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Genetic Engineering and Biotechnology Monitor

Issue No. 37 March 1992

This issue carries a special article by Dr. Kishore Singh on the management of science, industry and university collaboration in generating and commercialization of biotechnologies: an appraisal of the Indian approach.

This publication is distributed free of charge to developing countries

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A. NEWS AND EVENTS

UNIDO news

International Code of Conduct on Biosafety

The phenomenal advances in biotechnology and genetic engineering have already resulted in practical industrial applications in the fields of agriculture and health care. It is estimated that anywhere from $10-100 billion will be the market for biotechnology-based products in the agro- and food-processing sector alone by the year 2000.

The realization of the potential of these frontier technologies often entails production and release of genetically modified organisms (GMOs) into the environment. Several releases have already taken place in industrialized countries. Although to date there are no untoward incidents consequent to these releases, there is a potential for ecological disturbances that one has to guard against and a precautionary approach is needed. Cognizant of this eventuality and for promotion of sustainable industrial development, the Preparatory Committee on the Establishment of the International Centre for Genetic Engineering and Biotechnology (ICGEB) at its 14th session in February 1990 suggested that the Centre should play an important role in evolving and adopting of common minimum biotechnology safety guidelines among its Member States.

Concurrently, since 1985, an Informal Working Group on Biotechnology Safety, consisting of UNIDO, the United Nations Environment Programme (UNEP) and the World Health Organization (WHO) has been considering biosafety in relation to research institutions, industry and the environment. Recently, the Food and Agriculture Organization (FAO) has joined this group. In its fourth meeting in 1989, the Working Group recommended, among others, the promotion of an international code of conduct on biosafety and the establishment of an advisory group under United Nations auspices to assist countries, upon request, in the assessment of release of GMOs in the environment; establishment of an international database on releases; preparation of a biosafety manual and development of biosafety training programmes. The group authorized UNIDO to take the lead in each of these recommendations. It may be noted in this context that the first meeting of the Preparatory Committee of the United Nations Conference on Environment and Development (UNCED) was interested in the preparation of an International Code of Conduct on Biosafety and asked its secretariat to closely follow the progress of work undertaken by this informal working group.

According to the recommendations of the informal working group, UNIDO organized an expert group meeting in March 1991 in Vienna consisting of some 15 scientific experts from developing and developed countries and the Organization for Economic Co-operation and Development (OECD). The group prepared a draft code of conduct on the release of GMOs into the environment along with a recommendation for the establishment of an international biosafety information and advisory service. The draft was further examined by another group of some 35 experts with a greater representation from developing countries at a meeting convened in July 1991 at the ICGEB premises in Trieste (Italy). The final draft that emerged from this meeting was endorsed by the informal working group of UNIDO/UNEP/WHO/FAO. The UNCED secretariat has been informed of the activities of the informal working group at every stage of the development of this code.

Need for the Code

Few developed countries have already formulated special regulations on release of organisms into the environment. However, there is a startling lacunae in this area in many countries as is evident in a recent survey conducted by UNIDO. The Preparatory Committee for ICGEB requested UNIDO to collect existing information on biosafety guidelines in its member countries. The feedback is still coming in but the responses that were received revealed that most countries have no biosafety committees, regulatory requirements or approval bodies. It is of interest to note in this connection that even many industrialized nations have yet to develop guidelines on biotechnology safety. There is, therefore, a pressing need to formulate biosafety guidelines, risk assessment and a code of conduct for the release of organisms into the environment.

International cooperation is necessary in forming a basic set of guidelines that countries can make use of in order to avail themselves of the advances of frontier technologies to their benefit. These guidelines will:

(i) Serve to promote R&D and environmental applications of GMOs;

(ii) Provide guidance to national authorities to make quick decisions on proposals for introduction;

(iii) Help industry to commercialize GMO-based products;

(iv) Bring transparency and avoid trade barriers; and

(v) Facilitate consumer confidence and acceptance.

Code

The International Code of Conduct on Biosafety was prepared by experts, taking into consideration the existing efforts in the area of the Organization for Economic Co-operation and Development, the European Economic Community and of industrialized countries, with a view to harmonizing them under a United Nations umbrella. Basically, the Code attempts to capture the minimum commonly accepted principles in regard to the release of GMOs into the environment. It stipulates principles and obligations of governments, the proposer and the researcher intending to release the GMOs. The guidelines expressed in the Code are meant to be user-friendly without hindering the process of biotechnology progress. These can be modified or extended to suit specific situations, if the countries so desire.

Alongside the Code, the experts felt there was a need for, and developed the concept of an information-cum-advisory service, which could serve countries and enterprises on request. The structure of such an advisory service is under elaboration by UNIDO.

UN and other organizations' news

Malaria clinical trials

Clinical trials of three new drugs for malaria treatment will soon get under way, the result of a new emphasis by the World Health Organization (WHO) on fostering drug development in industry.

With malaria vaccine development stalled and mosquitoes in tropical regions fast developing resistance to existing drugs, new treatments are badly needed. The latest candidates are injectable derivatives of artemisinin, the active constituent of a Chinese herb traditionally used to combat fever. Clinical trials will take place over the next four to five years in the Netherlands and several African and Asian nations.

These drugs are the first that WHO has supported from the earliest stages of development through clinical trials - a new policy resulting from industry's "lack of interest" in developing drugs on its own. Previously, WHO concentrated on support for academic research and clinical trial management. (Source: Science, 1 November 1991, p. 639)

UNESCO Short-term Fellowships in Biotechnology

The UNESCO Short-Term Fellowship Programme in Biotechnology, aimed at promoting international cooperation in this dynamic field, is designed to stimulate research and facilitate training in plant and aquatic biotechnology and environmental biotechnology as it affects these two areas. Scientists, particularly from developing countries, are offered an opportunity to carry out research at well-established scientific centres and to learn techniques in the above-mentioned fields that are not normally accessible to them in their own country. Fellowships are not awarded for attendance at scientific meetings.

Fellowships, on a semi-annual basis, will be awarded to selected applicants wishing to spend one to three months in a scientific laboratory abroad. Fellowship grants provide for either partial or full travel expenses and/or a modest monthly subsistence allowance. Coverage for life, accident or health insurance is the personal responsibility of the individual or the host institute.

Applications for fellowships should be received either by 30 June or 30 December of each calendar year.

All applications must be submitted on the UNESCO/BAC application form that can be obtained from:

UNESCO Short-Term Fellowships in Biotechnology
Biotechnology Action Council
Division of Basic Sciences
UNESCO
1, rue Miollis
75015 Paris
France

(Source: News Release, August 1991)

Cancer will "overwhelm" the third world

An epidemic of cancer will sweep across the developing world in the next 30 years, a group of eminent epidemiologists is warning. At WHO in Geneva they accused industrialized countries of doing too little to help poor countries prepare for the epidemic.

According to Timo Kaulinen, professor of epidemiology and biostatistics at the Karolinska Institute in Stockholm, the number of people dying from cancer in developing countries is expected to jump in the next 30 years from 2.7 million a year to 6.5 million. This is an increase of 140 per cent. In the poorest countries of the third world, the number of new cancer cases each year is likely to double, rising from five to ten million.

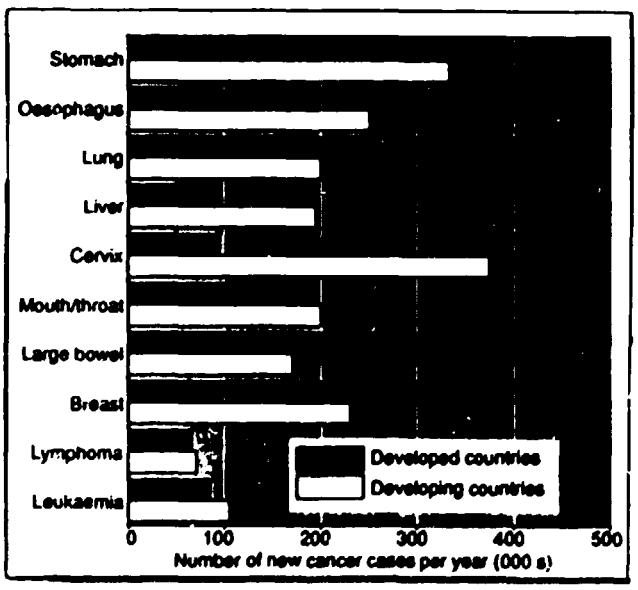
Over the same period, the number of people dying from cancer in developed countries will increase by 20 per cent, from 2.2 to 2.6 million a year. New diagnoses of cancer will probably rise by 25 per cent, from four to five million.

The reasons for the predicted cancer epidemic are simple. First, cancer is a disease of the elderly, and the elderly population of the developing world is expected to increase by 240 per cent over the next three decades. But the main reason for the epidemic is that people in poor countries are adopting the lifestyles of developed countries - particularly cigarette smoking. According to WHO, tobacco consumption is increasing by more than 2 per cent a year in the developing world. The result, WHO says, will be an extra 1.5 million cases of lung cancer, of which 90 per cent will be incurable.

Already well over half of the 9 million new cases of cancer discovered each year are in developing countries, says Howard Barnum, an economist at the World Bank. Around 80 per cent of cancers of the oesophagus, cervix and liver, 70 per cent of cancers of the mouth and pharynx, and just over half of all Hodgkin's lymphomas and leukaemias are diagnosed in developing countries. Despite this, there is little medical help for cancer sufferers there.

Jan Stjernswärd, the chief of the WHO Cancer Unit, says that 90 per cent of cancers in developing countries - over four million each year - are incurable by the time diagnosis is made. In developed countries the figure is below 60 per cent.

Without much chance of curing a patient's cancer, pain control is a priority, but there are 55 countries where "not a single morphine tablet can be found", largely because of outdated laws on the use of opium-based drugs. Many of these countries, China for example, are major opium producers. (Source: New Scientist, 14 December 1991)



UN initiates AIDS vaccines trials in third world

Four countries, Brazil, Rwanda, Thailand and Uganda, have been chosen by the United Nations Global Programme on AIDS as the first to take part in a massive AIDS vaccines trial. Incidence of infection by the human immunodeficiency virus (HIV) is widespread in these countries.

Medical facilities there will be strengthened in preparation for the trials, which are an extension of preliminary ones currently under way in North America and Europe. The programme is being administered through the Geneva-based World Health Organization.

WHO estimates that at least 9-11 million people are infected by HIV, and that at least 1.5 million have gone on to develop AIDS. A third of all AIDS cases involve children.

Vaccines currently on trial, says WHO, are showing some promise, and these and other experimental vaccines will be involved. After an experimental vaccine is proven safe and effective, studies will be carried out on thousands of volunteers clear of HIV infection. These will be followed up over several years to assess the degree of protection offered by the vaccine in question.

Selection of volunteers is a tricky question. Population groups will have to be chosen for their economic and political stability, their popular support for the trials, and, most importantly, lack of taboos that could make blood sample collection difficult.

More than 10 candidate vaccines are already being tested for safety. Three groups of product are being prepared for field trials:

- Preventive vaccines - these are intended to protect the general population from being infected with HIV. They are analogous to the classic virus vaccines such as measles and polio.

- Therapeutic vaccines - these are for those already infected by HIV, and are intended to prevent patients from progressing to AIDS.

- Perinatal vaccines - for administration to pregnant HIV-infected women preventing transmission of the virus to the foetus.

Dr. Michael Merson, director of the global programme, explains that it is essential to test promising vaccines in the regions for which they are intended because different HIV strains are found in different parts of the globe. A vaccine for one may not be effective against another.

Also, testing in the poor countries will accelerate the development of appropriate HIV vaccines where the need is greatest.

In addition to the WHO programme, trials will also continue in the richer countries of the world. Several are establishing national sites for vaccine trials and are working in partnership with developing countries. The steering committee of the WHO programme is encouraging the development of all vaccine testing sites and will provide expert advice for such national efforts.

Discussions are already under way between WHO and major drug companies, via the International Federation of Pharmaceutical Manufacturers Association, to establish a collaborative arrangement for the development and eventual world-wide availability of HIV vaccines. (Source: European Chemical News, 25 November 1991)

Release of organisms into the environment

The proceedings have been received of a UNEP/MSDN workshop organized by MSDN at the request of UNEP with co-finance from UNEP, USEPA, USDA, Environment Canada and the Commission of the European Communities (BRIDGE concertation action), held in Vienna, Austria and Rockville, Maryland, USA on 11-15 March 1991. The workshop on the needs and specifications for an Information Resource for the Release of Organisms into the Environment (IRRO) made several recommendations, some of which have been followed up in a meeting at the University of Nottingham, UK, of the IRRO steering group established in Vienna. This second meeting was held adjacent to "REGEM 2", the second meeting on the release in the environment of genetically-engineered micro-organisms.

It has been agreed to form an electronic network providing access to information on environmental releases, including release events, organisms, scientific, technical and regulatory information. The network will provide centralized access to existing data sources in different regions of the world for all those studying the release of organisms into the environment.

Details of report and network: IRRO Secretariat, 307 Huntingdon Road, Cambridge LB3 0JX; Tel:. (44)223277628. (Source: EBIS, No. 5, October 1991).

OECD looks at biotechnology for a clean environment

The OECD Committee for Scientific and Technological Policy has created a group of national experts to examine scientific and technical aspects of environmental applications of biotechnology and to draft a report on the subject. The group met for the first time on 11 and 12 July 1991 and selected as Chairman Dr. Michael Griffiths from the UK. A grant towards the work of the group has been made by the Commission, under the concertation actior of the BRIDGE programme.

The group is interested in gathering the views of industry (amongst others) on aspects of biotechnology covering the topics of prevention, detection and remediation of environmental damage. Interested firms/individuals should contact the OECD secretariat, Dr. S. Waid, OECD, 2 rue André Pascal, 75016 Paris, Fax: (33)145249767 or Dr. I. Economidis, Commission of the European Communities DGXII; Fax: (32)22355365. (Source: EBIS, No. 5, October 1991).

International agricultural research invites NGOs

The Consultative Group on International Agricultural Research (CGIAR) was established in 1971 through the efforts of the Rockefeller, Ford and Kellogg Foundations to find governmental partners for their Green Revolution research

around the world. The result was an entirely informal system. Northern governments and foundations provided approximately US$ 300 million per annum to support the work of 13 International Agricultural Research Centres (such as the International Institute of Tropical Agriculture (IITA) in Nigeria or the International Centre for Agricultural Research in Dry Areas (ICARDA) in Syria) in developing new breeding material for countries of the South.

NGOs have been critical of CGIAR for its narrow breeding focus on mass-market high-response/high-input crop varieties, which displaced traditional crops and varieties. CGIAR's research orientation has encouraged production systems biased to larger farmers to the detriment of the world's poorer farmers. Central to the NGO concerns has been CGIAR's insensitivity to democratic principles and the integrity of third world peoples and governments shown by the imbalance between Northern "donor" governments and token representatives from the South. Since CGIAR has no constitution or legal status, major global decisions concerning agricultural development affecting developing countries are taken without participation of the societies concerned.

As funds become scarcer, however, CGIAR has begun to rethink its orientation towards the Green Revolution. Invited by CGIAR and the World Bank (CGIAR's host and facilitater in Washington, DC, USA) in May, the Rural Advancement Fund International (RAFI) informally made the following recommendations in the context of a general shift towards sustainable agriculture and the greater participation of rural communities in both genetic resources conservation and plant breeding:

1. Regionalization of the CGIAR system with stronger representation from third world countries - including NGOs - and orientation of the International Agricultural Research Centres (IARCs) towards whole regions rather than specific crops;

2. Institutionalization of CGIAR on a one country - one vote basis;

3. Participation of NGOs in the CGIAR planning and reviewing processes including a special forum on NGO/CGIAR relations;

4. Possibility of NGO/farmer participation on the IARC Boards.

As a result, RAFI has been asked to help organize a meeting between CGIAR and a small group of NGOs on the future of international agricultural research. The meeting was held in Washington on 22 October 1991. The agenda included NGO work in plant genetic resources conservation and utilization, optimization of conservation concepts through formal and informal strategies, a possible strategy for cooperation and coordination of activities before and at the UN Conference on Environment and Development.

Follow-up discussions will be held with the International Board for Plant Genetic Resources (IBPGR - one of the IARCs) and, possibly, other IARCs. An African regional discussion of CGIAR is expected in Nairobi either at the end of 1991 or early in 1992. The Washington session is only the beginning of a hopefully major restructuring. (Source: African Diversity, No. 6, October 1991)

Local seed supply systems: call for documentation

A team of the Development Research Institute (IVO) in Tilburg, the Netherlands, and three teams in Costa Rica, Honduras and Nicaragua have started a project on "Local seed supply systems and food security in developing countries". The project will analyse the socio-economic importance and potential of the local seed systems for national food security. Information on practices used by small farmers to produce, obtain, store, select and use seed, the type of genetic material they use, farmers' criteria of crop and variety choice, etc., will be collected. The project will pay special attention to the role of women and ecological aspects. Case studies will be carried out in Honduras, Nicaragua and Costa Rica to actively search in the field for information and farmers' knowledge concerning the use of seeds. A final report will be published with recommendations concerning seed policy of governments and developing institutes in order to strengthen and improve local seed systems. All collected information on socio-economic importance and functioning of local seed systems will be compiled in a bibliography and form the basis of a literature study. Part of the documentation gathered will be in the form of so-called "grey" literature, so it can be made available to other people who are interested. Therefore, anybody who has interesting information and papers on this topic is requested to send this to: IVO - Project local seed systems, P.O. Box 90153, 5000 LE Tilburg, The Netherlands. (Source: Biotechnology and Development Monitor, No. 8, September 1991)

ABC opens European chapter/information office

The Association of Biotechnology Companies (ABC) has announced its first European chapter and information office in Hannover. The stated objective of this office is to provide ABC members in Europe and North America with better lines of communication on availability of capital, technology transfer, policy development and strategic alliances, etc.

Details: Tom Wiggans, Vice President of European Affairs for ABC, Serono Laboratories Ltd., 9c Bridge Road East, Welwyn Garden City, Herts., AL7 1BG, UK. Tel.: (44) 7073?1972.

Ethics

Ethics report condemns "ignorant" AIDS researchers

Ignorance and confusion about the ethical rules for research on people are widespread among scientists at the US National Institutes of Health. This is the conclusion of an internal report by the NIH which criticizes the institution's failure to protect people taking part in research carried out by its staff.

Although the NIH is responsible for protecting people who are involved in research by its staff, it has no policies or procedures to monitor such work, the investigation found.

The interim version of the report follows an investigation into joint projects between NIH scientists and the controversial French AIDS researcher, Daniel Zagury. Officials at the NIH stopped all collaboration between Zagury, the

institutes in France and Zaire where he works, and NIH staff after allegations that some projects had violated the NIH's ethical guidelines.

Scientists at the NIH who do any research on human subjects - including, for example, the analysis of blood samples - must gain approval for their work within rules spelt out by the NIH's Office of Protection from Research Risks. The rules apply to joint projects with foreign researchers as well as projects in the US.

The report looks at eight projects, including one in which 18 HIV-negative Zairian children received an experimental AIDS vaccine. Some of the children were only two years old. Another project concerned an immune therapy for AIDS patients in Paris. In both these projects, NIH researchers supplied materials such as HIV and vaccinia virus used in the research, and in others they analysed blood samples for Zagury. The American scientists say they provided the materials for animal research only.

The report finds fault with the NIH on six separate grounds for failing to protect people. It also says there is widespread ignorance among its scientists about their responsibilities under government regulations for work on human subjects.

The investigators are waiting for all involved to respond before publishing a final version. In future, says the report, there must be a single authority within the NIH to authorize all research projects on humans. The rules will also be overhauled. The responsibilities of scientists and administrators will be clearly spelt out, and scientists will receive "mandatory" education to make sure they understand the rules. (Source: New Scientist, 27 July 1991)

Regulatory issues

Ministers clash over rules for modified organisms

Europe's agriculture ministers have approved a directive regulating the sale of pesticides that conflicts with procedures drawn up by environment ministers in 1990. The clash is over the release of genetically modified organisms (GMOs) into the environment. Under the new directive, the release of organisms designed as pesticides - bacteria that secrete insecticide, for example - would be controlled by a committee of agricultural experts in Brussels, rather than by environmental authorities.

The environmental directive passed in 1990 requires a detailed assessment of the risks to the environment before a GMO may be released, either as an experiment or as a commercial product. The directive says GMOs may be regulated under other legislation, as long as a similar environmental assessment is made.

The new pesticide directive replaces national rules for the approval of pesticides. The decision to license a pesticide will be made by a committee of experts in Brussels appointed by member States, probably from the same ministries that control other agricultural chemicals.

The new directive does not include specific rules for assessing GMOs. The agriculture directorate of the European Commission has promised to add such criteria within two years, so that it will provide the same environmental safeguards as the earlier directive. National environment ministries will continue to control releases of GMOs for research. (Source: New Scientist, 3 August 1991)

General

The role of Law in the development of tropical natural product pharmaceuticals and the conservation of biodiversity

Tropical forests hold over half of the world's species. This diversity of life has produced many medicines, including treatments for childhood leukaemia, Hodgkin's disease, heart disease and glaucoma. Every year plant-based pharmaceuticals net tens of billions of dollars.

Tropical forest-derived medicines have a significant economic value, but this value is not always fully realized in tropical communities, where the lack of economic alternatives can lead to practices that destroy forests. Legal mechanisms that generate revenue for local economies from the development of plant-based drugs can be one important way to increase local incentives to conserve tropical biodiversity.

On 18 April 1991 the Periwinkle Project of the Rainforest Alliance hosted a workshop at the Environmental Defense Fund in New York. This workshop, "The role of Law in the development of natural products pharmaceuticals and the conservation of biodiversity", explored legal structures that determine the value of both plant genetic resources and indigenous peoples' knowledge of these resources. Participants included representatives of conservation and human rights organizations, scientific research institutions and industry, attorneys and government officials.

Participants examined proposed and existing contractual agreements, international laws, and foreign domestic laws that can ensure benefits from the development of natural product pharmaceuticals are shared with individuals or institutions within tropical countries. Both the enforceability of these measures and the significance of the benefits derived from their use were explored.

It was noted, however, that legal structures are one part of a larger issue, and must be applied in accord with a wide variety of strategies that include cultivation and harvesting practices; immediate monetary returns through collection agreements; sharing of laboratory results; building up R&D capabilities within tropical countries; immediate non-monetary compensation to participating communities in forms such as medical care and education.

The Periwinkle Project will produce a paper outlining and further discussing the issues addressed in this workshop. (Source: News Release, April 1991)

Genetic survey gains momentum

Last summer population geneticist Luca Cavalli-Sforza of Stanford University, molecular anthropologist Allan Wilson of the University of California, Berkeley, and others issued a call to action: an urgent plea for help - and money - to collect DNA samples from aboriginal populations around the world before those groups vanish. Now, just a few months later, even the proponents of this bold new plan seem amazed at the response.

As word gets out, numerous anthropologists are offering to help collect samples from the isolated tribes they study. And in an unexpected twist, several US federal agencies have approached the scientists - unsolicited - to see how they can help. Indeed, the agencies are already talking about picking up at least part of the tab, which could run to $20 million or more over the next five years.

The basic plan is to collect blood samples from members of at least 100 indigenous populations, such as the Bushmen of southern Africa and the Hill People of New Guinea. Such populations, isolated for hundreds or thousands of years, contain in their genes clues to human evolution, migration, and diversity. But the opportunity to analyse those genes is rapidly vanishing as society encroaches upon these once-distinct peoples. Once the samples are collected - probably from about 50 individuals in each group - the researchers would establish permanent cell lines to preserve the DNA in perpetuity, allowing it to be studied even after the tribes have disappeared. (Extracted from Science, Vol. 254, 25 October 1991, p. 517)

South-North Human Genome Conference

The first South-North Human Genome Conference will be held in Brazil next 12-15 May. The conference is being organized by UNESCO and the Brazilian Biochemical Society to inform the third world of progress on the Human Genome Project - a 15-year programme to map and sequence the human genome.

The project, which began officially last October in the United States, is expected to revolutionize medical treatments and diagnostic techniques.

Although UNESCO does not directly participate in the research, it provides fellowships to train scientists from the developing countries, works to promote cooperation and flow of information and materials between South and North and serves as a forum for discussion of the social and ethical issues involved. (Source: UNESCO Sources, No. 29, September 1991)

Malaria parasite gaining ground against science

According to a new report* from the Institute of Medicine (IOM), humans are on the retreat after making significant progress against the parasite in the 1940s and 1950s. The disease is still felling victims in 102 countries, killing more than 1 million people a year - most of them children. Though chiefly confined to poor nations, malaria recently has come knocking in the United States.

Researchers and fieldworkers battling malaria are hampered by more than the biology of the disease. The African countries where 90 per cent of the malaria deaths occur have been ravaged by warfare, making it more difficult to combat the disease, and the rich nations that fund most malaria research are cutting their budgets.

The IOM report makes it clear that scientists still have a long way to go in unravelling malaria's basic biology. For example, it is not known why some people living in malarious areas become violently ill while others develop an immunity. Nor do researchers understand why drugs derived from the bark of the Peruvian chinchona tree control the parasite in the bloodstream, although the curative power of chinchona - the source of quinine - was recognized centuries ago. As for the best modern drug, chloroquine, researchers do not know exactly how it worked when it was first developed - or why it has been losing its potency over the past 40 years. Vaccine development meanwhile has languished after a big push in the late 1970s and early 1980s when the US Agency for International Development (AID) invested heavily in targeted research.

The IOM did not confine its survey to basic research. One of the panel's assignments was to survey the entire field of anti-malaria work and report on promising new approaches. This proved difficult because the field is splintered into many competing camps - basic researchers, clinicians, and mosquito-control experts. In the end, the IOM panel did not single out any particular strategy for special attention, but embraced them all. One reason for this was that the panel included representatives from every speciality. Even so, the panel did agree on some specifics:

- Nations in the endemic malaria zone should try to develop long-term malaria-control strategies, and multinational businesses should be asked to "contribute substantially" to these control efforts;

- The United States could offer the greatest help by expanding research on vaccines and potential new drugs;

- A massive screening programme by the World Health Organization that checks 140 million blood slides each year (detecting only 3-5 per cent positive) should be "reoriented" to collect more specific data, focused on high-risk groups and potential epidemics.

* Malaria: Obstacles and Opportunities, Committee on Malaria Prevention and Control, chaired by Charles C. Carpenter, Brown University.

(Extracted from Science, Vol. 254, 11 October 1991, p. 190, Eliot Marshall)

Bt resistance bugs biopesticides

Researchers in the Far East and the US have unveiled some harrowing news for the potential future of biopesticides. Some insect pests, including the diamondback moth, are emerging that are resistant to the Bacillus thuringiensis toxin.

A meeting of experts in Washington, DC has warned that farmers and seed companies will have to adopt conventional pest-management techniques if the potential of Bt-based biopesticides is not to be lost. This includes crop rotation and a more sparing use of the biopesticide by farmers.

According to Bruce Tabashnik, professor of entomology at the University of Hawaii, resistance to Bt doubled in the diamondback population, affecting watercress and cabbage fields on the island of Oahu between 1986 and 1989. In all cases, the scientists noted, the farmers were using frequent and high doses of the biopesticide.

Only by allowing the pests access to untreated crops, and so allowing them to damage them, will it be possible to slow the advance of

creeping resistance. This means that non-resistant pests will also survive and will be able to breed with the resistant strains. Because the trait is thought to be recessive it will take longer to show up in the population. Failure to combat the growing resistance could sound the dealth knell for the fledgling biopesticide sector as well as undermine years of research effort by the agro-chemicals industry.

Monsanto has been developing a cotton that has been genetically modified to include the gene for the Bt toxin to protect the crop from attack by bollworms. It is expected that the company will be in a position to sell seeds for the transgenic cotton in the mid-1990s. Entomologists are now calling on the company to sell transgenic seeds in mixtures with wild type cotton, to prevent farmers planting entire fields of Bt toxin-containing plants. (Source: European Chemical News, 18 November 1991)

Senior Advisory Group on Biotechnology on environmental priorities

"Biotechnologies have the demonstrated potential to preserve natural resources, protect the natural environment and prevent environmental problems", says the Senior Advisory Group on Biotechnology (SAGB) in its latest publication, Community Policy for Biotechnology: Benefits and Priorities for the Environment. Among the examples the SAGB highlights are the following:

- The modification of a natural micro-organism to produce glucose-6-phosphate dehydrogenase has improved the production efficiency of this biochemical used for blood diagnosis. 1 cubic metre of fermentation capacity now replaces 600 cubic metres, giving dramatic savings in the consumption of raw materials, water and energy;

- Enzymes derived from modified micro-organisms are now used in more than 75 per cent of all "enzyme" detergents. These produce energy savings of 30 per cent or more by allowing washing to proceed effectively at lower temperatures.

This 18-page brochure argues that a central pillar of EC biotechnology policy should be to support the development and application of biotechnology's potential for solving environmental problems. Among the areas where the SAGB calls for policy actions are the following:

- Policies for specific industrial sectors;

- Agricultural and rural development policies;

- Regional policy and structural funding;

- Small and medium-sized enterprise policy;

- Policies to reduce and eliminate environmental contaminants;

- European aid to development and policies under the Lomé Treaty;

- European science and technology policy and programmes.

An affiliated association of CEFIC, the SAGB - whose founder members were the Ferruzzi Group, Hoechst AG, ICI plc, Monsanto Europe SA, Rhône-Poulenc, Sandoz Ltd. and Unilever - is a senior industrial forum for debating policy issues affecting biotechnology in the European Community. Partly in response to growing competition from the emerging European Secretariat for National Bioindustry Associations, which is in the process of setting up shop in Brussels, the SAGB is now seeking to expand its membership. Details from: Brian Ager, Director, SAGB, Avenue E. van Nieuwenhuyse, 4, B-1160 Brussels, Belgium. Tel.: +32.2.676.72.86; Fax.: +32.2.676.72.88. (Source: Biotechnology Bulletin, Vol. 10, No. 10, November 1991)

New scientists needed to save the Earth

The International Council of Scientific Unions (ICSU) called the conference, entitled "An Agenda of Science for Environment and Development into the 21st Century", to provide the interdisciplinary voice of the science community in preparation for the UN's Earth Summit in Rio de Janeiro next June.

The conference called for the international science community to "undertake a review of environmental ethics related to such issues as the intrinsic value of nature, environmental rights of citizens, communal rights for common properties (atmosphere and oceans, for example) and ethical responsibilities of scientists".

The secretary-general of the Earth Summit, Maurice Strong, called for science to "develop a code of environmental and development conduct, readily accessible to the public, so that its guiding principles are transparent and the scientific community itself [is] accountable to other sectors of society".

The "new scientist", he said, should gain power as well as responsibilities. New ways should be found to present to policy-makers "the best scientific views on major issues, even where there was as yet no consensus". One successful example was the Intergovernmental Panel on Climate Change that has advised on the greenhouse effect.

Scientists must rise to the challenge of their new responsibilities, he said. "Too often in the past, scientists have limited their involvement with policy-makers to merely presenting them with their research findings, and have often been far from satisfied with the manner in which their discoveries have been employed."

The conference largely agreed. It committed ICSU to a review of science's relationship with everyone from UN agencies, to industry, environmental groups and the media. The examination will look at the need for new openness within science. It "should cover the integrity of data collection and the rights to publish and communicate scientific findings".

The conference's conclusions were presented to a working group drafting the science section of a declaration about combining economic development with environmental protection in the coming century. The declaration will be one of the main outcomes of the Earth Summit. (Extracted from New Scientist, 7 December 1991)

New research facility for third world scientists

The US-based Scripps Research Institute and France's Orstom (Institut Francais de Recherche

Scientifique pour le Développement en Coopération) have signed a five-year joint agreement to establish the Laboratoire Internationale de Biotechnologies Agricoles Tropicales (ILTAB). The laboratory will be set up within Scripps' new cellular biology department, in the plant biology division and will be located in La Jolla, San Diego in California. The purpose of the agreement is to promote and transfer biotechnology for tropical plants to developing countries. A network to promote tropical plant biotechnology will be developed to provide links among the main laboratories of industrialized countries. ILTAB will be the first link in the scheme designed to open the doors of international laboratories to researchers in the developing countries. (Source: European Chemical News, 25 November 1991)

Scientists seek a free future for biotechnology

Biotechnology could solve burgeoning environmental problems and provide the key to future economic development as long as it is not stifled by legislation, according to leading industrial scientists.

European policy which is now being developed must encourage it to fulfil its potential, says a report published by SAGB, the Senior Advisory Group on Biotechnology.*

SAGB is an industrial forum set up to promote biotechnology in the EC. It includes the Ferruzzi Group, ICI, Rhône-Poulenc, Hoechst, Monsanto Europe, Unilever and Sandoz.

With the world's population set to double to 10 billion over the next 50 years and 95 per cent of the increase expected in developing countries, the task of finding new, more efficient means of growth is becoming increasingly urgent, says the report.

Major contributions could be made in areas ranging from waste and sewage treatment to pharmaceuticals and food. Biotechnology-based processes are already cutting the environmental impact of industries including tanning, paper, textiles and packaging.

The 18-page report urges the Community to encourage the industrial use of new technologies and to ease their economic and social acceptance. Mistrust of biotechnology, which some fear could lead to "genetic engineering", continues to be a problem for the industry. In order to promote public confidence the report stresses that in many cases biotechnology copies natural processes, but uses fewer raw materials and less energy, and produces less waste.

Costs, however, are high and the lack of an EC policy has increased the uncertainty factor in new company decisions. SAGB insists that an integrated European policy on biotechnology, which would reassure investors and promote new technology, is the answer.

* Community Policy for Biotechnology: Benefits and Priorities for the Environment. SAGB, Av. E. van Nieuwenhuyse 4, bte 1, B-1160, Brussels, Belgium.

(Source: The European, 9-10 November 1991)

CGIAR goes out on a limb

One of the world's key agricultural research organizations - the World Bank-affiliated Consultative Group on International Agricultural Research (CGIAR) - is preparing to expand its scope from the smaller flora of the world to include research on trees. After more than two years of debate, the organization is finally moving ahead to open a new institute on social forestry research in southern Asia in late 1992. It will become CGIAR's 17th international agricultural research centre.

The new institute, scheduled to open with a staff of 30 to 50 researchers, will focus on a mix of applied and basic research intended to improve understanding of forest management and the social and biological factors that lead to deforestation. It will also begin a programme aimed at preserving and storing the germ plasm of trees.

Several Asian nations, including Malaysia, Sri Lanka and Indonesia, are lobbying to host the centre which should initially bring in between $4 million and $5 million a year in research money, and perhaps as much as $15 million a year by 1996. (Source: Science, Vol. 254, 8 November 1991, p. 787)

International advanced course. Engineering of biological reactions and processes

The second edition of this international course was given in Guatemala last May. Organized by the International Organization of Biotechnology and Bioengineering (IOBB) and the Center for Scientific and Technological Studies of ICAITI in Guatemala City, the course offers cost-effective continuing education for less developed nations that have cadres of scarce technologists. The programme consisted of 47 morning lectures and ten computer afternoon sessions. This was not an elementary course. Most of the lectures dealt with advanced topics and new research. There was heavy emphasis on modelling, computer control, computer tools for analysis and artificial intelligence. Lectures were supported by computer sessions where teams of students exercised the simulations and tackled problems. In addition, participants were encouraged to make presentations about their own organizations and projects. There were 34 full-time participants from 12 countries. Each participant left with sufficient literature and computer programs that are ideal for self study. The third edition of the course has been planned for the end of 1993. More details from the IOBB Chairman: Prof. Carlos E. Rolz, Center for Scientific and Technological Studies, ICAITI, P.O. Box 1552, Guatemala 01901, Central America.

The plant genetic resources of Latin America

The discussion on the conservation and use of plant genetic resources has become a major theme in the general environmental debate, and is now also firmly linked to the discussion on "biotechnology and development". Of eight chief Centres of Origin of the world's cultivated plants (so-called Vavilov centres), two are located in Latin America. The origins of many of the world's most important food crops (including the third and fourth: maize and potatoes), as well as those plants important for industrial, nursery and medicinal uses are found in these centres. In some cases, however, this valuable genetic material is severely threatened or extinction has already occurred.

A special issue of Diversity* shows that considerable efforts are under way throughout Latin America to survey genetic resources and protect them in both gene-banks and in situ (in the field). This reflects the current awareness

in the region of the importance that the conservation of plant genetic resources has. For instance, the Government of Costa Rica recently created, through the Ministry of Agriculture and the Ministry of Science and Technology, a National Commission of Genetic Resources. Latin American countries also play a major role in the development of FAO's Global System of Plant Genetic Resources. Recently, journalists from Latin American newspapers signed their names to a resolution supporting the conservation efforts of the international organizations (the Declaration of San José).

Regarding the international efforts, much attention in this special issue is given to the conservation work of the International Agricultural Research Centers (IARCs), that are financed by the Consultative Group on International Agricultural Research (CGIAR). Latin America hosts three of these centres: the International Center for Tropical Agriculture (CIAT, Colombia), the International Maize and Wheat Improvement Center (CIMMYT, Mexico), and the International Potato Center (CIP, Peru). Using new biotechnological techniques, these centres have speeded up conservation efforts for their respective mandate crops. This work is coordinated by the CGIAR's International Board for Plant Genetic Resources (IBPGR). An important regional institute is the Tropical Agricultural Research and Training Centre (CATIE, Costa Rica), that stores genetic material of a wide range of Mesoamerican plants, in cold chambers, in field collections, and in vitro. A crop-specific regional initiative is the Latin American Maize Project (LAMP). Supported by the seed company Pioneer Hi-Bred International, 11 Latin American countries and the United States cooperate to evaluate the agronomic characteristics of maize accessions in Latin American and US genebanks.

These ex situ conservation efforts must be complemented by conservation in situ, in which case the plants are not separated from their natural environment. In an interesting contribution, Dr. Stephen Brush describes how and why Andean farmers maintain a rich varietal diversity of potatoes, despite the introduction of modern high-yielding varieties. On a national level, Brazil's National Centre for Research in Genetic Resources and Biotechnology (CENARGEN) and Costa Rica's National Biodiversity Institute, carry out major in situ conservation programmes. These programmes may benefit from "debt-for-nature swaps", whereby international and conservation organizations purchase debt titles at 15 to 20 per cent of face value. The reduction of the huge foreign debts of Latin American governments deserves a high priority. Firstly, because the short-term urgency of earning foreign exchange forces many countries to exploit and destroy its tropical forests, while Dr. Al Gentry (Tropical forest diversity vs. development: Obstacles or opportunity?) shows that the products harvested from an intact rainforest can be economically far more valuable than what can be harvested under alternative development schemes. Secondly, the debt crisis has resulted in structural under-funding of national conservation programmes, thereby in some cases transforming gene banks into gene morgues.

* Diversity is a quarterly news journal for the international plant genetic resources community published by Genetic Resources Communications Systems, Inc. Subscription rates are: US$ 35 (North America) or US$ 50 (outside North America) for government/non-profit institutions and individuals; US$ 55 (North America) or US$ 70 (outside North America) for all others.

This issue of Diversity (Vol. 7, Nos. 1 and 2, 1991) has been published in both Spanish and English, and can be obtained through: Diversity/GRCS Inc., 727 8th Street, NW, Washington, DC 20003 USA. Tel:. (+1 202) 5436843, Fax: (+1 202) 5442521.

(Source: Biotechnology and Development Monitor, No. 8, September 1991)

Plans for an Intermediate Biotechnology Service

A central point of contact for biotechnology appraisal in relation to crop agriculture in developing countries is under consideration at the CGIAR Taskforce on Biotechnology (BIOTASK). The idea of an Intermediate Biotechnology Service (IBS) is currently being discussed by a group of interested donor agencies.

The IBS should play a central role in advising developing countries on plant biotechnology research and training before they embark on research programmes that require major investments. The IBS should inform on technologies as well as on related legal and regulatory issues. IBS would assist in national policy formulation, priority setting, building of capacity, training, socio-economic analyses, technology assessment, information, legal issues and biosafety. It will utilize existing biotechnology research networks, international research networks (such as the CGIAR), and regional key institutes in biotechnology. These groups will be represented in the research advisory panel in order to short-circuit the discussions between its clients (national agricultural research institutes, universities, private foundations, and non-governmental organizations in developing countries) and experts. (Source: Biotechnology and Development Monitor, No. 8, September 1991)

Whittling down in biotechnology

Chiron's (Emeryville, California) merger with rival biotech health-care firm Cetus (Emeryville, California) could be just the tip of the iceberg. New alliances in the $2-billion/year-plus biotechnology-based human therapeutics business are expected as recession continues to pinch funding in this research-intensive sector.

A key player eyeing an acquisition could be BASF (Ludwigshafen), according to some industry observers. While the chemical firm has long been active in biotechnology, experts say it could be ready for a stronger push.

Slow progress in getting biotechnology products to market - in an industry where total US R&D spending in 1990 reached $1.8 billion, outstripping sales by $600 million - has biotechnology firms seeking strategic alliances to secure research and development funding. Roger Shamel, president of biotechnology advisor Consulting Resources (Lexington, Massachusetts), says the 300 firms operating in the sector could be whittled down to 150-175 within a decade.

Last year Genentech (South San Francisco, California), the world's largest biotechnology firm, sold a 60 per cent stake to Hoffman-La Roche (Basel). More recently, Genex landed Enzon as a partner. But while biotechnology firms offer good

research and products, it is the traditional pharmaceutical companies that generally have access to funding. They also have stronger distribution and a better knowledge of how to handle product approval applications with the US Food and Drug Administration.

Shamel notes firms that have yet to get marketing approval are the strongest candidates for alliances. Those likely to stay independent include companies with management commitment and a promisng product base.

While some observers questioned the wisdom of Genentech's decision to sell a majority stake to Roche, Shamel says the company may have picked a good time to sell, since sales of tissue plasminogen activator are beginning to flatten. But progress of the Roche/Genentech alliance has not been smooth, and the difference in corporate culture led to the loss of many Genentech scientists.

While some observers see the deal as better, short-term, for Genentech, Shamel believes Roche's strategy will be vindicated in the end. (Extracted from Chemicalweek, 7 August 1991)

The biotechnologies - a logical path to nanotechnology

There is much talk of the biotechnologies replacing micro-electronics as the business area for the 1990s and beyond. In terms of growth this is probably true, for the commercial derivation of the biotechnologies is as new as that of semiconductor based micro-electronics in the 1960s. But will the economic impact of the biotechnologies eventually match that of micro-electronics?

Perhaps the second decade of the 21st century might see the marriage of micro-electronics - approaching ever closer the limitations of Heisenberg, and of that established molecular discipline, molecular biology in its manifestations of protain design, genetic manipulation, etc.

Nanotechnology is receiving more and more attention as a number of new techniques offer the prospect of engineering at the molecular level. Nanotechnology is quite simply the application of established engineering principles on a much smaller scale than ever envisaged before. Electron beam techniques can sculpt silicon wafers with increasing precision, and scanning tunnelling devices can arrange a line of atoms with startling geometrical definition. Nanotechnology, as the word suggests, is engineering at the nanometer level. How can devices be built on the atomic and molecular scale?

One approach, perhaps the "classical" nanotechnology approach, is to use various particle beams or tunnel effect devices either to sculpture or arrange atoms and molecules. At present-day precision levels even "ordinary" multimegabyte memory chips have a very high failure rate, with as many as 75 per cent of the chips on a silicon wafer being rejected. Two often it has been easy to overlook the biological approach to zero defect manufacture, as characterizes living organisms and more recently biotechnological processes.

Molecular engineering has been an established art in chemistry for some 90 years, and in biology for some 20 years. Our recent understanding of the physical and chemical processes involved in muscle contraction and other bio-motive forces provides an interesting insight into the coupling of electronic and biological nanotechnologies. The biotechnologies present the tools with which to transform new developments in nanotechnology into effective everyday devices with applications in medicine and system control.

Growing understanding of the interaction of carbohydrates and proteins with charged and polar surfaces throws pointers towards the integration of biological devices with semiconductor-based electronic devices.

There are four major classes of macro-molecules involved in biological process. They all have potential as nanotechnological intermediaries.

Carbohydrates

Considered simply as energy reserves for much of the century, it is now becoming clear that carbohydrates are a class of structural molecules as important as proteins or nucleic acids. First reports are identifying carbohydrate-linked biological activities that were previously associated only with proteins or nucleic acids. Polymers of various sugar molecules form straight or branched chain structures which occupy typically half the volume of a glycoprotein. Work in the past decade has studied the use of chemically engineered cyclodextrins and crown ethers as artificial enzymes. This is real nanotechnology and promises to yield real benefits. The difficulties arise in our as yet incomplete knowledge of carbohydrate chemistry and control of genetic expression.

Lipids

Perhaps the least easily adaptable class of biological macromolecules, lipids may offer scope for incorporation in devices that require fixed or variable dielectric constants. Lipid membranes generated by biological or biotechnological processes are highly defined, but enzymatic activity and changing electrical environment can effect major changes in porosity, surface characteristics and affinity. As liposome or liposome-like structures they engage a useful role in compartmentalization and both spatial and causal separation. In complex form with other biological molecules almost infinite possibilities are afforded.

Nucleic acids

Although nucleic acids are the ultimate repository of information in biological systems, the complexities of information retrieval may preclude their adopting such a role in nanotech structures. Where nucleic acids do stimulate interest is in their capacity for adopting functional 3-D structures. Energy transduction processes in 3-D nucleic acids may be influenced by a number of factors affecting charge distribution and physical constraint. Stability may be a limiting factor in some applications, but ultimately the capacity for self-repair, correction and replacement is very attractive. Nucleic acids are at their most attractive as the

raw stuff of protein structure. It is easy to generate nucleic acids that will yield a specific peptide structure.

Peptides and proteins

These will be the primary stuff of 21st century nanotechnological advance. The word "bionic" has very trivial associations with popular TV shows, but by 2050, bionic arms and legs, half made, half "grown", could be real. Proteins can be configured by modern means to adopt highly stable forms which offer potentially long use lifetimes (today in affinity chromatography columns, tomorrow in molecular devices). Already today pioneers are interfacing protein films with electronics in a number of "biosensors". As such interfacing becomes better understood and more reliable, barriers to price and acceptance will fall. Our ability to genetically engineer proteins and peptides of many classes is moving ahead with our understanding of those natural algorithms that generate higher order structure in the originally one-dimensional amino-acid sequence. (Source: Biotechnology Forum Europe, Vol. 8, No. 10, October 1991)

B. COUNTRY NEWS

Austria

Biotechnology organization in Austria and relations with EFB

1. Relations with EFB (see figure 1)

In Austria four societies are full members of the European Federation of Biotechnology (EFB):

- Austrian Society of Biotechnology, ÖGBT, Vienna;
- Austrian Association of Bioprocess Technology, ÖGBPT, Graz;
- Society of Austrian Food and Biotechnologists, VÖLB, Vienna;
- Society of Austrian Chemists, GÖCH, Vienna.

Some other scientific societies are partly active in multi- and interdisciplinary fields of biotechnology as indicated in figure 1.

Recently the Coordinating Committee of Biotechnology in Austria (ÖKB) was installed in close connection with ÖGBT in order to channel interaction with EFB and to coordinate official national activities (e.g. selection of delegates for EFB Working Parties according to transparent rules, contacts between the national societies, structuring Austrian activities along the lines of EFB, official reports).

At the moment there are no Austrian national study groups analogous to the Working Parties. All engineering biotechnology activities are collected and stimulated through ÖGBPT. In 1989, 8 of the 10 EFB Working Parties included delegates from Austria. A first meeting of all Austrian delegates took place in 1990.

2. Coordination of industrial interests

At the moment there is no direct coordination of biotechnology industries in Austria. Some exchange takes place in the course of the meetings of ÖGBT and ÖGBPT.

3. Public perception

Only a poor level of public relations is maintained at the moment, mainly by the annual meetings of ÖGBT. Another contribution is made by a monthly series of lectures in Graz called "BIOTEC Seminar Steiermark", organized by ÖGBPT since 1986.

Recently a political programme called "Eco-Social Market Economy", which represents efforts in the direction of "Closed Cycle Production Systems", was chosen as a joint research activity according to the new definition of biotechnology given by EFB: "Biotechnology is directed towards the benefit of mankind by obeying biological principles".

4. Research at universities and other institutes

The following three institutes at three universities are heavily involved in biotechnological research:

- The University of Forest and Agriculture (Inst. Appl. Microbiol., H. Katinger et al.);
- Technical University Vienna (Inst. Biochem. Technol. & Microbiol., W. Hampel et al.);
- Technical University Graz (Inst. f. Biotechnology, Microbiol. & Waste Technol., A. Moser et al.).

There are three main areas of concentrated efforts in R&D:

1. Pharma-Biotechnology: ACC (Vienna, Linz);
2. Biopolymers: PHB, cellulose degradation (Graz, Linz);
3. Bioprocess Technology: Bioreactor systems, closed cycle production (Graz).

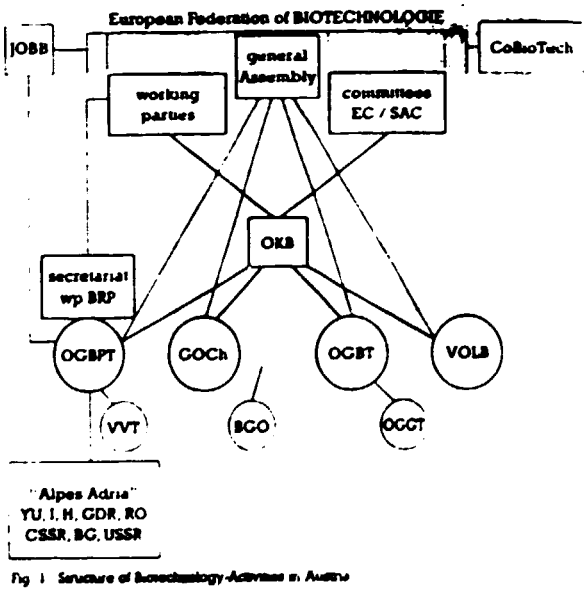


Fig. 1 Structure of Biotechnology-Activities in Austria

ÖKB Austrian Coordination Committee Biotechnology (Moser, Wohlmeyer, Katinger, Kininger)
ÖGBT Austrian Society of Biotechnology
ÖGBPT Austrian Association of Bioprocess Technology
VÖLB Austrian Society of Food & Biotechnologists
GÖCh Society of Austrian Chemists
VVT Society of Chemical Engineers
ÖGGT Austrian Society of Biochemistry
wp BRP EFB-working party "Bioreactor Performance"
IOBB Internat. Organization of Biotechnol. & Bioengng

ref. A. Moser (1989) report to EFB SAC/EC, in EFB Newsletter

5. Conclusion

The overall situation in Austria can be summed up as follows:

- Increased European activities (EFB, EC);
- Efforts in the direction of structuring biotechnological activities, e.g. by the OKB where there are difficulties due to a low critical mass, a West/East gradient and observable centralization in Vienna;
- Strong reputation of Austria as a "green" country with a high level of public consciousness for living quality leading, for example, to advanced concepts in R&D ("Model Austria" combining the use of raw material from agriculture and the environmental engineering efforts; the "closed cycle production systems", the "eco-social way") fulfilling the vision of "Biosociety" with a strong new dimension orientation on ethics.

(Reprinted from EFB Newsletter No. 23, September 1991)

Canada

Synergie in Quebec

In an attempt to increase the innovative technological capabilities of its university researchers and industries - and thus the province's competitiveness in international markets - the Quebec government has set up a programme called Synergie to encourage university/industry collaboration. It will distribute $32 million to successful applicants over the next five years.

Synergie will support projects that could help industry to produce new products or processes and commercialize them; that involve a level of risk a firm could not assume alone; that stimulate interest in innovation and technological development in research centres or industrial firms; or that promote development of the personnel required for innovation.

Researchers in universities, colleges and affiliated organizations can apply. Their projects must involve at least two participating Quebec companies, must cost more than $1.5 million and must last from one to five years. Companies must put up between 10 and 40 per cent of the cost, depending on their size.

The programme will be administered jointly by the departments of industry and higher education and science, and the first group of approved projects will be announced in March 1992. (Source: Nature, Vol. 354, 12 December 1991)

Research commercialization

Although Canada has not been as quick as other nations to recognize the importance of biotechnology to industrial growth, that situation is now changing. In recent weeks, the federal Government has released a report aimed at strengthening the Canadian biotechnology industry, and both Canada's science minister and the president of the National Research Council (NRC) have taken up the issue.

National Biotechnology Business Strategy: Capturing Competitive Advantage for Canada finds a variety of obstacles hampering Canadian biotechnology development.

The report's recommendations include:

- Creating funding pools of $35 million to $50 million for small-company investment, offering investors tax incentives and encouraging joint industry-provincial development funds;
- Setting up high-technology company management courses, and making immigration easier for foreigners with required skills;
- Upgrading university research through support of indirect costs; and
- Streamlining regulations and patent laws and harmonizing them internally and with those of other countries.

More than 200 Canadian companies already use biotechnology, but the report identified four areas in which significant market opportunities are matched by Canadian strengths: waste management, forestry, food and agriculture, and human biopharmaceuticals. (Source: Nature, Vol. 354, 12 December 1991)

China

China-EC Biotechnology Centre

A jointly funded China-EC Biotechnology Centre (CEBC) has been set up by the EC and the Chinese Government. It is located in Beijing within the National Centre for Biotechnology Development.

The main objective of CEBC is to promote scientific and technological cooperation between researchers from China and the Member States of the EC in the field of biotechnology applied to medicine and agriculture. The CEBC will aid in the establishment, expansion or improvement of cooperative links in these areas. The CEBC will also coordinate and manage joint EC-China biotechnology research activities.

The types of activities supported will include:

- Research visits;
- Collaborative research;
- Workshops;
- Training.

The establishment of the CEBC represents a significant opportunity for Irish laboratories to develop collaborative research links with China or to attract Chinese trainees.

For more information on CEBC and its activities contact: Dr. Jim Ryan, BioResearch Ireland, EOLAS, Glasnevin, Dublin 9. Tel: 353-1-370177; Fax: 353-1-370176 or Mr. Luc Vandebon, China-EC Biotechnology Centre, Ta Yuan Diplomatic Offices Building 2-6-1, Liang Ma He Nan Lu 14, Beijing 100600, People's Republic of China. Tel: 861-532-4443; Fax: 861-532-4342. (Source: Irish Biotech News, December 1991)

Costa Rica

Prospectors for tropical medicines

This year, one of the world's smallest countries will pair up with the world's largest drugs company to try something completely different. They believe they can extract valuable substances from the flora and fauna of the forest, sell them to the pharmaceuticals industry and, possibly, hold the bulldozers at bay. The experiment is called chemical prospecting, a term usually attributed to Thomas Eisner, professor of biology at Cornell University in the United States, Costa Rica, a Central American country about the size of Denmark, and Merck & Company of Rahway, New Jersey, are about to put it to work.

Endowed with one of the world's most diverse tropical landscapes, Costa Rica wants to turn itself into a kind of biological OPEC. It would protect its biota as other countries now do their oil or minerals, sharing it in return for a portion of the profits from its chemical bounty. Spearheading the plan is the National Biodiversity Institute (INBio) founded two years ago in Heredia, in the heart of Costa Rica's lush, agriculturally rich central valley. Says Rodrigo Gámez, a plant virologist who runs INBio: "We want to put our biodiversity to work for us. But we want to be perceived as partners, not as a resource to be exploited".

The agreement signed with Merck is the first of what Gámez hopes will be several partnerships with drug companies. Merck will provide $1 million over the next two years, which, along with launch funds from US and European universities, foundations and Governments, will help to build INBio into a chemical prospecting business. In return, Merck will acquire exclusive rights to screen for pharmaceuticals any plant extracts collected for it by INBio. INBio's prospecting for industrial clients will dovetail with its own ambitious 10-year scheme, already under way, to inventory its entire flora and fauna, the biggest biological project undertaken by any tropical country.

Costa Rica's gambit is designed to make its forests pay for themselves while the country acquires the technology needed to screen natural compounds in its own institutions. From now on, says Gámez, "we will have absolute control over who will be allowed to operate in protected areas". Biologists will have to get permits and deliver samples of everything they collect to INBio. Any profit made on their work must be shared with Costa Rica. According to Gámez, government officials from several tropical nations have consulted with him on how to set up similar schemes.

Income from prospecting will be used to support the country's huge conservation programme. Numerous donors have helped to landscape Costa Rica's green future. Money has come from the environment budgets of the MacArthur and Alton Jones Foundations and the Pew Memorial Trust (all in the US), from the Governments of the United States and Sweden as well as that of Costa Rica itself, and from numerous conservation groups and small private donors. The country has its own flourishing conservation movement and well established biological research organizations such as the Fundación Neotrópica based in San José.

Chemical prospecting will capitalize on an effort Dan Janzen began in the 1980s to create a corps of "parataxonomists". Convinced that those who understand the biology of the tropics will want to conserve it, Janzen, Gámez and collaborating scientists are educating the population, especially the youngsters, in tropical ecology. Costa Rica is fertile territory: 90 per cent of its adult population is literate, according to government figures.

The vanguard of the bioliterate are parataxonomists - farmers, housewives, bus drivers, former park guards and other lay people who are trained to become field collectors and paid for their work. After completing a six-month course covering botany, entomology and ecology, INBio's 31 parataxonomists have moved out into the country's biological reserves and parks. Splitting their time between home and a field station, they collect plants and insects. Every few days, their dried, pinned and boxed collections are driven to INBio. There, in an airy, high-ceilinged room lined with cases of specimens, curators preserve them and affix each with a bar-coded label for computer classification of its genus, species (if known), and where and when it was found.

Experience and advice offered by Janzen and visiting researchers from the Natural History Museum in London, the Smithsonian Institution in Washington DC, the Missouri Botanical Garden and other scientific centres have taught parataxonomists which insects to look for. They prepare the specimens with naphthalene, mount them, and regularly deliver them to INBio.

Tropical plants are especially well-endowed with chemical defences, as they must repel so many types of predators. Their armoury includes alkaloids, such as morphine and nicotine; phenolics and tannins, found in tropical trees like cecropia and mangrove; cyanogenic glycosides, in passion flowers and manioc, and terpenoids, found in more than 30 species of plant in Costa Rica's dry forest. About a quarter of all medical prescriptions in the US are formulations based on substances from plants or microbes, or are synthetics derviced from such sources. Alkaloids come from flowering plants, yet only about 2 per cent of these plants (some 5,000 of the estimated total of 250,000 species) have so far been examined for them. Eisner also notes that insects have never been systematically studied for valuable chemicals. He won fame for discovering the bombardier beetle's bizarre ability to defend itself with a spray of benzoquinones, and he believes insects are an untapped source of useful compounds.

Interest in botanicals at pharmaceuticals companies ebbed after the 1950s, when fermentation with micro-organisms (the source of penicillin) and synthetic chemistry became more popular. A few drugs companies such as Merck kept at it, but the work was viewed as laborious and highly speculative. Now things have changed. Charles McChesney, a natural products chemist at the University of Mississippi, has watched closely the "return to nature". "The synthetic chemists have made the easy molecules", he says; now they must synthesize and investigate some five to ten thousand chemicals to get one new drug lead. Given the high cost of chemical synthesis, says McChesney, companies are increasingly inclined to let plants and other organisms do the synthetic work.

Meanwhile, bio-assays that exploit new molecular techniques - such as the cloning of genes for receptor molecules, the usual targets for drugs on the surfaces of cells - are speeding up the process of screening plant extracts. Using cells engineered to carry a particular type of receptor, for example, researchers can home in on plant extracts that contain compounds which stimulate or block the receptor. A natural products laboratory, says Eisner, can now screen thousands of compounds in a week.

Even so, Georg Albers-Schonberg of Merck's natural products division is sceptical about chemical prospecting paying off soon or handsomely. In the past 25 years, the company has marketed only five drugs discovered by screening natural extracts, all from micro-organisms. So why the contract with INBio? One reason, says Albers-Schonberg, is the precarious state of the world's tropical forests. Merck executives have woken up to the fact that a vast reservoir of potential drugs is rapidly disappearing, and that it may be now or never for chemical prospecting. The emergence of faster screening techniques is another key factor. In the past, Merck has only dabbled with natural compounds, but it now realizes that for a relatively modest investment it can enter a partnership that could yield thousands of extracts for screening.

Other organizations are thinking along similar lines. The US National Cancer Institute in Bethesda, Maryland has created a repository for botanical specimens and raised its budget for collecting new species of plants and micro-organisms. Last month, the NCI renewed two five-year contracts with the Missouri and New York botanical gardens in which botanists will collect specimens for testing as anti-cancer and AIDS treatments. The chemicals company Monsanto recently signed a contract for several million dollars with the Missouri garden for three years of collecting. Monsanto calls the programme "bioprospecting" and is interested in soil micro-organisms as well as plants. Other companies are looking for botanists who can make sense of tropical flora. (Source: New Scientist, 19 October 1991)

European Community

Progress on EC biotechnology programme

The EC biotechnology programme now looks likely to issue a call for proposals early in the new year, following its approval by the Council of Ministers. The programme, which has a budget of 164 million ECU, will fund projects in basic biotechnology in the areas of:

1. Molecular approaches: Protein structure and function, and gene structure (including large gene-sequencing and mapping projects on yeast, Arabidopsis and other species).

2. Cellular and organism approaches: Cellular regeneration, reproduction and development of living organisms; basic metabolism; and communication systems (e.g. immuno and nervous systems).

3. Ecology and population Biology: Ecological implication of the release of GMOs and conservation of genetic resources. The call for proposals is unlikely to be before March 1991.

(Source: Irish Biotech News, December 1991)

National biotechnology associations launch new industry body in Brussels

Organizations representing the interests of bioindustries in seven European countries have taken a major step towards increasing their visibility and accessibility and making Europe a major force in the commercialization of biotechnology by establishing a joint secretariat and administrative centre in Brussels.

The new organization, called the European Secretariat of National BioIndustry Associations (ESNBA), has as its parent bodies the national bioindustry associations in Belgium, Denmark, France, Italy, the Netherlands, Spain and the UK. These seven organizations believe that Europe-wide coordination is vital for European companies to exploit the potential of emerging markets in the face of intense competition from biotech companies in the USA and Japan.

In addition to providing a European focus for the collation and dissemination of information on national and international issues, the seven founders hope the ESNBA will help them make an effective contribution to the development of EC regulatory policy and to the coordinated application at national level of EC directives affecting biotechnology.

The executive council of ESNBA will meet every two months to set policy and coordinate operations. Activities of the central office will be carried out by its own staff under the supervision of an Executive Secretary appointed every six months from the parent bodies on a rotation basis. The first to take up this position is the Executive Director of the UK's BioIndustry Association (BIA), Mr. Louis Da Gama. He believes that ESNBA will provide an excellent platform for European biotechnology associations and their member companies and says: "While we have been working closely together for several years, we have always suffered through lack of continuity of administration and follow-up. We now have a means of speaking with one voice on EC matters on behalf of our members and of working towards the best conditions possible to help European biotechnology companies compete effectively in world markets." The ESNBA address in Brussels is: Avenue Louise, 490 bte 9, B-1050 Brussels, Belgium. Tel.: 32-24-646-37-03; Fax: 32-2-640-37-59. Further information is available from: Mr. Louis Da Gama, Executive Secretary, European Secretariat of National BioIndustry Associations, c/o The BIA, 1 Queen Anne's Gate, London SW1H 9BT. Tel. 071-222-2809. (Source: ESNBA News Release, 16 December 1991)

In vitro test validation centre

During the development of new in vitro toxicity testing procedures a critical stage is the process of assessing their potential and validating their usefulness in regulatory toxicity testing systems. The European Centre for the Evaluation of Alternative Testing Methods (ECVAM) has now been established by the EC to assist this process.

The main tasks of the ECVAM are to:

- Validate testing procedures;

- Maintain a database of validated test methods and appropriate contacts for technical back-up;

- Promote exchange of information regarding testing methods;

- Coordinate communication between interested parties (e.g. scientists, animal protection groups etc.).

The centre is located in the EC Commission's Joint Research Centre and is supported by the JRC's technical infrastructure, in particular by its toxicological laboratories. For more information contact: The Director of the Environment Institute, Joint Research Centre, I-21020 Ispra, Italy. Tel.: +39-322-789-834; Fax: 39-322-789-222. (Source: Irish Biotech News, December 1991)

Biotech can make green contribution, says SAGB

SAGB, the Brussels-based Senior Advisory Group on Biotechnology, is calling on the EC and governments to establish policies that promote the environmental benefits of biotechnology.

"If Europe is to meet the environmental challenge of the next decade, an integrated approach using all available technologies must be employed", commented SAGB chairman Peter Doyle. The group argues that biotechnology must be part of that approach.

The SAGB in its latest paper, Benefits and Priorities for the Environment, says biotechnology will preserve natural resources, protect the natural environment and prevent environmental problems. "But to fulfil the potential it is essential that policy is in place that promotes routine use of technologies that offer environmental payoffs."

SAGB cites a number of examples which show biotechnology to be a "green" technology. Biotechnology's contribution to improved agricultural productivity, the ability of certain bugs to clean up polluted sites and treat toxic wastes plus the fact that most of its raw materials are renewable are among some of its more obvious environmental attractions.

Some advantages, however, are not so obvious. Biotechnology can curb the environmental impact of a number of activities. "Enzymes derived from modified microorganisms are now used in more than 75 per cent of 'enzyme' detergents. These produce energy savings of 30 per cent or more from lower temperatures."

Enzymes are also being used to cut the environmental impact of the leather and paper industries. They are being used increasingly to remove hair from animal hides and treat chrome shavings in tannery waste streams. In paper production, the enzymes are used to improve the separation of lignin from cellulose.

In each case the potential environmental payoff is very attractive, according to SAGB. Use of enzymes in leather production means less lime and sodium sulphide are needed to dissolve hair; the volumes of organic solvent used are reduced; the biological oxygen demand in waste water is cut and chrome salts can be reused rather than dumped as shavings. Use of enzymes by papermakers cuts chlorine bleach demand by some 35 per cent.

In other industrial processes, such as production of diagnostics, antibiotics or even bioplastics, environmental payoffs include dramatic reductions in consumption of energy and clean water, significantly reduced loads on waste-treatment systems and use of non-hazardous compounds and the utilization of renewable raw materials. (Source: European Chemical News, 18 November 1991)

France

French drug industry initiative

The French pharmaceutical company Rhône-Poulenc is expected to announce a new government/industry biotechnology initiative that could amount to between FF 1,000 million and FF 2,000 million ($170-340 million) in new research funding over the next five years. Known as Bio-Avenir, the project is part of a major shift in the mostly State-controlled French pharmaceutical industry towards more life sciences research - supported by an increase in the price of research-intensive drugs.

Bio-Avenir is to be split between industry and government research institutes, with between 30 and 50 per cent of the funding coming directly from the Government. Research priorities are expected to include cellular regulation, the structure and function of macromolecules and membrane transport.

Seeking to bring the domestic pharmaceutical industry more in line with European standards, French cabinet officials are also planning to propose major drug pricing reforms to Parliament in October. If the new plan is approved, French pharmaceutical companies will be able to charge enough for "innovative drugs" to recover research costs and keep up with their international competitors. State pricing controls now keep French drug prices some 30 per cent below the European Communities average. (Source: Nature, Vol. 353, 10 October 1991)

Germany

German biotech law centre seeks collaborators

A research centre for biotechnology and law has been established at the Universities of Luneburg and Hanover. The centre has a data bank covering German biotechnology laws (recommendations, decisions, comments, literature). They are now seeking partners in universities, firms or other organizations in EC member States who would be interested in establishing an international data bank. The objective is to provide a Europe-wide on-line source of information for consultation, communication and research that might aid in standardizing the law throughout member States. Details are available from: Prof. Dr. J. Simon, Forschungszentrum Biotechnologie und Recht an den Universitäten Hannover und Luneburg. Hanomagstrasse 8, D-3000 Hanover 91. Tel.: (49) 511-449-81-67; Fax: (49) 511-83-03-37; ECHO Euromail Nomos R 457 22 19 32 02. (Source: Irish Biotech News, August 1991)

Hong Kong

Biotech grows in Hong Kong

Several Asian Governments regard biotechnology as an obvious successor to consumer electronics in their struggle to succeed in the world's high-technology markets. The pursuit has plenty to recommend it to nations that are

relatively poor and often short of land. After all, biotechnology is scientist-intensive - research and development accounts for about 80 per cent of overall costs - and it does not require huge amounts of capital or working space.

For several years, Japan has played a small but significant role in the global biotechnology business. More recently, the Governments of Singapore and Taiwan have taken measures to encourage the growth of the biotechnology industries. Singapore has set up an Institute of Molecular Biology to undertake basic research and biotechnology, while Taiwan has funnelled several million US dollars into biotechnology-related industries such as agriculture and pharmaceuticals.

But the first effective biotechnological products to emerge from Asia that are not Japanese may well come from Hong Kong.

Three years ago, a small group of scientists founded the Hong Kong Institute of Biotechnology (HKIB). A year later, the non-profit institute received $22 million in funding from the Royal Hong Kong Jockey Club. This year, HKIB has started to produce results - a joint venture with the US pharmaceutical company Syntex that will search for new pharmaceutical products, and a memorandum of understanding with Radian, another US company, for a venture that will offer environmental technology services to local companies.

A major reason for the founding of the HKIB was the prospect that it would serve as a gateway to mainland China, which has both vast resources of natural products and a large reservoir of excellent biotechnologists.

HKIB's joint venture with Syntex, called HKIB/Syntex, will use Chinese resources in its first project. The objective is to screen synthetic and natural products from China - particularly those used in traditional Chinese medicine - for pharmaceutical potential. Scientists at HKIB and Syntex Research in Palo Alto, California, will carry out the screening. The raw materials will be gathered by researchers associated with the Chinese Academy of Sciences.

HKIB is also acting as the middleman in a more local project, designed to clear indigo dye from Hong Kong's waterways. The territory's garment industry uses about 4,000 tons of dye annually, to make blue jeans blue. According to Chinese University microbiologist Kai Keung Mark, about one tenth of that ends up in the waterways, which it stains an unpleasant blue/black colour.

Two years ago, Mark discovered a natural strain of bacteria that degrades indigo, converting it into colourless, non-toxic compounds. Now, Mark and HKIB are undertaking research on the compound. Investigations include determining how much the bacteria produce of the enzyme responsible for decolourizing indigo and analysing how long the bugs can withstand high concentrations of indigo in waste water from garment factories. Biologists hope that genetically engineered versions of the bacteria could replace the process of stone washing to give jeans the fashionably faded look, and could even remove the indigo from waste waters before they reach waterways.

HKIB's other main initiative, in cooperation with the US company Radian, shows the institution's pragmatic side. The aim is to provide clean-up services, such as water treatment, for Hong Kong companies, and the joint venture will not restrict itself to biotechnology- based services. It is prepared to offer whatever technology is needed for the jobs at hand. (Source: Nature, Vol. 352, 25 July 1991)

India

Challenge to AZT

India is the latest country to challenge the Burroughs Wellcome monopoly on AIDS drug AZT. Three Indian pharmaceutical companies expect to sell the drug on the domestic market and for export before the year's end.

The Indian Institute of Chemical Technology (IICT), which developed the process for synthesizing AZT, has licensed the process free of cost to Lupin, Cadila and Reddy Laboratories. According to Dr. A. V. Rama Rao, director of IICT, the Indian-made AZT will cost a quarter or less of the current Wellcome prices.

The fact that AZT has been at the centre of patent disputes in the United States and Canada does not affect India, which has not signed the Paris Convention and does not recognize patent protection for pharmaceuticals. Under Indian patent law, only processes, and not products, may be patented. Several Indian companies are exploring the foreign market in Africa and other areas where Burroughs Wellcome has no patent. The World Health Organization has shown interest in the Indian product and may become the largest buyer, Rao says. (Source: Nature, Vol. 353, 17 October 1991)

Japan

Energy and functional food in Japan today

The Japanese believe that food and medicine have exactly the same function which basically is health.

The food industry has discovered the beneficial effect of certain ingredients in the human body and a brand new category of products have found increasing space on the shop shelf: functional foods.

Industries producing such products are allowed to print an identifiable logo (1) on the packaging to make food recognizable by the consumer as having special healthy features and been previously reported and checked by appropriate government departments.

A definition of functional foods can be as follows:

- Containing components that are effective to prevent illness;
- Containing ingredients which are commonly used in food or existing as a standard micro component of ingredients.
- To be eaten as normal food without time restrictions.
- To be clearly described for its functionality on the label.

Functional food has become one of the most active categories on the Japanese food market and

its influence has reached almost every category as consumers are asking for increasingly healthy food with appropriate nutritional characteristics and the current market value is estimated to be $1.2 billion.

(1) Beverages

Producer	Product name	Function
Otsuka	Oranomin C	Anti-fatigue tonic
Otsuka	Fibe Mini	Dietary fibre supplemented orange
Asani Beer	Karkade	Relaxing flower-scented soft beverage
Shirakawa Sansai	Kenko-tea	Natural tea containing Dokudami as valuable anti-constipation
Maruzen Kogyo	Fruit Spinach	Iron & Vitamin C rich blend spinach/carrot
Nihon Kokumin	Jobury	Orange juice enriched with Ca from oyster shell
Elbee	Elbee Honey & Lemon	Lactic acid drink for growing children
Iwatani	Vivalth	Citric juice enriched with extract of turtle for easy digestion

(2) Chewing gum

Warner Lambert	Clorets	Containing chlorophyl derivate for fresh breath
Lotte	Super Black	Enriched in caffeine against sleep
Glico	Kiss-mint	Camomile enriched for relaxing effect
Meiji	Soft Taste	With functional stress-reducing ingredient

(3) Candy

Koyo Seika	Palatinose jelly	Calcium fortified Palatinose sweetened jelly
Ise Shokuhin	Ise No Tamago	Candy containing EPA and DHA effective for lowering cholesterol
Kenkyujn	Dr. Spirulina	Candy containing Spirulina, beta-carotin from algae functioning as easy to digest
Lotte	Yogurt 100	Containing living milk-oligosaccharide

(4) Miscellaneous

Nippon Synthetic	Borage	Flavoured dry mix for diluting, enriched with seed oil rich in gammalinoleic acid extracted from primrose
Asada-Ame	Eylume	Supplement food for reinforcing eyesight based on wild blueberry
Ichiwa	Koijin-A	Supplement food for eyes based on carp's organs and pearl oyster
Nissei	Health Spread	Vegetable spread based on 100% Omega-3 oil
Jap. Ind. Research	Tangerine Loaf	Bread produced using fresh skinned high fibre tangerines instead of H20

(Source: Agro-Industry Hi-Tech, August 1991)

STA to start nanobiology/micromachines project

The Science and Technology Agency (STA) will start a nanobiology project in fiscal 1992. It will bring together experts from the fields of biotechnology and electronic engineering to develop micromachines and bioelements. Living organisms consist of nanometer-size as proteins, nucleic acids, carbohydrates and lipids. The project will attempt to explain synergistic associations between these molecules and pathogenic substances to provide a database for new drug development. The STA project will also aim to unravel the mechanisms of action of cilia, flagella and other organelles in the hope of putting the principles to work in micromachines. (Source: McGraw Hill's Biotechnology Newswatch), 16 September 1991)

Portugal

Biotechnology in Portugal

1. Relations with the European Federation of Biotechnology

The Sociedade Portuguesa de Biotechnologia (SPBT) with 500 individual members and 20 collective members (industry) is the only representative of Portugal in the European Federation of Biotechnology (EFB).

The SPBT is an open section of the Sociedade Portuguesa de Bioquimica. The SPBT nominates Portuguese members for the Science Advisory and Executive Committees as well as for the Working Parties of EFB. The SPBT is organized in sectoral groups which correspond to the Working Parties of EFB. The Portuguese delegates in the Working Parties of EFB are sectoral group leaders in Portugal.

The SPBT was established at the end of 1981 and has been a member of EFB since 1983. A series

of national congresses (Congresso Nacional de Biotechnologia) has been organized biannually since 1982 to promote, discuss and develop biotechnological activities in Portugal. The national congress is the most important event in Portugal in this area as it provides a unique opportunity for members of the SPBT from all over the country to meet. SPBT is directed by a chairman and three co-chairmen who are elected in the General Assembly for a two-year period and who have the following responsibilities: overall coordination of SPBT, relations with EFB, coordination of the bulletin (Boletim de Biotecnologia), organization of the national congress, relations with industry, research laboratories and universities, and financing.

The SPBT is organized in two regional sections: Northern Section (based in Oporto) and Central Section (based in Coimbra).

Another important feature of SPBT is the publication of a bimonthly bulletin which acts as a medium of communication among the members and contains news, research and review articles, and announcements.

2. Biotechnology research in Portugal

Research programmes are coordinated by the National Board for Science and Technology (JNICT) in Portugal, an organism that belongs to the Secretary of State of Science and Technology. JNICT is organized into several Coordination Committees of Research (CCI) which correspond to the priority areas.

The CCI for biotechnology is made up of seven experts (researchers and university professors) including the chairman (J. M. S. Cabral) and a co-chairman (M. Mota) of SPBT with technical assistance from the staff of JNICT.

Biotechnological research in Portugal is mainly carried out at universities and national laboratories. The main centres of biotechnology R&D are:

- Technical University of Lisbon, Faculty of Engineering (Instituto Superior Técnico), Section of Biotechnology (J. M. Novais) with Enzyme Engineering (J. M. S. Cabral), Fermentation Technology (M. M. R. Fonseca), Microbial Physiology and Genetics (I. Sá-Correia), Downstream Processing (J. M. S. Cabral), Food Biotechnology (J. M. Empis), Environmental Biotechnology (J. M. Novais), Bioreactors and Measurement and Control (J. P. Cardoso and S. Alves);

- Technical University of Lisbon, Faculty of Agronomy (Instituto Superior de Agronomia), Section of Microbiology with Microbial Physiology of Yeasts (V. B. Loureiro);

- University of Lisbon, Faculty of Science, Department of Plant Biology with Plant Tissue and Cell Culture (M. S. Pais), Plant Physiology (J. Arrabaca), Plant Ecology (F. Caetano), Mycology (J. L. B. Ferreira), Microbial Technology (N. T. Rodeia) and Genetics (C. Queirós);

- New University of Lisbon, Faculty of Sciences and Technology, Section of Biotechnology with Molecular Biology and Human Genetics (L. Osório), Safety in Biotechnology (L. Archer), Department of Chemistry and Chemical Engineering with Fermentation Technology (J. P. Crespo). Other researchers and university staff from this university work in the Centro de Tecnologia Quimica e Biologia (CTQB);

- The Center of Chemical and Biological Technology (CTQB) in Oeiras (A. Xavier) was recently established to promote research in areas related to agriculture and agro-food industries. The main research groups in biological fields are: Molecular Biophysics (A. Xavier), Metallo-Proteins (J. J. Moura and I. Moura), in vivo NMR and Metabolism (H. Santos), Protein Structure and X-Ray Crystallography (P. Matias), Genetics of Anarobes (C. Araiano), Genetics of Bacilli and Streptomyces (H. Lencastre), Animal Cell Technology (M. Carrondo), Plant Genetics (J. Almeida), Plant Biochemistry (C. P. Ricardo), Microbiology (J. F. Marques) and Lactic Acid Bacteria (V. San Ramao);

- University of Porto, Faculty of Engineering, Department of Chemical Engineering with Bioreactors (M. Mota), Measurement and Control (S. F. Azevedo) and Food Engineering and Simulation (A. Sereno);

- University of Porto, Centre of Experimental Cytology with Medical Microbiology (T. Silva), Genetics (C. Sunkel) and Plant Biology (R. Salema);

- University of Porto, Institute of Biomedical Sciences (ISBAS) with Yeast Genetics (P. M. Ferreira) and Immunology (M. Sousa);

- Catholic University, School of Biotechnology (ESBUC) (A. Medina) with Food Engineering;

- University of Coimbra, Faculty of Sciences and Technology, Department of Chemical Engineering with Protein Purification and Enzyme Engineering (F. A. P. Garcia); Department of Chemistry with Enzyme Immobilization and Biosensors (H. Gill); Department of Biochemistry with Protein Purification and Enzymology (E. Pires) and Thermophiles (M. Costa);

- University of Minho, Braga, Department of Biological Engineering with Biofouling and Environmental Biotechnology (L. Melo and M. Pinheiro) and Fermentation Processes (O. Maia); Department of Biology (C. Leao) with Microbial Physiology and Plant Biology;

- University of Trá-os-Montes e Alto Douro (UTAD), with Food Technology and Lactic Acid Bacteria (A. Ferreira), Cellulases (A. N. Pereira) and Plant Genetics (H. G. Pinto);

- University of Aveiro with Environmental Technology (A. Duarte) and Immobilized Enzymes (I. Delgadillo);

- University of Azores, Department of Science and Technology (J. Medeiros) with Thermophiles and Food Engineering (D. Ponte);

- University of Algarve, Department of Horticulture (E. Faria) with Plant Tissue and Cell Culture.

The non-university institutes active in the field of biotechnology are:

- Gulbenkian Institute of Science (IGC) (H. Menano), Oeiras, a well-known research institute in biology with Microbial Physiology (N. van Uden), Cell Biology (D. Ferreira), Biomechanics (H. G. Ferreira), Biochemistry (C. Lechner), Virology and Immunology (C. Geraldes and J. V. Costa) and Molecular Biology of Eucaryotes (C. Pousada);

- National Laboratory of Industrial Engineering and Technology (LNETI), Department of Chemical Industry (DTIQI) (I. Florêcio) with Fermentation Processes and Biohydrometallurgy (J. C. Duarte), Protein Purification and Affinity Processes (A. Karmali) and Liposomes and Drug Delivery (E. Cruz); Department of Food Industry (DTIA) (A. Severo) with Biomass and Fermentation Processes (T. A. Colaco and J. C. Roseiro) and Dairy Industry (M. Barbosa); Department of Effluents and Industrial Analysis (M. V. Pinheiro) with Gas Effluent Technology and Phenol Degradation; Department of Renewable Energies, Group of Biomass (H. M. Fernandes) with Biogas (Santini), Algae Biotechnology (H. M. Fernandes) and Ethanol Fermentation (M. F. Rosa).

The major setbacks of biotechnological research in Portugal have been the lack of a "critical mass", of significant financial support for research projects, members of staff, modern equipment, e.g. pilot plants, specialized technicians, the hindrance by bureaucracy and structure and the lack of financial support for establishing and nurturing international contacts and collaboration.

It has to be mentioned that in Portugal the amount of money spent on R&D is relatively small. Only 1 per cent of the gross national income is allocated to research.

Recently the Science Programme (Programa Ciência) with financial support from the EC to cover and improve R&D in Portugal was approved. Biotechnology is a priority of this programme and 15 million ECU are allocated to basic infrastructure for the period 1990-1993 to establish new centres and/or reinforce existing ones. A programme for training and fellowship was also approved in the same programme to double the critical mass of research in the next four years. This programme is coordinated by JNICT. Every year JNICT launches calls for proposals for research projects; it has been the main financial support agency for the research groups working in universities, laboratories and industries. LNETI has also received strong support from the Ministry of Industry as it belongs to this department. The Technical University of Lisbon (Section of Biotechnology), the Gulbenkian Institute of Science, CTQB and the University of Porto (Department of Chemical Engineering) have also received financial support for projects approved in the biotechnology programmes, EAP and BRIDGE.

3. Biotechnology education in Portugal

Biotechnology education in Portugal is established at undergraduate and post-graduate level studies.

The following undergraduate courses related to biotechnology lead to the first university degree ("Licenciatura"):

- Technical University of Lisbon: Diploma in Chemical Engineering with specialization in Bioprocess Engineering and Diploma in Agro-Industrial Engineering;

- University of Lisbon: B.Sc. in Biochemistry and B.Sc. in Applied Plant Biology;

- New University of Lisbon: B.Sc. in Applied Chemistry with specialization in Biotechnology;

- University of Porto: Diploma in Chemical Engineering with specialization in Bioengineering and B.Sc. in Biochemistry;

- University of Minho: Diploma in Biological Engineering;

- Catholic University: Diploma in Food Engineering.

At post-graduate level there are the following M.Sc. courses (1 year course and 1 year research):

- M.Sc. Biochemical Engineering (Technical University of Lisbon);

- M.Sc. Molecular Biology (New University of Lisbon and Gulbenkian Institute for Science);

- M.Sc. Plant Biotechnology (Faculty of Sciences, University of Lisbon);

- M.Sc. Food Science and Technology (Technical University of Lisbon);

- M.Sc. Food Engineering (Catholic University);

- M.Sc. Immunology (Institute of Biomedial Science, Porto).

4. Bio-industries in Portugal

Portugal has a weak industrial sector in biotechnology. This is one of the major setbacks for the development of biotechnology in this country. While academic research and education have recently been encouraged and are expected to expand further in the next four years, Portuguese industry is not moving with these developments: only traditional biotechnological (fermentation and food) industries are established in Portugal.

The most active and important industry is the pharmaceutical industry, namely for production of antibiotics (CIPAN, Hovione, BIOFRANCO) and steroids (Hovione, QUATRUM). In addition to these national companies, Gist-Brocades has a

Penicillin G and a yeast producing plant, and other multinational companies (Schering, Hoechst, Ciba-Geigy, etc.) have small plants for drug formulation without industrial activities in biotechnology.

The agro-food industry also represents an important sector of Portugese economy. However, this industry is traditionally very conservative and only recently have biotechnological methods and approaches slowly been introduced. The wine industry represents a major sector with "Vinho do Porto" (Port Wine), "Vinho Verde" (Green Wine) and other common wines. Portugal also has breweries (UNICER and CENTRALCER), bakeries, meat and fish industry and dairies. Recently a new industry BIOROPE was established which deals with crop improvement.

The major problem in Portuguese industry is the lack of a critical body at research level, of trained personnel, industrial research and development, modern equipment and genetic manipulation techniques for improving microbial processes.

With the increase of R&D activities in the Science Programme, a positive input in Portuguese industry may be expected. The areas lacking biotechnological activity in Portuguese industry include health care which is without diagnostic kits (to be produced in Portugal) and various human and animal vaccines. The plant biotechnology area should also be developed to improve crops. Fishery and related industries should also be improved by marine biology, rDNA techniques (transgenic fishes) and process engineering. (Reprinted from EFB Newsletter, No. 23, September 1991)

Singapore

Asia-Pacific's industries of tomorrow need biotechnology today

The Asia-Pacific region's quest for biotechnology solutions continues to accelerate as the region expands into a higher level of industrialization. Biotechnology is seen to be crucial for assisting industrial growth and is being eagerly sought in a diverse range of industries which include, among others, the pharmaceutical, chemical, food, seed and agriculture, medical, energy, environmental and cosmetic.

Singapore is already among the newly industrialized nations, actively seeking to develop and promote widely the applications of biotechnology. Recent investment plans include:

- The introduction of research centres for different areas of biotechnology;
- Training engineers in bioprocessing to develop methods for mass production of new products;
- Setting up clinical research facilities for extensive testing of products before commercialization.

These investments, which are part of a wider development programme, will also help to service the needs of Malaysia, Indonesia and its other ASEAN neighbours, Australasia and other economies in the Asia Pacific region. Singapore still maintains its position as the commercial centre in the region. Due to its favourable economic and political climate, it is not surprising that international companies continue to set up their regional quarters in Singapore. The development of various biotechnology facilities which meet the needs of the growing industries in the Asia Pacific region will further strengthen Singapore's role as a service centre.

To stimulate rapid expansion and to foster international links the Economic Development Board of Singapore, together with the Commission of the European Communities, are jointly sponsoring the staging of a special three-day convention on biotechnology - BIO-INDUSTRY '91 - held on 1-3 October 1991 at the Mandarin Hotel, Singapore.

The BIO-INDUSTRY '91 Convention was specially designed so that participants from Europe and the Asia Pacific region can benefit from:

1. Attending a comprehensive seminar programme, presented by speakers from Europe and Singapore, covering government policies, state-of-the-art developments, industrial case studies and other important subjects;
2. The services of an on-site secretariat to arrange bilateral meetings with government officials and policy-makers, biotechnologists, industrialists, financiers, prospective customers and other participants;
3. The opportunity to publicize their interests, activities and projects to other participants on an information display panel (for poster sessions);
4. Listing contact details, activities, projects and interests of their oganizations in the Convention directory to provide a permanent source of reference for use during and after the Convention.

(Source: Agro-Industry Hi-Tech, August 199.)

United Kingdom

Regulation cost concerns

British biotechnologists are concerned that proposed genetic engineering regulations, published in October 1991 by the UK Government, will place British companies at a competitive disadvantage within the European Communities (EC).

The regulations are designed to comply with two EC directives regulating the contained use and deliberate release of genetically engineered organisms. Among other things, the directives say that no environmental releases of engineered organisms will be allowed without the prior approval of national authorities and propose that, once a product containing an altered organism is approved in one member State, it can be marketed throughout the EC.

But Louis De Gama, executive director of the BioIndustry Association, is concerned that the regulations will place a greater financial burden on researchers and industry than those being drawn up in other EC States.

The British Government estimates that implementing the new regulations will cost between

£3 million and £10 million over the next five years. Most of this money will come from companies and research institutes, which will be charged for consents to market products containing engineered organisms and to release altered organisms into the environment.

Officials in the Environment Directorate-General of the European Commission, which drafted the two EC directives, say that the member States will be left to draw up their own charges for consents to release organisms. Britain is one of four EC States so far to have passed laws to comply with the directive on environmental release. Among the others, Denmark and Germany are proposing similar fees for consents. (Source: Nature, Vol. 354, 7 November 1991)

Department of the Environment publishes GMO regulations for consultation

Britain's new regulations on genetically modified organisms (GMOs), due to come into force six months after the October 1991 deadline set by the European Community, have been published for consultation by the Department of the Environment. Copies are available from: Department of the Environment, Room A338, 43 Marsham Street, London SW1P 3PY. Comments need to be in by 22 January 1992. A useful review of the current status of the background to these regulations can be found in ENDS Report 201, available from Environmental Data Services Ltd., Finsbury Business Centre, 40 Bowling Green Lane, London EC1R ONE or on 071-278-4745/7624. Fax: 071-837-7612. (Source: Biotechnology Bulletin, Vol. 10, No. 10, November 1991)

Nuffield Council on Bioethics

The Nuffield Foundation has announced the 14 eminent members of the Nuffield Council on Bioethics which will be chaired by Sir Patrick Nairne. The Foundation's initiative in establishing a Council on Bioethics is in response to recent developments in biological and medical science which present ethical issues considered to be of great potential difficulty and increasing importance.

The terms of reference of the Council are:

1. To identify and define ethical questions raised by recent advances in biological and medical research in order to respond to, and to anticipate, public concern;

2. To make arrangements for examining and reporting on such questions with a view to promoting public understanding and discussion; this may lead, where needed, to the formulation of new guidelines by the appropriate regulatory or other body;

3. In the light of the outcome of its work, to publish reports; and to make representations, as the Council may judge appropriate.

For further details contact: David Shapiro, Nuffield Foundation, 28 Bedford Square, London WC1B 3EG; Tel.: (44)-71-631-0566; Fax: (44)-71-323-4877. (Source: EBIS, No. 5, October 1991)

NEDO predicts explosive growth in exploitation of biotechnology

UK sales of biotechnology products are expected to exceed £350 million in 1991, with just under half of that value being exported. In addition, biotechnologies support sectors of the economy - including chemicals, pharmaceuticals and agriculture - which together account for 21 per cent of UK gross domestic product.

At the launch of a new report by the National Economic Development Office (NEDO), the Government's chief scientific officer, Professor William Steward, said that the UK must get three issues right if it is to make a commercial success of biotechnology. The key issues are: public perception and regulation; the scientific research base; and technology transfer from the laboratory to industry.

NEDO concludes that "identifiable biotechnology products have sales of billions and show growth rates of 30-40 per cent per annum". The report, New Life for Industry, assesses the position of the UK in a global context and includes specially commissioned research to show: which industries will be affected; where the leading businesses are headed; and how markets will develop. Details of the report, priced at £95.00 (plus £2.50 postage and packing) from: NEDO Books, National Economic Development Office, Millbank Tower, Millbank, London SW1P 4QX or on 071-217-4037. (Source: Biotechnology Bulletin, Vol. 10, No. 9, August 1991)

Biotech means business

The UK Department of Trade and Industry (DTI) is to set up a new biotechnology initiative, aimed at encouraging better collaboration between the science base and British industry. Trade and industry secretary Peter Lilley hopes that the new programme, "Biotechnology Means Business", will make UK companies more aware of the opportunities offered by biotechnology.

The announcement came as a consortium of experts outlined possibilities for a national biotechnology strategy. The Biotechnology Joint Advisory Board (BJAB), set up in 1989 and headed by British Bio-Technology chairman Brian Richards, advises the DTI and Britian's research councils on strategy, funding for biotechnology R&D, training and education, and technology transfer.

In its new report,* BJAB sets out research priorities for eight major industrial sectors: pharmaceuticals, agriculture, chemicals, food, diagnostics, environment, animal health and process engineering. As part of its strategy for the chemical industry, BJAB hopes to encourage the application of biotechnology "beyond the high value area", with a focus on the use of biocatalysis in production. Efficiency, process replacement, product improvement and routes to new products are identified as priorities in this area.

* "Biotechnology: A strategy for industry strength", BJAB. Contact the Biotechnology Unit, Laboratory of the Government Chemist, Queens Road, Teddington, Middlesex TW11 0LY.

(Source: Chemistry & Industry, 7 October 1991)

Oxford University seeks partners

Researchers at Oxford University in the UK are looking for industrial partners to commercialize a technology that uses a microbial filter to remove toxic compounds from waste streams.

The filter, which employs the soil bacterium Citrobacter, relies on the principle that many compounds are rendered insoluble with the addition of a phosphate group to their molecular structure.

A phosphatase enzyme in Citrobacter is able to transfer phosphate groups from donor molecules to compounds containing heavy metals such as uranium or caesium. The Citrobacter also offers the advantage that it is not poisoned by the heavy metals and can tolerate high salt concentrations and wide temperature variations.

The Oxford team has succeeded in growing the bacterium on glass beads that can be packed into cartridges. The filter cartridge is then placed in the flow of the waste stream enabling treated compounds to be trapped within the filters.

Initial tests indicate that the filter is capable of removing up to 95 per cent of metals from solutions. (Source: European Chemical News, 11 November 1991)

Genome Project

Even as UK scientists criticized the US National Institutes of Health (NIH) for raising the spectre of commerce in trying to patent gene sequences, the UK Genome Project has been holding its sequences secret while it prepares to sell them to industry.

Over the past year, researchers working on the Human Genome Mapping Project of the UK Medical Research Council (MRC) have identified about 2,000 human genes, in the form of sequences of fragments of complementary DNA, or cDNA. But rather than publish these sequences or make them available to other scientists, project officials have kept them in closely guarded storage while they developed a database that would allow them to charge industry for access.

Because cDNA, which is the genetic material actually expressed in the body, represents functioning genes, rather than just genetic material that may or may not have a function, researchers consider cDNA sequences more marketable than simple DNA fragments.

The UK project is preparing to sell access to its genome databases at an initial cost of £5,000 per company per year, plus £1,000 for each additional user within the same company. Academic scientists who agreed to sign a non-commercialization agreement would get free access. More than 700 such academics are now using the existing DNA databases of the MRC, which do not yet include the cDNA libraries. No companies have yet been given access to the databases. Although project officials explain that they are simply applying standard MRC policy to "take opportunities for commercialization where they arise", this is believed to be the first time a government has decided to sell its portion of the international genome effort. (Extracted from Nature, Vol. 354, 14 November 1991)

United States of America

US biotechnology in good health

The United States is still number one in the commercial exploitation of biotechnology, but progress in the development and marketing of new products made through biotechnology has been slower than expected, according to a report* released by the congressional Office of Technology Assessment (OTA). The report emphasizes that the key to maintaining a competitive position in the world marketplace depends less on the targeted sponsorship of biotechnology by the federal Government and more on a strong research base.

According to OTA, biotechnology-based drug development is flourishing. To date, 15 drugs and other biological products have been approved by the US Food and Drug Administration (FDA), and more than 100 others are in various stages of development. 1991 has been the best year since the stock market crash of October 1987 for biotechnology companies hoping to raise capital in the public markets.

OTA reports that the commercialization of biopharmaceutical products developed using biotechnology has been slower than expected and that the impact of biotechnology on other sectors of industry - agriculture, the chemical industry and the environmental business - has been limited.

Also, six years after the Coordinated Framework for Regulation of Biotechnology was first proposed and four years after it was made final, regulations for genetically-modified pesticides and certain micro-organisms are still not in place. This failure has led industry representatives to complain that the approval process as it stands is unclear and serves as a disincentive to investment.

Other policy issues singled out by OTA as relevant to US competitiveness include the need to structure coherent tax policies and adequately protect intellectual property rights. As markets in biotechnology become increasingly global, OTA says that protection of intellectual property is likely to become less of a domestic issue and more of an intenational one.

* US Congress, Office of Technology Assessment, Biotechnology in a Global Economy, OTA-BA-494 (Washington, D.C.: US Government Printing Office, October 1991)

(Source: Nature, Vol. 353, 31 October 1991)

US biotech sales step up

Revenues for the US biotechnology industry climbed to $5.8 billion in 1991, a 23 per cent jump from 1990, according to consultants Ernst & Young (San Francisco). The firm puts biotech product sales at about $4 billion, a 38 per cent rise from last year. Ernst & Young also notes that the biotech industry raised roughly $2 billion through initial and secondary public offerings during the year, achieving a total market capitalization of $35 billion, up 75 per cent from the previous year. The firm puts research and development costs for biotech's public companies at $1.3 billion, up 18 per cent. (Source: Chemical Week, 2 October 1991)

US okays rDNA rabies vaccine

The US FDA has given the go-ahead for the first use in North America of a vaccine produced by recombinant DNA technology. The vaccine, developed by Du Pont and Rhône-Mérieux with the involvement of a number of other research bodies, will be used to control rabies. A major programme of eradication of the disease is due to start shortly in the eastern states of the US.

The product, Raboral, is administered to wildlife capable of carrying the rabies virus. It has already proved effective in France and Belgium, where it has been used mainly with the red fox. The drug is administered orally through special baits which the animals are attracted to eat. In the US, the racoon and skunk will also be included in the eradication programme.

The animal vaccine uses a porcine vector. Work is currently under way at Rhône-Mérieux on a human vaccine based on a fowl vector. It has reached the clinical development stage, with the first trials just commencing in Rheims, France.

The recombinant technology also opens up prospects for other vaccines. Mérieux is preparing a measles vaccine, while a malaria vaccine is at an advanced stage, according to Philippe Desmettre, head of the company's vaccines research effort. (Source: European Chemical News, 25 November 1991)

Approvals still slow, but pipeline full

One hundred and thirty-two drugs and vaccines are now in development at US biotechnology companies, a 63 per cent increase since 1988, according to a report released by the US Pharmaceutical Manufacturers Association (PMA) entitled "Biotechnology Medicines in Development". Of these, half are being tested for cancer, or cancer-related conditions.

But although the future clearly looks bright, biotechnology in the present is still more smoke than fire. Just three biopharmaceuticals have been approved by the US Food and Drug Administration (FDA) in the last 16 months, the date of the last PMA survey, and only 14 such biotechnology products have been approved over the last nine years. Given this disturbing trend, the PMA has estimated that, at current staffing and funding levels, it would take the FDA 13 years to approve the 21 medicines already awaiting approval.

The United States can, however, draw comfort from the fact that of the 169 genetic engineering health-care patents issued in 1990, 82 per cent were of US origin; Japan was second with 11 per cent. (Source: Nature, Vol. 353, 17 October 1991)

California tackles insurance

The California state legislature is poised to pass a bill that would place an eight-year ban on the use of genetic information to discriminate among people in selling health insurance. If the bill is not vetoed California will become the first state to prevent health insurers from using the results of genetic tests to influence underwriting decisions.

The bill would also ban the use of genetic test information in employment decisions. The original draft proposed an indefinite ban on health insurers using genetic test results, but in a compromise to reduce opposition from the insurance industry, the bill emerged from the state Senate Judiciary Committee with the health insurance ban curtailed to an eight-year moratorium.

The bill is now expected to be passed by the legislature within a matter of days, and then needs only the governor's signature to become law.

Insurance companies argue that genetic test results are no different from the other medical data they use in underwriting health insurance. The industry fears that if applicants for health insurance are able to withhold genetic information, those whose genetic test results reveal that they are likely to have high health care costs will seek out health insurance in greater numbers. The result would eventually be higher outlays for insurance companies, and the undermining of the industry, insurers say.

On the other hand, some medical geneticists argue that genetic information is fundamentally different from the other data used by health insurers. If tests become available to identify a wide range of genes that confer susceptibility to particular health problems, they say, the whole notion of "shared risk" that underlies the insurance business will be subverted, and people whose genetic makeup indicates a higher probability of illness will find it difficult to get affordable health insurance. (Extracted from Nature, Vol. 353, 5 September 1991)

Convicts' DNA prints added to US police files

Law enforcement agencies in the US are starting to collect DNA samples from convicted criminals. Their aim is to keep such "genetic profiles" on file, just as they keep fingerprints. Since June 1990, the state of Virginia has collected blood samples from 33,000 people convicted of serious offences, and 2,000 more samples are added every month. The purpose of these DNA banks is to help solve future crimes. Police will try to match DNA patterns from blood, hair or semen stains found at the scene of a crime to DNA data on past offenders. Thirteen states now have laws allowing police to collect samples of DNA from convicts. Seven states are sharing their data as part of a pilot programme organized by the FBI. Virginia, however, is far ahead of the other states in developing its programme. Law enforcement agencies in the US already maintain larger collections of genetic data than all academic and research institutions combined, and their data banks are growing very rapidly.

Many states now allow much broader use of DNA data banks, usually covering anyone convicted of a serious criminal offence. Iowa's law allows police to collect DNA samples from those convicted of minor offences as well. The Pentagon, meanwhile, is looking into the possibility of collecting DNA samples from all its soldiers and keeping them on file. This information could help identify soldiers killed in combat. (Extracted from New Scientist, 21 September 1991)

Yugoslavia

Biotechnology organization in Yugoslavia and relations with European Federation of Biotechnology (EFB)

1. Links with the European Federation of Biotechnology (see Fig. 2)

Two Yugoslav professional societies are members of EFB:

- Association of Yugoslav Microbiological Societies (AYMS);
- Society of Chemists and Chemical Engineers of Croatia (SCCEC).

Other academic and professional societies which promote biotechnology in the country are:

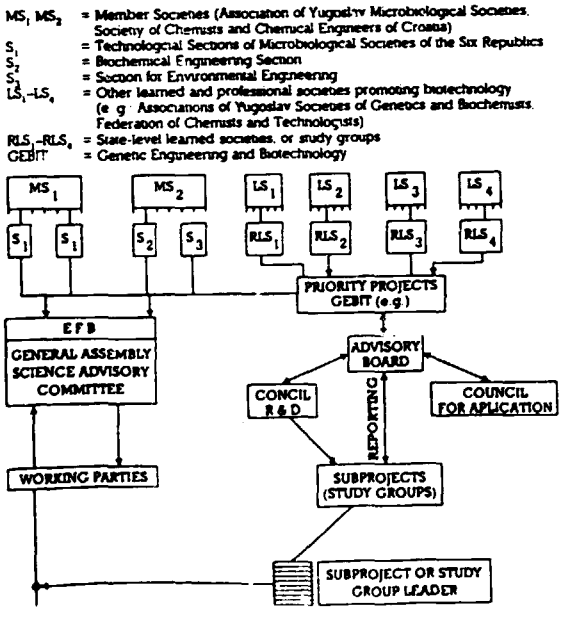
- Association of Yugoslav Societies of Geneticists (AYSG);
- Society of Yugoslav Biophysicists;
- Association of Biochemical Societies of Yugoslavia;
- Federation of Chemists and Technologists of Yugoslavia.

At present, no Yugoslav Biotechnology Society exists. Biotechnologists, as members of the societies listed, are active in their specific groups or sections. Some of the most active are:

- Technological Sections of the AYMS;
- Biochemical Engineering Section of the SCCEC;
- Groups for Molecular Biology of the AYMS.

These sections/groups nominate the Yugoslav members for the Science Advisory and Executive Committees, as well as for the Working Parties of EFB.

All of the Yugoslav representatives in the EFB Working Parties are actively involved in one of the three Yugoslav priority projects in biotechnology. Some of them are leaders of subprojects or study groups. The above described structure is shown below.



2. Coordination of industrial interests

The coordination of industrial interests is effected by the Federal Committee for Science and Technology (FeCoST), recently renamed Federal Committee for Development (FeCoD), and by the Union of Self-management Communities for Science (USCoS). Government policy is defined by a "Strategy of Technological Development". This means that FeCoST (FeCoD) and USCoS give priority to those projects aiming at specific target products or processes. These projects must (1) have considerable financial support of the industry/industries interested and (2) include universities or research institutes from two Republics at least. On that basis, the following projects in biotechnology have been set up:

- Biotechnology of the future;
- Genetic engineering and biotechnology;
- Chemical and biochemical manufacture of maize.

A few industrial research departments (PLIVA and KRKA Pharmaceuticals, PODRAVKA Food Industry, for instance) are involved in these projects.

3. Public perception

The attitude of the general public towards modern biotechnology is generally positive. General information on biotechnology is supplied by mass media and journals for popularization of science. New developments in biotechnology and processes using genetically manipulated micro-organisms have not encountered an emotional response.

4. Research at universities and institutes

Six universities (of the existing 19) and six outstanding research institutes are engaged in priority and other biotechnology projects. These institutes are: Boris Kidrič, Vinča; Rudjer Bošković, Zagreb; Jožef Štefan, Ljubljana; Institute for Molecular Genetics and Genetic Engineering, Beograd; Institute for Biological Research Sinisa Stanković, Beograd; Research Center for New Technologies, Skopje; Faculties of Natural Sciences and Mathematics at Beograd, Zagreb and Novi Sad Universities; Faculty of Food Technology and Biotechnology, University of Zagreb; Biotechnical Faculty, University of Ljubljana; Faculty of Technology and Agriculture, University of Novi Sad; Central Institute for Tumours, Zagreb; Maize Institute, Zemun Polie and several others.

5. International relations

International collaboration is fairly well developed with a number of research institutes, including grants from the EC, as well as from American foundations.

Successful collaboration is organized by the interregional organization Alpe - Adria. The Institute for Molecular Genetics and Genetic Engineering in Beograd is a regional centre of the UNIDO network with seat in Trieste (International Centre for Genetic Engineering and Biotechnology). The Department for Biochemistry of the Institute Jožef Stefan in Ljubljana is a reference laboratory of a similar UNESCO network.

6. Education

The training of biochemical engineers, biotechnologists, molecular biologists and microbiologists is offered at many Faculties of the Universities of Beograd, Zagreb, Ljubljana, Novi Sad and Skopjie on undergraduate and graduate level. International seminars on graduate level are also initiated in successful collaboration of the universities, institutes and industry.

7. Conclusion

Biotechnological activities in Yugoslavia are limited by chronic underfinancing, regional isolation, inadequate internal structure and organization and a lack of strictly formulated common objectives. The foundation of a Yugoslav Biotechnological Society would help to overcome some of these limitations; this seems to be one of the first common targets. (Reprinted from EFB Newsletter, No. 23, September 1991)

C. RESEARCH

Research on human genes

Ni(II) complexes induce DNA cleavage

Square-planar Ni(II) complexes of polyazamacrocycles can catalyze the oxidation of guanine residues in DNA, leading to strand scission, say Xiaoying Chen, Steven E. Rokita and Cynthia J. Burrows of the State University of New York, Stony Brook. They find that only macrocyclic Ni(II) complexes with vacant coordination sites, a positive charge on the complex, and a relatively high Ni(III)→Ni(II) reduction potential are effective agents for DNA oxidation. In addition, oxidation is specific to sterically accessible guanine sites. All guanines are equally reactive in single-stranded DNA, but only accessible guanines are oxidized in double-stranded DNA, such as those at helix termini. The researchers believe oxidation may occur by direct metal binding to DNA, followed by activation of an external oxidant for site-specific modification and strand scission. The Ni(II) complexes could potentially be used as probes of nucleic acid structure and as therapeutic agents. (Reprinted with permission from Chemical and Engineering News, 29 July 1991, p. 19. Copyright (1991) American Chemical Society)

Marfan syndrome linked to gene

Researchers in the US have identified a gene linked with Marfan syndrome. Evidence from separate teams leaves little doubt that the syndrome is caused by defects in fibrillin, a protein in connective tissue. By analysing the role played by the normal protein in the tissue, researchers aim to discover how its abnormal form causes symptoms of disease.

People with Marfan syndrome have a wide variety of problems, including eyesight defects, heart disease and abnormally long limb bones.

Last year, researchers led by David Hollister at the University of Nebraska found defective fibrillin in people with the disease but could not prove a link. Francesco Ramirez and his team at Mount Sinai School of Medicine, New York has now cloned the gene for fibrillin and mapped it to a segment of chromosome 15. In studies of families with the disorder, he found a tight linkage between the gene and the syndrome.

Ramirez and his colleagues also found a gene on chromosome 5 that is similar, but not identical, to the gene on chromosome 15. Both, it seems, are involved in coding for fibrillin.

After examining families with various manifestations of the disorder, they found that the gene on chromosome 5 was linked with a related syndrome, congenital contractural arachnodactyly (CCA).

Lyn Sakai and her colleagues at Shriners Hospital in Portland, Oregon, have sequenced the gene for fibrillin. Knowing its nucleotide sequence and structure will help to explain the protein's function and what happens when its structure is abnormal, says the team. And in a third paper, Harry Dietz at Johns Hopkins University has identified a new mutation in the fibrillin gene on chromosome 15 in two patients with Marfan syndrome. Neither patient had a family history of the disease, so the presence of the mutation together with the disease is further strong evidence of the link, says the team. (Source: New Scientist, 27 July 1991)

Do genes play a role in AIDS?

Some people may carry genes that slow the course of AIDS, say researchers in California. HIV-positive men who remain healthy are more likely to have a specific "signature" of human leukocyte antigen (HLA) genes on chromosome 6 than men who have AIDS or early signs of the disease.

The HLA genes govern a vital part of the immune system. They encode proteins, or antigens, that enable the T-cells of the immune system to "recognize" foreign proteins. T-cells will recognize such proteins only when they are bound to HLA antigens. The HLA genes are some of the most variable in the human genome, and everyone has a slightly different set. They are classified into two groups: class I, which govern "killer" T-cells and class II, which control the "helper" T-cells.

Because HIV attacks helper T-cells, scientists have wondered whether different alleles, or alternative forms, of HLA genes might be associated with the strength of a person's immune response to HIV. Several small studies have already reported links between certain HLA alleles and the severity of AIDS. However, they have all identified the HLA signatures of their subjects using a relatively crude technique, tissue typing.

Now Mary-Claire King, Leslie Louie and Beth Newman at the University of California, Berkeley, have used direct analysis of DNA to study the HLA signatures of 114 HIV-positive men. This method, which uses the polymerase chain reaction and gene probes, is far more accurate than tissue typing, say the researchers.

The men were selected from a group of more than 1,000 men, infected and uninfected, who have been examined regularly since 1984.

Most doctors trace infected individuals' progression to AIDS by measuring how the levels of T helper cells, or CD4 cells, decline in their blood. The researchers found that certain linked alleles, including DRB1*0702 and DQA1*0201, were linked with the rate of decline of these cells. However, the links were weak. The two linked alleles that were common in symptom-free men may not in themselves be responsible for slowing progression to AIDS, the researchers warn. This particular combination of alleles is only one of about 20 combinations of DR and DQ alleles, all of which are tightly linked on the chromosome. Other combinations may also be involved.

The researchers hope that by learning which HLA antigens help to slow disease progression, they may gain clues to which part of the immune response to HIV is useful in fighting the virus. This could have implications for future therapies. (Source: New Scientist, 24 August 1991)

Unravelling the ageing mystery

The basic genetic mechanisms of ageing are the focus of a $4.6 million grant recently awarded to The University of Texas Health Science Center at San Antonio by the National Institute on Ageing. Researchers are studying the human transferrin gene - which manufactures a protein that transports iron throughout the body. Previous tests have revealed that as humans age there is a decrease in the production of transferrin, which compromises the availability of iron to the cells. The result is that all organs function less vigorously, which may partly explain why people lose energy as they grow older. Researchers hope to learn how the expression of several important genes changes as humans age. These findings may lead to better treatment of a variety of blood diseases such as haemophilia, and endocrine-related disorders such as infertility. Other genes under study produce proteins to combat inflammation, regulate sex hormone function and regulate the process of blood clotting - all of which are adversely affected by age.

For more information, contact Cary Corbin, Robin Magers or Donna Butler, Dublin-McCarter & Associates. Tel.: 512/227-0221. (Source: Biobytes, San Antonio Biotechnology News & Information, August 1991)

RNA polymerase activity viewed close up

The first close-up view of RNA polymerase in action has been obtained by biologists at Washington University in St. Louis. RNA polymerase is a cell enzyme that reads, or transcribes, genetic information in DNA. The researchers attached molecules of this enzyme to a glass slide. Then, using a sophisticated light microscope connected to a video camera, they recorded the movements of a 40-nm gold particle attached to the end of a DNA molecule that was being transcribed by the RNA polymerase. As the DNA molecule ratcheted through the polymerase, the length of the gold particle's DNA tether increased, allowing the particle a greater range of Brownian motion. By analysing the particle's Brownian motion, the researchers were able to measure the rate at which the polymerase molecule moved along the DNA strand. The work was reported by Robert C. Landick and Dorothy A. Schafer of Washington University, Jeff Gelles of Brandeis University and Michael P. Sheetz of Duke University Medical Center. The technique they describe is expected to lead scientists to a better understanding of how RNA polymerase starts and stops transcription. This has implications for ailments such as cancer, where transcription goes awry. (Reprinted with permission from Chemical and Engineering News, 12 August 1991, p. 27. Copyright (1991) American Chemical Society)

Gene jam holds hope for leukaemia therapy

The gene that causes a common type of leukaemia can be blocked in cancerous cells without damaging healthy ones, say scientists in the United States. The findings suggest that gene therapy for the disease is a distinct possibility, if an expensive one.

"This is a first step", says Cezary Szczylik, a member of the team who led the work in Bruno Calabretta's laboratory at Thomas Jefferson University in Philadelphia. Although the team has worked only with cells in culture so far, they expect to start studies in mice soon.

About one in 10 of the new cases of leukaemia diagnosed every year is chronic myelogenous leukaemia (CML) - a disease which results from a swap of genetic material between chromosomes 9 and 22. A piece of the so-called "breakpoint cluster region" on chromosome 22 becomes attached to chromosome 9, while chromosome 9 loses a gene known as abl which fuses to the remainder of the breakpoint region on 22. The altered chromosome 22 is known as the Philadelphia chromosome.

Instead of simply rearranging the genetic material, this swap creates a new "hybrid" gene on 22. Known as bcr/abl, it codes for a particular protein in cells carrying the hybrid gene. People affected have abnormal stem cells in their bone marrow, which produces more of the protein encoded by bcr/abl, leading to the production of leukaemic cells. Eventually, this chronic disease progresses to an acute stage known as blast crisis.

For years, scientists had suspected that bcr/abl caused CML, but it was not until last year that they proved it. Mice injected with the gene developed CML.

The new study goes a stage further. The team made a short stretch of single-stranded DNA only 18 nucleotides long. The sequence of the DNA is "antisense", or complementary to, the portion of the hybrid gene where bcr and abl join: nine nucleotides correspond to bcr and nine to abl. By binding specifically to this junction section, the 18-nucleotide strand "jams" the whole gene and stops it from being transcribed. Adding the artificial strand to colonies of cultured leukaemic cells taken from patients heavily suppressed their growth. By contrast, cultures treated with another, mismatched DNA sequence grew fast. Normal cells were unaffected.

Previous attempts to block the bcr and abl genes separately with antisense strands had succeeded, but only by damaging healthy cells. (Source: New Scientist, 10 August 1991)

Circular DNA excels at nucleic acid recognition

Eric T. Kool has a novel idea: circular DNA oligonucleotides are better than conventional ribbons of DNA at recognizing nucleic acid sequences.

He has discovered that these DNA circles bind nucleic acid sequences "several orders of magnitude more strongly" than standard linear oligomers do, and they are more selective for the correct sequence. "To our knowledge, these are the strongest known intermolecular nucleic acid complexes under physiological conditions", says Kool, an assistant professor of chemistry at the University of Rochester, New York.

"Although circular polynucleotides are abundant in nature", Kool notes, few studies have focused on small, synthetic DNA circles. And no one else, as far as he knows, has addressed their potential in molecular recognition, he adds.

Cyclic oligomers have potential applications in the design of DNA-based drugs that target nucleic acid sequences, e.g., in messenger RNA or viral RNA. Researchers at a number of laboratories, for example, have been trying to use antisense oligonucleotides - strands complementary to RNA's "sense" sequence - to specifically inhibit gene expression. Linear antisense oligomers have been shown to have some antiviral activity, Kool says. Circular DNA, with its greater binding strength and specificity, may lead to better antisense agents he believes. (Extracted with permission from Chemical and Engineering News, 12 August 1991, p. 29, by Ron Dagani. Copyright (1991) American Chemical Society)

Research on animal genes

Gene-spliced fish may be on the menu

The aquaculture industry has been targeted by a number of biotechnology companies, with opportunities in the areas of fish vaccines, diagnostics, growth hormones and genetic manipulation. While work is moving ahead on vaccines and diagnostics, which are becoming essential components of aquaculture, some genetic engineers are turning their eyes to the possibility of genetically engineering fish and shellfish.

Rearing fish in freshwater ponds and sea pens is now big business (Science, Vol. 253, pp. 512-513). World-wide sales topped $22 billion in 1990, according to the UN Food and Agriculture Organization (FAO). Farmed fish now account for around 15 per cent of the fish consumed world-wide - and by the turn of the century that proportion could be 20 per cent, says FAO.

One obvious way to breed bigger or better fish would be to feed them synthetic growth hormone. Trials have shown that hormone-fed fish gain weight twice as fast as normal fish, but the approach is expensive (the hormone is expensive to produce), inefficient (the fish did not always absorb the hormone) and likely to be unpopular (remember the BST controversy?).

So now the target has shifted: scientists are aiming to transfer cloned genes into fish which will boost the production of natural growth hormone. The transfer is achieved by the micro-injection of DNA into the fish egg. For example, researchers at the University of Maryland's Center for Marine Biotechnology have injected a cloned growth hormone gene into carp and rainbow trout embryos. About half of these embryos survived, with an average of just under half of the survivors integrating the new genes into their own DNA. The transgenic fish and their offspring both grew from 20 per cent to 46 per cent faster than ordinary fish. At Auburn University in Alabama, genetically engineered carp are being kept in high security outdoor ponds, to see how they respond to "natural" conditions. Next, the researchers plan to see whether fish can be engineered to better resist disease and cope with colder conditions.

Scientists at the Memorial University of Newfoundland are inserting a gene extracted from the winter flounder, an Arctic species which seems to have its own natural anti-freeze compounds to keep it from freezing solid in icy waters, into Atlantic salmon. The "anti-freeze genes" have been seen circulating in the blood of the transgenic fish.

These trends will inevitably cause concern among environmentalists - indeed, it is interesting to see a paper on the subject of fish-farm biotechnology appearing in the June issue of Biotechnology and Development Monitor (No. 7, pp. 3-6). The Monitor is a joint publication of the Dutch Directorate General for International Cooperation at the Ministry of Foreign Affairs and the University of Amsterdam.

Details from: Biotechnology and Development Monitor, University of Amsterdam, Department of International Relations and Public International Law, Oudezijds Achterburgwal 237, 1012 DL Amsterdam, the Netherlands, or on Tel.: +31 20 525 2177. Fax: +31 20 525 2086. (Source: Biotechnology Bulletin, Vol. 10, No. 7, August 1991)

Research on plant genes

Researchers identify gene that controls oil quantity

Researchers at Iowa State University have found a carrot gene that controls oil quantity. Geneticist Eve Wurtele and biochemist Basil Nikolau made the discovery of the gene which encodes the enzyme acetyl-CoA carboxylase. By introducing the gene into oilseed plants such as soybeans, it may cause them to produce greater quantities of oils.

A longer goal of such research is to cause the plants to produce hydrocarbons that could be used as petroleum replacements. (Source: Science, 5 July 1991, p. 33)

GIRIN synthesizes plant growth regulators

A group at the Government Industrial Research Institute, Nagoya, Japan (GIRIN), a research arm of the Agency of Industrial Science and Technology, have synthesized three compounds that can regulate plant growth. The new compounds are variants of trifluoroindoleacetic acid, a derivative of the commonest naturally-occurring plant auxin, indoleacetic acid (IAA). The group made the compound by binding three fluorine groups at different sites in the acetic acid side chain of IAA. They added aqueous solutions of the compounds to soils supporting the growth of Chinese cabbage, tobacco, horseradish, rice and corn. All three compounds led to a remarkable increase in the rate of root growth relative to equivalent plants given unmodified IAA. This resulted in an increased level of water and nutrient uptake, thereby promoting overall growth of the plants. The presence of fluorine in the derivatives also appeared to provide the plants with lipophilic, acid-resisting properties. The group says its IAA derivatives can be used to accelerate the growth of plants in environmental bioremediation programmes and improve the harvest of plants under cultivation for alternative fuel production by biomass conversion. (Source: McGraw Hill's Biotechnology Newswatch, 19 August 1991)

Transformed potato resists antibiotics

The National Agriculture Research Center of Japan's Ministry of Agriculture, Forestry and Fisheries has transformed a potato with genes encoding resistance to the antibiotics kanamycin and hygromycin. The researchers finely sliced cultured potato tubers, then infected the cells with Agrobacterium tumefaciens. New tissue was

subcultured on selection media containing the antibiotics to yield potato cells with wide-ranging antibiotic resistance. The cells were regenerated into plantlets and cultivated to produce a variety of genetically transformed potato. It plans to modify the plants with genes for nutritionally complete proteins, and for resistance to herbicides and insect pests. (Source: McGraw Hill's Biotechnology Newswatch, 16 September 1991)

Research on viral genes

Glycolipid may usher HIV into neural cells

The CD4 receptor is the portal through which the human immunodeficiency virus (HIV) invades the helper T-cells of the human immune system. Many cells in the nervous system, liver, and other tissues do not carry the CD4 receptor, yet they are still prone to HIV infection. Researchers at the University of Pennsylvania Medical Center in Philadelphia may have discovered a possible new HIV entry point common to neural cells. Their results implicate galactosyl ceramide (GalC), a prominent glycolipid of the brain and peripheral nervous system. The researchers, Janet M. Harouse, Shama Bhat, Francisco Gonzalez-Scarano, and four other co-workers, found that antibodies against GalC inhibited the entry of HIV into two kinds of infectable neural cells in vitro. These cells contain GalC but not CD4. Furthermore, they found that gp120, the glycoprotein "key" that HIV inserts into the CD4 "lock" to gain entry to a cell, also binds to GalC but not to other glycolipids. These results suggest that GalC, or another receptor molecule much like it, is a likely candidate for the HIV portal in cells lacking CD4. (Reprinted with permission from Chemical and Engineering News, 22 July 1991, p. 16. Copyright (1991) American Chemical Society)

Molecular "chimera" saves chimps from HIV

Chimpanzees can be protected from HIV infection by an artificial molecule that "mops up" the virus in the bloodstream. This discovery, by researchers in the United States, shows for the first time that a drug rather than a vaccine can prevent the virus from taking hold in the body. And since the molecule can cross the placenta, it raises hopes of a treatment to stop the spread of HIV from women to their unborn children.

Rebecca Ward at Genentech in San Francisco and her colleagues have developed an ingenious idea first raised more than two years ago. They have attached a soluble form of CD4, the molecule on cell surfaces that acts as the main receptor for HIV, to the back half of an antibody, IgG. The resulting "chimeric" molecule acts as a decoy, fooling the virus into binding to it, instead of binding to the real CD4 on cells. It also disables the virus by stripping off gp120, the part of its protein coat that binds with the receptor molecule.

In the past, scientists had thought that soluble CD4 alone might keep the virus from entering cells. But trials of this molecule in people have been disappointing. The kidney rapidly excretes soluble CD4, so its half-life in the body may be too short to be useful. The chimeric molecule, by contrast, has a much greater half-life because the antibody fragment fools the body into thinking it is ordinary IgG.

Last year, the researchers found that, unlike soluble CD4, these chimeric molecules could cross the placenta in monkeys. So they started thinking about using the molecule to block infection in pregnancy.

They gave two chimpanzees each two doses of the chimeric molecule then injected live HIV into their bloodstreams. For the next nine weeks, they continued to give the animals regular injections of the molecule. A third chimpanzee, acting as a control, was also given HIV. This animal tested positive for HIV infection after seven weeks. By contrast, the two treated animals are free of infection after almost a year.

The researchers do not believe the molecule would be a realistic way to protect uninfected adults from HIV. This is because the molecule must be present at high concentrations to be effective, and gradually disappears after treatment stops. Few people can predict when they will be exposed to the virus, so they would need to have frequent injections and permanent treatment to avoid the risk. But, for a foetus, the "danger time" may be predicted to within months or weeks.

Ward cautioned that there are several unanswered questions. First, it is too soon to conclude that foetuses would be protected by the chimeric molecule. Secondly, most test-tube studies showing CD4's success as a decoy have been done with laboratory strains of HIV. These strains have been cultured, which may alter their behaviour. Strains taken directly from people seem to be relatively resistant to soluble CD4. (Source: New Scientist, 3 August 1991)

Viruses in neurons hide from killer T-cells

Scientists have puzzled over how nerve cells infected with viruses escape detection by the immune system's cytotoxic T-lymphocytes. These T-cells recognize and kill infected cells on whose surface are viral peptides complexed to glycoproteins of the class I major histo-compatibility complex (MHC). One possible explanation is now suggested by Etienne Joly, Lennart Mucke and Michael B. A. Oldstone of Scripps Clinic and Research Foundation, La Jolla, California. They find that neuronal cells do not express enough class I MHC molecules to serve as targets for the killer T-cells. By contrast, infected neurons experimentally primed with genes encoding the class I MHC molecules were readily targeted and destroyed. The researchers say the absence of these target molecules on the surface of most infected neurons may represent an important "selective survival mechanism" for avoiding destruction by the immune system. Unlike other cells, once neurons die, they cannot be replaced. But because of this survival mechanism, viruses often persist in neurons and can affect nerve function. (Reprinted with permission from Chemical and Engineering News, 16 September 1991, p. 22. Copyright (1991) American Chemical Society)

Mouse model for screening AIDS drug

An animal model to screen drugs for efficacy against human immunodeficiency virus (HIV) has been developed by researchers at North Carolina State University and Burroughs Wellcome Co. Veterinary medical professors Wayne Tompkins and Mary Tompkins, graduate student Calvin Johnson, and technician Tedd Childers of NCSU joined with

virologists M. Nixon Ellis and Dean Selleseth of Burroughs Wellcome to graft thymus, liver, lymph node and spleen cells of cats into mice bred to have severe combined immunodeficiency disease (SCID). This gave the mice functioning feline immune systems. They will test drug candidates in such mice, which they call SCID-fe, after injecting them with feline immunodeficiency virus (FIV), which is related to HIV. Other workers have developed similar mice with human immune cells, called SCID-hu, to screen drugs after infection with HIV. But because the feline virus does not infect humans, the costly containment measures needed for work with HIV will not be necessary with FIV. (Reprinted with permission from Chemical and Engineering News, 16 September 1991, p. 22. Copyright (1991) American Chemical Society)

Research on bacterial genes

Toxin genes more potent in biopesticides

Two independent research groups have reported important progress in the development of baculoviruses as biological pesticides. Baculoviruses - viruses that infect insects - can be genetically engineered to produce a specific toxin that will kill the insect host. The two groups have shown that a baculovirus will kill its host more quickly if toxin-producing genes from arthropods are inserted into the viral genome. The toxin produced by female mites of one species, for example, can paralyse insects 150,000 times their size. The gene encoding for this toxin was cloned and inserted into a baculovirus by Michael D. Tomalski and Lois K. Miller of the University of Georgia, Athens (USA). Larvae infected with the modified virus became paralysed within minutes. At the NERC Institute of Virology and Environmental Microbiology in Oxford, UK, Robert D. Possee and colleagues constructed a recombinant baculovirus containing the gene for a quick-acting insect-specific neurotoxin from a species of scorpion. Like the mite toxin, the scorpion toxin is harmless to mice, but it brings a swifter end to the insect host, thus reducing the amount of plant damage it can wreak. Both baculoviruses can be engineered to persist in the environment. (Reprinted with permission from Chemical and Engineering News, 8 July 1991, p. 32. Copyright (1991) American Chemical Society)

How ancient bacteria handle the heat

Researchers in Germany have found a new clue to how archaebacteria survive at extremes of temperature. Karl Stetter and Angelika Hoffmann of the University of Regensburg and their colleagues from the Max-Planck Institute for Biochemistry at Martinsried, Munich, have discovered large quantities of a cylindrical protein complex in the cells of Pyrodictium occultum. They believe that the complex returns bacterial proteins to a correctly folded state.

This bacterium is one of the most thermophilic known, preferring temperatures of 105°C. Wolfgang Baumeister and Barry Phipps came across the complex when they were studying the bacteria using electron microscopy. Some of the cells had burst, releasing particles made up of two stacked polypeptide rings, each of eight oval-shaped subunits. The protein is an enzyme that breaks down adenosine triphosphate (ATP). This activity was strongly dependent on temperature and reached an optimum at 100°C. When the researchers increased the surrounding temperature, P. occultum produced more and more enzyme, until at 108°C it made up almost three quarters of the soluble protein.

The German team suspects that the enzyme complex works as a molecular chaperonin in thermophilic archaebacteria.

Molecular chaperonins are thought to surround the denatured protein and bind to exposed hydrophobic groups so that the protein cannot form aggregates with other denatured proteins. When the stress is removed, the chaperonins split off again. (Source: New Scientist, 10 August 1991)

E. coli suicide plasmid developed for releases

Yasuo Kobayashi of the Faculty of Agriculture at the Tokyo University of Agriculture and Technology has developed a suicide plasmid that specifically destroys recombinant E. coli strains. He claims the plasmid has ten times the potency of its conventional counterparts. Kobayashi produced the construct by inserting a lethal gene and an upstream promoter sequence obtained from the Bacillus subtilis into a vector that infects both E. coli and B. subtilis. The lethal gene functions only when the promoter sequence is activated by the presence of gluconic acid. Engineered E. coli containing the sequences can be eliminated by exposing the culture to gluconic acid. Kobayashi developed the suicide plasmid to control the spread of recombinant E. coli developed for open-air use in environmental bioremediation and crop protection projects. (Source: McGraw Hill's Biotechnology Newswatch, 19 August 1991)

Cholera under attack from "altered" vaccine

A genetically engineered vaccine against cholera began trials in Chile in late 1991. The vaccine, which is taken by mouth, has so far proved much more effective than any of its predecessors and hopes are high that it could halt future epidemics.

Cholera has swept through Latin America and Africa this year. At least 300,000 people world-wide have contracted the disease and more than 6,000 have died. The existing licensed vaccine, which is based on killed bacteria and has to be injected, protects only half of those vaccinated - and then only briefly. The World Health Organization does not recommend it.

The new candidate, by contrast, has protected all the volunteers in a trial in the United States. The volunteers were deliberately infected with cholera after receiving the vaccine; none of them developed the disease. "This is an extraordinary breakthrough for a cholera vaccine", says Myron Levine. who led the team developing it at the University of Maryland in Baltimore. Unlike its predecessors, the Baltimore vaccine is live.

Vibrio cholerae, the bacterium that causes the disease, can kill because it produces a toxin that paralyses the gut. The ensuing diarrhoea causes rapid dehydration and ultimately death. The Baltimore team reasoned that if it could remove the genes that code for the toxin or part of it, they might be able to render the bacterium harmless, yet still stimulate the immune system to protect the body against the real organism.

Levine believes the vaccine is more effective than its predecessors because it is live. Researchers have recently discovered that V. cholerae switches on genes that change its

protein coat when it moves from contaminated water into the human gut. The changed coat appears to be important in stimulating an immune response. Killed bacteria in a conventional vaccine may lack the elements of the coat that provoke the strongest reponses.

The trials in Chile are designed to confirm that the vaccine is safe and produces an immune response. Another trial is under way in Indonesia in young children, who are particularly vulnerable to cholera. Levine also plans trials in Lima, and San José, Costa Rica.

If the safety trials go well, a large controlled field trial will follow to test whether the vaccine actually protects a population at risk of natural infection. A decision could be made in early 1992 and field trials could start by 1993, possibly in Indonesia, Bangladesh or Peru.

Meanwhile, WHO and the Brazilian Government are planning field trials in Brazil of another experimental oral vaccine based on killed bacteria. So far, Brazil has escaped the epidemic that hit Peru and Ecuador but researchers fear it could still reach Brazil in the coming months. The vaccine is closer to being licensed than the Baltimore vaccine because it has already completed field trials in Bangladesh. It is more effective than the existing vaccine because it protects for three years, but it still only works in about 50 per cent of those vaccinated. (Source: New Scientist, 24 August 1991)

Research on yeast genes

Hydroxylase made in r-DNA yeast

Japan's Government Industrial Development Laboratory at Hokkaido is making hydroxylase in a genetically engineered strain of Saccharomyces cerevisiae, baker's yeast. If the group can scale up the technique, hydroxylase-mediated reactions at room temperature may replace costly inorganic-catalyst-mediated treatment of industrial substrates at high temperatures. Hydroxylase is a mono-oxygenase enzyme that catalyzes reaction of a substrate with molecular oxygen in which only one of the oxygen atoms is introduced into a compound. The enzyme can be used in the synthesis of a wide range of useful compounds. The researchers transformed yeast with a hydroxylase-encoding gene isolated from mouse-liver cells. The r-DNA yeast produced large amounts of the enzyme under low-cost culture conditions. The group is now looking for ways to use the enzyme in low-temperature production of pigments and drug components from liquefied coal. (Source: McGraw Hill's Biotechnology Newswatch, 16 September 1991)

Research instrumentation

Western blotting detection kits with new stable substrates

Cambridge Research Biochemicals have announced the launch of a new range of Western blotting kits, which contain purified antibody-enzyme conjugates that are specific for either sheep, rabbit or mouse immunoglobulin and optimized to give minimal background. Both horseradish peroxidase and alkaline phosphatase versions are available.

Each kit contains a new, stable colour liquid substrate formulation, either TMB in the HRP kits or BCIP/NBT in the alkaline phosphatase kits, obviating the need to weigh out powders or make up fresh solutions every day. These substrates are supplied in a convenient spray bottle for easy application and for protection against enzyme contamination. The substrate is applied only where needed and with no waste.

Also available are kits containing the Lumi-Phos chemiluminescent substrate, supplied in the same spray bottle. These kits give the opportunity of obtaining permanent results on film. The kits can include a carefully selected PVDF membrane for optimum results.

A 10 x concentrate of blocking buffer is also supplied to reduce non-specific background problems. These kits are suitable for all Western blotting applications. Sufficient reagents are provided to blot 4,000 cm^2 of membrane.

Further details from: Simon Douglas, Senior Product Manager, Bioscience, Cambridge Research Biochemicals Ltd., Gadbrook Park, Northwich, Cheshire, CW9 7RA. Tel.: (0606) 41100. Fax: (0606) 49366. (Source: CRB News Release, 23 July 1991)

Adsorbents for protease purification/removal

A range of affinity adsorbents for protease purification and removal is now available from Affinity Chromatography Ltd. The agarose-immobilized amino acids and amino acid analogues (lysine, arginine and aminobenzamidine) are especially useful for binding serine proteases such as trypsin and plasminogen. Ultra-stable epoxide bonding chemistry is used exclusively, which imparts a high degree of chemical stability and virtually eliminates ligand leakage. The adsorbents may be cleaned and sterilized with sodium hydroxide and are manufactured to GMP standard.

Further details from Joy Cornforth, Affinity Chromatography Ltd., Freeport, Ballasalla, Isle of Man, UK. Tel.: (0624) 823 519. Fax: (0624) 824 957. (Source: ACL News Release, August 1991)

Triazine activated agarose 4XL

A new inexpensive alternative to CNBr agarose which utilizes a novel triazine bonding chemistry is now available from Affinity Chromatography Ltd. Triazine Activated Agarose 4XL, supplied as a freeze-dried powder in a variety of pack sizes, is highly reactive with proteins. Antibodies or enzymes can be bonded to the cross-linked agarose support under relatively mild conditions with very high coupling efficiencies which minimizes loss of activity and wastage of valuable protein. The new triazine chemistry has many advantages over cyanogen bromide coupling, in particular its high reactivity at near neutral pH and the generation of a stable neutral bond.

Further details from Joy Cornforth, Affinity Chromatography Ltd., Freeport, Ballasalla, Isle of Man, UK. Tel.: (0624) 823 519. Fax: (0624) 824 957. (Source: ACL News Release, August 1991)

Second Messenger

Issue 2 of AFFINITI Research Products Ltd.'s quarterly Newsletter, Second Messenger, has just been released. Describing over 40 new products, focused on neuroscience research and researchers, the Newsletter coincides with the launch of AFFINITI onto the US market.

New products include three high sensitivity RIA kits for members of the endothelin family, including ET-3 and big-endothelin; antibodies and DNA probes to fos-related proteins; antibodies to drugs of abuse, and the outstanding range of antibodies, including polyclonal antisera to catecholamine-synthesizing enzymes and to dopamine, GABA and serotonin from Eugene Tech International Inc.

Copies of the Newsletter and information on AFFINITI's products and services can be obtained by contacting Dr. Ian M. Varndell at AFFINITI; Tel.: +44/0 602 442232; Fax: +44/0 602 442313. (Source: AFFINITI News Release, 23 September 1991)

Lyme disease antigen detector

A new device allows the disease-causing organism, a spirochete, to be directly withdrawn from the skin and inserted into the culture medium in one single step. The new method provides an irrefutable confirmatory diagnosis that a patient has been infected with Lyme disease. Serological tests are not adequate for this purpose because antibody tests are often inconclusive. This is an ideal test for physicians' offices or for public health testing. (Patent rights available.) Further details from Mr. Shelby Calvert Morss, Technology Transfer Officer, Harvard University, 124 Mt. Auburn Street #256, Cambridge, Massachusetts 02138. Tel.: (617) 495-3067. Fax: 495-9538. (Source: International New Product Newsletter, September 1991)

Viable bacteria reader

The mass of viable bacteria, yeast or other micro-organisms in a fermentation broth can be read directly on a new instrument. The Biomass Monitor uses electrical measurements to determine active biomass and thus is unaffected by such physical characteristics of the broth as opacity. The rugged four-electrode probe may be inserted into process pipework or directly into the fermentation vessel through a standard 25 mm port. The meter measures the capacitance of the medium at low radio-frequencies and from this calculates the viable-cell concentration in either mg/ml or cells/ml and displays the results immediately. The instrument can also measure the conductivity of the medium, a useful parameter for monitoring the progress of a fermentation. (Rights available.) Further details from Mr. B. Wise, Aber Instruments Ltd., Science Park, Aberystwyth, Wales SY23 3AH. Tel.: (44) 970 615284. Fax. (44) 970 623311. (Source: International New Product Newsletter, September 1991)

Bacterial cultures

Bacterial cultures in combination with enzymes formulated to be used for industrial, municipal and agricultural waste management are available. The products are designed for use in drain cleaners, grease traps, septic systems, human and animal waste processing such as pig, cattle or chicken manure pits, and leaf and grass mulch, as well as municipality sewer treatment processing, including digesters, oxidation tanks, trickling filters and ponds, etc. (Licence rights available.) Further details from Ref. No. 5, Hem Vakharia, President, Specialty Chemical Consultants, Inc., 3959 South Victoria Court, New Berlin, Wisconsin 53151. Tel.: (414) 784-5017. Fax. (414) 789-0614. (Source: International New Product Newsletter, September 1991)

Miscellaneous

Melbourne skull may hold clues to origin of man

Australian scientists have isolated DNA from a 15,000-year-old skull found at Kow Swamp, north of Melbourne. This is now the oldest known human DNA.

"The finding raises the exciting possibility that we can test some of the ideas that have been developed over the years to explain the origin of the Australians", says Alan Thorne of the pre-history department at the Australian National University (ANU) in Canberra.

Thorne also believes that with such early DNA it might be possible to resolve the debate about whether modern humans originated in Africa or if they evolved simultaneously in Africa, Asia and Europe.

Working with Thorne were Tom Loy, another prehistorian from ANU, and biochemists Liz Dennis and Jim Peacock of the division of plant industry at CSIRO, the Australian national research organization. The team used techniques pioneered by Loy to extract minute amounts of mitochondrial DNA from the ancient skull and then amplified the DNA with the polymerase chain reaction.

The next step, says Thorne, is to sequence the DNA and compare what has been preserved of the genome with DNA from more recent bones. Thorne also hoped to compare the DNA with modern samples. (Source: New Scientist, 27 July 1991)

Conjugate vaccine fights meningitis

Researchers have used bioconjugate chemistry to create an experimental vaccine that promises to eradicate three types of bacteria that cause meningitis in children. Until now, a vaccine has not been available to protect children from Escherichia coli K1 and group B meningococcus. Although a vaccine is available for group C meningococcus, it cannot be used in infants because their immature immune systems do not respond to it. Researchers Sarvamangala Devi, John Robbins and Rachel Schneerson of the National Institute of Child Health and Human Development (NICHHD), in Bethesda, Maryland, have now got round this problem by chemically linking a polysaccharide capsule from E. coli K92 (a bacterium that does not cause meningitis) with a protein (tetanus toxoid). The K92 capsule is used because it has structural elements in common with capsules from the three meningitis-causing bacteria. In experiments in mice, the polysaccharide-protein conjugate vaccine is recognized by the immune system and elicits production of antibodies against the three disease-causing bacteria, in addition to tetanus toxoid. According to NICHHD, this is the first time a single-component vaccine has been developed

that can protect against four different pathogens. (Reprinted with permission from Chemical and Engineering News, 19 August 1991, p. 20. Copyright (1991) American Chemical Society)

Iron chelators starve malaria parasites

Israeli chemists have developed a novel series of iron-binding compounds that destroy malaria parasites resistant to standard anti-malarial agents. The researchers find that the most potent member of the series, an isoleucine derivative dubbed SF1-ileu, swiftly enters red blood cells infected with the malaria parasite, binds available Fe^{3+} ions, and removes them from the cell, depriving the parasite of this essential nutrient. The result is a sharp drop in protein and DNA synthesis (a sign of parasite death) in treated malaria cultures within a half hour after exposure. SF1-ileu is found to be effective at all stages of parasite development and on at least four rampant strains of the organism, two of which are resistant to several widely used anti-malarial drugs. In related studies, the potential drug caused no damage to various types of cells in tissue culture. SF1-ileu is not expected to interfere significantly with normal iron metabolism in the body. However, systematic toxicity tests will need to be carried out before clinical trials are contemplated. The work was reported by Abraham Shanzer and Jacqueline Libman of the Weizmann Institute of Science, Rehovot, and Z. Ioav Cabantchik, Simon D. Lytton and Hava Glickstein of Hebrew University, Jerusalem. (Reprinted with permission from Chemical and Engineering News, 19 August 1991, p. 20. Copyright (1991) American Chemical Society)

DNA synthesized sans protecting groups

A procedure to synthesize DNA oligomers of short to moderate length using phosphoramidite chemistry, but without resorting to use of nitrogen-protecting groups, has been developed by Sergei M. Gryaznov and Robert L. Letsinger of Northwestern University. N-protecting groups are used almost universally in oligonucleotide synthesis because they prevent reaction of phosphoramidites with nucleoside amino groups, allowing reaction to proceed only at the hydroxyl groups. However, their use requires two additional steps (introduction and removal) and limits the synthesis to addition of nucleosides that are not attacked by N-deblocking reagents such as NH_4OH. The new technique allows the phosphoramidite reaction to occur at both amino and hydroxyl groups. Selectivity is achieved by group transfer of nitrogen-linked phosphoramidites to aniline, leaving the desired phosphorus-oxygen linkages intact. A disadvantage is that yields are not as high as with N-protection. The primary advantage is the capability to synthesize modified oligonucleotides (up to about 20-mers) containing substituents sensitive to N-deblocking reagents. Such modified oligonucleotides are of interest as recognition systems for antisense nucleic acids. (Reprinted with permission from Chemical and Engineering News, 5 August 1991, p. 15. Copyright (1991) American Chemical Society)

Artificial antibody

A new type of artificial antibody that could cross the blood-brain barrier has been developed by researchers at the University of Pennsylvania School of Medicine (Philadelphia) and the University of Illinois (Chicago). The antibody (called a mimetic) contains no amino acids, and so could be long-lived, escaping destruction by the immune system and enzymes. The mimetic stimulates the growth of cells that sheathe neurones in the central nervous system. It is a version of a mimetic loop on a mouse antibody, which bonds to a specific part of viral coats. Natural antibodies have six loops. The synthetic mimetic is based on the carbon skeleton of the loop, and so has no amino acids. Adding side chains to the mimetic allows the researchers to produce custom-made antibodies. The mimetics are water-soluble and can be administered orally. In addition to tests against rheoviruses, researchers hope to test the mimetics against multiple sclerosis, where the mimetics might help restore nerve sheaths. (Extracted from New Scientist, 24 August 1991)

Metals trace the secrets of nitrogen fixation

Chemists in Britain and the United States are near to a breakthrough in understanding how the enzyme nitrogenase works. The enzyme turns nitrogen (N_2) from the air into ammonia (NH_3), the compound which living cells need in order to make their amino acids and essential organic bases. Now chemists know not only the molecular structure of the enzyme but also how it is able to trap and "fix" nitrogen, releasing hydrogen gas (H_2) at the same time.

To change one molecule of nitrogen into two molecules of ammonia and make one molecule of hydrogen requires a supply of hydrogen atoms and electrons - eight of each. Bacteria which can accomplish this contain an enzyme composed of two proteins. The smaller protein, which has a molecular mass of about 60,000 daltons, supplies the electrons, while the larger, weighing in at about 250,000 daltons, carries out the ammonia conversion. The smaller proteins contains iron and the larger one both iron and molybdenum, though this protein will still function if vanadium replaces the molybdenum.

Jeff Leigh, Rafael Prieto Alcón and Roger Sanders at the AFRC Nitrogen Fixation Laboratory at the University of Sussex find that when a nitrogen molecule is caught between two vanadium atoms, it can be reduced to ammonia by a process which involves extracting electrons from vanadium (Journal of the Chemical Society Chemical Communications, 1991, p. 921).

Leigh and another colleague, Manolo Jimenez-Tenorio, carried out a separate experiment with molecular nitrogen attached to iron (Journal of the American Chemical Society, Vol. 113, p. 5862). They found that ammonia is again produced but now molecular hydrogen is given off - as in the natural system. Why this happens is a mystery. However, chemists expect to understand it once they get to the bottom of the mechanism of nitrogen fixation. In other experiments, Robert Eady at Sussex has shown that even iron alone can carry out the vital N_2-capturing function.

According to Leigh, the active site in the larger protein may hook the nitrogen molecule from the air by using its molybdenum, vanadium or iron. It passes this to a neighbouring iron atom for the actual reduction to ammonia to take place.

Leigh proposes the nitrogen-fixing enzymes, which were the first to evolve, may have relied entirely on iron to capture molecular nitrogen and reduce it. Enzymes which developed later incorporated vanadium, which made capture easier. Later still, a molybdenum variant emerged, which

was even better. In the enzyme, these metals are held in place by sulphur atoms.

Another team led by Douglas Rees at the California Institute of Technology in Pasadena has grown crystals of the smaller protein and analysed them with the technique of X-ray diffraction. This reveals a "cluster" of four iron atoms and four sulphur atoms which are set on the surface of the protein in a shape that Rees likens to a diamond ring. The cluster is the gemstone which protrudes. Rees believes it has this structure to touch the larger protein and pass electrons to it.

Chemists have now switched their attention to the larger protein, which has two molybdenum atoms. Its structure is much more complicated, and it behaves in a way which continues to puzzle them. Jeff Bolin and his colleagues at Purdue University have shown that this protein has two active metal regions. These are 700 picometres (7×10^{-12} metres) apart, which Bolin says indicates they are near the surface, on opposite sides of the protein. This conflicts with previous theories which assumed the two molybdenums were close together, and that each grabbed one end of a nitrogen.

Each active region also consists of two components - M-sites and P-sites - which are about 190 picometres apart. The P-sites are thought to be where the smaller protein off-loads its electrons. The M-sites pluck the molecular nitrogen from the air and are called FeMoco, which is short for iron molybdenum co-factor.

Carol Gormal, Ray Richards and Barry Smith at Sussex and David Garner at the University of Manchester have used the techniques of X-ray absorption and electron paramagnetic resonance spectroscopy to probe the FeMoco "cluster" of metal atoms and sulphurs. Richards has devised a method of extracting FeMoco from bacteria in "high yield": five kilograms of bacteria will make 15 milligrams of FeMoco.

FeMoco is very sensitive to oxygen, and great care has to be taken to prevent air reaching the material when it is extracted and crystallized. In addition to one molybdenum atom, each FeMoco cluster is formed from six or seven iron atoms and about the same number of sulphurs.

The current work on nitrogenase has implications in a very different area of chemistry - one which has important industrial applications. Chemists who are looking for better ways of removing sulphur from oil, to reduce the sulphur dioxide given off when it is burnt are studying hydrogen atoms attached to metals which are supported by sulphurs. Richards has already found new molybdenum compounds with both sulphur and hydrogen atoms attached to the metal in what he believes may be similar to the molecular environment within the enzyme. (Journal of the Chemical Society Dalton Transactions, 1991, p. 1813) (Source: New Scientist, 31 August 1991)

Genetic test reveals transplant errors

As many as a quarter of transplanted kidneys are not matched closely enough to transplant patients because of errors in the matching process. This mismatching probably accounts for many otherwise unexplained kidney failures in transplant patients.

These are the conclusions of German immunologist Gerhard Opelz of Heidelberg University, who coordinated a study of more than 4,000 transplants across Europe and the United States. Opelz and his team uncovered the discrepancies with a recently developed DNA-based tissue-typing technique, which appears certain to improve matching and extend the life of transplanted kidneys.

Opelz says if typing errors are eliminated, all matched transplants could be as successful as those between brothers and sisters. Of these, about 93 per cent survive for more than a year. (Extracted from New Scientist, 31 August 1991)

Pioneers push back the limits of gene therapy

Three experiments to insert genes into people either with cancer or an inherited liver disease will begin within months in the United States. The novel treatments go well beyond anything yet attempted in humans.

A special panel of the National Institutes of Health's Recombinant DNA Advisory Committee approved the experiments in August 1991. One trial would insert a gene from the herpes virus into cancer patients. The gene should make tumour cells appear like herpes, which could then be killed by drugs that fight the virus. Another cancer treatment would "immunize" patients against their own tumours. A third experiment is designed to treat an inherited blood disease.

The proposals require further review by senior scientists at the NIH and the Food and Drug Administration, but are expected to be accepted. The herpes and blood disease experiments also require some refinement before human trials can begin. (Extracted from New Scientist, 10 August 1991)

Genome assignment for industry

One of the big questions for the Human Genome Project is who will actually slog through the sequencing of millions and millions of nucleotide bases. Should project leaders follow the usual route and pass the chore to graduate students, or should they try something different - namely, call on industry?

Now, for the first time, the US National Institutes of Health's (NIH) genome centre has awarded a $5-million, three-year grant to a company, Collaborative Research, Inc. (CRI), in Bedford, Massachusetts. CRI plans to tackle the genomes of two mycobacteria that cause leprosy and tuberculosis, each about four million bases long. This will be no small feat - the largest complete genome sequenced to date is that of cytomegalo- virus, with 250,000 bases. The company plans to do the sequencing for 50 cents a base by using a promising but relatively untried technique called multiplexing, developed by George Church and colleagues at Harvard.

Genome officials see the grant as a test of industry capability. But CRI's vice-president for research, Gerald Vovis, says he is already convinced that if the entire human genome is ever to be sequenced, it will have to be industry that does the job. (Source: Science, 16 August 1991, p. 743)

Genome funds

American researchers taking part in the international project to map the human genome are squandering hundreds of thousands of dollars in futile attempts to patent sequences of human genetic material.

European partners in the project are angry at what they see as a waste of money and are seeking urgent discussions through the Human Genome Organization (HUGO), an alliance of scientists coordinating the project - to avoid a transatlantic split in the programme.

Walter Bodmer, the president of HUGO, told the British Association for the Advancement of Science that American researchers funded by federal agencies, including the National Institutes of Health and the Department of Energy, are filing patents for some 1,000 partial sequences of human genetic material each month. With each application costing $30, this amounts to some $30,000 a month.

As the human genome programme progresses and scientists build up a working manual of the human body, there will be huge opportunities for improving health care. Scientists will discover the identities of natural biochemicals with unique pharmacological value and pinpoint the genes responsible for making them. But pharmaceuticals companies wishing to patent the chemicals or the genes responsible for their production face enormous problems. (Extracted from New Scientist, 7 September 1991)

D. APPLICATIONS

Pharmaceutical and medical applications

A new breed of drugs

By genetically altering goats, sheep and cows, scientists appear to have taken several key steps towards creating dairy animals that secrete valuable medical drugs in their milk.

In three papers published in the journal Bio/technology, groups from the United States, Britain and the Netherlands show the concept to be not only possible but commercially feasible. With a variety of new techniques, the papers claim livestock can be engineered far more easily than previously thought, becoming living factories for certain types of drugs that are currently very difficult or expensive to manufacture.

One of the papers, for example, shows that goats can be used to produce the heart-attack drug TPA, one of the most expensive clot-dissolving drugs on the market. Like other candidate drugs, TPA is a naturally produced protein for which the normal gene can be obtained from one species and spliced into the genetic material of another.

The beauty of producing proteins and other pharmaceuticals with a lactation system is that a normal animal is performing its normal functions.

The basis of barnyard biotechnology is now the standard technique of injecting human genes into the fertilized eggs of other animals, thus endowing the embryo with a human gene that will be duplicated and passed on to each new cell as the embryo develops.

The goal of a number of researchers has been to exploit this technique commercially. Several valuable drugs currently in use - like TPA - are now produced in vats of cultured transgenic cells, a complicated and sometimes expensive process.

By putting the genes for these proteins into dairy animals biotechnologists hoped cows or other farm animals could be given the ability to simply manufacture the human protein at the same time that they made their own milk protein. The morning milking would yield a few grams of TPA in each quart.

Extracting the drug from the milk is, in principle, little different from extracting the drug from the cell culture vats. The barnyard idea seemed a potentially low cost alternative.

There were, however, two drawbacks. Although it is relatively easy to create transgenic mice, the process was difficult and very expensive in larger mammals and had never been shown to work in dairy cows - the animal of choice for barnyard biotechnologists.

Secondly, in the one instance where the technique had worked in larger animals - sheep bioengineered by a British team - the human protein was produced in the sheep milk in such small quantities that it was difficult to see any commercial advantage.

The Bio/technology papers appear to provide at least a partial way around these obstacles. (Source: International Herald Tribune, 28 August 1991)

New cancer therapy to be tried

Injecting genetically engineered tumour cells into ovarian cancer patients will be attempted as a way to make all the cancer cells susceptible to chemotherapy. The US National Institutes of Health Human Gene Therapy Subcommittee has provisionally approved the experiment, to be done by Scott M. Freeman of the University of Rochester Medical Center. Final approval could come in eight months. In trials with mice, injecting engineered tumour cells into cancerous mice allowed ganciclovir to kill not only the engineered cells, but existing cancer cells as well. The engineered cells incorporate the thymidine kinase (tk) gene from herpes simplex virus. Thymidine kinase plays a key role in DNA synthesis and cell reproduction. But the gene is sensitive to ganciclovir. It is not clear why the existing cells also become susceptible. It may be that the gene is absorbed by tumour cells when the engineered cells die. Or it may be that the ganciclovir sets off some immune response.

Elizabeth Nabel of the University of Michigan (Ann Arbor) proposes using the tk gene as a suicide gene along with any other gene to be inserted into the human body. This would give doctors a way to turn off any engineered cells that go awry. (Extracted from Science News, 3 August 1991)

Rosenberg plans biological "one-two" punch against cancer

Dr. Steven Rosenberg, chief of surgery at the US National Cancer Institute in Bethesda, Maryland, plans to turn the tables on his earlier work involving altering cancer patients' white

blood cells to boost their cancer-fighting ability. The US National Institutes of Health have approved a proposed experiment in which Dr. Rosenberg will treat cancer patients with infusions of their own cancer cells - genetically redesigned to trigger a stronger immune response from the patient's body.

In what he termed a biological "one-two" punch, cancer cells will be taken from each patient. These would then be spliced with a gene for a known cancer-fighting protein (such as interleukin-2 or tumour necrosis factor) and reinjected into the patient's body. The result, Dr. Rosenberg hopes, will be that the patient's immune response is much more vigorous.

At the end of three weeks, the patient's lymph node would be removed and its cancer-fighting cells harvested. These would then be encouraged to multiply, before being injected into the patient for the second phase of therapy. Although Dr. Rosenberg has recently focused his gene therapy work on malignant melanoma, the new experiments - provided they win approval from all the relevant regulatory authorities - could target a number of different cancers, including colon cancer. This form of therapy is still extremely experimental, however, and Dr. Rosenberg is stressing that he will only try it on patients who have failed to respond to conventional forms of treatment. (Source: Biotechnology Bulletin, Vol. 10, No. 9, August 1991)

Chemical bombshell explodes in tumour cells

Chemists in New Zealand have designed an anticancer compound which they believe could become a model for drugs capable of treating solid tumours, cancers which are notoriously difficult to treat with conventional drugs or with radiation. The compound contains the metal cobalt, together with a chemical which can kill cells.

Cells found in solid tumours replicate slowly, which means they are not vulnerable to the normal anticancer drugs that act by interfering directly with DNA as it replicates. Solid tumours are also difficult targets for drugs. This is because the blood vessels which feed them are distorted and so carry blood very inefficiently.

However, another effect of the ineffective blood supply and the pressure exerted by the solid tumour is that little oxygen reaches it. It is this hypoxic condition in the tumour which the New Zealand chemists have exploited in designing their drug.

David Ware and his colleagues at the University of Auckland made their drug from a cobalt (iii) metal ion that was surrounded by stabilizing methylpentanedionato chemical groups. They used so-called nitrogen mustard as the cell-killing, or cytotoxic, component.

This is not the first attempt to exploit tumour hypoxia. In fact, the search for suitable drugs, commonly referred to as bioreductive agents, has become a major focus in the search for anticancer drugs.

The first bioreductive compounds were discovered serendipitously and resemble the antitumour antibiotic mitomycin C. They are poised to enter clinical trials over the next year. Ware's cobalt compound is important because it is the first attempt to rationally design an "inorganic" compound to work in this way.

According to Ware and his colleagues, "It is much too early to say whether this new approach will lead to a practical drug". The chemists are currently studying versions of their compound in which the reduced complex is more stable. Such versions should be selective in their action, the scientsts believe. (Extracted from New Scientist, 31 August 1991)

Synthetic taxol produced

A new technique to produce a synthetic taxol, an anticancer drug, has been patented by Dr. Robert Holton at Florida State University (Tallahassee). Dr. Horton's hemisynthesis technique links a synthetic chain with baccatin III to produce a compound identical to taxol, a bark extract of mature Pacific yews. Florida State has granted an exclusive licence for the technique to Bristol-Myers Squibb (Princeton, New Jersey), which has been buying taxol from Hauser Chemical Research (Boulder, Colorado). The raw material used in Dr. Horton's technique is obtained from the needles of the English yew, which can be grown in nurseries. The hemi-synthesis technique uses 1 kg of needles, about the number from six English yew trees, to produce 1.3 g of the synthetic taxol. The bark of five to seven mature Pacific yews is needed to produce a similar amount of natural taxol. About 2 g of taxol/patient is the normal dosage for cancer patients.

Taxol has shown good results in early clinical trials as a treatment for ovarian cancer, a silent cancer that causes some 12,400 deaths/year due to the lack of early detection. The compound stabilizes the activity of microtubules, which are normally involved in changes of cell motility and shape and in cell division. As the drug attacks cells undergoing changes, it causes such side effects as hair loss and nausea. Taxol's side effects are less severe than those of other chemotherapeutic agents. Bristol-Myers Squibb is conducting Phase III clinical trials of taxol as an ovarian cancer treatment and Phase II trials as a treatment for other tumours. (Extracted from Genetic Engineering News, August 1991)

Botanical AIDS cure?

New compounds that show anti-HIV activity in vitro have been identified in Chinese medicinal plants by Sylvia Lee-Huang of New York University and colleagues at American Biosciences and elsewhere. The compounds are not only able to inhibit infection of cells by the AIDS virus, but they also prevent replication of HIV in cells that are already infected, according to Lee-Huang.

One protein, dubbed MAP 30, comes from the seeds of the bitter melon, Momordica charantia, and another, TAP 29, comes from the root of the medicinal plant, Trichosanthes kirilowii. Lee-Huang and her colleagues also found three other proteins in the seeds of a Himalayan medicinal plant, and in the leaves of the carnation, Dianthus caryophyllus.

The proteins show no toxic effects in human cells in vitro, and will next be tested for

toxicity in clinical trials. The fruits and seeds of M. charantia are used in traditional Chinese medicine to strengthen the immune system, while T. kirilowii has been used to induce both labour and abortion, and to treat some tumours.

Lee-Huang hopes that, in addition to potential use as therapeutic agents in AIDS and HIV-infected patients, the compounds might be used to treat blood supplies in blood banks. "These compounds might even be used in condoms, vaginal jellies, toothpastes, mouthwashes or detergents and soaps to minimize the transmission of HIV", she adds. (Source: Chemistry & Industry, 2 September 1991)

New test detects early exposure to AIDS virus

The US National Cancer Institute researchers think they may have a way of telling whether an individual has been exposed to human immunodeficiency virus (HIV) as much as a year before current tests show infection with the virus. In preliminary studies, the new test signalled HIV exposure in two high-risk, initially uninfected persons, in one case 14 months and in the other case six months before standard tests showed they had become infected. Exposure to HIV, however, does not necessarily lead to infection.

Current tests for HIV depend on infection and detect either the immune response to the virus (antibodies), pieces of viral proteins (antigens), or genetic material from the virus. The test reported by the NCI researchers detects interleukin-2, a protein released by T helper cells when they come in contact with foreign antigen. To run the test, T-cells are separated from blood and stimulated in vitro with synthetic HIV peptides. T helper cells previously exposed to HIV in vivo will release IL-2. The presence of this protein is detected by its proliferative effect on a cell line that requires IL-2 for growth.

Some 150 individuals considered not to be at risk for HIV infection tested negative for HIV exposure. The T helper cell test takes about seven days to perform, so is not suitable as a rapid screening method. (Abstracted with permission from Chemical & Engineering News, 8 July 1991, p. 35, by Ron Dagani. Copyright (1991) American Chemical Society)

* Drug developed that prevented HIV in chimpanzees

Genentech (San Francisco, California) researchers have developed a chimeric molecule that prevents HIV infections in chimpanzees. The molecule uses a soluble form of CD4 attached to part of the IgG antibody. CD4 is the molecule which HIV attaches to in the human body. Tests used two chimpanzees receiving a dose of HIV and regular doses of the molecule, and one chimpanzee only receiving HIV. The control became HIV-positive and the two test animals were uninfected after a year. Previous tests only with soluble CD4 were unsuccessful because of a short half-life. Since the drug can cross the placenta, it may be useful in preventing pregnant women from passing the disease on to their children. (Extracted from New Scientist, 3 August 1991)

Compound delivers to brain

Neuropharmaceutical firm Alkermes (Cambridge, Massachusetts) has filed an application with the Food and Drug Administration to begin clinical trials of its RMP-7 compound, designed to help various drugs cross the blood-brain barrier. If RMP-7 proves effective, Alkermes believes various existing anti-infective and anticancer drugs would be more accurate, since they could enter the brain in larger amounts. Later this year, Alkermes hopes to test RMP-7 with several drugs. (Source: Chemicalweek, 25 September 1991)

Dutch scientists plan new approach to gene therapy

Scientists in the Netherlands are planning a new approach to gene therapy for a rare immune-deficiency disease. The treatment, which would involve adding a gene to the patient's bone marrow cells, builds on a therapy first developed by scientists in the US. Unlike the American approach, however, the Dutch gene therapy would need only one treatment instead of many repeated transfusions.

The aim is to treat a patient who has a disease known as severe combined immune deficiency (SCID), caused by lack of the enzyme adenosine deaminase. People with this defect suffer from a build-up of a toxin which prevents the maturation of T-cells, a vital component of the immune system. As a result, sufferers are vulnerable to many infections and must sometimes live in a plastic bubble.

Now researchers at the University Hospital of Leiden and the Dutch research organization, TNO, in Rijswijk, plan to add the gene for adenosine deaminase to a patient's bone marrow cells.

The researchers first take stem cells from the bone marrow of the patient, then introduce the gene, isolated from healthy people, by means of a recombinant retrovirus. Dinko Valerio of TNO says that the proposed therapy will not only be a remedy for individual patients, it will also be a testing ground for other gene therapies. He says the technique could also be used for the genetic treatment of blood diseases such as thalassaemia and haemophilia, and other genetic disorders of the metabolic system.

In a sense, says Valerio, gene therapy of ADA-SCID is an "easy" first step, because it concerns "easy to reach" bone marrow cells. The regulation of expression also seems to be uncomplicated, because the ADA-gene is expressed in all cells of the body. With other types of gene therapy, researchers have to carefully control the expression of the newly inserted genes in the target cells.

According to Valerio, a recent independent survey carried out in the Netherlands revealed a great acceptance of such gene therapy experiments. In all, 70 per cent of those questioned said they approved of experiments, as long as they were used for severe genetic disorders. Forty per cent of respondents considered genetic experiments of this type important. (Source: New Scientist, 31 August 1991)

Aerosol gene therapy

Another gene therapy first has been reported by Vanderbilt University lung specialist Kenneth L. Brigham, who has been using positively charged liposomes to introduce novel genetic material into rabbits' lungs.

Liposomes are those fatty globules that cosmetic manufacturers tout as skin moisturizers. They can also, according to pharmaceutical manufacturers, target drugs to particular cells. Now the tiny micrometer-sized globules have taken on yet another clinical role: as biological couriers, they deliver a gene to prevent certain lung disorders.

In the May issue of Clinical Research, Brigham reports that the new genes were coded for the production of alpha-1 antitrypsin, a protein that inhibits the kind of protein breakdown associated with adult respiratory distress syndrome. It is thought that gene treatment works better than conventional medication because it does better at targeting the protein inside cells.

The experiment, says Brigham, marks the first time that liposomes have been delivered by a simple noninvasive technique - an aerosol device - to transform cells genetically in living animals. If the gene-carrying liposomes can be easily sprayed into patients' lungs, thousand of deaths might be avoided, according to Brigham.

As with other gene therapies, a major challenge is to ensure that the inserted gene is well regulated, producing enough of the enzyme at the right time, and that it does not disrupt normal cell activities. (Source: Science, Vol. 253, p. 964, 30 August 1991)

Research collaboration established by BRI

A collaborative effort aimed at finding the genetic defect responsible for the human inherited disorder, Malignant Hyperthermia, has been established through BioResearch Ireland between the research groups of Dr. Tommie McCarthy in the Dept. of Biochemistry at University College Cork and Dr. Ken Siggens at the Dalgety Research Laboratories in the Leicester Biocentre. The Dalgety group will establish a procedure to allow rapid screening of regions of the MH gene from affected individuals for mutations(s) that cause this disorder. Once such regions are identified, the mutations contained in them will be characterized in Leicester and Cork using newly developed DNA sequencing approaches.

The MH disorder is a genetic disease which can kill the affected person during surgery, due to an adverse reaction to the anaesthesia used. Currently the only valid test for MH is a highly invasive test that relies on monitoring the reaction to standard anaesthetic agents of strips of muscle tissue obtained by biopsy. The identification of specific defect(s) in the MH gene means that it will be possible in the future to develop a simple blood test to screen for the presence of malignant hyperthermia in high-risk patients before anaesthesia. (Source: Irish Biotech News, August 1991)

Recombinant hgh may speed healing

Genentech's Protropin somatrem recombinant human growth hormone may speed healing from injury, surgery or chronic disease, according to Dr. Louis Underwood of the University of North Carolina (Chapel Hill). Researchers have focused on metabolic measures to assess the drug's efficacy, but are now turning to clinical effects. Underwood tested the drug in seven chronic obstructive pulmonary disease patients, who gained an average of 2.16 kg, with a general improvement in exercise tolerance and a mean pulmonary function increase of 23 per cent. The drug has the unpleasant side-effects of glucose intolerance and hyperinsulinaemia, however. The drug has also been effective in shortening healing time in burn patients, according to researchers at the Shriners Burns Institute (Galveston, Texas). (Extracted from Medical World, July 1991)

New biopolymer

Bioelastics Research (Birmingham, Alabama) will commercialize a technology for a new biopolymer called a bioelastic that was developed at the University of Alabama (Birmingham). The bioelastic is being tested for such uses as muscle-like robotic grippers and special drug-delivery systems. The new material is a synthetic muscle-like fibre that contracts and expands after sensing temperature or chemical changes in its environment. The new fibre is modelled on elastin, which is a protein that is the basic content of elastic tissue. The new fibre comprises a polymer chain whose single links comprise the amino acids valine-proline-glycine-valine-glycine, making it a polypentapeptide. Possible uses for bioelastics are in rotary engines, in desalination, and in burn-cover applications in which they would temporarily substitute for skin. Bioelastics Research was created by members of the University of Alabama's Laboratory of Molecular Biophysics. (Extracted from Mechanical Engineering, July 1991)

Livestock applications

Transgenic poultry work at Institute for Animal Health

Two male and four female adult chickens have been reared from embryos in which the primordial germ cells were exposed to infection by the initial replication-defective vector developed in the AFRC Institute for Animal Health.

Southern blot analysis of DNA from germinal tissue of embryos and from semen of the two male birds has shown that proviruses corresponding to the vector are present in these tissues - indicating for the first time that a defective virus can be used for this purpose in the absence of a helper virus. The intensity of the signal from the sperm DNA suggests a substantial proportion of these males will be transgenic. Unfortunately, however, thus far matings using these males have not produced fertilized eggs. This may be due to problems of husbandry, which are being addressed. For further details contact: AFRC Institute for Animal Health, Compton, Newbury, Berkshire RG16 ONN or Tel.: 0635-578411. Fax: 0635-578844. (Source: Biotechnology Bulletin, Vol. 10, No. 7, August 1991)

Bacteria make a meal of pig manure

Dutch biotechnologists have found a way to recycle the most polluting part of pig manure, ammonia. Using gentically modified bacteria, they have converted large amounts of the ammonia into a harmless protein which can be fed back to the pigs. "It's what I would call the ultimate in recycling: effectively allowing animals to consume their own purified waste," says Johan Sanders, who led the research.

In 1986, the biotechnology company Gist-Brocades, based in Delft, began looking for a bacterium which could convert almost all of the ammonia in pig manure into an amino acid, lysine, a protein used in animal feed. The company used a traditional technique in biotechnology in which micro-organisms are cultured and then irradiated with ultraviolet light to generate random mutations in the bacteria. Bacteria are then selected according to specific criteria for further reproduction.

Tests are currently being carried out in a small-scale experimental fermentation vessel. The researchers are juggling the controls to find the ideal conditions of heat, movement and aeration under which the bacteria produce lysine. The conditions will then be replicated in an industrial-scale fermenter with a capacity of more than 100,000 litres.

The final step will be to separate out the lysine from the remaining manure. This will be achieved, Sanders says, by concentrating the lysine as much as possible and then filtering away the solids left in the manure. Other soluable compounds in the manure will be drained away and the amino acid solution will be evaporated to leave a pure powder of lysine.

Ground water can also be contaminated by phosphate from manure. Pigs need phosphate in their diet, so it is added to their feed. This can be avoided by adding an enzyme called phytase instead. Phytase breaks down a substance which plants use to store phosphorus, releasing it in a form that the pigs can absorb. Using phytase in pig feed instead of phosphate cuts the amount of phosphate in manure by over a quarter.

The fully integrated process is expected to be in commercial operation by 1994. It will treat up to 500,000 cubic metres of manure, about 15 per cent of the Netherlands' manure-processing capacity. (Source: New Scientist, 3 August 1991)

Agricultural applications

Bumper transgenic plant crop

Although it may seem hard to believe, it's been almost 10 years since researchers showed that they could use gene transfer technology on plants. Since then the plant genetic engineers have taken great strides. With several dozen field trials already under way, they may soon achieve their original goal - the development of high-yielding plant varieties with enhanced resistance to herbicides, disease, or insects. So now the researchers are branching out, beginning to design plants with improved consumer appeal, such as tomatoes that hold up better to freezing, as well as creating plants that can serve as factories for pharmaceuticals and industrial oils, just as researchers are now attempting to use pigs to make human haemoglobin. Here is a rundown on some of the weird and wonderful plant varieties being developed.

Researchers at the Scripps Clinic and Research Foundation, La Jolla, California, have genetically engineered tobacco plants to produce functional human antibodies. Plant biologist Mich B. Hein says that these "plantibodies" are not quite the same as those produced by traditional monoclonal antibody techniques, but test tube studies show that the plantibodies behave enough like more typical monoclonals to suggest that they can be used for diagnosing and treating human diseases. Hein and his Scripps colleagues will start pharmacological testing to see how the plantibodies behave when they are injected into mice.

Scripps is also expanding its plant efforts. The institute has recently brought in Roger Beachy, a pioneer in plant genetic engineering, from Washington University to start up a plant science section. The ultimate goal for such work is to harvest high-value pharmaceuticals from common crops, such as alfalfa.

Plants may also become more efficient production factories for oils. Two Iowa State University researchers, geneticist Eve Wurtele and biochemist Basil Nikolau, have discovered a carrot gene that controls the quantity of oils produced. By introducing extra copies of the gene, which encodes an enzyme called acetyl-CoA carboxylase, into plants such as soybeans, it might be possible to induce them to increase their oil production. A more distant goal for this line of research is to switch plants from making the usual cooking and salad oils to producing high-value hydrocarbons, which can be used as petroleum replacements for industry.

At the Oakland, California laboratory of DNA Plant Technology researchers, have cloned the gene for a protein that helps keep the winter flounder from freezing, and inserted it into tomatoes and tobacco. Based on knowledge that freezing and thawing damages plant structures, the company's Gary Warren predicts that fruits and vegetables containing this antifreeze gene will have an improved, firm texture after freezing and thawing. Field trials of tomatoes transformed to make the antifreeze protein began in northern California the week of 20 June 1991.

For people who enjoy a large helping of refried beans, but suffer from the intestinal unpleasantries associated with the digestion of legumes, Agracetus, Inc., of Middleton Wisconsin, has good news. Working with researchers at the University of Wisconsin, Madison, and the University of California, Davis, this biotechnology company has transferred new genes into dry, navy, and green beans. While the company has so far concentrated on improving the plants' disease resistance, another priority is to alter the chemical composition of beans to reduce the flatulence they can cause.

This latter goal, however, may be tougher to realize, says Agracetus' David Russell. He notes that while the traits that affect disease resistance are reasonably well known, the sugars thought to be the culprits in flatulence have not been positively identified, and therefore plant scientists do not yet know how to redesign bean plants to eliminate the undesirable components. But when they do find out the job should be well within reach of the techniques available for the genetic engineering of plants. (Reprinted from Science, Vol. 253, 5 July 1991, p. 33, by Anne Simon Moffat)

Genes for trees

Wisconsin, a US state known for its evergreen forests, now has the world's first conifers that have been genetically altered to kill pests.

The trees' pest-killing genes come from one of nature's best insecticides, the bacterium

Bacillus thuringiensis (Bt). A natural inhabitant of soil, Bt has been used whole to fight plant pests for decades. But scientists now prefer to remove its pest-fighting genes and transfer them into the plants.

Researchers at the University of Wisconsin and the company Agracetus used the genes to arm conifers against spruce budworm, which they say has been the object of more pesticide spraying than any other forest pest in North America.

The researchers coated tiny gold pellets with DNA containing instructions for a protein from Bt that kills the budworm. The pellets were "shot" into spruce embryo cells, which were then induced to grow. (Source: New Scientist, 24 August 1991)

Biodiesel

Gegenbauer farm in Wolfern in northern Austria cultivates wheat, barley, oats, turnips and sugar beet using tractors made by Italy's SAME Group. The unique thing about these tractors is their fuel - vegetable oil, a form of bio-diesel. In the EEC, other manufacturers such as Citroen and Lamborghini are also running tractors, cars and other vehicles on bio-diesel, in this case made from rapeseed oil. Its proponents, such as Melvyn Askew, a consultant to the UK Department of Agriculture, argue that bio-diesel is renewable, more environmentally friendly than ordinary diesel and can easily be recycled.

The company that has pioneered the bio-diesel technology and procedure, which is basically cheap and simple, is Bioenergie-GmbH of Austria, which in 1991 will produce 10,000 tons for local use. A French company is in the process of building an even bigger bio-diesel plant.

Bio-diesel is made by mixing rapeseed oil (ESO) with methyl alcohol to produce methyl RSO. Glycerol is then added to produce rape methyl ester (RME) - known as MRE in Germany and diester in France - as well as high value glycerine which is used in the explosives and pharmaceutical industries. One of the advantages of bio-diesel is that it produces fewer noxious emissions than diesel, particularly sulphur and nitrous oxides.

If the economies of cash- and energy-starved developing countries can structure their farming policies, bio-diesel could represent a break-through for them. Bio-diesel is also used as lubricating oil for vehicles - even buses could be run on the fuel. A major problem is the quantity of rapeseed required. The EEC produces 6.5 million tons per year (tpy) which is not enough to produce the quantities needed to compete with mineral diesel. (Source: South, August 1991)

Dead bacteria give life to "friendly" pesticide

By packing a toxin into dead bacteria, the biotechnology company Mycogen of San Diego has become the first company to win approval from the US's Environmental Protection Agency for the release of a genetically engineered pesticide.

Mycogen's toxin is a naturally occurring protein called Bt, produced by the bacterium Bacillus thurengiensis. Certain strains of the bacteria produce Bt proteins that are toxic to specific pests, such as caterpillars and beetles, but harmless to other wildlife. Mycogen says that it has tested Bt on seven of the most common beneficial pests, as well as on mammals, with no adverse effects.

The effect of Bt has been known for a long time but users found that B. thurengiensis biodegraded within four days. Mycogen has bypassed this problem by inserting the gene that produces Bt into another bacterium, Pseudomonas fluoroscens. The company used a patented recombinant DNA technique, called Cellcap, in which researchers remove genetic material and plasmids from the first bacteria, splice them together outside the cell, clone them, and then insert the cloned copies into the second bacteria. Once inside the new bacteria, the gene causes its host to manufacture Bt. The host bacteria are then killed by heating and immersion in iodine.

Research is also being conducted into altering the strains of Bt to produce pesticides toxic to several pests at once. Another company, Ecogen, is also marketing a genetically altered B. thurengiensis which lasts longer than the natural bacteria. (Source: New Scientist, 10 August 1991)

Fettuccine con worms

William Connick Jr. makes his own pasta but his recipes call for some unsavoury ingredients: fungi and worms. The noodles are a new idea in biological pest control that Connick, a chemist at the US Department of Agriculture in New Orleans, calls Pesta.

Fungi can be effective weed killers and tiny parasitic worms called nematodes devour many insect larvae that kill crops, but researchers who want to package these natural bullies as pesticides face a problem. They have to bundle the fungi or worms in stable granules to ensure that they have a long shelf life, yet they cannot use chemical solvents or high temperatures to do this - it would kill off the killers before they did their job.

Connick bought semolina and a countertop pasta machine, plant pathologist Douglas Boyette sent him spores of the fungus Colletotrichum truncatum. This fungus attacks hemp sesbania, a weed that chokes cotton, rice and soybean fields. Connick mixed his dough with the fungus spores and rolled out some lasagna-shaped noodles. He let the Pesta dry overnight, crushed it into granules, and sent it back to Boyette.

When Boyette mixed the granules in the soil, the fungus kept hemp sesbania seeds from sprouting. In a more elaborate test the fungal Pesta wiped out existing hemp sesbania plants but had no effect on cotton or soybeans that had been growing alongside the weeds.

Pesta with worms has had more modest success. When the granules get wet, the worms squirm their way out and into the soil. In a greenhouse test Pesta with Steinernema carpocapsae worms destroyed 63 per cent of a batch of corn-rootworm larvae. The drawback is Pesta's short shelf life; while the fungal variety has lasted up to a year at room temperature, the worm noodles need to be refrigerated. Even so, Connick

says, wormy Pesta is easier to make and safer to store and handle than many chemical pesticides. Source: Discover, August 1991)

Winter wheat takes off on a magic carpet of clover

British agronomists have unveiled the first alternative to traditional fertilizers and pesticides that will not cost farmers any money: clover.

This lecuminous plant has long been known for its ability to absorb the most important fertilizer, nitrogen, from the air and deposit it in the soil. This process is mediated by bacteria in nodules on the clover roots. For this reason, farmers occasionally plant clover along with rye-grass to provide good grazing. But researchers at the Agricultural and Food Research Council's Institute of Grassland and Environmental Research, at Hurley in Berkshire, have come up with a new way of exploiting clover - by planting it alongside cereals.

Surprisingly, the clover not only fertilizes the crop but also protects it from pests. The researchers think that this may be because beetles and spiders make homes in the clover, preying on aphids and other insects.

Lewis Jones, the agronomist leading the research, says he now recommends clover to some farmers as the first practical alternative to chemical fertilizers and pesticides. The rotational set-aside scheme is a European Community measure to shrink the cereal mountain. Under the scheme, farmers are paid to leave a different part of their land fallow each year. Jones says farmers using rotational set-aside will get the same results from planting clover alongside winter wheat as from adding commercial nitrogen fertilizers.

Since 1988, Jones has been comparing plots of cereals fertilized using chemicals with neighbouring land that had been planted with white clover before the cereal was planted. In each year, the mixture of clover with winter wheat did at least as well as winter wheat fertilized with commercial fertilizers. As the cereal grows taller it cuts off the light to the clover, killing some and releasing nitrogen into the soil just as the crop needs it. The clover transfers 100 kilogrammes per hectare of nitrogen to the soil, as much as a farmer would apply.

By planting the cereals far enough apart, Jones found that some clover would have enough sunlight to survive past the harvest to recolonize the plot in time for the next crop. Winter wheat proved the most successful because, unlike other cereals, it does not spread out around each stalk.

Although untreated with pesticides, clover plots had fewer aphids and slugs than neighbouring land. Jones suspects that poisonous spores from fungus growning on clover may help to kill off the aphids.

According to Jones, the clover-wheat combination could be used without breaks, but leaving the field without cereal for a year gives the clover more time to recover. (Source: New Scientist, 10 August 1991)

Australian company near to a blue rose

The Australian biotechnology company Calgene Pacific estimates that it will be marketing blue roses by 1997, now that it has successfully isolated a blue pigmentation gene from other flowers. Such a rose cannot be produced by normal breeding techniques since roses do not have the necessary pigment.

The company says the blue roses will be sold initially at about US$ 80 a stem.

Michael Dalling, managing director of Calgene Pacific, says the company has already developed an implantation technique for putting new genes in flowers by adapting a mechanism used by the crowngall disease virus. It has used the technique to alter the genetic makeup of other flowers, he says. For instance, Calgene recently grew a batch of several thousand carnations with a gene for extended life. The company still has to marry the gene implantation technology with the new gene, which was isolated from delphinium flowers, but believes it will be able to do so within schedule. (Source: Nature, Vol. 352, 22 August 1991)

Food and food processing applications

Battling bacteria in meat products

A bacteriocin-producing Lactobacillus has prevented Listeria monocytogenes from growing in fresh Mettwurst (German sausages), report researchers at the Federal Centre for Meat Research's Institute for Micriobiologoy (Kulmbach, Bayern, Germany). Their work suggests that this and other Lactobacillus strains could be incorporated into meat products as a means of combating food-borne infections caused by Listeria monocytogenes. The infections - collectively known as listeriosis - are potentially fatal and are increasing in many countries, not least because Listeria monocytogenes can grow at the comparatively low temperatures (down to 0.5°C) that are within range of those used in order to preserve prepacked cook-chill foods. The organism, which is a particular threat to immunocompromised patients, is also relatively tolerant of low pH and high salt concentrations. (Extracted from Bio/Technology, Vol. 9, August 1991)

Industrial microbiology

Degradable polymers

Eyeing the market for biodegradable packaging materials, Cargill (Minneapolis) is developing a series of corn feedstock-based processes to make lactic acid and degradable lactic acid polymers. Pilot plant quantities to represent commercial plant production should be available by March 1992. Cargill's proprietary processes are designed to economically transform corn into lactic acid that can be converted into lactic acid polymers, tailored to customer needs. Full-scale commercialization, which could occur in late 1994, will be driven by customer demand and successful demonstration of product performance, says Cargill. (Source: Chemical Week, 30 October 1991)

Biosensors

In the days before the safety lamp, nervous coal miners used to inch towards the coal-face clutching a canary. If it died, that was early warning of explosive or asphyxiating gases. Canaries, however, have drawbacks. They need food and water, and are liable to do many things besides dropping dead for the convenience of miners. The ideal artificial canary would ape the sensitive biological detective work of a real

bird, and link it with some untemperamental technology to give the warning. Biosensors aim to do just that.

Modern biosensors are useful for monitoring environmental pollution. Japanese scientists, led by Isao Karube of the University of Tokyo, have developed devices to check both general water pollution (by measuring the oxygen uptake of pollution-causing bugs) and particular unpleasant substances, such as phenols. But it is in the field of medicine, where biosensors were first developed, that they are most useful.

All biosensors are an uneasy a..iance of two components. The biological part is usually a protein (either an enzyme or an antibody) that reacts only with the relevant chemical. The technology is a device that detects the electrical or optical convulsions which this reaction generates and then reports them to the outside world.

About 100 enzymes have been incorporated into biosensors, enabling doctors to keep an eye on the chemical health of their patients.

Antibodies (proteins used by bodies to recognize foreign molecules) provide an alternative tool for the biosensor builders. Jerome Schultz of the University of Pittsburgh is using them to attack diabetes from a different direction. Unlike devices based on enzymes, which need a drop of the patient's blood, his sensor sits in the bloodstream and monitors glucose levels continuously. With luck it will eventually be linked to a portable, insulin-injecting pump to create a sort of artifical pancreas.
Dr. Schultz's detector uses a surrogate antibody - ConA - and a large sugar-like molecule called dextran, both contained inside a special membrane. ConA can combine either with glucose (which can leak in through the membrane) or dextran (which is too big to leak out).

Such protein-based sensors are robust and fairly simple. Some researchers have been experimenting with biosensors which are neither: they use intact tissues from plants and animals. Garry Rechnitz and his colleagues in the University of Hawaii at Manoa have made biosensors using banana pulp (which detects the neurotransmitter dopamine), maize kernels (pyruvate - a chemical that figures in energy production), rabbit liver (guanine - one of the components of DNA) and sugar beet (tyrosine - another neurotransmitter). They even tried using the antennule (a small sensory organ) from a blue crab.

These whole-tissue biosensors have two big problems: they do not last long; and joining the living material to a tiny electrode or optical fibre is as much an art as a science.

Uses for biosensors are proliferating. Biotrace, a German company, has invented a device for monitoring the brewing and fermentation of beer, while Britain's Cranfield Biotechnology hopes to make a colour-coded card that will tell you if you have drunk too much of it.

Biosensors are not yet big business: a recent report from Cranfield Biotechnology tentatively estimates a world market of $360 million by 1996. They are, however, themselves tell-tale indicators of an inexorable process: the evolution of industrial biology from cottage craft to mass production. (Source: The Economist, 28 September 1991)

Energy and environmental applications

Finns clean up paper plant with enzymes

Biotechnology has been helping a paper manufacturer in Finland to clean up its factory. Liquid effluent from wood pulping mills usually contains highly toxic chlorinated organic compounds, and some of the chlorinated waste can discolour the waterways it is dumped in.

Chlorine is normally required to pre-treat wood pulp before it is bleached with chlorine dioxide to make it white enough for the production of quality paper. Finnish scientists are attempting to carry out the pre-treatment with enzymes, which do not form toxic chlorinated waste products.

Liisa Viikari and colleagues at the Technical Research Centre of Finland in Helsinki worked alongside researchers at the Finnish Pulp and Paper Research Institute to conduct the largest trials ever attempted using an enzyme system for pulp bleaching.

The trial ran throughout most of April 1991 in a plant producing 1,000 tons of wood pulp daily, sited at Aanekoski, 70 kilometres north of Helsinki. During the trial the amount of chlorine used for pre-treatment was reduced by 25 per cent, and the amounts of chlorine and chlorine dioxide combined fell by 15 per cent. The researchers say this reduced levels of chlorinated organic compounds by 40 per cent.

Pre-treatment of the pulp removes lignin, the natural "scaffolding" in wood which supports the cellulose and hemicellulose fibres which are processed into paper. Any residual lignin imparts a brownish "paper bag" colour to the pulp.

Researchers have found that, like chlorine, some families of enzymes can attack and alter lignin chemically so that it becomes soluble and can be drawn off in alkaline fluids prior to brightening.

The team in Finland used xylanase enzymes extracted from a fungus called Trichoderma longibrachiatum. Xylanases make lignin soluble by dissolving the bonds between lignin and the fibres it supports.

Viikari says that Novo Nordisk, a Danish biotechnology company based in Copenhagen, is about to begin selling a xylanase that works in alkaline conditions. Other companies are investigating similar techniques. The US chemical company Sandoz has devloped an enzyme-based product specificially for pulp pre-treatment. Known as Cartazyme, it is a mixture of hemicellulose enzymes and could, according to Jean-Pierre Carrard of Dandoz's chemical arm in Britain, dispense with chlorine altogether. Several paper makers are running trials with Cartazyme.

Gordon Hoffman, of Sandoz Chemical in Charlotte, North Carolina, says that alternative delignification techniques that are less environmentally harmful than chlorine already exist including the use of oxygen and ozone, but

these require a new pulping plant to be built, entailing a huge capital outlay. Enzymes, by contrast, can be adopted with a minimum of plant modification. (Source: New Scientist, 15 June 1991)

E. PATENTS AND INTELLECTUAL PROPERTY ISSUES

Genentech's TPA patent sets precedent in Japan

In what analysts have seen as Japan's first major biotechnology case, Genentech has won a preliminary injunction in the Osaka District Court against Toyobo Corp. - ruling that the Japanese company's sales of tissue plasminogen activator (t-PA) infringed the US company's patent. Court bailiffs promptly seized t-PA from Toyobo's plant in Katata. The ruling leaves Genentech as the only supplier of t-PA in Japan, which approved the drug for sale in May. The Japanese market is estimated to be worth $80-100 million a year, or around half the size of the US market. On the face of it, since Genentech - and its licensees, Mitsubishi Kasei Corp. and Kyowa Hakko Corp. - have supplied around half of the Japanese market, their share could double if the ruling holds.

Although Genentech could have licensed Toyobo, it decided to take the higher risk strategy of fighting the case through the courts - and filed suit in 1987. If Genentech succeeds in forcing Toyobo's t-PA off the market, but then loses on appeal, the US company could end up owing considerable sums in damages for lost sales. Any appeal could take two years to decide. Genentech company was required to post a bond of 100 million yen ($760,000) to cover the possibility that such an award might be made in Toyobo's favour. Details from: Genentech Inc., 460 Point San Bruno Boulevard, South San Francisco CA 94080, USA. (Source: Biotechnology Bulletin, Vol. 10, No. 10, November 1991)

New Patent Act in Indonesia

The Indonesian Patent Act of 1989 came into effect on 1 August 1991, and provides a patent term of 14 years from the date of filing with a possible single extension of two years. Inventions for processes for production of food or drink, new types of varieties of plant or animals, or processes for cultivating plants and animals, as well as the products of these processes, and inventions for methods of treatment or diagnosis of human or animal body, are not patentable. (Source: Australian Biotechnology, Vol. 1, No. 2, October 1991)

Revision of New Zealand practice on patentability of naturally-occurring micro-organisms and biological compounds

The New Zealand Patent Office has significantly relaxed its restrictions on patentability of biotechnology-related inventions. Claims will be accepted if they are worded so as to exclude substances or organisms in their naturally-occurring state or environment. Thus permissible claims will now include claims for:

(a) Biological compounds in a stated degree of purity;

(b) Substances, except when found in nature;

(c) Biologically pure cultures; and

(d) DNA sequences.

A number of applications that have been held up in prosecution due to the previous more rigid practice can now be accepted, and these cases will be taken up by the Patent Office in chronological order. (Source: Australian Biotechnology, Vol. 1, No. 2, October 1991)

Reservations against "Patents on Life" in Europe

Last September the powerful Agriculture Committee of the European Parliament rejected the European Commission's proposal for a Council directive on the legal protection of biotechnological inventions, which would allow patents on life, even on human genes or body parts. The proposal would be "likely to have an impact on the economic, social, ecological and ethical bases of our society" and "involves changing the structure of agriculture", concluded the Committee.

Genetic Resources Action International (GRAIN) and other Europe based NGOs welcomed this vital decision as they are convinced that the proposed patent system would lead to concentration of ownership of vital resources, promote environmentally inappropriate research, deny farmers the right to plant back seed from their previous harvest and undermine negotiations for a global agreement on protecting biodiversity.

The overwhelming majority of the Committee warned against pressurizing the European Parliament into making a hasty decision on life patenting in favour of the competitiveness of the biotechnology industry. Equally, it warned against deliberately playing down the social, ecological and ethical aspects of the patenting of living organisms. Both the Committee and the NGOs hope that the full Parliament will not only reject the Commission's proposal but will address the wider fundamental issues about claiming ownership over life. Before the full European Parliament meets in Strasbourg to consider the matter, the Legal Committee will make its formal recommendation.

In a related decision, the Agriculture Committee endorsed plans worth two million ECUs (about US$ 2.5 million) in 1992 for a European Programme on the Conservation of Plant Genetic Resources to coordinate the efforts of Member States. The programme is designed to support both the formal gene banks and the informal work by Community organizations to protect crop diversity in farmers' fields, as well as awareness raising efforts on the importance of genetic resources for farming, the food supply and the environment. It was later approved by the Budget Committee, but still has to go through the Legal Committee and plenary. It certainly indicates a favourable climate for genetic resources in Europe. (Source: GRAIN Press Release, 25 September 1991)

F. BIO-INFORMATICS

UNEP report on deliberate release information resource needs

The United Nations Environment Programme (UNEP) has now published the proceedings of a workshop on "Needs and Specifications for an Information Resource for the Release of Organisms

into the Environment (IRRO)", held in Vienna, Austria and Rockville, Maryland in March 1991. The workshop was supported by the Microbial Strain Data Network (MSDN), the Commission of the European Communities (DG XII/F/1), the US Environmental Protection Agency (EPA), the US Department of Agriculture (DOA) and Environment Canada.

Among the workshop's conclusions were the following:

- A not-for-profit, integrated information resource on the introduction of organisms into the environment should be established;
- The resource should be international in scope and accessibility;
- Information on both non-modified and genetically modified organisms should be included;
- The resource should be a distributed network linking existing resources - with new databases developed only to fill identified gaps.

Details from: Barbara Kirsop, MSDN, 307 Huntingdon Road, Cambridge CB3 0JX or Tel.: 0223 276622. Fax.: 0223 277605.

Biotechnology: EEC policy on the eve of 1993

Although the EEC has the human, scientific and material resources to compete globally in the biotechnological race, it has failed so far to match strides with its main rivals - the United States and Japan. The failure may be attributed to several factors:

- Fragmentation of research efforts;
- Compartmentalization of the EEC market, as a result of disparate standards and regulations;
- Absence in the Community of the correct supportive context and infrastructure to allow biotechnology to emerge;
- Lack of a unified market, thereby discouraging companies from making the substantial investment required for the commercial and industrial exploitation of new discoveries;
- Inadequate patent protection for biotechnological inventions.

Recent developments suggest however that the Community is beginning to make the political choices needed to fulfil its potential. On 22 April 1990, the Member States adopted two Directives which go a long way towards establishing a regulatory framework for the biotechnology industry, whilst a Directive on worker protection is expected to be agreed shortly. Steps have also been taken to facilitate the development and placing on the market of high-technology medicinal products, and the "Twelve" are currently examining a proposal for a Directive on the legal protection of biotechnological inventions.

To help keep abreast of likely developments in this fast-evolving sector, which is capital for the future of EEC industry, agriculture and healthcare, European Study Service has just published a 400-page study entitled "Biotechnology: EEC Policy on the eve of 1993". The study analyses the technical, economic and political aspects of this crucial issue and is supplemented by comprehensive annexes containing all relevant EEC documentation. Further details from: European Study Service, Avenue Paola 43, 1330 Rixensart, Belgium. Tel.: (+32 2) 653 90 19; Fax: (+32 2) 652 03 02.

UNESCO Series of Manuals in Biotechnology

With a view to diffusing authentic scientific laboratory research protocols for research in the biotechnologies and to overcoming the isolation of young researchers from modern advances, a series of manuals in biotechnology will be made available, free of charge, to scientists and institutions particularly in the developing countries. The following manuals are available:

1.	Plant Tissue Culture Manual	K. Lindsey, Kluwer Academic Publishers
2.	Plant Molecular Biology Manual	S. B. Gelvin, R. Schilperoort, Kluwer Academic Publishers
3.	Molecular Cloning: A Laboratory Manual	J. Sambrook, E. E. Fritsch, T. Maniatis, Cold Spring Harbour Laboratory Press

Researchers and institutions in the developing countries desirous of obtaining one or more copies of each of the above manuals are required to provide a one-page description of the applicant's research programme which must be accompanied by two representative publications on the subject. This statement must also specify which manuals are needed and a justification for the request being made. Requests from individuals must be endorsed by the Head of the Institute. All requests must be submitted to:

UNESCO Short-Term Fellowships in Biotechnology
Biotechnology Action Council
Division of Basic Sciences
UNESCO
1, rue Miollis
75015 Paris
France

(Source: News Release, August 1991)

WFCC Technical Information Sheets available

Scientists using micro-organisms and cell cultures in their investigations are usually faced with numerous bigger or smaller problems. Some of these problems concern safe handling, cultivation, maintenance, preservation, identification, availability, packing, shipping or deposition of micro-organisms and various other collection-related matters. To meet the need of scientists especially in the developing countries, the WFCC Education Committee has initiated, with financial support from UNESCO, the production of Technical Information Sheets (TIS) on all above matters. The following TIS have been published and are available (limited number) free of charge.

1. Prevention of mites in cultures, by A.H.S. Onions

2. A quick method for estimating the percentage of viable cells in a yeast population, using methylene blue staining, by K. Painting and B. Kirsop

3. Cryopreservation of yeasts in polypropylene straws, by J. Henry and B. Kirsop

4. Cryopreservation of bacteria with special reference to anaerobes, by Khursheed A. Malik

5. Cryopreservation of fungi, by Peter Hoffmann

6. Cultivation and preservation of members of the family Halobacteriaceae, by Brian J. Tindall

7. Freeze-drying of micro-organisms using a simple apparatus, by Khursheed A. Malik

8. Liquid-drying of micro-organisms using a simple apparatus, by Khursheed A. Malik

9. Instructions for packing and shipping of biological materials, by Dieter Claus

10. Some universal media for the isolation, growth and purity check of a broad spectrum of microorganisms, by Khursheed A. Malik.

Requests for free copies should be addressed to WFCC Education Committee (Dr. Khursheed A. Malik, DSM-Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH, Mascheroder Weg 1 B, D-3300 Braunschweig, Federal Republic of Germany) or to your regional MIRCEN.

TIS are edited by Dr. Khursheed A. Malik. All material should be sent to the Editor if you would like to contribute to the preparation of additional TIS. We all perform specialized technical activities that may not be known to others but may help in solving problems or just help doing things better, easier or quicker.

Information kit on agroforestry technology

The International Institute of Rural Reconstruction (IIRR) has prepared an "Agroforestry Technology Information Kit" for the use and guidance of social forestry officers and technicians.

This handbook was developed through a workshop involving 39 participants representing a variety of organizations concerned about environmental problems and agriculture. Sections include soil and water conservation, annual cropping systems, seed and plant propagation, trees and their management, livestock production and home-lot technologies.

This kit contains a variety of important, interesting information that would be especially valuable for extension workers and farmer-motivators. It is written with the Asian audience in mind but has broad applications for the humid and sub-humid tropics.

Meanwhile, a second kit for agricultural trainers titled "Regenerative Agricultural Technologies" has also been compiled by IIRR. This kit contains a variety of information sheets covering topics necessary for development and maintenance of a regenerative agricultural system for small farmers. Included are designs for 1,000, 2,500 and 10,000 square metre foodlot modules which integrate gardens, grains, trees, fish, snails, chickens and pigs.

These kits are available through the IIRR, Siland, Cavite, Philippines for the cost of printing and postage.

ICARDA issues book on agricultural sustainability in West Asia and North Africa

For thousands of years, farmers have tilled the soil of West Asia and North Africa. Yet after millennia of food self-sufficiency, this region is no longer capable of feeding itself, and today imports more food per capita than any other area on earth. Inexorable market forces are compelling farmers to wrest from the earth a level of food production it simply cannot sustain. Soil erosion and nutrient exhaustion are becoming ever more common. Scarce water resources are being rapidly depleted. Overgrazing is creating deserts.

A book shortly to be issued by the International Center for Agricultural Research in the Dry Areas (ICARDA), entitled Agricultural Sustainability Research at ICARDA, outlines some of the work being done to develop practical, realistic solutions to these problems. Central to these solutions is an acute awareness that gains in productivity in this generation must be weighed against the land's ability to provide for future generations, in other words, sustainability.

The experience of the last three decades has shown that increased crop productivity in and of itself is only part of the solution to feeding the world. An integral approach to agriculture, an awareness of both the long- and short-term effects of any given crop or farming practice, is critical for sustained food crop production.

Despite this, only in recent years has sustainability become an issue. This is partly because of increased environmental awareness, but also because prior to the introduction of mechanized agriculture, most agricultural systems were by their very nature sustainable. Agricultural mechanization, pesticides and chemical fertilizers have enabled farmers to realize amazing yield increases capable of feeding the world's growing population.

But these innovations also led to a fundamental loss of equilibrium. "Miracle" technologies made it easy for farmers (and agricultural researchers) to forget the importance of maintaining the fine balance between man's needs and the laws of Nature. With growing public concern over global warming, environmental pollution, toxic wastes and the like, the concept of sustainability has finally begun to receive the attention it rightly deserves.

Agricultural Sustainability Research at ICARDA features concrete examples of ICARDA research aimed at limiting soil erosion, restoring range vegetation after years of overgrazing, and increasing the efficiency of water and fertilizer use.

For a copy of Agricultural Sustainability Research at ICARDA, simply contact Information Services, ICARDA, P.O. Box 5466, Aleppo, Syria. (Source: News Release, 16 September 1991)

Biotechnics and Society: The Rise of Industrial Genetics by Sheldon Krimsky

Impacts of technological change have historically been assessed only after the passage of a significant period of time. It is then that historians recreate the decisions that were made, sort out the influencing factors, and debate in hindsight the options that were available at the time. Sheldon Krimsky, consistent with the importance of his subject, telescopes this process by providing contemporary readers a broad overview of the first ten years of the industrial revolution in applied molecular genetics. He discusses the birth and expectations of the biotechnology industry, the response to products of genetic engineering, perspectives on risk assessment from different sectors of the scientific community, and public initiatives to regulate new products. Krimsky explores the social and political discourse on the direction of biotechnology, and offers the most detailed examination to date of the controversy over the environmental release of genetically engineered organisms. Finally, he takes a critical look at the conventional role of technology assessment and suggests an alternative model that fits more closely with the needs of an environmentally sensitive world.

Krimsky's thought-provoking work offers readers a unique opportunity to understand what questions were being asked, what options were available, and what decisions were being made when the industrial application of genetic technologies was still in its infancy. His insider's perspective will interest those working in the fields of biology and social issues; science, technology, and society; and the sociology of science. Challenging, cautioning, and balanced, this book is required reading for all who are seriously concerned with the relationship of emerging technologies to society. Sheldon Krimsky is Professor of Urban and Environmental Policy at Tufts University. Price $17.95. ISBN 0-275-93860-3. 280 pages. July 1991. A hardcover edition is available: 0-275-93859-X. C3859. $47.95. Greenwood Publishing Group, Inc., 88 Post Road West, Box 5007, Westport, Connecticut 06881. Tel.: (203) 226-3571.

G. SPECIAL ARTICLE

Management of science, industry and university collaboration in generating and commercialization of biotechnologies: an appraisal of the Indian approach

by
Dr. Kishore Singh*

Industrialization of research results is becoming a touchstone of scientific and technological (S&T) development policies. The main drawback of S&T development strategies has been the isolation of research and development (R&D) from industry and the productive sector. The experience of developing countries shows that the interface between the R&D and the system of technology production is a common problem they face.

As a recent UNCTAD study has pointed out, in almost all developing countries, including the more advanced ones, the scientific and technological knowledge produced in research institutions is insufficiently used in the industrial sector. Indeed, the lack of adequate linkage between the knowledge-generating sector and the production sector is the main source of difficulties for the technology innovation process in developing countries. 1/ A question which will increasingly draw the attention of policy planning bodies and technology development agencies is: how to ensure continual feedback between research and industry, and forge points of contact between R&D/S&T and industrial management?

Experience available in developing countries shows that constraints and limitations on industrialization of research results emanate from the diminishing policy concern with the process of innovation. Policies in developing countries have generally tended to be weaker with respect to progressive measures required to be taken in different phases of innovation. Due to scant outlays on developmental R&D, policy concern is characterized by regression as one gets closer to the market. With a perspective, limited to technology generation, and at best inventive activity, technology policies in developing countries have generally proved highly inadequate when it comes to the tasks involved in commercializing technologies generated indigenously. This is, inter alia, on account of the fact that the magnitude of resources and expertise devoted to developmental R&D after the inventive activity, gets reduced instead of being progressively increased. In fact, the process of innovation is not understood as being a continuum of inventive activity. 2/

Biotechnology development priorities and thrust areas

Currently evolving policies for promoting biotechnology development in India seem to have taken due cognizance of these problems and strategies are being evolved to minimize them. Measures being taken for commercializing R&D results are primarily concerned with forging necessary linkages with the productive sector. Industry and universities are being actively involved in developing biotechnologies.

Biotechnologies are being recognized in India as a frontier area of scientific research and application and in a number of areas, biotechnology development programmes have been launched in the country.

Major thrust areas for R&D are:

(i) Plant molecular and agricultural biotechology;

(ii) Biological pest control;

(iii) Fuel, fodder, biomass, horticulture, plantation crops and sericulture;

(iv) Environmental biotechnology;

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The opinions expressed and viewpoints presented are those of the author and not of the organizations for which he works.

(v) Aquaculture and marine biotechnology;

(vi) Veterinary biotechnology;

(vii) Medical biotechnology;

(viii) Biochemical engineering, downstream processing and instrumentation;

(ix) Microbial biotechnology;

(x) Industrial biotechnology;

(xi) Basic research, emerging areas and R&D facilities;

(xii) Bio-informatics; and

(xiii) Integrated manpower development.

Technology innovation: highlights

In some areas, programmes relating to biotechnology development have been successfully carried to the stage of innovativeness, and technology transfer activities are now in the process of realization so that product development or generation of know-how is profitably used by the industry or productive sector concerned, after going through pilot plant stage and demonstration of technologies developed.

In the thrust areas in medical biotechnology - DNA technology, development of diagnostic kits, drug delivery systems, development of DNA probes, development of cholera vaccines, biosensors, prenatal diagnosis of genetic disorders - innovations have already been realized, and attempts are being made now to commercialize technologies.

Sustained support to development, validation and commercialization of immuno-diagnostic kits of relevance to major diseases prevalent in the country is a continuous programme of activities in India. For instance, two kits - one for detection of bancroftian filariasis and a pregnancy detection kit - were commercialized through private sector industry. Besides, M/S Ranbaxy Ltd., New Delhi, released the first of the three immuno-diagnostic kits licensed by the National Institute of Immunology (NII) for the diagnosis of pregnancy. The tests employing specific and high affinity monoclonal antibodies (Mabs) have produced a test with improved stability of working in tropical countries.

Another major biotechnology programme relates to the Embryo Transfer Technologies (ETT). Projects for embryo transfer in cattle and buffaloes are being implemented through the National Dairy Development Board (NDDB) as the lead agency. The main embryo transfer laboratory has been established at Baidaj Gujarat which provides central facilities for training, research and cooperation under the project. More than 1,000 frozen embryos are in germ plasm banks in India.

Research projects for embryo transfer have resulted in some major achievements:

(i) The first ever buffalo calf named Pradham born following in vitro fertilization of cocyte and subsequent embryo transfer was reported during 1990 at the National Dairy Research Institute, Karnal;

(ii) The Central Institute of Freshwater Aquaculture, Bhuneshwar, has succeeded in producing the seed of the air breathing catfish, Clarias batrachus, continuously from April to October 1990, through proper maintenance of breed stock, coupled with hormone treatment;

(iii) The animal birth control vaccine - Talsur - has been developed at the National Institute of Immunology (NII), New Delhi, with the aim of reducing the number of unwanted animals and eliminating the stray-dogs menace. Field trials have been conducted for large-scale application and popularization, and the Drug Controller of India, New Delhi, has approved it for commercial production and application. The NII has signed a Memorandum of Understanding (MOU) with M/S Karnataka Antibiotics & Pharmaceuticals Ltd., Bangalore, for the use of large-scale manufacture of the product. 3/

Given these cases of success, need for disseminating ET technologies throughout the country is being felt. As such, 25 State level centres are being created for the popularization of ET technologies for the benefit of farmers.

As regards the Aquaculture and Marine Biotechnology Programme, technology generation activities relating to semi-intensive prawn farming with the application of biotechnologies have begun showing results and are nearing the completion of the innovation chain, after demonstration of being technologically feasible and commercially viable.

In the area of tissue culture, 4/ biotechnology development has been notable. As part of the All-India Coordinated Programme on Plant Protection, the project on tissue culture of cardamom has been developed to the stage of demonstration of performance of high yielding in vitro cloned cardamon. Technology development efforts in this respect have involved the private sector. AVT & Co. - a private sector company - supplies elite tissue culture plantlets and is closely associated with implementation, monitoring and evaluation of the Tissue Culture Cardamom Project Plan, which was launched in 1989 in collaboration with the Spices Board and the Ministry of Commerce. It may be mentioned that the Microbial Type Culture Collection Bank (MTCC), which is a national facility sponsored jointly by CSIR and the Department of Biotechnology - has more than 900 cultures in stock.

International collaboration for biotechnology development

Biotechnology development programmes have also drawn upon international collaboration. These have been mainly in the form of technical assistance and joint development programmes. Some of the notable examples covering current collaboration are:

(i) A public sector company: Bharat Immunogicals and Biologicals Corporation Limited (BIBCOL) was established for moderating manufacture as well as R&D in the area of immuno-biologicals - vaccinology and related subjects - with its Oral Polio Vaccine (OPU) Unit. Under a technical consultancy

cooperation with the USSR, 14 million doses of OPU were imported in the latter half of 1989.

(ii) Indian Vaccines Corporation Ltd. (IVCOL) - a company in the joint sector - was established in March 1989 to undertake manufacture cum R&D of viral vaccines, promoted by the Department of Biotechnology, Indian Petrochemicals Corporation Ltd. (IPCL) and Pasteur Merieux Serum and Vaccines (PMSV), Lyon (France). Bulk import from PMSV would be followed by indigenization.

(iii) M/S Organon Tecknika, The Netherlands, along with their Indian associates M/S Infer India, Calcutta, have agreed to supply AIDS diagnosis kits and set up manufacturing facilities. Over 20 reputed international companies are participating in other programmes. 5/

Besides, several projects with the cooperation of international bodies as well as industrialized countries are being carried out presently to promote agricultural productivity growth, covering areas such as development of drought-resistant plant varieties, integrated nutrient management, animal and fish genetic resources conservation, post-harvest technology, embryo transfer technology, agro-forestry research, tissue culture in horticulture, crops, etc. 6/

Modalities of collaboration between research institutes and industry

As regards technology transfer in the area of biotechnology in India, transactions are based on working relationships. Collaborations between R&D institutes and industry has taken the form of a Memorandum of Understanding, spelling out the interest and commitments of industry and tasks assigned to research institutes. These MOU provide channels for technology transfer from R&D institutes to user agencies and industry, and purport to technology licensing.

Among the current cases of transfer, the following may be noted:

(i) A Memorandum of Understanding was signed between the All-India Institute of Medical Sciences (AIIMS) and M/S Ranbaxy Laboratories, New Delhi, for the procurement of techniques for typhoid fever detection from AIIMS and for their introduction to the market after developing a commercial kit.

(ii) Another MOU was signed between the National Institute of Immunology and M/S Cadila Laboratories Ltd., Ahmedabad, transferring clones and techniques of blood grouping developed at the National Institute of Immunology, New Delhi.

The modality of the Memorandum of Understanding is also being used as regards international cooperation in the area of agricultural research and biotechnologies.

Growing role of universities in generating biotechnologies and in providing support services

In these efforts towards technology generation, the collaboration of universities and academics is more and more becoming a contributory factor. Research programmes in several universities, initiatied in recent years, are being geared towards generating biotechnologies, often by way of collaborative arrangements. Universities are also increasingly becoming seats of learning in this area, thus creating a technical knowledge base. On the basis of expanding research and teaching activities, universities in India would become better equipped to form and supply the necessary expertise and specialized skills for executing biotechnology development programmes. 7/

As part of an integrated programme on human resources development and skill formation, graduate and post-graduate research and study programmes have been introduced in Indian universities in recent years. At present, M.Sc./M.Tech./Post-doctoral teaching is provided at 12 Indian universities in different areas such as biochemical engineering, agricultural, veterinary, medical and marine biotechnologies, etc. This will lead to the formation of expertise and specialization in diverse areas of biotechnology. These activities are promoted by the National Board of Studies.

University-industry interaction and collaboration is indeed becoming a commendable feature of biotechnology development programmes in India. Several biotechnology programmes are being currently implemented at different research institutions and universities in the country:

(i) A project on poultry broiler production on growth promotion aspects by means of immunization of birds against somatostatin has been implemented at the Madras Veterinary College. Financial support for this activity was obtained from M/S Godrej Soap Limited, Bombay.

(ii) A research programme promoted by the Department of Biotechnologies is on transgenic fish production. Madurai Kamaraj University has standardized the technique to produce transgenic fish through the expression of growth hormone genes micro-injected into the eggs of commercially imported fish.

(iii) PGIMER and the Department of Human Biology and of Human Genetics, Guru Nanak Dev University, Amritsar, have a joint project for diagnosis of genetic disorders with the objective of developing DNA probes.

(iv) The Indian Institute of Technology (IIT), Bombay, is entrusted with a project on membrane-bound enzyme sensors for use in biotechnology and biomedical engineering.

(v) The University of Delhi has started research in liposome technology.

Commercializing R&D results: new institutional mechanisms

Several tasks require to be undertaken for transfer and commercialization of biotechnologies: feasibility studies, field demonstrations, validation, marketing, testing and certification, marketing surveys, apart from further process development after initiating production development. 8/ Moreover, experience

shows that a major limitation on technology development in developing countries is that these countries prefer technologies that are proven and commercialized, rather than take risks, in developing technologies from the inventive stage. Hence the need for risk-coverage mechanisms, in addition to a diverse range of technical assistance.

Therefore, as a follow-up to a proposal by the Department of Biotechnology for setting up a bio-venture company, 9/ a new institutional mechanism - M/S Biotech Consortium of India Ltd. (BCIL) - was incorporated by the Industrial Development Bank of India (IDBI) in September 1990, with the participation of financial institutions, nationalized banks and industry.

The main objectives of the BCIL are to:

- Develop one-to-one tie-ups with industries, entrepreneurs and R&D institutes, along with financial institutions;
- Support the development of prototypes and establishment of pilot plants and assist in the validation, field trials and approach of the products developed;
- Enable basing and renting of national facilities for product and process development;
- Produce pre-feasibility reports as well as detailed project reports;
- Carry out cost-benefit analysis to minimize risk capital investments for production of value-added products;
- Assist in the transfer of relevant technologies from indigenous or international sources and to assist in screening and evaluation of these technologies. 10/

Sinc BCIL, has just started, it is premature to attempt any kind of performance evaluation. However, its activities would have significant bearing on:

(i) Risk-coverage modality;

(ii) Licensing arrangements and intellectual property rights; and

(iii) Innovation promotion.

Risk coverage

Risk capital by way of loan agreements to entrepreneurs, enterprises, institutions, etc. undertaking development of indigenously generated biotechnologies will be provided by BCIL on concessional terms, with provisions for profit and risk sharing with the project sponsors. BCIL may also hold equity shares. In case of commercially oriented, successful programmes, the return to BCIL will be in the form of royalty on sales for a mutually agreed rate and period. However, only 5 per cent of the loan amount would be recovered if the project is not commercially successful.

Licensing and intellectual property rights

In case of commercially successful ventures, while respecting intellectual property rights of technology developers, BCIL would expect a share in the commercial licensing of technology/process patents, etc. though BCIL will not normally claim ownership of intellectual property rights (know-how, patents, etc.). It will also reserve to itself the right of compulsory licensing in cases where potentially useful products or processes are developed as a result of work financed by BCIL, but the applicant chooses to neither commercialize it, nor licence such products or processes. In that case, BCIL would, as of right, commercialize such products/processes through any other agency it may select at its discretion. If so required by BCIL, the promoter will execute a disclaimer release assignment in favour of BCIL or any other agency, as BCIL may direct.

Innovation promotion

The activities of BCIL are expected to promote activities of innovations by way of development work proposed for assistance, and coverage of risks involved. A perusal of proposals to be covered by BCIL indicates that innovation promotion would be the main purpose of assistance. Assistance would be provided for:

(a) Setting up of pilot plant/demonstration plant (where justified)/prototype/software development based on laboratory process/detailed designs developed in-house or in any of the national/other laboratories with a view to ultimately commercializing the product;

(b) Technological innovation leading to substantial quality upgrading, reduced material consumption, cost reduction, improved competitiveness mainly in the field of biotechnology;

(c) Adaptation/modifications to processes/products which were imported so as to make it suitable for Indian conditions. The modifications would also include substitution of imported raw materials/components with indigenous material to suit wider domestic applications in the field of biotechnology. 11/

Planning and execution of biotechnology programmes in India is being premised on growing interaction and development cooperation between R&D institutes, industry, academics and financial institutions. Programme planning in this field has been done in a larger perspective in such a way that India can draw upon the expertise available locally, as well as abroad. Teaching and research aimed at generating biotechnologies and development of R&D infrastructure have been encouraged and supported on the one hand, while on the other, business transactions with some private sector companies have been made to complete the process of innovation and to commercialize technologies generated indigenously.

India's approach to biotechnology development has high relevance for other developing countries, especially as regards emphasis placed not only on the technology generation, but also on innovation, transfer and commercialization of technologies. It shows that without a closer interaction between research and development institutions and industry, as well as academic and financial institutions, innovative activities and their transfer to the productive sector is not possible. Mechanisms for providing venture capital, risk-sharing and associated promotional measures are crucial if the process of innovation has to be completed.

India will, however, have to mobilize resources on a much broader scale and substantially increase her outlays on R&D in order to be internationally competitive. At present the total annual budget for biotechnology (estimated for 1991-1992) is Rs. 74.06 crores, that is, around US$ 30 million, devoted to as many as 13 thrust areas in R&D. Besides, the proposed share capital of BCIL is only Rs. 5 crores, that is, around US$ 2 million. One may expect that the financial resources would see further increase rapidly for developing biotechnologies, especially given the performance in industrialization of research results.

A greater involvement of private sector firms could be significant. Large firms will have to be encouraged to undertake their own in-house R&D programmes, supported and encouraged by a vigorous government role. Some firms in India, like Hindustan Lever, already undertake biotechnology development activities. Need for increased foreign collaboration in the area of biotechnologies is recognized, notably as regards imports of new recombinant DNA-based biotechnological processes, products and technology. In the field of tissue culture propagation of plants, during the year 1990-1991, more than a dozen proposals were approved for the setting up of basic facilities in the country. This collaboration, mainly with the Netherlands, France, the United Kingdom, Belgium and Italy, covers production and export of flowering plants, for which the germplasm is to be imported and the tissue culture raised to be exported. India's New Economic Policies for rapid industrial growth 12/ would have the impact of increasing collaboration with foreign partners, including the private sector. A major challenge before biotechnology development in India, is whether avenues being opened and the opportunities created by the New Economic Policies can be fully taken advantage of, blending these with the commercialization of R&D for productivity growth.

Notes

1/ Policies and Instruments for the Promotion and Encouragement of Technology Innovation - Preliminary Report by UNCTAD Secretariat, TD/B.C.6/123, 15 August 1984 (pp. 8-9).

2/ Kishore Singh "Technology Innovation and Evolving Regime of Intellectual Property Rights: perspectives for Developing Countries", Journal of Scientific and Industrial Research (Special Issue on Technology Innovation), Volume 50, February 1991 (pp. 145-155).

3/ For further information, see Annual Report 1990-91, Department of Biotechnology, Ministry of Science and Technology, Government of India, the Annual Report of the Director General of the Indian Council of Medical Research, 1990-91, New Delhi, and Annual Report 1990-91 of the Department of Agricultural Research and Education, Ministry of Agriculture, Government of India, New Delhi.

4/ On plant tissue culture, see National Facility for Plant Tissue Culture Repository (NFPTCR), National Bureau of Plant Genetics, Pusa Campus, New Delhi, 1990.

5/ Annual Report of the Department of Biotechnology 1990-91, op. cit.

6/ Annual Report 1990-91, Department of Agricultural Research and Education, Ministry of Agriculture, Government of India, New Delhi. See Post-Graduate and Post-Doctoral Teaching Programme in Biotechnology, Department of Biotechnology, Ministry of Science and Technology, Government of India, New Delhi, March 1989 and Short-Term Training Courses (1988-89 and 1989-90), Department of Biotechnology, Ministry of Science and Technology, Government of India, New Delhi, February 1989.

8/ A Workshop on Potential Commercial Applications of Biotechnologies, organized by the Department of Biotechnologies and the National Board of Studies at the M.S. University, Baroda, in August 1987.

9/ These proposals were the outcome of the Science-Industry meeting held in April 1990 for catalysing interaction between industry and the R&D institutes, including universities.

10/ See Portfolio of Activities: Biotech Consortium India Ltd. (BCIL), New Delhi, 1991.

11/ Ibid.

12/ See "India's New Economic Policies" (regarding industrial licensing, foreign investment approvals and foreign technology agreements). Government statement on Industrial Policy of 24 June 1991, Department of Economic Affairs, Government of India, New Delhi.