investment in technological development and technology transfer, the Information Centres will equally promote trade which , in testing the market, represents a first step towards investments and joint ventures.

All the countries who participate in the System , which could be called **INFO-BIO-LAT**, will be beneficiaries in an initiative which should result in an increasing attraction of national and foreign investment to the bio-industry sector.

C. INSTITUTIONAL FRAMEWORK

Biotechnology business associations which have been set up in Latin America in recent years (Brazil, Uruguay, Argentina, and Mexico) or are in the process of formation (Chile, Andean Pact) are the ideal institutional base for hosting the Information and Support Centres.

Business associations have a continuity in time and autonomy in the generation and administration of resources which government bodies often do not possess. The existence of such associations is at the same time a symptom that the country has established a certain critical mass in the area. In certain cases regional rather than national Centres may be preferable (Andean Pact countries, Central America).

In the case of the advanced countries participating in the project, their respective associations of biotechnology enterprises could likewise provide the counterpart institutional base.

D. COORDINATION ARRANGEMENTS

The decision to create a Latinamerican Federation of Biotechnology Industry Associations (**FELAEB**), taken in October

1989 at a meeting organised by the BIO-RIO with the help of the UNDP, provides the projects with both a national and a regional bases of support. Alongside the national association the FELAEB could become the principal interlocutor with the UNDP in directing and evaluating the project.

E. DEVELOPMENT OBJECTIVE

The creation of a permanent mechanism for the exchange of information and support for firms and groups interested in the technological, industrial and commercial potential of biotechnologies in Latin America.

F. INTERMEDIATE OBJECTIVES , OUTPUTS AND ACTIVITIES

- 1) The creation of a support system for bio-industrial investment in the principal countries of the regions, or at the level of subregions, which will be interlinked between all the countries of the continent.
- 2) The linking of this system with correspondents in the advanced countries.

G. ACTIVITIES

1. The first year of the project should involve the selection of one country for the implementation of a pilot experience. We would propose that Brazil is the most adequate country for initiating the project since it possesses an already consolidated Biotechnology Business Association, has developed a first experiment in data bank organisation (SINBIO), has offered its services to the project (see Annex III), and is an attractive option for the advanced countries because of its size and potential.

1.1. This first Centre should define the different types of relevant information, their form of organisation and programmes to be used, together with the telecommunications system which will serve as a support for the system as a whole. From the outset there should be an interchange of information and ideas with the other future Centres and correspondents outside of the region, to determine the type, format, and most adequate system for the circulation of information. (Four months).

1.2. Once the technical parameters have been established a systematic survey of data will be undertaken after which the data bank will be permanently updated. (Six months).

1.3. The data bank will then be connected to terminals located in regional centres (possibly the principally State-based Biotechnology Poles).

1.4. At the end of the first year, and on the basis of careful preparatory work, the Information and Support Centre will be connected to a similar Centre located in a developed country.

2. On the basis of the Brazilian experience three further Centres will come into operation as regional poles: Argentina (Southern Cone - Uruguay, Paraguay, Chile); Mexico (Central America and the Caribbean) and the Andean Pact.

2.1. The creation of these three poles will follow a similar dynamic to the establishment of the first Centre. On the basis of the criteria previously established the data banks will be fed first with national and sub-regional information. (Six months).

2.2. Subsequently the different Centres will be linked up with each other and with correspondents from the developed countries.

GRAPHICAL REPRESENTATION

National Terminals	Information and Promotion	Centres in the Advanced Countries
Uruguay ← - - - Chile ← - - -	→ Argentina ↑ ↓	← - - - - - - - →
State-level Units ← - - -	→ Brazil ↑ ↓	← - - - - - - - →
Central Amer. & Caribbean ← - - -	→ Mexico ↑ ↓	← - - - - - - - →
Andean Countries ← - - -	→ Host Country ↑ ↓	← - - - - - - - →

3. Once the system is fully established in the third and fourth years, its functioning can be tested and promotion and dissemination activities developed (24 months).

3.1. A survey will be carried out among the users of the system to detect limitations, problems and the potential for improvement.

3.2. A publicity campaign will be developed among potential users of the system, including national and international meetings with institutions and firms either interested or able to divulge the services offered by the systems.

3.3. An evaluation will be carried out based on users of the system by a consultancy agency contracted for this purpose.

3.4. From the fourth year on services will be charged, with the resources being used to finance the system without however the objective of generating a profit.

B U D G E T

BUDGET FOR SETTING UP THE LATINAMERICAN SYSTEM

(UNIDO support does not include participants from outside the region).

1st Year (US\$)

Consultants

General Coordinator (part-time)	3.500 x 12	42.000,00
National Expert	2.500 x 12	30.000,00
Travelling Coordinator		8.000,00
Expert in Informatics		12.000,00
Travel - data collection		5.000,00

Equipment

Computers/Soft/Fax		30.000,00
Regionals terminals/Fax	3.000 x 5	15.000,00

Miscellaneous

Telecommunications		3.000,00
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Sub-total		145.000,00
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2nd Year (US\$)

Consultants

General Coordinator	3.500 x 12	42.000,00
National Experts	4 x 2.500 x 12	120.000,00
Local Informatics Experts	3.000 x 3	9.000,00
Travel - General Coordinator		16.000,00

Equipment

3 Computers/Soft/Fax	30.000 x 3	90.000,00
14 Terminals/Fax	5.000 x 14	70.000,00

Miscellaneous

Telecommunications		24.000,00
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Sub-total		371.000,00
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3rd Year (US\$)**Consultants**

General Coordinator (part-time)	3.500 x 12	42.000,00
National experts	4 x 2.500 x 12	120.000,00
Travel - General Coordinator		12.000,00

Miscellaneous

Telecommunications		36.000,00
Publicity/Dissemination		12.000,00

Sub-total		222.000,00
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4th Year (US\$)**Consultants**

General Coordinator (part-time)	3.500 x 12	42.000,00
National experts	4 x 2.500 x 12	120.000,00
Travel - General Coordinator		12.000,00
Project Evaluation Mission		25.000,00

Miscellaneous

Telecommunications		36.000,00
National & International Meetings		75.000,00

Sub-total		310.000,00
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General total		1.048.000,00
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Budget (National Contribution)

Each country hosting a Centre should commit itself to the following expenditures:

1. Premises.
2. Computer Operator.
3. Costs relating to periodic collection of data (after the completion of the basic survey).
4. Administrative support structure for the Coordinator of the Project and the National Expert.
5. Continuation of the Project once ended the four year institutional support period.

ANNEX 1

BIOTECHNOLOGY IN: BRAZIL
ARGENTINA
URUGUAY
CHILE

This Annex was compiled in collaboration with Dr. John Wilkinson and is based on personal interviews, bibliography, and material gathered at international conferences. The names of the persons who have contributed specifically to the report are indicated in each country study.

BRAZIL - BIOTECHNOLOGY PROFILE

Brazil was one of the first developing countries to elaborate a national biotechnology programme. With the end of the military regime in 1985 Science and Technology policy was raised to ministerial status. Funding, while a long way short of developed country parameters has been far healthier than in the rest of the Southern Cone countries, averaging some 0,8 of the GNP.

Differently from Argentina and Uruguay also, special financing exists for the commercial promotion of biotechnology. Institutionally, support for science and technology is divided at Federal level between three organs. The National Research Council (CNPq) is responsible for funding training and basic research. Biochemistry would seem to be the strongest of the relevant disciplines with 300 researchers and 18 Doctorates per year, followed by Genetics and Microbiology. Molecular Biology is critically weak, as also Virology and Parasitology. In addition to problems of equipment and laboratory material, there is a need for special initiatives to break the vicious circle of a lack of high level researchers in key areas to form the necessary critical mass. International cooperation, in the form of a variety of training initiatives, is currently being negotiated to tackle this problem.

The Financing Body for Studies and Projects (FINEP) is responsible for more applied research and development. and administers the bulk of funding via the Programme for the Support of Scientific and Technological Development (PADCT).

And finally the National Economic and Social Development Bank (BNDES) opened a line of special credit for biotechnology industrial projects. This however was closed in 1989.

The five year PADCT programme was budgetted at US\$42,6 million. By the end of 1988 however a little under US\$13 million had been allocated. These funds were administered basically by the CNPq and the FINEP. While according to the Programme some 75% of the funding should go to training, in fact two thirds of the resources were applied in research and development projects by

the FINEP.

Since 1984 the FINEP has allocated US\$6 million to 54 biotechnology projects in agriculture. 15 of these were for biological nitrogen fixation, 13 for seed improvement, 10 for the control of phytopathogens, and 10 for the improvement of vaccines. In the health field the FINEP has financed some 57 projects since 1979 to the value of US\$13.3 million. Over half of these resources involving some 40 projects were directed to the pharmaceutical industry. Areas supported included monoclonal antibodies and reagents for diagnostics, enzyme and protein research, together with training in genetic engineering techniques.

For its part the BNDES has allocated US\$25.5 million to four leading firms involved in biotechnology, two in agriculture (AGROCERES, BIOMATRIX), and two in health (BIOBRAS, CIBRAN), with a further application by VALLEE NORDESTE, also active in the health field, under consideration. This credit line was suspended however in 1989.

In addition to these Federal resources, biotechnology activity receives an important boost from State financing particularly in São Paulo, via the Secretary for Industrial Technology, but also in the southern States in the promotion of biotechnology poles.

While initially the National Biotechnology Programme essentially supported whatever existed in areas relevant to biotechnology, strategy has now shifted to the promotion of multidisciplinary and multiinstitutional research and development geared to a closer articulation of public and private actors. This orientation has crystallised in the promotion of Biotechnology Poles, the first of which was developed in the State of Minas Gerais. Similar Poles now have now been consolidated in the Southern States, São Paulo and Rio de Janeiro.

The BIORIO initiative deserves specific mention, involving the consolidation of a University-Industrial complex within the campus of the Federal University and equipped with an incubator for the testing and development of up to 22 industrial projects in conjunction with interested firms. Two firms have already established themselves in the complex. BIO has also the participation of FIOCRUZ, the principal centre for public health research, development and production, thereby complementing university expertise in agricultural biotechnology. FIOCRUZ is now developing vaccines and diagnostic kits using genetic engineering and monoclonal antibody techniques for the following diseases - Hepatitis B and meningitis. In addition it has now been awarded a US\$20 million grant from the Panamerican health Organisation (OPAS) and designated the Latin American Centre for Genetic Engineering Research into new vaccines for endemic diseases.

In São Paulo two major biotechnology poles have emerged around the São Paulo (USP) and the Campinas Universities. The USP Centre has some fifty researchers involved in 30 projects and among its major results to date is the creation of a culture medium by microbial fermentation which it is claimed will economise millions of dollars in imported nutrients. A "processing

privilege" claim has now been made to the National Institute for Industrial Property (INPI), a juridical mechanism for guaranteeing production rights. Other projects include the development of national techniques for the production of insulin using yeast and the isolation of bacteria responsible for the deterioration of latex. The Centre also serves as a pole of attraction for the Butantã which is the second major public health research centre and principal producer of serum with an annual production of 400,000 ampoules. The Butantã is now developing vaccines for poliomyelitis and tetanus using genetic engineering. The Butantã in its turn has created a Centre for Health Biotechnology and one of its major projects is the production of albumin, a protein obtained from human placenta which may substitute for blood transfusions. A further target is the production of purified factor 8 which would eliminate blood transfusion risks for haemophiliacs.

Also associated to the USP Centre is the São Paulo Institute for Technological Research (IPT) which has its own biotechnology programme. The Institute has a long history in fermentation and digestion technologies, receives strong support from the São Paulo Secretary for Industry and Trade, and has a successful record in commercial appropriation of research results. Involved for over twelve years in the Proalcohol Programme the Institute is now researching flocculating yeasts in continuous fermentation processes. In addition to alcohol, the IPT is developing the fermentation phase of vitamin C production using domestic microorganisms and raw material. Anaerobic digestion technology has now been transferred to a number of firms in beer and soft drinks production, in addition to the public of the Proalcohol. This technology is now being extended to waste treatment in a broad range of agroindustrial activities -slaughter houses, vegetable oil processing, the milk industry, paper and cellulose. Priorities for research at the IPT are based on the potential for commercial application, and in the case of enzymes attention has been given to amilases (beer, bread making), invertases (which hydrolyse sugar syrup for the soft drink industry), lactases (milk), proteases (protein processing), pectinases (fruitjuices) and cellulases (hydrolysis of sugar cane). Research into biodeterioration has similarly wide industrial applications (leather, paints, paper, textiles, packaging, plastics, adhesives, wood products). In the area of natural products, research which has included wax from sugar-cane, sweeteners from Stevia, is now directed to the study of marine algae (extraction of commercial inputs). These different research activities are supported by a microbiology sector which is developing a bank of microorganism strains and studying processes of contamination in fermentation processes.

The Industrial Technology Foundation (FTI) which specialises in the development of technology for transfer to industry also works closely with the USP. Long active in manioc alcohol research, the FTI has recently established a Centre for Biotechnology and Chemistry with support from FINEP. In its traditional area the FTI is now researching into the production of high quality alcohol from tuberculars to develop international competitiveness in perfumes and drink, and is looking for a partner for the production from its pilot project. Research into the hydrolysis

of manioc has led to priority for research into the transformation of lignocellulosic material. The microorganism *Phanerochaete chrysosporium*, which produces enzymes for lignine has been imported from England. Research into the genetic manipulation of microorganisms is currently being developed in conjunction with the Chemistry Institute of the USP.

The University of Campinas UNICAMP in its turn has developed a Biotechnology Programme involving natural products, biological tests and standards, molecular biology, and food. An interdisciplinary structure has been established for systematic research into the economic and particularly medicinal properties of Brazilian plants. International training agreements have been reached with universities in England, the USA, and Belgium, and contacts established with Germany and Japan. Bioinsecticides for application in soybean and sugarcane production, together with a vaccine against parasites in cattle are currently being developed.

In the area of food technology, research is being carried out into the genetic improvement of the *Xanthomonas campestris* microorganism to make xanthane gum production economically viable. A further project aims to produce and purify bacterial enterotoxines as the basis for the development of antibodies in the detection of infections. A third area involves the control of thermophylic microorganisms which are responsible for the deterioration of canned foods. And finally in enzyme research priority is given to the hydrolysis of lipids of interest to the detergent industry.

Plant research has been facilitated by the purchase of Monsanto's sophisticated research centre, renamed the Pluridisciplinary Centre for Chemical, Biological and Agricultural Research (CPQBA). The Centre specialises in the development of projects for commercial use, the counterpart being secrecy with regard to projects under development. Growing interest has been shown by industry, from multinational to small firms and business associations.

Each of the Southern States has also taken initiatives to develop regional biotechnology poles. In the highly agroindustrial State of Parana a networking arrangement has been promoted between the three major research centres in the interior of the State, comprising the Universities of Londrina and Maringa, and the agricultural research unit IAPAR. Research is concentrated on animal vaccines, natural product substitutes for chemical inputs - bioinsecticides - and the development of new products - Stevia a natural sweetener, and artificial skin from cellulosic bacteria. This network of biotechnology centres has guaranteed State funding and is supported by eleven local industries which have formed a State Association of Biotechnology Industries. Mention should also be made of the Parana Technology Institute (TECPAR) which is Brazil's sole producer of anti-rabies vaccine for animals.

Further to the South in Santa Catarina, a Biotechnology Development Centre (CDB) has been established in the industrial town of Joinville. Supported by local industry to the value of

US\$1 million and the State's three Universities, and with the promise of further funding from the CNPq, the Centre aims to work preferentially on the production of biotechnological inputs for the food, animal feed, and pharmaceutical industries, particularly aminoacids, enzymes, and vitamins which are currently heavily dependent on imports. The FINEP has approved funds to the values of US\$2 million for the following projects: the development of technology for the industrial production of lysine and riboflavin via fermentation; lactic fermentation of milk serum for the production of nitrogenated concentrates as protein supplements in animal feed. The basic orientation of the research and development programme in this heavily agroindustrial State is to substitute imports for the growing animal feed supplements market. The CDB is developing a joint project with the German research centre, Gesellschaft Biotechnologie Forschung (GBF), which in addition to training the critical mass for this research programme, proposes to research the secondary characteristics of tropical plants for commercial exploitation in international markets beginning with the extraction and purification of caffeine from the Amazon plant guarana.

In Rio Grande do Sul, Brazil's southern most State, applied research is being conducted at the University of Caxias do Sul in close collaboration with the local wine industry on the development of new yeasts using genetic engineering. After ten years of research a modified yeast has now been developed (MB7) which reduces the level of malic acid, the most difficult element to control in the making of wine and the factor responsible for "hangover" symptoms in the case of red wine. The research team has already requested "privilege of use" from the National Industrial Property Institute (INPI), the first step for the concession of patent rights, not only in Brazil but also Germany and the United States which have both shown interest in the research. Advanced genetic engineering techniques are also dominated at the Biotechnology Centre of the Federal University where research is underway on vaccines and plant genetic improvement.

In the pioneering State of Minas Gerais a regional industrial biotechnology pole is now emerging around two of the major national biotechnology firms - Biobras and Vallee Nordeste - which will be examined in more detail below. These firms are especially active in animal and human health and have established close manpower and contract research links with the regional agricultural Institute Viçosa and with the State University while maintaining sustained in-house research activity.

In 1987 the Interministerial Committee for Fine Chemicals and Biotechnology was established. While the boundaries between these two areas are increasingly blurred, research and development

policy for the former have been heavily influenced by efforts to counter the dependence on multinational firms in the drugs industry. The Technological Development Company (CODETEC), was set up in 1976 in Campinas, with the objective of developing the active ingredients of drugs based on the systematic exploitation of information contained in internationally registered patents. A large number of such active ingredients have now been developed and placed at the disposal of national industry. The Centre has now moved explicitly into biotechnology with an investment of US\$2 million for the development of antibiotics, hormones, reagents form diagnostic probes, enzymes and vitamins. Technology Centres in cooperation with industry are also being projected for the three petrochemical poles - Bahia, Rio Grande do Sul, and Rio de Janeiro (in process of implantation).

In dealing with the principal institutions involved in the regional biotechnology poles we have discussed the major research, development and production being carried out in the health field. For plant and animal biotechnology at public level we must refer above all to the National Agricultural Research Enterprise (EMBRAPA) and particularly its genetic engineering nucleus at the National Genetic Resource Centre (CENARGEN). In 1986 the CENARGEN was renamed the National Centre for Genetic Resources and Biotechnology responsible for leading and coordinating EMBRAPA's biotechnology activities. The research team already dominates the majority of genetic engineering techniques and is currently being reinforced in the areas of protein engineering, peptidic synthesis, and monoclonal antibodies. Competence extends also to tissue culture, embryo transfer (including bipartition and the production of identical twins), biological pest control (studies of Baculovirus, Beauveria and Nomurea fungi, and Bacillus sphaericus). The biotechnology programme incorporates plant and animal genetic improvement, plant and animal health, biological control, animal production, microbiological production, fermentation, and genetic resources. Priorities for research are being defined on the basis of the identification of the following principal problems :

- limited genetic base of the priority crops for agricultural research;
- lack of knowledge of sampling techniques for the collection of germplasm from perennial tropical crops;
- lack of new agricultural alternatives;
- accelerated genetic erosion with the loss of species, populations, local races and cultivars, partly as a result of the inexistence of criteria for "in situ" definition, and the inexistence of criteria for recovery at the specific level;
- lack of morphological-physiological characterisation of plant germplasm accesses;
- lack of reproductive characterisation of germplasm accesses;
- lack of biochemical characterisation of plant germplasm accesses;
- lack of biochemical- genetic evaluation of variability contained in the plant germplasm accesses;
- lack of knowledge on the system for longterm preserving orthodox seeds;
- lack of techniques for the preservation of recalcitrant seeds and tuberose species;

- lack of knowledge on the longevity of pathogens transmitted by seeds;
- need for the regeneration of plant germplasm collections;
- lack of forestry genetic reserves for "in situ" conservation of species;
- lack of germplasm banks of target species and tests for "in situ" conservation;
- inadequate preservation of naturalised races of cattle, sheep, goats, horses and pigs;
- development of techniques for the micromanipulation and criopreservation of embryos;
- development and adaptation of tissue for the formation of transgenic herds with greater capacities and resistance to disease;
- the low qualitative and quantitative value of root, grass, vegetable and tubercular crops of agronomic importance for genetic engineering techniques;
- limited use of biological controls for pests and diseases;
- lack of methodologies for the cultivation and regeneration "in vitro" of plants of interest for research programmes;
- lack of fermentation techniques for the production of microorganisms for biological control and the production of cellular proteins and metabolites;
- lack of studies on bioproductivity at molecular level in relation to rates of photosynthesis;
- need for the development of biological probes for diagnosis of plant and animal diseases;
- lack of immunological methods adapted to the production of monoclonal antibodies and vaccines;
- lack of biochemical-molecular studies on the mechanisms of plant stress.

Different patterns of competitive pressure are stimulating demand for biotechnology in a number of key economic sectors. The crisis surrounding the Proalcohol programme is forcing greater preoccupation with cost cutting and productivity innovations. An indication of this tendency can be seen in the recent investments by Copersucar responsible for 35% of total production which has accelerated its biotechnology research, investing US\$2,5 million over the last two years in a new Technology Centre. Research projects are underway with Germany and Japan and new fermentation technology is being experimented which would permit productivity increases of up to 50%. The Centre is also researching the development of co-products ranging from animal feed, and fertilizer, to acetone-butanol and lactic acid. Copersucar has also been active in the development of new sugar cane varieties, and has recently signed a US\$200,000 three year agreement with Cornell University for the development of a genetic engineering programme applied to sugar-cane.

A question mark on the other hand hangs over the Alcoholchemicals sector. Considered by the President of the Chemicals Industry

Association to be technologically superior to any other country, the sector's future is tied to the subsidy, productivity levels of the Proalcool. Eleven industries, including the multinationals Union Carbide, Stauffer, and Rhodia, and major national companies such as Elekeiroz and the Companhia Brasileira de Estireno use up to 500 million litres of alcohol per year. Depending on subsidies, some US\$100 millions are exported annually, principally to Japan. According to a working group of the Secretary for Science and Technology in São Paulo the alcohol chemicals sector will probably develop as the result of a diversification on the part of existing distilleries.

Energy costs have also become an important motive for resorting to the potential of biotechnology. Wood is increasingly used as fuel in the steel industry and major firms such as Acesita are financing micropropagation research for the rapid renewal of eucalyptus plantations. This same firm is negotiating an ambitious joint venture with an Italian group for the development of biomass conversion technology as is also Biopart, a Minas Gerais biotechnology firm. Altogether some nine Brazilian firms are studying cooperation projects for the development of biomass technology promoted by an initiative of the Commission of the European Communities.

The paper and cellulose industry is one of Brazil's most competitive export sectors. Maintaining such competitiveness however will depend on the ability to incorporate new technologies both in the area of cloning and micropropagation and the enzymatic processing of cellulose. As we have seen earlier, research activity is now underway in relation to this latter, and the former has been one of the stimuli to the emergence of a tissue culture entrepreneurial sector. Bioplanta, the largest tissue culture firm is a subsidiary of Souza Cruz (British American Tobacco) which in turn has a 30% share in Aracruz Celulose one of the largest firms in this sector, in addition to its own forests for the generation of energy. Other firms participating in the promotion of biotechnology research and development are the Companhia Suzano de Papel e Celulose and Klabin Florestal Guaiba Ltda, both national companies and together with Aracruz, leaders in the sector.

While the modernisation of the Brazilian agrofood system has been dominated by multinational, national firms have gained important spaces in specific sectors. In the hybrid seed market, national presence is dominant through the leading position of Agroceres which controls some 50% of the hybrid corn market. Strong competition however is provided by the multinationals Cargill, Pioneer, Ciba Geigy, Asgrow Seed Co. and Continental Grain. Of these Ciba Geigy and Pioneer are known to be involved in the production of herbicide resistant seeds using genetic engineering. To maintain competitiveness therefore Agroceres will be forced to increase its activity in advanced biotechnologies, if not through in house activity, then through joint ventures.

In the animal genetics sector Agroceres has already made major advances. Brazil is the world's second exporter of poultry but as yet has not dominated the production of matrilines. Through a technology transfer agreement with the English firm Ross Breeders

which may prefigure similar moves in relation to plant biotechnology, Agroceres will now internalise technology for the production of matrizes.

Brazil is also emerging as a major exporter of beef and processed meat products, and has now superseded Argentina as the Southern Cone's leading exporter. The competitiveness of international markets has led to the adoption of advanced genetic technologies in animal health and reproduction. By 1983 some 23 firms were known to be operating in the production and commercialisation of semen, and 8 firms were registered as involved in embryo transfer.

Given the importance of its research and development and the strength and diversity of its economy it is not surprising that a significant private biotechnology industrial sector should have emerged in Brazil. In this process two national biotechnology associations emerged - ABRABI, the Brazilian Association of Biotechnology Industries with more than 30 associates and ABIVEG, more specialised in plant biotechnology. At State level, the Parana Association of Biotechnology Enterprises (APEBI) has some eleven firms. If we add to these the nine firms involved in biomass conversion mentioned earlier, eight firms identified in biological nitrogen fixation, together with a further eight active in embryo transfer, the number of firms active in biotechnologies would approach eighty.

Some of these firms as in the case of nitrogen fixation are entirely dependent on public sector research. Others are essentially laboratory inputs suppliers, not involving any significant scale up. Two significant areas however account for the majority of these companies, tissue culture and micropropagation in the agricultural sector, and diagnostic kits in health, each of which involves some ten firms.

In the tissue culture sector the most important national firms are BIOMATRIX, THE BRAZILIAN SEED COMPANY (SBS), and COTIA. Biomatrix was formed in 1984 by researchers at the Federal University of Rio de Janeiro headed by Prof. Antonio Paes de Carvalho, to produce and market tissue culture products, especially vegetables and ornamental plants, and is now part of Agroceres. In 1988 it marketed products to the value of US\$1 million, particularly in forestry, tropical fruits, ornamental plants, palm olive species, and is initiating work with potatoes, tomatoes, temperate climate fruits. In addition to the sale of products, Biomatrix sells technology in the form of the elaboration of micropropagation methodologies for specific species on demand which can then be developed by the client.

SBS is following a similar trajectory to Biomatrix. begun as potato producer based on imported seed, SBS opened a laboratory in 1983 for the development of virus free seed varieties using tissue culture techniques. While it is also active in other products (banana, pineapple and especially strawberry) the firm's expansion is seen in terms of the Brazilian potato seed market, actually around US\$10 million but with an estimated capacity of US\$100 million. Having now integrated all the stages of potato seed production, the SBS has been recognised by the Ministry of

Agriculture within its national potato production programme, and is projected to occupy 25% of the basic seed market. Expansion however depended on the injection of new capital which was made possible through the US\$450,000 funding from the FINEP.

Other firms in the agricultural and livestock sector are in a position to benefit and absorb advanced technologies, particularly the large Cooperatives, some of which as for instance COTIA, a major horticulture producer active also in the new cereals frontier, have substantial investment capacity. COTIA is now developing its research capacity in tissue culture.

The use of inoculants for the biological fixing of nitrogen is widespread in the soybean producing areas and a number of firms have emerged on the basis of close collaboration with the relevant research centres -TECPAR in Parana and MIRCEN-RG in Rio Grande do Sul. Collaborative research and development involving EMBRAPA, a wide range of Cooperatives in the South and the IPT in São Paulo have led to the widespread use of bioinsecticides. Agroggen, a firm specialising in bioinsecticides for use in soybean and sugar-cane production, plans regular production of Diaggen (for sugar-cane) and Polyaggen (for soybeans) as from 1990. Export production is also planned.

Two firms in the pharmaceutical sector stand out for their R&D and production capacity. BIOBRAS could be considered the first pharmaceutical firm based on private national capital with a modern vision centred on the development and absorption of technological innovations through in-house scientific capacity and close relations with the academic community. On the basis of an association with Eli Lilly, Biobras now dominates the production of insulin for the Brazilian market and exports to a variety of other countries. It also produces reagents for diagnostics together with a wide variety of enzymes. Through the creation of BIOFERM it has begun to enter the market for fermenter plant inputs. More recently it has established cooperation with BIOSIDUS to develop interferon using genetic engineering techniques. Contract research with the University of Minas is also underway for the production of AZT. Biobras has a turnover of some US\$15 million and reinvests 7% of this on new research. Such a high rate of R&D investment however is unsustainable in the long term and Biobras is looking to the establishment of more systematic public sector research cooperation.

Vallee Nordeste has a different trajectory although it shares with Biobras, the objective of becoming a pharmaceutical firm with a strong science and technology base. The firm which belongs to CARFEPE based on agricultural activities was founded in 1978 continuing on the activities of the Vallee Institute centred on the production of foot and mouth vaccine. In 1987 Vallee Research was created to expand into the area of human health, and in the same year Innovall was set up as the result of an association with the Merieux Institute for the production of triple vaccines, haemoderivatives, and also for the marketing of a line of Merieux products. This joint venture includes technology transfer and the

training of technicians in Merieux's laboratories.

The largest national antibiotics firm, CIBRAN, with an annual turnover of some US\$30 million, has recently involved itself in the improvement and selection of strains for its fermentation production which accounts for some 25% of total production. It has also shown interest in genetic engineering.

A variety of firms are active in diagnostic reagents production. EMBRABIO, has recently launched an AIDS test Imunoblot. A further product Hemobio AIDS uses informatics to detect the presence of the antibody HIV for blood transfusions. Embrabio with a turnover of US\$1 million is also active in embryo transfer. BIOTEST and SALK of similar size are also active in diagnostic reagents.

A number of firms specialise in the production of laboratory inputs. MICROBIOLOGICA, another firm with University origins produces plant hormones, active ingredients for drugs, immunological reagents, and culture medium. CULTILAB in its turn specialises in the research and development of cell cultures.

ENGENHO NOVO which is responsible for the development of a continuous fermentation process for sugar-cane alcohol, specialises in innovations for agroindustry and has a particular interest in biotechnology opportunities.

ARGENTINA - BIOTECHNOLOGY PROFILE¹

Institutional responsibilities for biotechnology in Argentina are divided between three bodies. The CONYCIT, the National Science and Technology Council invests in the area of basic research - molecular biology - involving high risk capital in the words of Nestor Bianchi. On the other hand the National Programme for Biotechnology under the auspices of the Secretary for Science and Techniques gives priority to projects which have medium term applicability. And finally the CABBIO, the Argentine-Brazil Biotechnology Cooperation Programme, supports projects which have a commercial dimension.

Articulation between the three major actors - State, University, and Enterprise - can take a variety of forms. The State traditionally finances University research and promotes technology transfer through University- private sector association. Firms on the other hand may establish their own Research and Development Laboratories and contract services from the State. This is the case in the paper-forestry sector in Argentina. The State in its turn may create Research Institutes, an example of which would be the Institute for Biotechnology and Ecology in Argentina. In this case the State shares responsibility with the PNUD which administers funding thereby facilitating imports.

In practice in Argentina the private sector receives no special support from the State. As a result, although the idea of integration has advanced considerably, there is resistance to the use of university research funding for the development of industrial products, and effective transfer of technology has been quite modest. The CABBIO for its part has only received funding as of 1988.

While therefore Argentina has a strong tradition in biology with three Nobel Prizes it has little industrial biotechnology. The Argentine Biotechnology Forum was formed to counter lack of support for the biotechnology industry and research and development in this area. With Aldo Ferraz as its President, the Forum functions as a Chamber of Industry and has a membership of thirty three firms. These include firms involved in both classical and modern biotechnology, together with firms interested in accompanying developments in the area.

¹ Special thanks are due to Dr. Bianchi for information supplied.

The main areas of activity covered include:

monoclonals for diagnostics;
vaccines for foot and mouth;
embryo transfer;
genetic engineering.

BIOSIDUS is the most important modern biotechnology firm in Argentina. Founded ten years ago it now has the best research and development laboratories in Latin America. Its history is an example of the complementarity between scientist and businessman. The original project was interferon. Biosidus had its origins in a pharmaceutical firm and was originally conceived as providing services for pharmaceuticals rather than being specifically a biotechnology firm. Initial investments were heavy with no immediate returns but the firm now has complete biotechnology laboratory facilities, permitting the use of genetic engineering techniques, protein purification, monoclonal antibodies, and tissue culture. The laboratory therefore which was established for the production of interferon is now in condition to produce a wide variety of other substances. Total investment has been within the order of US\$10 million with no help from the State.

In relation to interferon, Biosidus produces all types of leucocytes, and is scheduled to produce recombinant alpha in 1990. In addition it produces superoxides and is developing insulin and interferon gamma. It was initially intended to allow Biobras (Brazil) supply the market for bovine insulin. This market however has now been occupied by an Argentinian firm. Cooperation is underway however with Biobras for the production of human insulin.

The National Biotechnology Programme has given priority to the following areas for the purposes of financing:

- the development of biotechnology productive processes (with special emphasis on those which imply the use of advanced biochemical engineering);
- biological nitrogen fixation (with special emphasis on the plant molecular biology and tissue culture);
- production of vaccines and the active ingredients of drugs;
- reagents for diagnostics.

As from 1989 animal production and health have been included as also the establishment of infrastructure of broad utility for biotechnology projects. In this sense priority has been given to animal and plant germplasm banks, banks of cell-lines in culture, together with microorganism banks.

Some 45 projects were approved within the 1988 budgetary programme.

The University of Buenos Aires has three projects in the Faculty of Medicine - the development of biotechnology systems for the detection of Toxoplasmosis and Mideatidosis, and the study of the polymorphism of the DNA; four projects in the Faculty of Pharmacy and Biochemistry - preparation of synthetic antiserum ,

monoclonal antibodies for diagnosis for human and bovine brucellosis, production of steroid compositions from plant cell culture in bioreactors, detection of the presence of plasmids in bacterial strains of *Clostridium acetobutylicum* from agroindustrial waste;

one project in the Faculty of Natural and Exact Sciences for the development of enzymatic bioelectrodes; and one project also from the Faculty of Law and Social Sciences on the application of industrial property to biotechnology.

The National University of Cordoba has two projects, one in the Faculty of Medical Sciences for the development of monoclonal antibodies, and the second in the Chemical Sciences Faculty on the development and application of genetic probes for the detection of enteropathogens in cases of acute gastroenteritis.

The National University of Cuyo has three projects in the Faculty of Agrarian Sciences - optimisation of culture medium for "in vitro" micropropagation, potato micropropagation, micropropagation of selected biotypes of algaroba.

The La Plata National University also has three projects in the Faculty of Exact Sciences - molecular cloning and expression of the N gene of the glycoprotein of the Junin virus, production of bioinsecticides for the control of mosquitos, operation of bioreactors in transitory states applied to microbiological processes.

The Universidad Nacional Litoral participates with one projects in the Faculty of Biochemistry and Biological sciences - mapping the immunological response in animals infected with Brucellas and development of rapid diagnostic tests.

The Mar del Plata National University has one project on the isolation and cloning of a potato protein involved in resistance to the fungus *Phytophthora infestana*.

The Rio Quatro National University has three projects in the Faculty of Exact Sciences - the study of genetic control in the case of bovine mastitis, the effect of agrochemicals on the nodules of the *Rhizobium-alfafa* and soja systems, and the production of phytohormones in *Azosp. rillum* sp.

The Rosario National University in its turn has five projects in the Faculty of Biochemical and Pharmaceutical Sciences - the differential expression of carbon fixing enzymes in the different photosynthetic cells of superior plants, regulation of gene expression (tomatoes), construction of gene expression vectors, non symbiotic nitrogen fixation, and biotechnology studies in *Stevia rebaudiana*.

The Universidad Nacional del Sur has one project in the Agronomy Department on plant improvement in the semiarid zone of the Pampas.

Outside the University structure the following projects were approved:

CERELA - molecular biology and genetic engineering of lactic ferments;

CEVAN - expression of the glycoprotein and other genes of the Tacaribe virus in eukaryot cells;

CEVEG - "in vitro" micropropagation of wood plant species;

PROIMI - agroindustrial waste treatment with recuperation of single cell proteins;

INGEBI - cloning, isolation, characterisation and production of T.cruzi antigens (Chagas disease), production of antibodies against micotoxins (Tricotecenus ? and its metabolic products);

CEFAPRIN - isolation and analysis of thermosensitive mutating bacteria, and production of prototype vaccines against cattle disease;

INTA - variability in foot and mouth disease. Characterisation of strains active in Argentina, production of subcellular antigens of Brucella abortus using molecular biology and genetic engineering;

Centre for Research in Agricultural Sciences - obtention and study of mutants of agronomic interest using bioengineering techniques.

Technological Centre for Mineral and Ceramic Resources - bioleaching of minerals and bioaccumulation of metallic ions.

Centre for Applied Biological Research - molecular study of plant response to stress.

THE ARGENTINE BRAZILIAN BINATIONAL CENTRE FOR BIOTECHNOLOGY (CABBIO)

In the wake of the policies promoting greater Southern Cone integration the Argentine-Brazilian Binational Centre for Biotechnology (CABBIO) was created. This has led to the establishment of a binational training course, the development of binational research projects, and has provided a favourable climate for the establishment of joint ventures as in the case of Biobras and Sidus for the development of interferon. The main lines of cooperation were established at the Brazil-Argentine Biotechnology Meeting in 1985. At this meeting four working groups were formed to discuss priorities in health, agriculture, biochemical engineering, and financial and institutional mechanisms.

Lines of collaboration for health were divided into three categories: technology transfer, interchange of products and inputs, joint development of technologies and products for general use. Technology transfer from Brazil to Argentina would include - production of vaccines against measles, production of immunoglobulines from large animals, diagnosis of acute respiratory infections, production of insulin and other hormones. Technology from Argentina would cover - diagnosis for fixing solid phase macromolecules in suspension, production of interferon using cell culture and recombinant genetics, concentration and purification of macromolecules by absorption or affinity.

The following products and inputs were discussed for the purposes of exchange - vaccines (BCG, measles, meningitis, poliomyelitis), serum of blood types, antibiotics, reagents for diagnosis of pregnancy and diverse pathologies, interferon.

Joint initiatives could be developed in relation to the following - production of polyclonal immune serum and purification of subproducts, industrial scale animal cell culture, immobilisation of molecules, development of new generation vaccines by genetic manipulation including the use of recombinant virus, and chemical synthesis of oligopeptides, technology for the production and purification of proteins, including vaccine antigens and haemoderivatives, quality control including specifications and standards, development of antibiotic producing microorganisms, production of inputs for biotechnology, development of non-radioactive DNA probes, development of diagnostic methods for transmittable diseases.

The following priority areas were identified in the area of agriculture and livestock:

Biological nitrogen fixation - commercial scale fermentation of inoculants, methods of quality control applicable at commercial scale, scientific exchange for the genetic selection of *Azospirillum* spp.

Tissue and Cell Culture - intensive formation of human resources through the exchange of personnel and courses, interaction in the production of virus free potato seed using Argentine regions free from bacteria and virus, development of inputs and equipment

industry (phytohormones, cellulase, agitators), development of efficient methods for phytodiagnosis using advanced immunological and molecular technologies, synthetic seeds and the regeneration of forestry species, germplasm exchange.

Genetic Engineering - establish competence in recombinant technology through exchange of professional and intensive courses following the EMBRAPA -INTA model.

Biological Control - survey into the potential of both countries. Phytohormones and Growth Regulators - development at industrial level.

The Biochemical Engineering Group established the following as areas of mutual interest - training of human resources; development of collections of cultures of microorganisms of industrial interest in specialised laboratories and the creation of mechanisms facilitating exchange; development and construction of equipment for research in biochemical engineering (reactors, sensors, and control instruments); establishment of means to facilitate the interchange of raw material for industrial fermentation; development of technology for the production of agricultural inoculants together with complementary guarantee quality systems; treatment of industrial and domestic waste by anaerobic digestion with the production of biogas; development of technology for the production of enzymes, particularly - pectinases, cellulases, xylanases, ligninolytic enzymes, and amylases; development of supports and techniques for the immobilisation of biological molecules (enzymes, antigens, antibodies) and cells, together with the development of reactors and processes for their use; development of technology for the production of human insulin, interferon, and reagent for the diagnosis and recognition of molecules; development of new techniques for alcoholic fermentation; technical cooperation for the production of antibiotics of interest to both countries; development of technologies for the production of biopolymers (pullulan, xanthane etc).

In 1987 the Brazilian Argentine Centre for Biotechnology launched a tender for projects in three areas of biotechnology with funding of US\$4 million. In the health fields projects should be related to studies in triple vaccine, the production of diagnostic reagents and vaccines for Hepatitis B, fermentation antibiotics, monoclonal antibodies and diagnostic probes. In agriculture and livestock the areas contemplated were plant improvement, vaccines and diagnostic reagents for animals, animal reproduction and improvement, together with technological innovations in inoculants. The third area, complementary activities, includes protein purification, enzymes production, reagents for genetic engineering, and scaled-up production of monoclonal antibodies.

URUGUAY - BIOTECHNOLOGY PROFILE¹

Background

Uruguay has a population of some three million, and its economy is highly dependent on world markets and those of its neighbouring giants - Brazil and Argentina. As a result its GDP suffers significant oscillations from year to year in line with the fluctuations in world markets. Rates of investment are low - around 10% of gross domestic production.

Uruguay has only one University although it is now developing a Regional Pole in the North of the country. Support for Science and Technology research is low. Global internal financing amounts to only 0,01% of GDP, with external financing accounting for 0,06%. By contrast the Uruguayan Technological Laboratory (LATU) which is responsible for quality control of export products has a budget of 0,14% of GDP. The Laboratory however carries out no technological research.

Institutional financing for Science and Technology has been channelled through the Programme for the Development of the Basic Sciences covering physics, chemistry, biology, informatics and mathematics with co-financing on equal terms by the UNDP. An indication of the impact of this support can be gathered from the increase in the number of scientific publications which have more than tripled over the last two years. The number of Masters and Doctors have increased at a similar rate although from a very low base line. Productivity is stimulated by co-responsibility for the management of funds.

In the University a National Fund of US\$150,000 has been used to support some sixteen projects. Outside financing comes principally from the Swedish Government and the EEC, with support also from Japan, Italy, and the OEA.

Research relevant to biotechnology has traditionally been developed in two areas. Within the Ministry for Education and Culture, the Institute for Biology Research, Clemente Estable has been responsible for the development of molecular biology. Various biotechnology related programmes have been developed in plant and animal health, serum and vaccines involving the molecular biology, cytogenetic, biochemical and microbiological laboratories. Total funding for 1988 amounted to US\$770,000 with US\$300,000 representing non-budgetary resources.

¹ This report has benefitted from the information kindly provided by Carina Bertulo and Raquel Rodrigues Sanguinetti.

Within the Ministry for Livestock, Agriculture and Fisheries, research has been concentrated in the Miguel C. Rubino Institute for Veterinary Research. A National Institute for Agricultural and Livestock Research has just been created with the responsibility of organising different laboratories within a network structure.

In 1986 the National Committee for Biotechnology was created. Its first initiative was to promote a Seminar with the presence of nationals resident abroad. A National Development Plan for Biotechnology was subsequently elaborated. The following objectives were highlighted:

- promote the development of biotechnological processes which result in the short and medium term in services and goods of use to the country, substituting imports and generating exports;

- stimulate and coordinate the development of biotechnology through the high level training of scientific and technical personnel; through financing research and development projects, through coordinating the activities of research units with the private sector;

- contribute to implementing subregional integration.

The Plan however was not put into effect and as a result the National Committee was limited to coordinating participation in the Latin American Biotechnology Network, and more recently in the Argentine-Brazilian Biotechnology initiative CABBIO.

Support for Science and Technology from the Interamerican Development Bank has singled out biotechnology and the creation of a Faculty of Exact Sciences as its priorities.

With the return to democratic government, university practice has shifted from a posture of confrontation to one of dialogue with the State and an openness to civil society. Current University policy is promoting a greater integration between the University and society, and internally is stimulating a multidisciplinary approach, more in line with the demands of advanced technology. As an example of the above changes the Immunology Department in the Chemistry Faculty could be singled out. Under the Directorship of Dr. Nieto it has been possible to generate funds in the order of US\$120-150,000 per year for a staff of 20. In 1988 they created a Development Laboratory for the production of reagents and have now produced two kits, for the detection of antitoxoplasm and antidactic antibodies and juridical mechanisms are now being elaborated for the sale of technology.

In spite of limited funding the University concentrates competence in the wide range of advanced techniques including genetic recombination, DNA manipulation, production of monoclonal antibodies, tissue culture, plant micropropagation, enzyme production, fermentation, "in vitro" fertilisation, embryo transplants.

The dimensions of biotechnology activity in Uruguay can best be appreciated from the survey undertaken by the National Committee for Biotechnology. Some 63 entities, public and private, were identified as being involved in biotechnology - 21 of these were State bodies and 22 located in the University; 17 were private national firms and 3 were foreign. In all 188 researchers were involved - 79 State, 68 university, and 41 within private firms. The profile of research projects was as follows - 35 basic research, 63 applied, 11 experimental development, with nothing in the area of product development.

Some twenty biotechnology firms are present therefore in the private sector. These firms are in general small (only five have a turnover of more than US\$100,000) and their directors are young with university training, normally occupying both management and research positions. In 1987 these firms formed the Uruguayan Association of Biotechnology Enterprises. The following is a list of the principal firms involved:

LIST OF FIRMS IN AUDEBIO

Proteinas Uruguayas S.A.
 Laboratorio Santa Helena
 Semillas Santa Rosa
 Vinos Finos Juan Carrau
 Calister S.A.
 Frigorifico Carrasco S.A.
 Frigorifico San Jacinto
 Granja Roland
 Enzur
 Sirex Uruguay S.R.L.
 Urutec
 Norteña
 Granja Rowland

The Laboratorio Santa Helena was founded in 1959 by University Professors and produces vaccines, serum, reagents, and drugs. Sales are estimated at US\$1,3 million. Of a staff of 36 some 80% are qualified. The Laboratory has developed associations with a wide range of foreign firms: the Instituto de Sanidad Ganadera in Argentina for vaccines, the Apotevery Labororium in Norway for Antibiotics, Langford Inc in Canada at the level of representation and for biotechnology products, Colorado SERUM in the US for vaccines, and the Medical Research in Australia. Exports account for 20% of production basically vaccines to Argentina. They are currently in the process of building a new plant, costing some US\$1,5 million for the production of a foot and mouth vaccine. The plant will comprise a high security cell culture and microbiology laboratory including work on recombinant DNA. This line of activity will be developed specifically by the Empresa Uruquaya de Biotecnologia S.A. a subsidiary of the Santa Helena Laboratory. It is also involved in the production of enzymes for leather treatment which is a new area in Uruguay, together with biotechnology products

for foot rot and botulism.

The Laboratory is interested in contacts for the development of synthetic vaccines and monoclonals. Santa Helena considers itself competitive in comparison with multinationals operating in Uruguay and is the only national firm with know how in REPISO. Currently it is involved in three research projects: - with the State

(Clemente Estable) for research into foot rot in sheep using genetic engineering: with the University Chemistry Department (Imunology) for the production of diagnostic kits: and with the Panamerican health Organisation in the case of foot and mouth.

Two firms are active in plants - Semillas Santa Rosa and Calister S.A. The directors of Santa Rosa are Italians who settled in the country in 1980 and have now become advisors to the Government. It is essentially a firm involved in basic and applied research for the improvement and creation of commercial seeds for horticulture, fruticulture, cereals and other plants, using micropropagation and cloning techniques. and employing a staff of some 21 persons. In addition it provides farm support services and market evaluations. Sales are estimated at US\$200,000, including exports to Italy and Argentina. Diversification is planned for the development of "moras" "claveles" and roses, and the firm is interested in cooperation for "alcauciles", and with research firms for specific projects (the black pest in the case of tomatoes).

Calister S.A. on the other hand is a small firm with a staff of ten which works essentially on rhyzobium inoculants. Works in association with Agrosan S.A. which markets its products. sales are estimated at US\$300,000 including exports to Brazil and Argentina.

In food there are two Meat Packing firms - Frigorifico Carrasco S. A. and Frigorifico San Jacinto. The Carrasco Frigorifico is one of the most important in South America, with more than a thousand employees and wide range of exports. This firm is currently concluding research into techniques for tenderising meat, and is involved in biomass research for the treatment of waste products.

Three firms work in the area of industrial processes. Enzur S.A. produces inoculants and enzymes for a variety of applications, but basically for the textile industry.

Vinos Finos Juan Carrau a leading quality wine producer is basically involved in traditional biotechnology but is now concluding research into the use of malolatic bacteria in red wines. Sales are estimated at US\$500,000, with exports representing 2%. Biofur Ltda which also belongs to the group produces fertilizer, fruit juices, and dried yeast. The firm is interested in foreign cooperation for technology in the area of industrial microbiology, machinery for fruit juices and for the industrial scaling up of dried yeast.

Proteinas Uruguayas S.A. This firms works with proteolytic yeast and produces a hydrolyzate whose basic raw material is fish. The firms principal product is a protein concentrate for human use

which has all the essential and non essential aminoacids in free form (Bio Proteo Catenolizado) .This is used as a natural organic revitaliser.The firm was founded in 1976 with support from the BID for the construction of a plant capable of an annual production of 120 tons.The project for the production of BPC was declared of national interest in 1978.A variety of combined foods with different bromatological compositions and with perfectly mixed and homogeneous ingredients can be produced using the same methods.Proteinas Uruguayas is interested in cooperation in the area of proteolytic yeasts. high value prepared foods, and natural products. Biological deoderisation is also an area where it is thought cooperation could lead to product improvement. Contacts have already been established with Buittoni which is interested in BPC for biscuits.

Two firms work in the area of services: Sirex uruguayaya S.R.L. and Coasin

Biotechnology has not been declared of national interest.While there is agreement on the potential of biotechnology strong investmnet is needed in human resources, equipment, and venture capital.

The key sectors of industry - milk production, pulp and paper, the beer industry - are not integrated into this new area of biotechnology.

Projects in Development (CONICIT-BIRD). Areas selected for research:

Human and animal health: vaccines -BCG, diagnostic kits;
 Animal Production: production, sexing, and frezzing of embruos not only of cattle but also sheep.
 Plant health: certification of genetic material, desease diagnosis;
 Plant production: micropropagation of horticulture, fruticulture and forestry plants; genetic improvement of cevada; production of virus free potatoes.
 Energy: production of alcohol e biogas.
 Environmental contamination - waste treatment;
 Industrial production - enzymes.

Areas where there is demand for cooperation include:

Plant production - molecular biology, transgenic plants, genome markers, "in vitro" multiplication;

Plant health - virology, microbiology, plant aquaculture, imunodiagnosics, recombinant DNA for diagnostics;

Human health - production of monoclonals, imunodiagnosics;

Animal health - microbiology, virology, imunology, imunodiagnosics, recombinant DNA for diagnostics, vaccine production;

Biotechnology Services - DNA diagnostic probes, synthesis and sequencing of nucleic acids.

CHILE - BIOTECHNOLOGY PROFILE ¹

The National Biotechnology Committee was formed in 1983 with the general objectives of elaborating and implementing a national programme for biotechnology. Such a programme however inspite of significant efforts still does not exist. More specifically the Committee aimed to promote the relevant disciplines within a multidisciplinary and multiinstitutional perspective, and stimulate integration between the private and public sectors.

In addition the following priority areas were identified:

- i) bacterial mineral leaching;
- ii) biological nitrogen fixation;
- iii) plant tissue culture;
- iv) anaerobic digestion of biological residues;
- v) diagnostic reagents for plant, animal and human disease;
- vi) large-scale cultivation of microalgas;
- vii) lignocellulose processing;
- viii) industrial enzymes;
- ix) embryo transfer;
- x) marine biotechnology.

The Committee has in addition been active in the promotion of the Latinamerican Biotechnology Network.

From a comparative advantage standpoint forestry and fruticulture are the most promising areas. Pine trees in Chile reach maturity very rapidly and fruit is able to command high out of season world prices. Chilean exports have been increasing at a rate of 20% per year and reached the value of US\$7billion in 1988. Four categories account for 85% of these exports - mining, forestry, fishing and fruticulture.

In terms of projects Chile has a specific interest in the following:

- i) development of alfalfa germplasm;
- ii) tipification of virus;
- iii) fermenter design for hyaluronic acid;
- iv) development of vaccine for Hepatitis B;
- v) potato improvement;
- vi) biological nitrogen fixation for beans.

¹ We would like to thank Dr. Yudelevich who kindly provided material for this report.

The UNDP is currently funding the following initiatives:

- i) bacterial leaching;
- ii) antigens for vaccine against brucellosis;
- iii) production of B-caratene from microalgae;
- iv) cellulose research;
- v) plant micropropagation.

The following are some of the major biotechnology firms in Chile:

BIOPLANTA is linked to the principal Chilean tobacco company which in its turn is linked to NPI and the multinational BAT corporation. It works on plant meristem micropropagation, and carries out research and development in genetic engineering.

BIOSCHILE ENGENHARIA GENETICA was created in 1986 and is associated with Laboratorio Chile S.A., the largest Chilean pharmaceutical company. BIOS-Chile is active in the area of diagnostics (monoclonal antibodies for HCG and HL); vaccines (Hepatitis B); diagnostic tests for pregnancy and the identification of blood groups; growth hormones for the treatment of human deficiencies and hormones for the stimulation of growth in fish (salmon); production of proteins (erythropoietin), rennin by genetic engineering, and yeasts.

BIOTECNICA DE CHILE has foreign capital participation and is active in the following areas: diagnostics, production of veterinary hormones, agroindustrial enzymes (pectinase), "anabolizantes"

LEFFERS ALIMENTOS, traditionally active in the production of yeasts and has now created a Biotechnology Department for research and development in this area. Has established a jointventure with IGENE (?) to research into pigmentation for salmon.

SOC.TEC.CONESUL, active in marine products, and is a model for academia-industry integration. Works on the isolation of bio-adhesives (choro?), the organic interface between metals, used in the immobilisation of enzymes in bioreactors.

Biotechnology projects in Chile receive funding from five institutions:

- 1) The National Science Research and Technology Fund (FONDECYT);
- 2) UNDP;

3) National Science Foundation (NSF) in agreement with CONICYT and others;

4) International Scientific Foundation (ISF);

5) The CORFO Fund for Productive Development. (FDP).

Projects supported by the FONDECYT comprise the following areas and institutions:

- Isolation and characterisation of nitrogen fixing bacteria (Rhizobium Frankia) - Univ de Chile Fac. de Ciencias;
- Physiological changes associated with hydric stress in gramineos and possible effect on interaction between plants and insects - Univ. de Chile Fac de Ciencias;
- Evaluation of a non radioactive genetic probe for the identification of pathogenic strains of Yersinia Enterocolitica - Univ Chile Divisao Ciencias Med Oriente;
- Participation of the E. Coli antihemorrhagico (ECECH) in the Sindrome Hemolitico Uremico in children - Ur.iv. Chile Div. Ciencias Med. Oriente;
- Participation of Lactic Bacteria and Yeasts in the production of acetic acid in slow fermentations - Univ Chile Inst. Nutricao y Tec. de los Alimentos;
- Sperm antigens involved in the interaction of Gamezos - PUC de Chile Fac. de Cs. Biologicas;
- Identification, Purification and Characterisation of Cellulases in Native Fungus - PUC de Chile, Fac de Cs. Biologicos;
- Development of Systems for the "in vitro" micropropagation of fruit species using interspecific cultivars - PUC de Chile Fac. de Cs. Biologicos;
- Adherence of Thiobacillus Ferroxidase to copper minerals - PUC de Chile Fac. Cs. Biologicos;
- Production by fermentation and immobilisation of lactose yeasts for the milk industry - Cath. Univ of Valparaiso, Fac de Ingenieria;
- Biological control of Rhizoctonia Soliani using antagonistic bacteria -Univ. Austral de Chile , Fac de Ciencias Agrarias;
- Specific DNA probes to identify ovas responsible for the vertical transmission of infectious diseases in Salmon -U. Austral de Chile Fac de Ciencias Agrarias;
- Clonal micropropagation in marine Agarophyte Algae - U. de Valparaiso Fac de Medicina;
- Effect of the inoculation of microrizogenous fungi (VA) in plant production - Univ. de la Fronteira Fac de Ingenieria;
- Structural and biochemical characterisation of the modification-restriction system of the Bacillus Stearothermophilus Y. - Univ. de Talca Fac de Cs Agrícolas;
- Genetic expression for thermotolerance and resistance to injury in two Chilean trees: Prosopis Chilensis and Araucaria Araucana - Univ de Chile, Fac de Cs;
- Development and Implementation of modern immunochemical technology for the detection of molecules of biomedical importance: application to the diagnosis of the Chagas disease and tuberculose - U. de Chile Fac de Medecina;

- Determination of polycyclical aromatic Hydrocarbons in particulated material from the air of different zones of Santiago. Biochemical and toxicological studies for the analysis of possible risks from exposure -U. Chile Div. Cs. Medicas Norte;
- Micromorphological and Chemical study of the "Palo podrido" , a natural process of biopulping - U. Chile Inst. de Nutrição e Tec. de los Alimentos;
- Bacterial degradation of lignine : identification of the enzymes which catalyse ruptures in the intermonomer links and the cloning of those genes which code for them -PUC Chile Fac de Cs. Biologicos;
- Development of non radioactive molecular probes for the rapid diagnosis of virus and pathogenic bacteria - PUC Chile Fac de Cs. Biologicos;
- Bioseparation of fatty acids, protein concentrates, and pigments in algae - PUC Chile Fac de Ingenieria;
- Foods of intermediary humidity based on pelegic marine resources - PUC Chile Fac de Ingenieria;
- Identification of the tuberculosis mycobacterium in clinics through the hibridisation of nucleic acids. Molecular characterisation of Chilean strains -PUC Fac de Medicina;
- Reproducxtion control in Salmonideos. Productioin of monosex and triploid fish - U. Catolica de Valparaiso, Fac de Recursos Naturales;
- Biotechnology applied to the study of Brucella and Brucelosis. Creation of a Reference Centre, Training , and Pilot Plant production facilities for Vaccines and diagnostic antigens - U. Austral Fac de Cs. Agrarias;
- Production of chimeras and interspecies gestation of sheep and goats - U. Austral Fac de Cs. Veterinarias;
- In search of genes resistant to cold in superior plants - U. de Talca Fac de Cs. Agrícolas y Rec. Nat.

The UNDP in its turn is supporting the following projects:

- Biological processes applied to the cellulose and the forestry waste treatment industries - Consorciun of Chilean Universities;
- Study on the uses of lignine - PUC de Chile;
- Production of B- Carotene from the Dunaliella Micralgae - INTEC;
- Development of biological processes and their application in the bacterial leaching of Chilean minerals ;
- Obtention of products of biological and nutritional interest on the basis of microalgas - PUC Chile;
- Pulping of Pinus radiate using organic solvents - U. de Concepcion;

Cooperative Research Agreements with the participation of the CONICYT cover the following projects:

- Genetic and biochemical studies of lignolytic bacteria (NSF) - PUC Fac de Cs. Biologicos;
- Monoclonal antibodies in comparative studies in Immunology. Study of hexokinase isozymes (NSF) - Univ de Chile Fac de Cs.;
- Development of technological processes for the production and use of thermostable B. Galactosidase (NSF) - Univ de Concepcion;
- Protheglycan Sulphotransferase (NSF) -PUC Chile. Fac de Cs. Biologicas;
- Enzyme activity in the biosynthesis of proline in cevada tissue (DAAD) - Univ de Chile Fac de Cs.;
- Behaviour and Differentiation of the metabolism of Glucose in the Docito de la nana (DAAD) - Univ de Chile Fac de Cs.;
- Biorganic studies (CNPq) - Univ de Concepcion.

The International Scientific Foundation is currently supporting the following projects:

- The development of a simple microbial technology to remove heavy metals from mine drainages - Univ de Chile, fac de Cs.;
- Enhancement of productivity in the conversion of ligno-cellulosic waste to ethanol by microbial delignification - Univ de la Frontera;
- Antigenicity of different preparations of Brucella protein and the role of the contaminant LP as an inbuilt immunomodulator - Univ Austral;
- Electrochemical pathways for the oxidation and reduction of glucose obtained from cellulose hydrolise using elecycrocatalytic processes.

And finally the Fund for Productive Development is supporting the following industrially oriented projects:

- Methods of "in vitro" cultivation of arandanos - Carlos Munoz S.;
- Kits for pregnancy diagnosis -Bios Chile S.A.
- Micropropagation laboratory - Espinoza y Urzua Ltda;
- Development of vaccines against Hepatitis B - Bios Chile;
- Biotechnological propagation of fruit plants - INTEC;
- Salmon growth hormones -Bios Chile S.A.
- Chemical synthesis of the pheromone Rhyscionia Buoliana to control pollila del pino - Forestal Pedro de Valdivia S. A.;
- "In vitro" micropropagation - Fruticola y Forestal Sudamerica.

ANNEX III

DECLARATIONS OF INTEREST



Rio de Janeiro, 13 de fevereiro de 1990.

DR. BERNARDO SORJ
Rua José Linhares, 150 aptº. 401
Rio de Janeiro - RJ

Prezado Dr. Sorj:

Li com muito interesse o projeto sobre "Informação e Apoio ao Investimento Bio-Industrial".

A ABRABI tem desenvolvido, nos últimos anos, esforços no sentido de uma rápida e adequada circulação de informações sobre oportunidades tecnológicas e industriais no Brasil na área de Biotecnologia.

Sua proposta, portanto, vem ao encontro de nossas expectativas podendo contar com o apoio da nossa Associação no que for preciso para encaminhamento do projeto.

Cordiais saudações,

ANTONIO PAES DE CARVALHO
PRESIDENTE

APC/er