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18984

Genetic Engineering and Biotechnology Monitor

Issue No. 28 April 1990

Special in this issue: An article on safety, biotechnology and the problem of international trade-offs, prepared for the Monitor Dr. Morris Levin and Dr. R. Wachbroit of the Centre for Public Issues in Biotechnology, Maryland Biotechnology Institute, USA.

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A. POLICY, NEWS AND OTHER EVENTS

UNIDO news

Meeting on biosafety

The fourth meeting of the UNIDO/WHO/UNEP Informal Working Group on Biotechnology Safety (Working Group) was held in Vienna on 18-19 December 1989 by invitation of the United Nations Industrial Development Organization (UNIDO) and co-sponsored by the International Centre for Genetic Engineering and Biotechnology (ICGEB). The meeting was attended by representatives of UNIDO, the United Nations Environment Programme (UNEP), the World Health Organization (WHO), invited experts and observers from the ICGEB, the United Nations Conference on Trade and Development (UNCTAD), the US Department of Agriculture (USDA), the United Kingdom Health and Safety Executive (UKHSE), the Commission of the Economic Community (EC), and the Food and Agriculture Organization of the United Nations (FAO). The FAO expressed an interest in joining the Working Group and was welcomed as a new member. The purpose of the Working Group was established in 1985 as being "to establish a process through which the potential risks arising from (biotechnology) can be assessed and appropriate safety measures designed".

Following reports on the implementation of recommendations of its third meeting and presentations by the invited experts, the Working Group focused on the issues concerning the development of global biotechnology safety guidelines for environmental and industrial applications as well as in laboratory health. The members of the Working Group felt they could play a useful role in biotechnology safety by preparing a manual for the purpose of education. The manual would be directed initially at those responsible for providing advice within the developing countries, and it should both raise an awareness of the problems arising from the practice of biotechnology and the distribution of biotechnological products in the developing countries, as well as work towards the preparation of an international code of conduct in biotechnology. Development of an international code of conduct for the distribution and use of biotechnology would serve to increase international confidence in the availability, regulation, marketing and use of biotechnology. The manual may include annexes reviewing safety guidelines from existing codes in the areas of laboratory health and safety, environmental safety and industrial practice. It is envisioned that sufficient progress can be made on the preparation of the manual to enable the new Working Group (UNIDO/WHO/UNEP/FAO Informal Working Group on Biotechnology Safety) to meet in late 1990, with a full draft available for critical evaluation during 1991.

UN and other organizations' news

UNESCO Workshop

A successful UNESCO Workshop on "Biotechnology-Microbial Technology with Application to the Food Industry" was held at the University of New South Wales in February 1989 in association with the 8th Australian Biotechnology Conference.

The Workshop was an activity carried out under the auspices of the S.E. Asian Regional Network of Microbiology. It included discussions and lectures on the use of monoclonal antibodies and DNA probes in food analysis, plant tissue culture techniques, developments in membrane technology and the drafting of new food regulations for microbial cultures produced using recombinant DNA technology.

Participants came from the ASEAN countries as well as South Korea, Hong Kong and Fiji and presented reports on food biotechnology initiatives in their own countries. (Source: Australian Journal of Biotechnology, Vol. 3, No. 3, July 1989)

The role of biotechnology in CGIAR (Consultative Group on International Agricultural Research)

CGIAR is an assocation of Governments, international organizations and private institutions, co-sponsored by the World Bank, FAO and UNDP. CGIAR first met in 1971 when members agreed to support a co-ordinated, well-defined and closely monitored programme of research on food commodities and on food production in various agro-ecological zones. CGIAR started with a nucleus of four existing international agricultural research centres, CIAT, CIMMYT, IITA and IRRI. The number of centres has since increased to 13. Some centres focus on one or more commodities (see overview below), others perform specialized functions in the fields of food policy research, genetic resource conservation, and strengthening national agricultural research in developing countries.

Food abundance has been the overriding goal of CGIAR since its inception. The much debated "Green Revolution" was spearheaded by the IARCs.

Due to the successes of traditional breeding methods, CGIAR formulated a biotechnology policy rather hesitantly. In 1988 however, the Technical Advisory Committee (TAC) drew up a policy document entitled "The Role of Biotechnology in the CGIAR". The document is intended to be used as a guideline for the application of biotechnology in the IARCs. In the same year, CGIAR's International Service for National Agricultural Research (ISNAR), World Bank and the Australian Government, through the Australian International Development Assistance Bureau (AIDAB) and the Australian Centre for International Agricultural Research (ACIAR), decided to undertake a joint study to consider the opportunities and constraints to the use of agricultural biotechnology in stimulating the agriculture of developing countries. The study is based on a series of invited background papers on the technical, management and policy aspects of agricultural biotechnology and on case studies initiated in various developing countries. There are six particular issues on which the study has focused:

1. The possible impact of biotechnology on agricultural production, productivity and international trade;

2. The changing role of public and private sector investments in agricultural research;

3. The ecological implications of the release of genetically engineered micro-organisms, plants and animals;

4. The influence of patent law, plant variety protection and national incentives on biotechnology activities;

5. The institutional and social issues likely to be associated with biotechnology;

6. Mechanisms to facilitate international assistance in biotechnology for developing countries.

Two important recommendations are made considering the establishment of an Orphan Commodities Programme and a Biotechnology Transfer Unit. The Orphan Commodities Programme should facilitate the early application of modern biotechnology to those commodities important to the developing countries for which there are presently minimal investments in modern biotechnology, because of their lack of importance in the industrial world. The Biotechnology Transfer Unit should facilitate the transfer of new biotechnologies from industrialized to developing countries, by acting as a broker and adviser, to countries interested in accessing new technologies and to public and private sector institutions interested in expanding their activities in the developing countries.

The Synthesis Report served as a document for discussion at the seminar "Agricultural Biotechnology: Opportunities for International Development" held in Canberra on 24-26 May 1989, sponsored by the World Bank, ACIAR and ISNAR.

The recently installed CGIAR Taskforce on Biotechnology (BIOTASK) held its first meeting in May 1989. The activities of BIOTASK are:

1. Inventory of activities/information systems;

2. Regulatory issues and environmental release;

3. Public/private sector collaboration;

4. Cross-centre collaboration.

All commodity-oriented IARCs of CGIAR make use of biotechnology. There are considerable differences amongst IARCs in their current involvement in modern biotechnology, with some having substantial programmes, while others show only minimal involvement. Although the programmes of the centres vary, common components include genetic resource conservation and classification as well as biological research to increase yields by genetic improvement and to achieve greater resistance to pests and diseases.

Developing countries are likely to be the major clients of IARC-efforts in biotechnology, rather than the more advanced countries that have already developed their own capacity in biotechnology. The increasing dominance of private sector R&D in agricultural biotechnology may increase the cost of access by the developing countries to advances in science and technology. IARCs may function as windows of access to advanced technologies for national agricultural services (NARs) in developing countries. IARCs could play an important role under the "Biorevolution". In order to play this role to its full potential, shifts in research strategies, and the reallocation of resources and personnel in some centres will be necessary. (Source: Biotechnology and Development Monitor, No. 1, September 1989)

Regulatory issues

Controls needed on release

New legislation to back up a system of compulsory registration and licensing for any release in Britain of a genetically engineered organism is advocated in a report published last week by the Royal Commission on Environmental Pollution (RCEP). To release an organism without a licence should be a criminal offence.

The Commission's long delayed but carefully considered report argues against immediately categorizing any types of release as sufficiently free of risk not to require individual scrutiny by experts and licensing by the Secretary of State for the Environment and the Health and Safety Commission (HSC). But it recommends against any moratorium on releases. The report says that releasers must be required not only to monitor and report their results for the agreed duration of the experiment, but to continue monitoring for "an appropriate period" thereafter, with a degree of imagination to catch any unexpected signs of damage. Compliance would be checked by appropriately trained inspectors, while Britain's army of amateur natural historians could be expected to notice any untoward effects.

Public access to information on releases is essential, says the Commission. There should be a public register of applications for experiment and product licences and public advertisements of proposed releases. The public should also have access to the information on the basis of which the expert committee has made a recommendation, taking into account any need for commercial confidentiality.

Should the RCEP's recommendations become the basis of new legislation, Britain would have a law largely similar to that in Denmark, the only existing European law. The British law would however be considerably more restrictive than that proposed by the European Commission, and now the subject of considerable debate in the European Parliament and Council. (Extracted from Nature, Vol. 340, 13 July 1989)

Tests of gene-altered organisms deemed safe

A study by the US National Research Council of the risks involved in the release of genetically modified plants and micro-organisms for scientifically controlled field tests finds there is little or nothing to worry about. It concludes that field-test experience to date gives scientists sufficient information to evaluate risks and make safe decisions.

The report divides the field-testing universe into plants and micro-organisms. It does not cover larger animals or the use of genetically engineered organisms to produce other products. The report was done at the request of the inter-agency Biotechnology Science Co-ordinating Committee, which is composed of the five federal agencies most involved with biotechnology and genetic engineering.

The most significant contribution of the report is a detailed, tiered decision-making framework for the government offices to use when faced with approving a field experiment.

The framework has three major criteria. The most important factor is familiarity. This refers to how well researchers understand the plant or organisms and how much information has been gained from previous experiments. With regard to plants, familiarity is high because years of traditional crossbreeding research has provided much data. But familiarity with micro organisms is less because they have been studied for less time.

Overview of biotechnology activities in CGIAR-Centres

CIAT

(Centro Internacional de AgriculturaTropical)
Apartado Aereo 6713Cali, Colombia

Product	Technique	Aims
cassava	tissue culture	virus elimination and distribution
	in vitro culture	storage of genetic material (gene-bank)
	genetic engineering	increased protein production; virus resistance
common beans	tissue culture	regeneration of plants from tissue culture
	embryo rescue	wide crossing with wild species
	genetic mapping	screening for resistance to bacterial blight

CIMMYT

(Centro Internacional de Mejoramiento de Maiz y Trigo)
PO Box 6-641, Mexico 06600, Mexico D.F.

Product	Technique	Aims
wheat	tissue culture	selection for tolerance to salinity
	monoclonal antibody tests (MAb-tests)	detection of yellow dwarf virus
	electrophoresis	provide biochemical markers for alien germplasm in wide crosses
	genetic engineering	incorporate salt tolerance
maize	genetic engineering	cob colour and rust resistance

CIP

(Centro Internacional de la Papa)
Apartado 5969 Lima, Peru

Product	Technique	Aims
potato	tissue culture	development and distribution of disease- and virus-free clones
	tissue culture	in vitro selection for tolerance to salinity and drought; selection of clones with high starch content; gene-bank
	electrophoresis	verify duplicate accessions in gene-bank
	MAb-tests	detection of viruses Y, A and leafroll
	DNA-probes	identification of spindle tuber viroid
potato	genetic mapping	construction of molecular map for use in backcrossing
	genetic engineering	insertion of synthetic genes to increase protein production; resistance to leaf roll virus and potato spindle tuber viroid; resistance to fungal and bacterial diseases
sweet potato	in vitro culture	gene-bank
	embryo rescue	wide crossing with wild species
	MAb-tests/DNA-probes	detection and characterization of viruses

ICARDA

(International Centre for Agricultural Research in the Dry Areas)
PO Box 5466 Aleppo, Syria

Product	Technique	Aims
lentil	tissue culture	selection for resistance to diseases and environmental stresses
faba bean	embryo rescue	wide crossing with wild species

CGIAR

ICRISAT

(International Crops Research Institute for the Semi-Arid Tropics)
Patancheru PO, Andhra Pradesh 502 324, India

Product	Technique	Aims
chickpea	tissue culture	selection for salt tolerance
groundnut /pearl millet	tissue culture	plant regeneration from tissue culture
mandate crops	embryo rescue	wide crossing with wild species
mandate crops	MAb-test	identification of viral diseases

IITA

(International Institute of Tropical Agriculture)
PMB 5320 Ibadan, Nigeria

Product	Technique	Aims
cassava	tissue culture	multiplication and distribution of disease-free clones; selection for acid tolerance
sweet potato	tissue culture	multiplication and distribution of disease-resistant clones
	embryo rescue	wide crossing with wild species
sweet potato/yam	in vitro culture	gene-bank
	MAb-tests/DNA-probes	improved virus detection (several yam and sweet potato viruses)
cooking bananas/ plantains	tissue culture	multiplication and distribution of black-Sigatoka resistant cooking bananas as substitutes for plantains
cowpea	tissue culture	selection for low pH, high aluminium content, cold tolerance; selection for pest resistance
	genetic engineering	resistance to coreid bug and pod borer
	embryo rescue	crossing with insect resistant wild species
	MAb-tests	virus strain detection

ILCA

(International Livestock Center for Africa)
PO Box 5689 Addis Abeba, Ethiopia

Product	Technique	Aims
forage crops	tissue culture	storage and multiplication of disease-free clones

ILRAD ILCA •

(International Laboratory for Research on Animal Diseases)
PO Box 30709 Nairobi, Kenya

livestock	in vitro cultivation of parasites; MAb-tests/DNA-probes; rDNA-techniques	developing new diagnostic techniques and vaccins for animal diseases theileriosis and trypanosomiasis (tsetse)
livestock	embryo transfer	resistance to trypanosomiasis

IRRI

(International Rice Research Institute)
PO Box 933 Manila, Philippines

rice	tissue culture	selection for tolerance to salt and aluminium; yield improvement; resistance to pests and diseases
	embryo rescue/protoplast fusion	resistance to brown planthopper; increased yields; disease resistance; stress tolerance
	MAb-tests/DNA-probes	diagnostics for rice tungro and rice grassy stunt viruses, rice blast and bacterial blight
	genetic mapping	identify genes for resistance to diseases and planthoppers

WARDA/IRRI

(West African Rice Development Association)
01 BP 2551 Bouake 01, Cote d'Ivoire

rice	tissue culture	selection for tolerance to salt and drought

CGIAR Technical Advisory Committee, *The Role of Biotechnology in the CGIAR*, Washington DC, United States, August 1988.

Persley, G. (ed.), *Agricultural Biotechnology; Opportunities for International Development*, World Bank-ISNAR-AIDAB-ACIAR, May 1989.

Directorate General for International Cooperation, Section for Research and Technology, NGO, Education and Research Programmes Department, *Biotechnology and Development Cooperation - Inventory of the biotechnology policy and activities of a number of Donor Countries and Organizations, UN Agencies, Development Banks, and CGIAR*, The Netherlands, February 1989.

Annual Reports of CGIAR centers.

Source: Monitor Biotechnology and Development, September 1989.

Confinement or control of the organism is the second major criteria on which the report says decisions should be based. Because modified plants are tested in small field plots, confining them is relatively easy, but control of micro-organisms is more difficult.

The third major criterion is concerned with the probable environmental effects should an introduced organism or genetic trait last longer than intended or spread away from the intended target. Questions that need to be asked include: What is the potential for persistence of the organism in the environment? Can it spread to non-target environments? And what is the chance of genetic exchange between the target and indigenous micro-organisms?

The committee's report, "Field Testing of Genetically Modified Organisms: Framework for Decisions", is available for $19.95 from the National Academy Press, 2101 Constitution Ave., N.W., Washington, DC 20418. (Abstracted with permission from Chemical and Engineering News, 2 October 1989, p. 16, by David Hanson, copyright (1989), American Chemical Society)

Evidence for toxin gene transfer during field tests

A communique from the Rural Advancement Fund International (RAFI-1989) calls attention to the first experimental evidence of an ecological risk in releasing microbes that have been genetically modified with the endotoxin gene for Bacillus thuringiensis (BT). The biotechnology industry has lobbied extensively for an accelerated review process, citing specifically the inherent safety of genetically engineered organisms (GEOs) with the BT toxin.

The Maryland biotechnology firm Crop Genetics International carried out small scale field tests in which microbes with the BT toxin gene were injected into corn plants. The company defended the safety of that test on the claim that the altered microbe takes its residence exclusively in the plant's vascular system. According to RAFI, the company disclosed to the US Environment Protection Agency (EPA) that the BT gene was discovered in flea beetles during the field tests. A plausible explanation for this is that an insect feeding on the corn plant picked up the BT gene and became a vector for transferring the gene to non-target species.

In written comments to EPA, Rebecca Goldburg of the Environmental Defense Fund referred to certain subspecies of bacteria selected to host the BT endotoxin that are toxic to native moths and butterflies - not the designated targets of the microbial pesticide. Commercial uses of those genetically engineered host organisms, Goldburg states, would pose unacceptable risks.

These examples highlight the complex problems that may arise in the environment from the release of GEOs and support the recommendations of the report to the Ecological Society of America that calls for case by case review by interdisciplinary scientific teams. (Source: GeneWATCH, Vol. 5, No. 6)

Biotechnology law in North Carolina seen as model

Legislation enacted into law in North Carolina to regulate the planned introduction of genetically engineered organisms into the environment has the strong support of the biotechnology industry, which says the measure should serve as a model for other states and the Federal government.

The North Carolina legislation will permit industry to proceed with the large-scale field testing needed to prove that products are commercially viable and safe. (Extracted from Chemical Marketing Reporter, 14 August 1989)

Federal Republic of Germany's gene technology law

The Federal Republic of Germany's Government has drafted legislation on safety measures to be applied at facilities that handle genetically engineered organisms. The proposed law establishes four categories of organism, from "safe" products like E. Coli to viruses and other organisms. Provisions for each category cover areas such as containment requirements and waste-water treatment. The legislation faces a rough ride because of its provisions for public involvement in permitting procedures. Environment minister Klaus Topfer - backed by some opposition parties - proposes public involvement at each stage of permitting procedures, while industry and some ministers want the public's role to be more restricted. The law is scheduled to come into effect in 1991. Chemical industry leaders contend the legislation is seriously hampering development in the biotechnology sector by German companies. (Source: Chemical Week, 2 August 1989)

General

Biotechnology coming of age

The biotechnology industry is a reality that is here to stay - the industry as a whole reported sales exceeding $2 billion last year - but as commercial biotechnology enters the 1990s, uncertainties about its future abound.

A survey released by Ernst & Young's high technology practice bears out both the certainties and uncertainties of this fast-growing industry: an unprecedented 74 per cent of all biotechnology firms now have products for sale, but the average company survival index for the industry has shortened from 49 months in 1988 to 35 months in 1989.

Many certainties about the industry arose from the survey. One is that the industry is fundamental. Another is that powerful new products will be introduced in the 1990s by the larger segments of the industry-therapeutics, diagnostics, agriculture and instrumentation.

A third certainty is that the pipeline is now full and turning out commercial product. Product sales in 1988 averaged $8.2 million per company, up 33 per cent over 1987, and represent 65 per cent of all industry revenues.

A final certainty is that the industry will continue to spawn new companies in the 1990s. Even when the stock market was poor in 1988 36 new biotechnology companies opened their doors. As of the middle of July 1989, 31 new companies have been formed.

However, one of the major uncertainties, according to the survey, is where these and other fledgling companies will obtain financing. Almost two thirds of all companies expect to need major financing by year end 1990, and 90 per cent by the end of 1991.

Moreover, the industry as a whole anticipates, on average, the need for $55 million per company in external financing over the next decade. Such money will not be easy to raise and will only come if the public markets continue their recovery from the 1987 stock market crash and begin again to respond to the needs of the growing industries. One way to get around the need for cash is through strategic alliances with larger corporations to finance R&D and achieve marketing and manufacturing goals beyond a new company's power.

While such an approach betrays the ideal of self-sufficiency and totally proprietary products, sometimes it is the only realistic solution to cash problems.

And despite such partnering, another uncertainty - consolidation - is sure to be a factor in the 1990s. The Ernst & Young survey indicates that fully 66 per cent of biotechnology companies expect to be acquired sometime in the 1990s.

Some of this acquisition will probably occur in a third area of uncertainty, the global arena. Today, more than half of large biotechnology companies have sales in Western Europe, Japan and Canada, but the need for capital is causing these same companies to consider the rest of the world as more than just an end market for products.

Foreign investors are already more active in US biotechnology than meets the eye, the survey indicates. There have been few major acquisitions by foreign firms, but minority equity positions are increasingly common, and there is nothing to prevent outright acquisition when the time and price are right.

Indeed, this year's survey shows the majority of US firms are currently negotiating strategic alliances with foreign firms, which may well expand as time goes on.

Regardless of who owns whom, products will not reach the marketplace without co-operation from regulators here and abroad. A majority of survey respondents believe FDA, EPA and USDA are meeting their responsibilities well, but most also believe the situation could be improved.

Of primary concern are the issues of patents and product liability. Fully two-thirds of all large companies have been involved in patent disputes requiring litigation, while nearly half of the industry expects product liability concerns will significantly affect their ability to commercialize products in the future.

Also, while the FDA has approved, in record time, a number of biotechnology drugs to help the desperately ill, respondents express concern about overall new product approval times.

A final regulatory issue concerns third-party reimbursement policies, a factor that companies introducing recombinant therapeutics need to consider very carefully. (Source: Chemical Marketing Reporter, 25 September 1989)

New diagnostic products under preparation

Biotechnology firms are preparing to introduce diagnostic products based on monoclonal antibodies. These new diagnostics will be more effective in pinpointing diseases such as cancer. Centocor's (Malvern, PA) new monoclonal antibody imaging agent indicates the amount of damage caused by a heart attack by measuring the amount of dead heart tissue. Neorx's (Seattle) diagnostic for melanoma and Centocor's monoclonal antibody imaging agent have still not received FDA approval in the US, but Centocor's product is already availabe in Europe. The new monoclonal antibodies are joined to a radioactive isotope and injected into the patient. Antibodies bind to the target (e.g. tumour) and gamma-ray detection cameras are used to detect any radioactivity. Monoclonal antibodies will eventually be used to treat diseases, but this will probably not happen for several years at least.

Imaging is less complex than treatment and clinical trials necessary for approval are shorter, enabling the products to be launched sooner than therapeutics. Imaging agents will also lay the groundwork for therapeutics, in terms of demonstrating effectiveness and safety. Antibody imaging agents are more effective in pinpointing malignant tumours than other diagnostic methods, such as CAT scans. They can also detect tumours anywhere in the body, while CAT scans are usually limited to a certain area or areas of the body. Antibodies might also be able to locate smaller tumours that escape detection by other means. Imaging agents for cancer diagnosis could generate sales of $5-100 million/year, depending on the type of cancer. Neorx is completing clinical trials on imaging agents for two forms of lung cancer, while Cytogen is concentrating on colorectal cancer diagnostics. (Extracted from New York Times, 28 August 1989)

US clinical immunology and cellular diagnostics reagents market growth

The current US clinical immunology diagnostic reagents market is worth over $130 million, according to a new report from Biomedical Business International (BBI). This market is projected to grow to $220 million by 1993, says The Clinical Immunology and Cellular Diagnostics Reagents Market.

Clinical immunology tests help characterize and monitor various immune system parameters, including white blood cell components indicative of such disorders as systemic lupus erythematosus, mixed connective tissue disease and progressive systemic sclerosis. The clinical reagents market is divided into four major segments, namely allergy and non-allergy immunoglobulins, auto-immune antibodies, complement proteins and cell surface markers. (Source: Biotechnology Bulletin, Vol. 8, No. 7, August 1989)

Vaccines will build a giant US market for the 1990s

AIDS vaccine development programmes naturally get the most attention - and money. At least 34 programmes are under way, according to a new Frost & Sullivan report, Emerging Business Opportunities in New Vaccines, though no new AIDS vaccine is expected on the market before 1995.

But AIDS is by no means the only target. As the Frost & Sullivan study points out, altogether there are more than 400 US programmes in progress, either to develop new vaccines or to improve existing vaccine products. The various forms of hepatitis, malaria, herpes - these and many other diseases are the subjects of intense vaccine development activities.

Vaccines already make up one of the fastest growing areas among infectious disease product markets. Frost & Sullivan predict that estimated

sales of $547.4 million in 1988 will increase to $922.5 million by 1993. The most significant growth, however, is expected after new vaccines currently in development hit the market in the mid-1990s. The study sees a likely vaccine market of over $2.5 billion by the year 2000.

Some of the most intense activity target diseases for which vaccines already exist. Pertussis (whooping cough) is an example.

Hepatitis B is another example. Hepatitis B vaccines - mainly due to Merck's highly successful introduction in 1986 of a recombinant DNA product - now make up the single largest product market: $91 million of sales in 1988 and soaring. The size of the hepatitis B market and its obvious growth potential have stimulated more than 30 programmes to develop alternative vaccines. Some of these have recently been launched, with complex licensing agreements and possible patent challenges.

Analysing development in areas where products do not now exist, the study expects the following new vaccines to be on the US market by the mid-1990s: a gonorrhea vaccine; various herpes vaccines; hepatitis A vaccines; AIDS vaccines; cytomegalovirus vaccines; and human synctial virus vaccines. Some of these, notably herpes and rotavirus vaccines, could emerge in the early 1990s.

In addition, there is a long list of diverse development programmes likely to produce vaccines for the US market within the next decade. Diseases targeted include chlamydia, Lyme disease, salmonella, shigella, syphilis, streptococcus and rhinovirus (the common cold), among others. Then there are programmes applicable to third world areas, targeting diseases such as Dengue fever, malaria, leprosy, Lassa fever and cholera, among many others. Some, such as the cholera programme, are in advanced stages. (Source: Biotechnology Bulletin, Vol. 8, No. 8, September 1989)

World markets for drugs to treat and prevent strokes caused by blood clots

The markets for drugs to treat and prevent strokes caused by blood clots will exceed $1 billion worldwide by 1994 and $1.8 billion by 1999, according to the Technology Management Group (TMG). In a new report, Treatment and Prevention of Strokes - A Worldwide Market Study, TMG points out that drugs that can be used to treat strokes immediately after their occurrence include tissue plasminogen activator (TPA) and other clot-dissolving agents. The range of therapeutic products being developed include oxygen radical scavengers, such as superoxide dismutase.

Products that can be used to help prevent strokes include drugs that control high blood pressure and clot-inhibiting agents. At least 41 companies are working on products for the multi-billion dollar hypertension market. Drugs that will probably be used to prevent strokes in at-risk patients include platelet anti-aggregants and calcium channel blockers.

As second generation TPA products become available, a substantial price reduction is likely to occur. These products are now used for heart attack treatment. Strokes are their next large application area. As understanding of TPA and other clot-dissolving agents increases, each drug is likely to become the first choice for certain types of strokes.

Over 100 companies and over 60 other organizations are now involved in research, development or production of products for strokes. Seven companies currently have drugs in clinical trials to determine their effectiveness in stroke treatment. The preliminary results of the trials, TMG says, appear encouraging. (Source: Biotechnology Bulletin, Vol. 8, No. 7, August 1989)

ATCC expands repository

The American Type Culture Collection's Department of Molecular and Plasmid Biology has received approval from the US National Institute of Child Health and Human Development to include mouse genomic materials in the three-year-old NIH Repository of DNA Probes and Libraries, which is maintained at the ATCC. The repository currently has over 700 genetic materials of human origin available for distribution to researchers. Clones from the mouse genome will be added at a rate of 100 per year.

Information about materials currently in the repository is available from both a printed catalogue and on-line databases. Each information format includes descriptive data such as: gene name, locus abbreviation or DNA segment name, map position, sequence content, literature citations and enzymes for detecting RFLPs.

The ATCC has also announced the availability of the 1988 ATCC Fungi/Yeast Update, a supplement to the 1987 ATCC Fungi and Yeast Reference Catalogue. The 1988 Update includes 1,150 strains, representing 600 species, that have been added to the ATCC's collection since the printing of the 1987 reference catalogue. As with the 1987 reference catalogue the Update contains scientific information useful to industry and academia, such as literature citations which indicate uses of the cultures, recommended growth media and media formulations. Both the 1988 Fungi/Yeast Update and 1987 Reference Catalogue are free to US researchers. A modest shipping and handling fee is charged for catalogue shipments to locations outside the USA. The same applies to the ATCC's July 1989 supplement to its 1986 Animal and Plant Virus Catalogue. The supplement lists several new accessions available from the ATCC Plant Virus Collection for distribution, including: 6 [illegible]uses, 20 polyclonal antisera and 14 molecularly cloned viruses. Among the viruses are blackeye cowpea mosaic virus, lettuce mosaic virus, tomato spotted wilt virus, zucchini yellow mosaic virus and their respective antisera.

Enquiries should be directed to: ATCC/Mkting NR24, 12301 Parklawn Drive, Rockville, MD, 20852, USA. (Source: Australian Journal of Biotechnology, Vol. 3, No. 3, July 1989)

New York State leads on genetic fingerprinting

The first attempt in the United States to regulate the forensic use of 'genetic fingerprinting' was announced by the director of justice for New York state, John Poklemba. According to a plan likely to be approved and implemented in 1990, the state would establish a committee to set and monitor standards, and a scientific board to examine the accuracy of test results before they could be presented in court.

There is at present no federal or state legislation regulating DNA testing in private or public laboratories. Although the need for some kind of monitoring is widely acknowledged, there is

much dispute over who should do it. And the dispute will grow hotter as more state forensic laboratories carry out DNA testing.

The report also warns that if no national regulatory action is taken, "continued case-by-case examination of proper technical and operational standards could slow full implementation of forensic analysis using DNA typing".

The Federal Bureau of Investigation (FBI), a leader in forensic DNA analysis, is holding a series of meetings with researchers and laboratory representatives aimed at reaching a consensus on technical standards. The group is said to be close to agreement on the main issues.

However there are objections to the leading role of the FBI, an investigative and law enforcement body, in setting standards.

The National Academy of Sciences will begin a comprehensive study of the technical, legal and ethical issues involved in the forensic use of DNA analysis, having obtained promises of funds from a variety of sources including the FBI, the National Institute of Justice and the National Institutes of Health. A report is expected in late 1990.

The regulations proposed for New York have been warmly welcomed by researchers and lawyers grappling with the problems created by the transfer of the techniques of DNA analysis to the courtroom. (Extracted from Nature, Vol. 341, 14 September 1989)

Search continues for European standard on DNA probes

Scientists in Europe are trying to make DNA profiling, the process which identifies the genetic sequence of DNA taken from the scene of a crime, a more efficient tool for the police. Twelve of the frontline forensic research laboratories of Europe are swapping samples of DNA to compare their results in a first step towards agreeing to a Europe-wide standard on the best probes with which to produce DNA profiles.

Each laboratory is using the same restriction enzyme to chop up the samples, and the same probe to profile them. They will each produce 10 profiles from each sample and pool their results at a meeting in the Hague.

The Forensic Science Service of the Metropolitan Police in Britain pioneered the project, and is trying to persuade the main forensic laboratories of Europe to agree to use a set of common probes to help to speed up those criminal cases in Europe which rely on such evidence.

Co-ordinating the probes that Europe uses will benefit not only the case work of the police authorities but also the researchers in laboratories and companies throughout Europe who will be able to conduct their research within an agreed framework, but there will be some associated risk that important areas of research might not get the attention they deserve.

One drawback in attempts to co-ordinate international collaboration may be that the main laboratories in the US have more or less reached consensus on the enzyme they will use to cut their DNA samples, the Hae III enzyme. European laboratories, however, are gradually falling in line behind a different enzyme, called Hinf I. (Extracted from New Scientist, 12 August 1989)

Fingerprinting failure

A judge trying a murder case in New York has dismissed as evidence DNA fingerprints that he says do not satisfy standards of scientific certainty. The ruling is the first to reject DNA prints in the US and is expected to prompt higher standards for DNA prints.

Judge Gerald Sheindlin of the New York Supreme Court in the Bronx ruled that existing techniques of genetic fingerprinting can work in theory and practice. But the fingerprints presented in the case before his court, which matched blood on a suspect's wristwatch to blood of a murdered woman and her daughter, were done improperly.

Scientists had argued in pre-trial hearings that the company, Lifecodes of New York State, had not established how rarely the DNA sequences it uses for fingerprinting occur in subpopulations, such as Hispanics. Without such data, the chance of an accidental match could be understated, the scientists said. (Source: New Scientist, 26 August 1989)

Human genome mapping progress

At the recent 10th International Human Gene Mapping Workshop at Yale University researchers reported on progress in gene mapping. It was announced that since the last meeting in 1987, 53 new genetic diseases have been mapped to locations on specific human chromosomes. The diseases include breast and colon cancers, diabetes, rheumatoid arthritis and manic depression.

Researchers also announced that by using a new gene mapping computer system they had identified 700 more genes, taking the total number verified to 1,700. However, as Yale geneticist Frank Ruddle pointed out, there may be as many as 100,000 human genes, which means 98 per cent of them are still undiscovered. The amount of data on human genes is currently doubling every three years. (Source: Australian Journal of Biotechnology, Vol. 3, No. 3, July 1989)

A common language to express findings

Human Genome I, which convened in San Diego to ponder the $3 billion, 15-year project, featured a proposal for streamlining the work by adopting a common language instead of the prevailing scientific "Tower of Babel". The proposal is that scientists express their findings by giving the precise sequence of a short piece of DNA and its approximate location on a chromosome in a form called "sequence-tagged sites", or STS.

Even though the project is imprecise, the STS strategy could yield a crude map of the entire human genome, or genetic code, in as little as five years. Reducing all descriptions of key genetic landmarks to such shorthand would also let scientists merge their findings in a common database, and lessen if not eliminate the need to store vast fragile samples of actual DNA.

How fast the project moves is of more than academic interest. There are, by current estimates, 4,000 inheritable diseases from sickle cell anaemia to haemophilia, muscular dystrophy and cystic fibrosis. About 400 of those are linked to the X chromosome and passed from mothers to sons.

Tasuku Honjo of Kyoto University in Japan and Hans Zachau of the University of Munich reported

finding some surprising "acrobatics" in the genome, among them the ability of major clusters of immunoglobulin genes - as many as five or eight at a time - to jump from their home on chromosome 16 to chromosome 14. In the immune system, such "cutting and pasting" of genes does happen as the body acquires immune response, but the gene shifts are smaller and more local. (Extracted from Wall Street Journal, 6-7 October 1989)

C.A.B. International Mycological Institute

The C.A.B. International Mycological Institute (CMI), formerly the Commonwealth Mycological Institute, is one of the four scientific institutes of C.A.B. International. The Institute is the largest centre concerned with systematic mycology in the world. Founded in 1920 it is sponsored by 30 Governments. These were formerly Commonwealth Governments, but following the adoption of a new constitution in 1985, other countries can now join C.A.B. International. The first of these is Hungary, which joined in 1989. The Institute has from the first provided world services to mycologists and workers in related disciplines, particularly plant pathology, medical and veterinary mycology, and increasingly to industrial mycology and biotechnology.

Key areas of the Institute's activities being extended are consultancies and contract research. With some 350,000 reference specimens of microfungi (over 13,500 also in the Culture Collection), a substantial library, online database, and access to electron microscopes (SEM and TEM), computer, chemotaxonomic, and biochemical facilities, the Institute is well-placed to help solve problems or resolve confusions which involve microfungi. In 1987 additional research microscopes, a replacement Hitachi scanning electron microscope (with an Emscope cryo-fixation facility and image store), new spectrophotometer, liquid nitrogen storage system and incubated culture shaker, were purchased to further enhance the resources available.

Development of the Institute's services, research and project activities has resulted in increased pressure on space and facilities which have become a constraint on further progress. As an interim measure, while long-term options are reviewed, the Royal Botanic Gardens, Kew, has generously made available temporary new storage for the herbarium, and C.A.B. International is to fund some refurbishment and upgrading of facilities.

The two major EEC contracts awarded to CMI under the Biotechnology Action Programme, which started during 1986, are now in their fourth and final year. The first is to act as the UK node for input into MINE (Microbial Information Network Europe), in effect a computerized integrated catalogue, and the second to develop improved methods for the preservation of fungus strains (in collaboration with laboratories in Belgium, France and The Netherlands).

Support from the UK Department of Trade and Industry continues to enable the Institute to provide associated services to industry, including biological testing (the Industrial Laboratory is accredited under the National Testing Laboratories Accreditation Scheme - NATLAS/NAMAS), and also to build up biochemical data on strains held. The data on the physiology and biochemistry of strains are now also available online through the computerized MICIS data base being transferred from the Department to the Deutsche Sammlung von Mikroorganismen and Zellkulturen GmbH, Braunschweig, Federal Republic of Germany.

The Institute has been operating with the University of Umeå (Sweden) in the publication of the twice yearly Systema Ascomycetum since 1982; this is a current awareness journal also developing a new classification of the group and including original papers. Production methods have been improved from the December 1987 part. The new computerized production system for the Index of Fungi and Bibliography of Systematic Mycology introduced in 1987 is now fully operational and all issues are now on schedule, including a new supplement on family names. This has enabled a much greater level of indexing to be incorporated into the bibliography, down to the generic level.

Attention is also drawn to two particularly important new publications due to appear during 1989 on "Opportunistic Mycoses of Man and other Animals" (Professor J. Smith, New Zealand) and "Aspergillus species on stored products" (Dr. Z. Kozakiewicz, CMI).

Results of the major contract work undertaken for the UK Science & Engineering Research Council (SERC) on a multidisciplinary approach to the systematics of microfungi of biotechnological and industrial importance, which started in 1984 and was extended to the end of 1988, are currently in press. This has pioneered the application of bacteriological approaches to the filamentous fungi and shed new light on the extent of infraspecific variation and its genetic basis in Penicillium. Biochemical studies are now being carried out at the Institute on many groups. An in-depth project aimed at the biochemical separation of special forms in Fusarium oxysporum supported by the Overseas Development Administration started in the summer of 1989. In collaboration with the Royal Botanic Gardens, Kew, Birkbeck College, and the C.A.B. International Institute of Biological Control, investigations into microbial pesticides initiated in 1987 are continuing and options for the future development of the programme are currently being considered.

Training is the Institute's fastest-growing service. Postgraduate training is being actively developed, particularly in co-operation with the University of Reading, of which CMI became an Associated Institution in October 1984. In 1989/90 CMI announced the introduction of a new MSc in "Fungal Technology" in collaboration with the University of Kent at Canterbury; this is expected to be of particular value to students from developing countries and is being sponsored also by UNESCO. The number of training courses including one-day, one, two-, and six-week courses at CMI was maintained in 1989. That on plant pathogenic bacteria is proving particularly popular and will be repeated. A special course on medically important fungi was also held for the second time in 1989. Courses in Egypt and Chile were held in 1985, in India and Kenya in 1986, in the Republic of China and Egypt in 1987, and in 1988 in Brazil and Malaysia. Ones for Argentina and India were held in 1989.

The Institute has concluded an agreement on collaboration with the Systematic Mycology and Lichenology Laboratory of the Institute of Microbiology, Academia Sinica in Beijing in 1988. Under this agreement, botanical specimens and cultures are being exchanged, collaboration in training is underway, and CMI is assisting with the editing and refereeing of papers for the Laboratory's new journal "Mycosystema".

Further information on the work and services of the C.A.B. International Mycological Institute may

be obtained from Prof. David Hawksworth, Director, CMI, Ferry Lane, Kew, Surrey TW9 3AF, United Kingdom. Advert. (Pamphlet)

Culture Collection

The Culture Collection (incorporating the UK National Collection of Fungus Cultures) is one of the largest service culture collections of fungi in the world, holding over 13,500 isolates of living microfungi. These isolates are maintained by a wide range of modern techniques, in keeping with the CMI's role as a centre of research in this field. The greatest emphasis is on the maintenance of Zygomycetes, Oomycetes, Ascomycotina and Deuteromycotina. Yeasts, Hymenomycetes (other than plant pathogens or those of educational interest), fungi pathogenic to man and animals, actinomycetes, bacteria, and algae are not kept.

The majority of cultures (over 10,000) which will survive the process have been freeze-dried (lyophilized). Many special cultures (over 4,500 isolates) such as those derived from types, biochemical strains, patent strains, particularly delicate fungi or those that will not lyophilize, are also maintained at ultra-low temperatures in liquid nitrogen (-196°C). Sensitive strains are preserved by more than one means and may have special treatment, e.g. aquatic oomycetes are kept in water, genetic strains of Neurospora and Aspergillus are processed in silica gel, and Fusarium species are grown in soil. Different media, temperatures, and degrees of illumination are employed when growing cultures for preservation according to the groups concerned. Further information is provided by Smith & Onions (1983).

A key feature of the collection is quality control. Each time a strain is preserved or its viability examined the cultures are examined by the mycologist responsible for that group to ensure it has not become contaminated or modified in any way. The Biochemical Laboratory also assists in this task to ensure metabolic or other activities of importance are retained. The names under which strains are kept are also the responsibility of CMI's specialist taxonomists; all deposited material is checked by them when received to ensure names are correctly applied.

The strains held are of interest to plant pathologists, those concerned with research and teaching, testing of materials and preservatives, systematic mycology, and other areas of applied mycology. Fungi of industrial importance, as potential product producers, deteriogens or of other biotechnological interest are also being actively collected. Over 1,950 new isolates were added to the collection in 1988. Strains with biochemical documentation are particularly sought, enabling the metabolic sections of the Culture Collection's Database to be extended.

A printed catalogue listing isolates available from our open collection is available (1988 edition, Spring 1988, price 25 pounds sterling, post free).

An accession form to facilitate the supply of useful data is available on request for regular depositors of cultures.

Donors of organisms for inclusion in the open collection are provided with a culture for checking after preservation if requested and may request one free culture of their own deposit at any time within one calendar year of the deposit in the CMI collection, for each new isolate deposited, although more may be negotiated through the Curator.

Culture Prices

When ordering cultures, please ensure that you check the current price. The prices from April 1989 are given below.

40 pounds	Standard price. Post free worldwide (by air where appropriate)
25 pounds	Teaching use; University and Government non-commercial reasearch. C.A.B. International member countries only. Post free worldwide
35 pounds	Biodeterioration test strains, per culture as part of a complete test set (not less than 4 strains per set). Post free worldwide
	VAT will be added where applicable - 10% discount on orders over 150 pounds excluding VAT

Please note that customers eligible for the bona-fide teaching rate (25 pounds) may choose any cultures in our lists. We have no restrictive lists for teaching use.

For further information on culture prices, ordering, restrictions on pathogens, and teaching strains please consult the current edition of our Culture Collection Catalogue. If in doubt as to which price applies, please contact the Culture Collection Sales Department.

Users of MSDN (Microbial Strain Data Network) should note that the CMI Culture Collection now has a sales box on that system: CMI Sales Box, ID DBI 0257, Enter "CMI REQUEST" to see orders form.

Take it or leave it, gene banks versus conservation in the wild

Although everyone agrees that we have no choice but to conserve as much plant genetic material as we can, as fast as we can, the use of gene banks raises serious questions about our agricultural development. We have backed ourselves into a corner as far as the genetic diversity of our crop plants is concerned.

Our strategy of breeding improved varieties with narrow genetic backgrounds and promoting their use globally, either directly by technology transfer, or indirectly by economic pressure, forces us to rely more and more on gene banks to safeguard genetic diversity. It is the same as saying "We no longer need evolution. We have, inside our gene banks, enough genetic diversity for now and forever." We have placed in the hands of scientists the responsibility that nature once had for ensuring the evolutionary development of our food crops.

Some people suggest that crops should be conserved in their natural environment as well as in gene banks. The idea is to allow crops to evolve alongside their wild relatives, in much the same way as they have since Neolithic times. The suggestion is fundamentally flawed, however. The only way that such a system could work would be to prevent communities from developing their agricultural systems. They would have to remain stationary, using only those varieties that they have always used and capitalizing on whatever nature throws them. They would become anachronistic curiosities.

It would not be enough merely to pay farmers to grow traditional varieties instead of improved modern ones. Evolutionary forces do not confine their actions to fit neatly with the growing seasons of particular crops. Conservation in situ makes sense only when the management of the whole ecosystem is left to nature.

Conserving durians is a good example. The durian is an excellent candidate for in situ conservation, not least because the fruit is such big business in Southeast Asia, yet its continued survival is by no means secure. Durian flowers are pollinated almost entirely by one species of fruit bat that lives in the limestone caves of West Malaysia. As David Lee points out in his book The Sinking Ark, if Malaysians wish to continue enjoying the fruits of the durian tree they may well have to stop quarrying the caves where the fruit bat roosts.

The Soviet Union has established reserves in the Caucasus mountains to protect wild relatives of wheat and fruit trees and in the Kopet mountains, north of the Iranian border, to protect wild pistachio, apricot and almond. India's first reserve is for wild relatives of citrus in the Garo Hills. Influenced by the International Union for Conservation of Nature and Natural Resources and World Wide Fund for Nature, many countries are now looking at existing nature reserves as in situ gene banks for threatened and rare species. By 1988, there were more than 3,500 protected areas in 125 countries and covering an area of more than four million hectares.

Some information on what is held in those reserves is kept on a database maintained by the World Conservation Monitoring Centre (WCMC), run by IUCN, the United Nations Environment Programme and the WWF, based in Britain. The WCMC's Threatened Plants Unit has limited data on 51,000 species of plants, of which about 19,000 are threatened. The information lists species, which protected areas hold them, their world status and the sources that provided the data. The database will become more useful as more studies are carried out. Such studies would ideally by "ecogeographical", looking at the geographical distribution and ecological preferences of the plants. Field surveys would add information on diseases, pests, resistances and tolerances to environmental conditions. Laboratory studies of samples would separate genetic variation within the species from environmental factors.

"Biosphere reserves" that conserve genetic resources and representative examples of the world's ecosystem types already exist. Since 1974, 269 protected areas in 70 countries have been designated as biosphere reserves and are part of UNESCO's Man and Biosphere Programme. Scientists, the seeds industry and conservationists reached an agreement last year at the Keystone International Dialogue on Plant Genetic Resources, that a varied approach to conserving diversity is the best one. Conservation in gene banks and conservation in situ complement each other and should no longer compete. (Source: New Scientist, 5 August 1989)

B. COUNTRY NEWS

Australia

French seeds in Australian link

French seeds concern, Limagrain has been selected by Australia's public R&D agency, the Commonwealth Scientific and Industrial Research Organization (CSIRO), to form a joint venture. The new company, to be called Gene Shears Proprietary, will develop the commercial applications of a technology based on a new family of ribozymes discovered by CSIRO.

Ribozymes are fragments of RNA enzymes capable of catalyzing biochemical reactions, in particular "shearing" certain genes. According to the Australian researchers, Jim Haseloff and Wayn Gerlach, who discovered the technology, ribozymes introduced into the gene will selectively destroy it.

Limagrain is involved, through its biotechnology affiliate Biosem, in research into plant resistance against viral diseases as well as other areas of plant genetic engineering research through two EUREKA programmes with Nestlé and Rhône-Poulenc and other Italian, FRG and Dutch concerns.

The next technical advance could be the application of gene shearing technology to the whole plant, rather than just plant cells, confirming what is viewed as a major advance in genetic engineering. (Source: European Chemical News, 18 September 1989)

Secondary metabolites used as food flavourings

Secondary metabolites used as natural food flavourings can be produced from tissue culture, according to A. Lane of the Food Research Laboratory (Sydney, NSW). Secondary metabolites are often hard to extract in quantity from crops, so artificial flavourings have been developed. The new technique puts the plant tissue in a fermenter, where conditions can be controlled to encourage production of the secondary metabolites. Production can also continue year-round. Sirius Biotechnology will commercialize the technique. Natura' flavourings made with the technique could be available in four years. (Extracted from New Scientist, 15 July 1989)

Brazil

Brazilian firm's vaccine first

Brazilian biotechnology firm Biobras has announced it is to begin industrial production of the world's first leishmanioses vaccine at Montes Claros, Minas Gerais state.

Project manager Wellington Pereira said the first batch of 10,000 units will be produced and delivered in late October, with an additional 30,000 units by the end of the year. The main client will be the Brazilian health authorities.

The product, named Leishvacin, was targeted to meet local demand of one million units/year; but will also be exported to other endemic leishmanioses areas such as Colombia, Venezuela, Argentina and parts of the United States.

The disease is transmitted through the insect Lutzumya and causes frailty in humans.

In 1988, following trials on Amazon-based Brazilian army soldiers, which showed an immunization rate of 50 per cent, the vaccine's registration was accepted by the Brazilian drugs agency Dimed. It was recommended for widespread use by the World Health Organization in 1987. (Source: European Chemical News, 18 September 1989)

Bacterium raises sugarcane yield

Brazilian State owned Embrapa has isolated a bacterium which may save the country $150 million in nitrogenous fertilizer imports consumed by sugarcane agriculture. The biological fertilizer may also

revive Brazil's depleted alcohol programme. The bacterium, Acetocter diazotrophicus, is found in some varieties of sugarcane. Field tests of sugarcane innoculated with the bacterium are reported to have shown productivity increases from 60 to 180 ton/hectare in most species. (Source: European Chemical News, 2 October 1989)

Denmark

Denmark is [illegible] country to clear IL-2 for marketing

Danish regulators have cleared Cetus Corp.'s experimental anti-cancer drug, interleukin-2 (IL-2), as a treatment for advanced renal cell carcinoma, or kidney cancer. The move came less than six weeks after a European Community review panel recommended that its 12 member nations grant approval for the genetically engineered drug. Kidney cancer affects about 80,000 people in the US and Europe. (Source: Biotechnology Bulletin, Vol. 8, No. 6, July 1989)

Release of altered beet

The authorities in Denmark have approved the release of genetically modified organisms. It is the first test of Europe's only existing law to govern the deliberate release of altered organisms.

The Danish Parliament has approved plans by the sugar company Danisko, based in Copenhagen, to plant modified sugar beets next spring on a field of 5,000 square metres. One set of beets, comprising several varieties, will carry a foreign gene which confers resistance to rhizomania, a major disease of beets. The virus which causes rhizomania is carried by a fungus. It is decimating beets in southern Europe but has not yet reached Denmark.

Another set of beets will carry a different gene, licensed by Danisko from Monsanto. The gene confers resistance to glyphosate, a weed killer which Monsanto makes and sells under the trade name Roundup.

Afger Meulengracht, a biologist in the biotechnology office of the Danish government's agency for environmental protection, says that the release poses few risks. Because the beets will not be allowed to flower in the field, they cannot release pollen which might otherwise introduce the foreign genes into other beets, with unknown consequences. The experimenters will remove the flowers from any beets which bloom prematurely and cover them with plastic tents.

There is only one species of wild beet in Denmark which could interbreed with the modified beets. Any accidental crosses are unlikely to survive and compete successfully with normal beets, says Meulengracht.

The experimenters will transplant beets in a pollen-proof greenhouse and study the activity of the genes. They will investigate whether the introduced genes destabilize the rest of the beet's genome, the physical characteristics of the plants and their capacity to reproduce.

Denmark's approval of the beet experiment puts it among Europe's pioneers of deliberate releases of genetically altered organisms. The other major planned release, of petunias containing "jumping genes" from maize, was approved this year by the Federal Republic of Germany, but too late to allow planting until next year.

Denmark's law on genetic engineering prohibits all releases of genetically modified organisms unless special permission is granted. Conversely, a proposed law to govern releases in the UK permits release unless a particular case is prohibited. (Source: New Scientist, 26 August 1989)

Drug collaboration

Danish biotechnology leader Novo-Nordisk and SmithKline & French (Philadelphia), a subsidiary of pharmaceutical giant SmithKline Beecham have joined forces to develop and commercialize a new class of compounds. Called calcium channel blockers, the compounds are thought to prevent damage to neurons that leads to strokes and other central nervous system disorders. Under the agreement, the two firms will do the research at the Copenhagen laboratory of a Novo-Nordisk subsidiary where the compounds were discovered. The Danish firm will have exclusive marketing rights in Europe, while SmithKline & French will retain the rights for the rest of the world. (Source: Chemical Week, 30 August 1989)

European Community

Consumers and biotechnology: more information needed

As a step towards improving the quality of the public debate on biotechnology, a European Workshop on Consumers and Biotechnology was held in Brussels in February 1989. It was jointly organized by ERICA (European Research into Consumer Affairs), the Commission of the European Communities (DG XII) and the European Foundation for the Improvement of Living and Working Conditions.

The Foundation, which had already collaborated in a seminar on the Social Aspects of Biotechnology held in Dublin in 1987, concludes that the public has a good deal of catching up to do on biotechnology. Robert Anderson, its research manager responsible for biotechnology, notes that "in Europe, the public is fairly ill-informed about biotechnology, suspicious of the examples highlighted in the media (e.g. fertility drugs which produce multiple births), and vaguely hostile to the idea of this intimate interference with nature".

Information was held to be the key issue in this area, with several types of information now needed. These include information that will help the public understand the processes involved in biotechnology, the products of biotechnology and the likely effects on employment, food prices, the environment and so on. ERICA has been charged with preparing a discussion document based on the workshop and the results should be widely disseminated. Details from: European Foundation for the Improvement of Living and Working Conditions, Loughlinstown House, Shankill, Co. Dublin, Ireland or on Dublin 826888. (Source: Biotechnology Bulletin, Vol. 8, No. 6, July 1989)

Federal Republic of Germany

Genetic engineering law eased

Science organizations breathed a sigh of relief when the Government indicated that it would ease some of the most restrictive provisions in a new "basic law" to regulate genetic engineering. But the rest of the law may still be harsh enough to accelerate the exodus of pharmaceuticals research and development from the country.

The most welcome change for science organizations, including the Deutsche Forschungsgemeinschaft (DFG) and the Max Planck Society (MPS), was the dropping of a requirement for licensing of individual experiments with genetically modified organisms classified at "Level 1" or "not dangerous". DFG and MPS had warned at a closed hearing in Bonn on 15 May that such a licensing procedure could become a bureaucratic nightmare.

The regulations for handling riskier organisms or strains were also relaxed, making a general licensing procedure possible. A central licensing commission (ZKBS) will be called upon to assess experiments within 60 days after an application is submitted.

The effect of the new law on industry will depend largely on the amount of public participation allowed in licensing procedures. In the current version, the licensing of production facilities that use hazardous organisms will require public participation, which could introduce years of delay into the licensing procedure. Drawn-out licensing procedures are one of the main justifications for pharmaceutical producers such as Hoechst and BASF pulling some research and development out of the country.

An agreement reached in the European Communities (EC)'s council of environment ministers on 8 June 1989 provided inspiration for the changes in the FRG draft law. The new EC regulations (which have yet to take effect) will set minimum standards for genetic engineering research in the laboratory; standards for the release of genetically modified organisms into the environment still remain to be decided. (Extracted from Nature, Vol. 340, 13 July 1989)

BASF submits new plan for TNF production unit

BASF has submitted a new application to build a test plant for its genetically engineered anti-cancer drug tumour necrosis factor (TNF) at Ludwigshafen. The group's original plans, submitted in September 1988, met with considerable local opposition.

Under federal emissions control statutes, in effect since September 1988, plants using recombinant DNA technolgies are subject to a public hearing. Opponents also have the right to file written objections to the plans. Nearly 650 objections to BASF's project were received by the municipal authorities.

Although city officials were apparently satisfied with the information provided in the 15 page application, opponents claimed that details on product and safety precautions were "too fragmentary". During the public hearing in late April, the chemical group narrowed the scope of its application, limiting the project to TNF production with a laboratory culture of Eschericia coli K12.

BASF now says it believes the new application will have a better chance of being approved - possibly within six to eight months - than a revised draft. The scope of the document has been widened to 140 pages and encompasses detailed information on safety.

Among other precautions to be taken to prevent escape of the bacteria, a vat is to be installed beneath the fermenter to sterilize waste water. According to the company, its planned safety measures exceed those of the federal emissions control regulations.

Parallel to the Ludwigshafen project, BASF is planning a TNF test facility in Boston, US, scheduled to be started in 1991.

Meanwhile, the state of Hesse has said it will ask the Bundesrat to reinstate provisions for a public hearing for all genetic engineering projects in the new framework law passed recently by the cabinet. Part of the federal environment ministry's original draft, the requirement was dropped for all but high risk projects in the cabinet's version.

In other news, the federal biological authority (BBA) has received research ministry funds totalling DM 625,000 to study the safety of using genetically altered bacculoviruses in pesticides until 1992. (Source: European Chemical News, 4 September 1989)

Biotechnology licensing opposed

Opponents of genetic engineering from all over the country descended on the university town of Marburg to present a wide assortment of objections to a biotechnology plant for the production of the drug erythropoietin (EPO), which stimulates the creation of red blood cells in patients with kidney failure. In protesting against the plant, the opponents, led by the Green party, took advantage of a long-awaited opportunity: the first public licensing hearing in the FRG history for a gene-technology facility.

The licensing battle is an important test case for the future of industrial genetic engineering in the FRG. It could affect the "framework law" for genetic engineering scheduled to be debated in Parliament in autumn 1989. Other companies, including BASF AG, are facing similar hearings in the next few months.

Both Behringwerke AG, which owns the plant, and the Greens expect the plant to be licensed despite the protest, and both expect a legal battle to follow. Behringwerke had applied to produce EPO in 1988 but submitted its application again after the law was changed to require a public hearing.

The licensing authority, which in this case is the regional government in Giessen, announced that it would rule on the application by the end of the year. (Extracted from Nature, Vol. 341, 14 September 1989)

France

Squibb sets up genetics programme

Squibb Corporation and the University Louis Pasteur in Strasbourg, France, have entered a long-term research programme in molecular genetics to be directed by Professor Pierre Chambon.

The agreement is a joint initiative of the university, the Centre Nationale de la Recherche Scientific, the Institut National de la Santé et de la Recherche Medicale, and the Squibb Institute for Medical Research and Laboratories of France.

The agreement provides that Squibb will build a research facility - the Centre for the Study of Cellular and Molecular Biology and Genetics - and will support a variety of research projects. Professor Chambon will assist Squibb in identifying the specific research projects to be funded under the programme, and will direct and co-ordinate these projects. Funding for the research projects will begin this year.

Squibb will have access to certain discoveries of the centre related to such research projects and also has certain patent and licensing rights for such discoveries.

The agreement also provides for Squibb's support of up to 50 scientists and personnel at the centre when it becomes fully operational. The facility will be located in Illkirch-Grafenstaden, adjacent to the university campus, and construction is scheduled to begin in the near future. (Source: Chemical Marketing Reporter, 10 July 1989)

India

Cut-price fingerprints

The Centre for Cellular and Molecular Biology (CCMB), an Indian government laboratory in Hyderabad, hopes to provide DNA fingerprinting services to customers in India and abroad at a price much cheaper than the fees currently charged for similar service by UK and American companies. It is the first biotechnology-based service commercialized by India.

DNA fingerprinting was used for the first time in India last June to settle a drawn out paternity case in Madras. The Bureau of Police Research and Development under the Ministry of Home Affairs will set up a $6-million independent facility to exploit the technology for forensic science.

Services will be provided free for government agencies but a fee varying from $30 to $150 will be charged for others. With only a handful of private companies in the world offering DNA fingerprinting services, the CCMB hopes that the low-cost Indian facility will attract orders from overseas. (Source: Nature, Vol. 340, 20 July 1989)

Leprosy vaccines go on trial

After nearly four years of vacillation, the Indian Government has agreed to launch a human trial of the anti-leprosy vaccine developed by the World Health Organization (WHO). India will be the third country, following Malawi and Venezuela, to test the vaccine.

The WHO vaccine, a combination of live BCG and heat-killed Mycobacterium leprae derived from armadillo, has been cleared by the drug controller and, according to Dr. A.S. Paintal, director general of the Indian Council of Medical Research (ICMR), the trial, to be funded by ICMR, will start in January 1990.

The plan is to use the BCG-M. leprae vaccine in phase-two trials on a few thousand healthy people to determine if there are any adverse effects. The trial will last four months. After that, the vaccine will be evaluated, along with two (or possibly three) Indian vaccines, in a single "comparative" trial involving several thousand subjects at one location in south India. The vaccine that gives the best results, whether Indian or foreign, will be recommended for India's leprosy control programme.

The trial will be designed and conducted by a committee of experts chosen by ICMR. WHO will simply supply the vaccine and provide one scientist to sit on the monitoring committee. This arrangement constitutes a major change from earlier vaccine trials where WHO assumed total control while Indian participation was limited to provision of infrastructural facilities and manpower. By declaring it an Indian and not a WHO trial, ICMR hopes to save WHO from any possible future allegations that it manipulated the results.

The two Indian competitors in the race are the ICRC vaccine developed at the Cancer Research Institute (CRI) in Bombay and the vaccine developed at the National Institute of Immunology (NII) in New Delhi from a soil mycobacterium. A third Indian vaccine developed at the Central Drug Research Institute in Lucknow (from Mycobacterium habana) may also be included in the study.

The combined trial of all the vaccines is expected to put a stop to unhealthy competition among Indian groups. (Source: Nature, Vol. 340, 10 August 1989)

Tie-up with France on vaccine unit

A viral vaccines unit, Indian Vaccines Corporation Ltd. (IVCOL) is being set up in Gurgaon with French technical collaboration. The unit will manufacture 20 million doses of measles vaccine, 2 million doses of vero rabies vaccine, 50 million doses of inactivated polio vaccine and formulation of 40 million doses of quadruple (DPTP) vaccine.

The unit is being jointly set up by the Department of Biotechnology, Indian Petrochemicals Corporation and the Institute Merieux of France. Each of the three promoting partners will contribute 25 per cent of the equity shares capital. The balance will be obtained by public subscription through prospectus. Full autonomy and independence will be given to decide the composition and structure of the company. Dr. Raja Ramanna, an eminent scientist has been appointed Chairman of the Board of Directors.

The undertaking will be the biggest new vaccine manufacturing cum-R&D unit being set up anywhere in the world. (Source: The Hindustan Times, 14 September 1989)

Ireland

TDC genetics breakthrough

In August 1989 a research team at Trinity College, Dublin, announced a major breakthrough in the genetics of blindness.

The team, led by Dr. Peter Humphries, has succeeded in "mapping" the gene for a particular form of inherited progressive blindness, retinitis pigmentosa.

The disease generally develops during adulthood, and affected people usually notice first that their night vision is impaired. As the disease progresses, their peripheral and later their central vision may be lost. There are a number of types of RP, varying in the age at onset and severity of the condition, which may reflect differences at a genetic level.

A number of distinct genetic forms of RP are known. One form is X-linked, that is, the mutation occurs in a gene on the X chromosome; others are recessive (both copies of a particular gene must be defective for the disease to manifest itself) or, as in the form studied at TCD, dominant (a single defective copy of a gene is sufficient for the disease to develop). An estimated 2,000 to 3,000 people in Ireland are thought to have some form of RP.

In all cases, the mechanism for the development of the disease remains unknown: it takes its name

from the clumps of pigment which appear on the retina of the eye in affected individuals; however, the degree of loss of sight is not related to the amount of pigment present.

The TCD team's breakthrough was to locate the gene responsible among the genes in the human genetic library. The work entailed taking blood samples from 100 members of an Irish extended family, 50 of whom have RP. The DNA was extracted from the blood cells and fragmented using restriction enzymes.

A team of six geneticists then spent three years searching among the fragments to find the one containing the RP mutation, and so mapping the gene to chromosome III.

Now that the fragment containing the mutation has been isolated a simple and accurate predictive test can be developed for the disease. However, the gene has yet to be precisely located on the fragment, and this work may take another three to five years.

Once the gene has been located, though, it should be possible to sequence it and determine its function. That information should contribute to a greater understanding of the biology of the eye and of the nature of progressive diseases, as well as the development of a treatment or cure for at least one form of RP.

The TCD research, which was done in conjunction with the Texas Medical Centre in the USA and the Research Foundation of the Royal Eye and Ear Hospital, Dublin, was funded by the RP societies of Ireland, the UK and the USA. (Source: Technology Ireland, September 1989)

Japan

Plant biotechnology boost

Plant biotechnology in Japan is to be boosted by a new company formed by 20 Mitsui group firms. The new company, to be called the Mitsui Plant Biotechnology Research Institute, will have its research base at Tsukuba, and is designed to genetically engineer commercially important crops.

Japanese plant biotechnology is lagging behind US and European research, particularly in deliberate environmental release where the lag is believed to be approaching three years. The new company, capitalized at $720,000, will seek to redress the balance. (Source: European Chemical News, 21/28 August 1989)

Diabetes drug development pact signed by US and Japanese firms

Geritech Inc., Northvale, N.J., has announced signing agreements that will be the basis of a strategic alliance with Yamanouchi Pharmaceutical Company, Tokyo, to develop and commercialize a new field of biomedical technology that the two firms believe holds promise for treating many health effects of diabetes and aging.

The agreements cover technologies stemming from discoveries, made at Rockefeller University, about biochemical reactions that appear to play a role in diabetic complications. The Rockefeller scientists believe that these reactions also are involved in certain aging processes.

This research has already led to clinical trials of a drug for diabetic complications and eventually may yield treatments for some health effects of aging. (Source: Chemical Marketing Reporter, 4 September 1989)

The Netherlands

Biotechnology for small-scale farmers in developing countries

Research policy in the field of agricultural biotechnology in the Netherlands has not only denied all social interests except the economic ones, but also hampered independent universities to adjust their long term research programmes to the needs and interests of small-scale farmers in developing countries.

To point out research fields and research goals which would be appropriate to improve small-scale food production and sustainable rural development, the Free University in Amsterdam is carrying out a "programme study" on biotechnology for small-scale farmers in developing countries. It focuses on Pakistan and Zimbabwe. Comparisons will also be made with other countries in southern Africa (the SADCC countries).

Results of earlier agricultural innovations have shown that the introduction of new technologies was often inappropriate to meet the specific needs of (especially the poorest) subsistence farmers. High-yielding varieties, for example, are often inappropriate because subsistance farmers need their crops to be multifunctional.

Therefore, a new research method has been used for this programme study, called the "interactive bottom-up approach". It is divided into an inventory phase, an interaction phase, and a phase of institutionalization. The specific problems of small-scale farmers are identified in close co-operation with various local groups (government, farmers, women's organizations, scientists, environmental groups).

Biotechnological and conventional solutions to these problems are compared and prioritized by means of three main criteria:

(1) Inputs: Are the necessary inputs for the use of the (bio)technological innovation available? (Capital intensive inputs, norms and values concerning agricultural practices, etc.)

(2) Quality of the output: Will the innovation improve the quality of life (direct and indirect consequences)?

(3) Sustainability: Will the innovation not be destructive to the agro-eco system? Will it not harm the robustness (persistency against changes in e.g. climate; international trade developments; local maskets, etc.) of the farming system?

The interim report of the programme study will be finalized in November 1989, and the final report will be published in February 1990. The study is carried out by Joske Bunders et al., Department of Biology and Society, Free University, P.O. Box 7161, 1007 MC Amsterdam, The Netherlands. (Source: Biotechnology and Development Monitor, No. 1, September 1989)

Recombinant potatoes destroyed

In the wake of the disruption of field trials of genetically engineered plants in the USA, a Dutch

group calling itself The Seething Spuds claimed responsibility on 11 August for destroying 400 genetically manipulated potato plants. The protest was aimed at stopping an Agriculture Ministry research project. (Source: Biotechnology Bulletin, Vol. 8, No. 7, August 1989)

Spain

New biotechnology facility

Tres Cantos, north of Madrid, is the site of Spain's first genetic engineering facility. The $16.4 million R&D centre was made possible by an agreement between Laboratorios Serono S.A. (part of the Geneva, Switzerland-based Ares-Serono Group) and the Spanish Ministry of Industry's Centre for Technological and Industrial Development. First projects will be developing epidermal growth factor wound-healing products and corticotropin releasing factor, a diagnostic neurohormone. (Source: Bio/Technology, Vol. 7, August 1989)

United Kingdom

Institute of food research to place greater emphasis on food poisoning and biotechnology

The Council of the Agricultural and Food Research Council (AFRC) has decided to consolidate the work of the AFRC Institute of Food Research (IFR) at its Norwich and Reading sites, and to secure the future of these two laboratories. The laboratory at Langford, Bristol, will cease to be part of the IFR by the end of 1989, when AFRC funding will have been withdrawn.

Greater emphasis will now be placed on the basic and molecular sciences within the restructured institute, especially in key areas such as food safety, nutrition, consumer acceptability and biotechnology. More will be spent, for example, on research into food poisoning and on the design of rapid diagnostic tests of food quality and safety.

The AFRC argues that the restructuring will permit the consolidation and strengthening of the IFR's programmes on molecular sciences and biotechnology which offer major new opportunities for improved control of food safety. These include the new method for rapid detection of Salmonella enteritidis, the nucleic acid probes programme for rapid detection of Listeria at Reading, and the development of new routes to natural preservation. (Source: Biotechnology Bulletin, Vol. 8, No. 6, July 1989)

Catalysis research gets Government backing

Under a new scheme, government funding of 2.5 million pounds sterling for a new 5 million pounds sterling LINK programme, focusing on collaborative research into new catalysts and catalytic processes, will be shared equally between the Department of Trade & Industry (DTI) and the Science & Engineering Research Council (SERC). The funding will be matched by contributions from industry towards individual projects.

The programme will focus on seven research areas: (1) **C1 chemistry conversions**, including the conversion of syngas or methane to higher value products; (2) **hydrocarbon processing**, e.g. catalytic cracking of fuel oils in the refining process; (3) **environmental control**, including improved industrial effluent control and vehicle exhaust systems; (4) **electrocatalytic technology**, e.g. fuel cells for "clean" power generation; (5) **photocatalysis**, including water purification techniques; (6) **polymerisation**, including novel polymerization cayalysis; and (7) **enabling technologies for catalysis**, e.g. research into catalyst regeneration.

Forty-six industrial - and 17 science-based - organizations have been identified as having an interest in catalysis research. Organizations thought likely to participate in early projects include Liverpool Polytechnic, UMIST, British Gas, BP, ICI and Johnson Matthey.

The Government has also approved two biotechnology research programmes through the LINK programme. One, with the support of three research councils and the Ministry of Defence, allocates 9.6 million pounds sterling for protein engineering over five years. The other with 7.5 million pounds sterling in funding over five years, will be to research industrial applications of biotechnology. Novel extraction processes and new designs for fermenters are included in this project. It will also examine ways to protect the environment from the necessary organisms. (Source: Biotechnology Bulletin, Vol. 8, No. 6, July 1989 and New Scientist, 1 July 1989)

Genetics forum launched

The UK Genetics Forum was formally launched on 30 June. It called for increased public participation in decision making on biotechnology. Biotechnologists should be aware of the agenda it is advancing. Although it recognizes that the use of biotechnology could bring significant benefits, the Genetics Forum raises ten concerns in relation to genetic engineering and other advanced biotechnologies, summarized below:

(1) **Public information.** Public understanding of these revolutionary technologies remains minimal. What information there has been has generally been biased in favour of the technology.

(2) **Agriculture.** From the introduction of bovine somatotropin (BST) to the development of crop herbicide resistance, agricultural biotechnology has major implications. Agrochemical and other large companies are buying up seed companies and seeking to patent genetically engineered crops and livestock, threatening farmers with a loss of independence.

(3) **Animal welfare.** Genetic engineering of animals can produce unwanted side-effects. Transgenic pigs, for example, have suffered from crippling arthritis, infertility and other ailments. The first patented animal in the world was a mouse carrying a human oncogene which predisposed the animal to develop cancer within 90 days.

(4) **Biological warfare.** Genetic engineering is encouraging an insidious arms race. The Ministry of Defence directly funds at least 2 million pounds sterling of research into biowarfare a year in the UK. "The development of purely defensive biological agents is an illusory goal", the Genetics Forum suggests.

(5) **Civil and individual liberties.** New genetic screening techniques provide unprecedented power to identify and track individuals. This poses threats to privacy. In the future, companies could bar people with genetic susceptibilities to environmental pollutants

from certain jobs, rather than reducing workplace pollution levels, while Governments could illegally track people.

(6) **Environment.** A large proportion of the Earth's farmland could soon be covered with transgenic crops. Genetically engineered microbes will be released to the soil, watercourses and mines. Ecological disruption, unplanned gene transfers, alterations to global cycling of nutrients and reductions in local and global genetic diversity could result.

(7) **Ethics.** Genetic engineering raises fundamental questions about the relationship between humans and other organisms. It enables the production of organisms containing genes from unrelated species. Developments in human genetics raise the spectre of eugenics, of discrimination against disabled people and social pressures on prospective parents, especially women. Longer term, the technology will permit much greater control over human evolution.

(8) **Human health.** The escape of genetically engineered microbes from industrial applications could cause disease. For example, human pathogens could be created inadvertently. Working with recombinant DNA may also carry dangers, though the risks are thought to be low. Gene therapy and pregnancy intervention (for example, embryo biopsy) could lead to health problems.

(9) **Patenting of life.** Historically, living organisms have been excluded from the industrial patent system, but the consensus that they cannot be created and owned is breaking down rapidly under commercial pressures spawned by genetic engineering. Patents on life are morally questionable.

(10) **The third world.** The development of biotechnology is dominated by the industrialized countries, which are developing many applications inappropriate to - or too expensive for - developing countries, or which could undermine third world economies.

In its evidence to the Royal Commission on Environmental Pollution, the Genetics Forum recommended: **a partial moratorium** on releases of genetically engineered organisms to the environment until understanding of ecology has improved and a full public debate held; **the formation of a Public Biotechnology Commission**, with representatives from public interest and environmental groups to bring a public voice into biotechnology regulation; and the **development of criteria** to identify environmentally irresponsible biotechnological applications. "Those identified", the Genetics Forum concluded, "such as genetic engineering of herbicide resistance in crop plants, should be banned".

Following the publication of the Royal Commission's report (see above), the Genetics Forum renewed its call for a Public Biotechnology Commission. It also called for: the setting up of an authorization and licensing system for organizations wanting to make deliberate releases; the maintenance of a case-by-case system of expert scrutiny for every proposed release; the setting up of lineage registers to record the history of genetically engineered plant varieties and the full characterization of introduced DNA sequences; and the mandatory insertion of uniquely identifiable marker sequences into all recombinant organisms to be released. (Source: Biotechnology Bulletin, Vol. 8, No. 6, July 1989)

New pilot plant for blood components

Cambridge University has opened a production plant for genetically engineered blood components. The facility, at Cambridge's Addenbrooke's hospital, will initially produce test quantities of genetically engineered antibodies which show promise in fighting leukaemia.

The plant will inevitably bring some commercial advantages to the University but the intention is to decrease the time lag between innovation and availability to the patient.

The "Cambridge synthetic blood products unit", as the plant will be known, will enable clinical tests of the campath 1 rat antibody and humanized campath on 10-20 patients annually. There is already agreement with a drug company on the commercial exploitation of one of the products. Modified blood components for the control of blood-clotting and infection-free synthetic blood products will also be produced.

The unit is to be headed by Willem Ouwehand from the Netherlands Red Cross Blood Transfusion Service. The facility will receive its funding over the next five years from the Kay Kendall Trust, the East Anglia Regional Blood Transfusion service and the University's department of haematology. Contributions from industry and charities are also expected. (Source: Chemistry & Industry, 18 September 1989)

United States of America

Trade associations act in concert

Two Washington, DC-based biotechnology trade groups, the Industrial Biotechnology Association (IBA) and the Association of Biotechnology Companies (ABC), have issued a joint statement on proposed legislation that would impose a registration fee on facilities regulated by the Federal Drug Agency.

This marks the first joint action between the two groups, and may be the initial step toward consolidation into a single entity, which could then lobby more efficiently for its members' interests. IBA is the better financed of the two: its members include many of the larger biotechnology companies, while ABC represents the interests of many of the smaller firms. The Boards of Directors of the two groups are rumoured to be discussing a merger, most likely to occur later this year. (Source: Bio/Technology, Vol. 7, August 1989)

Biorational fungicide

EPA has registered a new biorational compound to control decay of pruning wounds in ornamental, shade and forest trees and internal decay of wood in fence posts, utility poles and playground structures. The new product, "Binab T", is a combination of two fungi, trichoderma harzianum and trichoderma polysporum, both of which are ubiquitous in nature. (Source: Chemical Marketing Reporter, 14 August 1989)

Dead microbes sidestep rules on genetic release

The US Environmental Protection Agency is expected to grant a licence soon for the first large scale field test of a biopesticide containing

genetically altered bacteria. The pesticide sidesteps laws governing the release of genetically altered organisms into the wild because the bacteria - which produce a toxin fatal to pests - are killed before they leave the factory.

If the EPA grants the permit then Mycogen of San Diego, California, will distribute its liquid pesticide to farmers in Florida and Texas to use against the caterpillar of the diamondback moth. This caterpillar attacks cabbages, broccoli and cauliflowers, and has built up a resistance to conventional chemical pesticides.

The product is the first to test a special category of regulation which the EPA has set up to cover such dead organisms. The company has simply to demonstrate that it can guarantee that its organisms are dead. Other companies have tested genetically manipulated organisms in small-scale field experiments, but they have had to destroy their crops because the effect of these life forms on the ecosystems into which they are introduced is relatively unknown.

The new biopesticide, called MVP (Mycogen Vegetable Product), relies on a gene taken from the soil bacterium Bacillus thuringiensis. The gene codes for a toxin that will attack the digestive system of caterpillars. Mycogen inserts this gene into a bacterium found on leaves, Pseudomonas fluorescens, which will produce the toxin, delta endotoxin, in far larger quantities than the gene's original host. In normal circumstances, the gene would produce the toxin as a crystal inside a cell which bursts open at the end of the life cycle of the bacterium. However, in its new host, the toxin forms in cells which stay intact.

The company grows the bacteria in a fermenter, then treats them with a chemical to toughen their cell walls and encapsulate the toxin. This natural barrier allows the toxin to remain effective for longer when exposed to the elements. The chemical also kills the bacteria, which the company then heats to guarantee that they are all dead. Over the next 10 days, the company takes samples from the fermenter and puts these into ideal conditions for any live bacteria to grow. This way the scientists can check whether live bacteria remain in the mixture.

Mycogen's scientists also engineer the bacteria to self-destruct. The first time a live bacterium tries to replicate it will be unable to form cell walls, and will die. The company is sufficiently confident that the EPA will approve the field tests to have signed manufacturing agreements with several companies, which have already begun producing MVP. The product has passed rigorous toxicology tests to demonstrate that it is not toxic to mammals, fish or birds. (Source: New Scientist, 7 October 1989)

Union of Soviet Socialist Republics

New institute established

The Shemjakin Institute of Bio-organic Chemistry of the Academy of Sciences of the USSR has been officially opened in Moscow.

It was built and equipped jointly by Terasbetoni OY (Helsinki) for building and services; OWEG Gmbh (Vienna) for equipment; and Techmashimport (Moscow) at a cost of $70 million.

The biotechnological research and experimental production centre of the Institute will facilitate in-depth research of various technological processes in the microbiology and biotechnology fields.

Sulzer subsidiary MBR Bio Reactor supplied biotechnological equipment covering a range of small and large scale bioreactors, measuring and control systems as well as the related engineering. (Source: Manufacturing Chemist, October 1989)

C. RESEARCH

Research on human genes

Submicroscopic defects in chromosomes can cause mental handicap

Many cases of mental retardation may result from submicroscopic defects in an individual's chromosomes, according to Sir David Weatherall of the Institute for Molecular Medicine at Oxford and his colleagues. Their research shows that "we can now detect defects in normal-looking chromosomes using DNA analytic techniques", says Weatherall.

The discovery raises the possibility that parents who have already had a mentally retarded child can have their own DNA and that of any subsequent foetus they conceive analysed for such microdefects. The parents would then have the choice of terminating the pregnancy.

The researchers noticed the chromosomal abnormality by chance, while studying a family in which the three-year-old son was mentally retarded and also had alpha-thalassaemia. This genetic disorder of haemoglobin, the oxygen-carrying molecule in the blood, is caused by mutations in alpha-globin genes. In the hope of finding some molecular clues to his mental handicap, they analysed the DNA at the tip of chromosome 16, the site of the alpha-globin genes, in the parents and their child.

To their surprise, they found that the mother carried a "balanced translocation" - the tips of the short arms of chromosomes 1 and 16 had swapped places, carrying the alpha-globin genes from chromosomes 16 to 1. Overall, the mother lost no genetic material in the transfer. But things were different for her children.

The boy inherited from his mother one of these translocated chromosomes - the chromosome 16 that had lost its alpha-globin genes. He developed thalassaemia. His mental retardation presumably comes either from the loss of the rest of the genetic material that is normally carried on the tip of chromosome 16, or from the extra dose of genes from the tip of chromosome 1.

A younger daughter, on the other hand, received her mother's translocated chromosome 1 bearing the extra alpha-globin gene: so she did not have thalassaemia, but she was also mentally retarded. Again, a loss or an overdose of certain genes seem to have led to her mental handicap.

The discovery radically alters the genetic counselling of couples who have had a mentally retarded child. Doctors treating this family had regarded the boy's mental retardation as a new mutation, and so told the parents that they need not worry about having more retarded children. They had attributed the girl's handicap to meningitis. (Source: New Scientist, 14 October 1989)

Cystic fibrosis gene found

Researchers from the US and Canada have identified the cystic fibrosis genetic defect. Cystic fibrosis causes various glands to fail to

work properly, resulting in the lungs clogging up with mucous, making the person susceptible to infections. Scientists found a mutation which causes a gene to produce a defective protein. This protein is what interferes with the movement of chloride and sodium atoms in and out of cells. Researchers discovered that the gene from cystic fibrosis patients was missing the "code" for an amino acid molecule at a single spot in the protein. The protein produced by the patients was therefore missing one amino acid molecule. The defect was found in the genes of 70 per cent of the 200 cystic fibrosis patients tested, while the other 30 per cent of patients were thought to suffer other kinds of mutations in the same gene. Researchers must now discover what the normal CFTR protein does and what the defective CFTR protein does not do to cause cystic fibrosis. (Extracted from Wall Street Journal, 25 August 1989)

New oncogene affects cyclic AMP synthesis

Because cyclic adenosine monophosphate (cyclic AMP) is an important messenger molecule in several biochemical pathways that stimulate cell growth, the genes that control its synthesis are likely candidates to become oncogenes. Henry R. Bourne of the University of California, San Francisco, along with co-workers there and at the University of Milan, Italy, have confirmed this hypothesis by identifying mutations that cause uncontrolled cyclic AMP synthesis in four growth hormone-secreting human pituitary tumours. The mutations lead to changes in one of two amino acids in the alpha subunit of a G-protein called G_s. Thus, the researchers have dubbed their new oncogene gsp. Because the role of G_s and its alpha subunit has already been studied extensively, finding a tumour-promoting mutated form of this protein offers what may turn out to be an important probe to see how mutations affect this cell-stimulating pathway. (Reprinted with permission from Chemical and Engineering News, 4 September 1989, p. 17. Copyright (1989) American Chemical Society)

Altered tPA may be more effective

Altered tissue plasminogen activator could last longer in the body and therefore be more effective than natural tPA, according to J. E. Sambrook of the University of Texas Southwestern Medical Centre (Dallas). The researchers hope to alter the structure of tPA so that it will not bind to its principal inhibitor. Since no one knows the structure of tPA, Sambrook worked with trypsin, a protein with many of the same amino acid sequences as tPA. This led to the discovery of a loop of 7 amino acids on the tPA molecule. Producing tPA without the loop rendered it incapable of binding with its inhibitor, but did not greatly diminish its ability to dissolve blood clots. It may also be possible to cover the binding site with sugar molecules, thus preventing liver cells from binding. (Extracted from Science News, 8 July 1989)

DNA triple helix blocks protein binding

Triple helix formation between a pyrimidine oligonucleotide and complementary homopurine homopyrimidine duplex deoxyribonucleic acid has been found to block the interaction between the DNA and sequence specific DNA binding proteins. California Institute of Technology chemistry professor Peter B. Dervan and colleagues have been investigating the formation of DNA triple helices between such pyrimidine oligonucleotides - that is, ones containing only cytosine and thymine - and homopurine homepyrimidine DNA for a number of years. They have shown that molecules containing 15 to 20 pyrimidines can site-specifically bind to a single complementary site in large, natural DNA. The chemists have now created a 21-base-pair homopurine site in a murine promoter sequence that was designed to overlap sequences recognized by a restriction endonuclease, a restriction methylase, and a eukaryotic transcription factor. Oligonucleotides containing 20 pyrimidines complementary to this site's homopurine strand bind to the DNA and block the activity of all three proteins, the chemists report. Such triple helix formation offers a new tool for analysing protein/DNA interactions; in some cases such oligonucleotides or their analogs might be designed to function as artificial gene-specific repressors in vivo, according to Dervan. (Reprinted with permission from Chemical and Engineering News, 21 August 1989, p. 18. Copyright (1989) American Chemical Society)

E. Coli produces human 5-lipoxygenase

Researchers at Nippon Tobacco Co. (Tokyo) have genetically engineered Escherichia coli to produce the human enzyme 5-lipoxygenase. This enzyme catalyzes the oxidation of arachidonic acid to 5-HPETE (5-hydroperoxyeicosatetraenoic acid), the precursor of a family of physiologically active substances known as leukotrienes. Leukotriene B4 (LTB-4), for example, plays an important role in allergic reactions by inducing inflammation of alveoli and contraction of the smooth muscles lining the bronchial airways.

The scientists isolated the cDNA for 5-lipoxygenase and introduced it into E. coli via a hybrid expression plasmid. The enzyme made by the bacteria has the same molecular weight (78,000) and activity as the authentic enzyme.

Although yields of the recombinant enzyme are still low, the researchers expect that - once they improve the expression plasmid and culture conditions - they should get about 100 milligrams enzyme per litre. Once large amounts of 5-lipoxygenase are available, it should be easier to develop enzyme inhibitors. (Source: Bio/Technology, Vol. 7, August 1989)

Arthritis is the target

Biopharmaceutical firm Celltech (Slough, UK) has cloned human enzymes believed to be involved in arthritis and is seeking ways to inhibit those enzymes as a possible treatment for the disease. The firm has now linked up with Merck (Rahway, NJ) to design and screen such enzyme inhibitors. (Source: Chemical Week, 9 August 1989)

The oncogene connection

So far none of the cancer-causing oncogenes have been found among the genes that control cell division, but recent discoveries indicate that the proteins encoded by these two groups of genes may be able to talk to one another and influence each other's activities. If so, the research may produce an improved view of oncogene action.

The activation of a protein known as maturation promoting factor (MPF) is the immediate trigger for cell division in higher organisms. Researchers have recently identified a kinase, an enzyme that adds phosphate groups to proteins, as one component of the maturation factor.

Now, James Maller's group of the University of Colorado School of Medicine in Denver, in

collaboration with that of David Shalloway of Pennsylvania State University in University Park, has found that the MPF kinase phosphorylates the protein product of the src "proto-oncogene". (Proto-oncogenes regulate normal cell growth, but can, if they malfunction, make cells cancerous). Harold Varmus, J. Michael Bishop, and their colleagues at the University of California, San Francisco, have made a similar observation about the src protein.

Earlier work by Shalloway and his colleagues suggests, however, that the phosphorylation may help to bring about the characteristic cell changes of mitosis. They found that certain specific amino acid residues in the src protein briefly acquire phosphate groups at mitosis - just when that kinase is active. Moreover, the current work shows that the MPF kinase phosphorylates those same amino acids.

Meanwhile, David Beach and his colleagues at Cold Spring Harbor Laboratory have evidence indicating that the src protein, itself a kinase, phosphorylates the MPF kinase protein. Neither the Maller nor Varmus group has been able to confirm this with the native protein, however, and the issue remains to be resolved. If the src protein does phosphorylate the MPF kinase in living cells, it could mean that the two enzymes engage in mutual communication and control during mitosis.

And just as important, it would mean that a natural target for the src enzyme has finally been identified. The oncogene was discovered more than 10 years ago, and researchers have been trying unsuccessfully ever since to find out what its targets are.

The src oncogene is not the only one that may interconnect with the MPF kinase. George Van de Woude of Bionetics Research Inc., in Frederick, Maryland, and his colleagues have evidence suggesting that the protein encoded by the mos proto-oncogene is a normal activator of maturation promoting factor during the meiotic divisions of frog and mouse eggs. Van de Woude does not yet know whether it has a similar role in the mitotic divisions of ordinary cells, but he points out, "the evidence is that what happens in meiosis and mitosis is the same".

Also unclear is the relation between the mos product and the second component of maturation promoting factor, the protein cyclin, which may also participate in the factor activation. The mos protein may act through cyclin, but that remains to be seen.

In any event, researchers now have evidence indicating that the normal products of at least two oncogenes interact with the machinery that immediately controls cell division. Possibly then the cancerous changes that the genes produce in cells when they malfunction may be the result of the cells inappropriately expressing mitotic features when they should be resting. (Abstracted with permission from Science, Vol. 245, p. 253, 21 July 1989, by J. L. Marx. Copyright 1989 by the AAAS)

Research on animal genes

Genetically engineered mice produce haemoglobins

Mice have been genetically engineered to produce human haemoglobin. Researchers at the University of Pennsylvania transplanted genes from human red blood cells to the mice, which now produce human haemoglobin, mouse haemoglobin, and two types of hybrid haemoglobin. The work may allow for animal studies of defects in haemoglobin, of the type that causes sickle cell anaemia (for which there is now no animal model). Further in the future, animals engineered to produce human haemoglobin might be used as factories to produce haemoglobin for transfusion. Mouse haemoglobin is different from human haemoglobin in that it releases oxygen much more readily. In larger animals, where oxygen must be transported longer distances, haemoglobin binds oxygen more tightly. The new work will also aid basic research in oxygen transport. (Extracted from Science News, 2 September 1989)

Drug delivery

Stomachs do not know the difference between food and medicine and thus have a tendency to try to digest treatments, rather than passing them on to the bloodstream intact. Nature has its own way around this drug-delivery problem, which scientists at Edinburgh University are now applying in various areas, from making asprin less damaging, to, perhaps, improving the treatment of Parkinson's disease.

A team led by Dr. Lindsey Sawyer in the biochemistry department of Edinburgh University has found a way to transport both aspirin and L-dopa through the stomach without the drugs affecting it or being affected by its digestive juices.

Their inspiration came from studying new-born calves. In their first days of life, before their immune systems are fully developed, calves need to be supplied with vitamins and immunoglobulins in their mothers' milk in order to make antibodies. Dr. Sawyer and his colleagues discovered that in order to ensure that the calf absorbs these vital substances, they are transported through the stomach and down into the intestine attached to a carrier molecule, the protein lactoglobulin. Vitamins attached to lactoglobulin are unaffected by stomach juices and pass through the intestine unscathed until they reach the absorptive tract. There, Dr. Sawyer found, lactoglobulin and its cargo of vitamins or immunoglobulin are absorbed through lactoglobulin receptors in the intestine wall.

Babies are protected in the same way. Dr. Sawyer believes that lactoglobulin can be used to bypass the stomach and transport other things to the intestine, where they can be efficiently absorbed through lactoglobulin receptors. He has cloned the gene for lactoglobulin (that is, implanted it in cell cultures, which then produce lactoglobulin) and engineered the gene to produce an altered version of the protein that binds to, and transports, L-dopa. He is now working to produce a version that carries aspirin. (Source: The Economist, 19 August 1989)

Research on bacterial genes

Redesigning nature's plastics factories

At the Massachusetts Institute of Technology, Anthony Sinskey and ChoKyun Rha are studying the mechanics of how bacteria manufacture their energy storing polymers. His team wants to understand the role of the different enzymes that direct the production of the polymers, with the goal of eventually controlling that production.

PHB production in A. eutrophus is carried out by three enzymes, Sinskey says. The first joins two molecules of acetyl CoA, a basic metabolic molecule found in all organisms, to form acetoacetyl CoA. A second enzyme modifies the composition of this

molecule slightly, and a third enzyme links these modified molecules together to make the polymer. The third enzyme is apparently the key to explaining why A. eutrophus makes different polymers when fed on different substrates, but since no one has identified the enzyme's structure, the process remains a mystery for now.

Rha is interested in the structure and design of bacteria-produced polymers. Her goal is to discover how the structure of a biopolymer determines its properties and to learn how to devise new polymers that will have certain desired characteristics.

Rha has a list of things she would like to try with biopolymers. By adding certain side groups to the long backbone of the polymer, for instance, it should be possible to put either a positive or negative charge on the molecules. Then the electrostatic attraction between the positively and negatively charged polymers could be used to bind them together to make hollow capsules that could be deployed, for example, in drug-delivery systems for implantation in the body.

With bacteria to do the work, it should also be feasible to build polymers with a row of side groups running along either side of the central chain - "like centipedes", Rha says. These rows of side groups should prevent the molecule from balling up, which would make the resulting polymer very stiff, she suggests. "We cannot produce such complicated molecules with any specificity using normal chemistry", Rha says. "The true advantage of biopolymer engineering is that we can specify such complicated designs. Biological systems can make it exactly so".

Sinskey says there are several ways to control the type of polymers produced by a bacterium. One is to vary the feedstock, which is straightforward and is being done in a number of places. Others involve changing the enzymes - the types of enzyme, their specificity, or when they are expressed - in order to alter the production process inside the bacteria. This is more difficult, but Sinskey has taken the first step. He has recently modified a single enzyme in one of the plastic-producing bacteria, he says, but he has not yet had time to see what the altered bacteria will produce. (Abstracted with permission from Science, Vol. 245, p. 1188, 15 September 1989, by Robert Pool. Copyright 1989 by the AAAS)

Ice nucleation protein's structural gene isolated

Research scientists in the School of Agriculture at Tokyo University have isolated the structural gene for a bacterial ice-nucleation protein. This protein probably causes frost damage to crops by stimulating the rapid formation of ice crystals at temperatures just below freezing.

The group isolated the gene for the ice-nucleation protein from a cDNA library cloned from a soil bacterium indigenous to Shizuoka Prefecture. The scientists then expressed this gene in Escherichia coli, with the same efficiency as in its natural host.

The protein encoded by this gene contains a 16 amino acid sequence that is repeated 70 times. Molecular modeling of this repeated amino acid segment suggests that it forms a structure with six-fold symmetry that matches the six-fold symmetry of ice crystals. This may be how the protein efficiently stimulates the nucleation of ice crystals. (Source: Bio/Technology, Vol. 7, July 1989)

Spiders' silk

Spider silk is by far the strongest natural fibre. Its ultimate tensile strength - a measure of how hard you have to pull it before it snaps - is similar to that of the strongest nylon, or aramid fibres like Kevlar (of which bullet-proof vests are made). Dr. Nicholas Ashley, of PA Technology in Cambridge, has found a way to make it on a large scale using E. coli, the intestinal bacteria whose willingness to make do with other creatures' genes has made them the workhorses of biotechnology. Such bacteria are not known for their ability to spin webs, so some sophisticated genetic engineering has also been applied. Spider silk is made up of proteins, which the spider's genes instruct its spinnerets to make. Different proteins make up each different type of silk; the spider uses various silks for different parts of his web and his cocoon.

Finding the genetic code for the silk proteins is no easy task. It is hidden deep somewhere in the spider's reams of DNA. Dr. Ashley's team has taken the easier course of examining the silk itself. A genetic engineer's toolbox includes a sequencer, which chemically snips amino acids off the silk protein one at a time and sorts out what order they come in. Once this order is known, it is a relatively simple task to assemble an artificial gene that will instruct a cell to manufacture the right protein.

The bacteria are grown in vats until the workforce is large enough. The stimulus that starts up the production line may be a chemical trigger, or a simple rise in temperature. The silk is formed in nuggets within the bacteria. These nuggets are collected, and the protein dissolved in a solvent.

To make a fibre, the solvent containing the protein is squirted in a fine jet into water. The solvent diffuses away quickly, leaving a thread of spider silk behind it. Dr. Ashley foresees a variety of applications.

Dr. Ashley's company is now looking for a partner to take the process from the laboratory to the factory floor. Biotechnology makes the production of silk in quantity far simpler than more traditional man-made fibres. The most complex parts of the production plant are the bacteria themselves. (Source: The Economist, 2 September 1989)

Research on viral genes

Structure of HIV enzyme determined

Successful determination of the crystal structure of a key protease enzyme from human immunodeficiency virus (HIV), which causes acquired immune deficiency syndrome (AIDS), could provide a route to the design of new AIDS drugs. The structure was determined by Alexander Wlodawer, Maria Miller, Mariusz Jaskólski, and colleagues at the National Cancer Institute's Frederick Cancer Research Facility and California Institute of Technology. The major structural proteins and enzymes essential for HIV replication are initially produced as high-molecular-weight polyproteins. The polyproteins are then cleaved by a viral protease to give the mature proteins and enzymes, including the viral protease itself. Now that the atomic co-ordinates of HIV-1 protease have been determined,

the structural information provided should facilitate systematic investigations of the mechanism of the enzyme with a view to design of specific inhibitors for use as potential therapeutics against AIDS. "It should be noted that one of the terminal strands contains a free Cys residue", the researchers say, "thus suggesting a site of covalent attachment for a compound designed along these lines". (Reprinted with permission from Chemical Engineering News, 14 August 1989, p. 24. Copyright (1989) American Chemical Society)

Vaccine protects monkeys against SIV virus

A vaccine has been developed that successfully protects animals against a disease related to AIDS, according to a small-scale study in monkeys. The vaccine prevented infection in two monkeys and has blocked development of symptoms in four infected monkeys. Of four monkeys which were exposed to the virus without receiving vaccines, three have died and one is ill. Researchers at the New England Regional Primate Centre (Southborough, MA) say that it is still not certain that a vaccine against AIDS in humans can be developed. Simian immunodeficiency virus (SIV) is the closest known relative of HIV, the cause of AIDS. The vaccine was made from killed SIV, and so it is similar to a killed virus vaccine developed by J. Salk. Some researchers say a killed virus vaccine is too dangerous to use against AIDS, since if just one viral particle is still viable, it could cause the fatal disease in vaccine recipients. Researchers in the latest study point out that they do not know why some of the macaques remained free from infection, while others did become infected. It is also possible that the infected monkeys may eventually develop the disease. (Extracted from New York Times, 15 August 1989)

Retroviruses turn up in more autoimmune diseases

Several autoimmune diseases have now been associated with retroviruses, according to speakers at the Seventh International Congress of Immunology (West Berlin). Studies at Middlesex Hospital and the Institute of Cancer Research (London) indicate that retroviruses are associated with the thyroid disorder Graves' disease.

Research at the University of Texas Health Centre (San Antonio) indicates that Sjogren's syndrome and systemic lupus erythematosus (SLE) are both associated with retrovirus. Fourteen of 20 Sjogren's patients (who show variable symptoms including inflammation, arthritis, and dry eyes and mouth) had antibodies against the p17 and p24 core proteins of HIV-1. So did 21 of 60 SLE patients. Critics say the findings have not been substantiated elsewhere.

F. Krapf of the University of Erlangen-Nurnberg has found DNA sequences that closely match retroviral genes in SLE patients. Just how retroviruses might cause autoimmune diseases is not known. The source of the retroviral DNA is also a mystery. (Extracted from New Scientist, 12 August 1989)

Water hides a host of viruses

Viruses could be the most important form of life in both freshwaters and the sea, according to a group of scientists from the University of Bergen, in Norway. Almost every textbook of marine ecology ignores viruses. And, until now, most microbial ecologists thought that viruses were an insignificant part of the ecosystem.

Gunnar Bratbak and his colleagues used a transmission electron microscope to count the numbers of tiny planktonic organisms in water. They included bacteria and viruses, belonging to the femtoplankton, which are smaller than 0.2 micrometres in size.

The largest number of virus particles the researchers found was 2.5×10^8 per millilitre of water, which is about 10 million times as many as anyone had recorded before. The highest numbers came from water from Lake Plussee in the Federal Republic of Germany. Samples of seawater taken from Norwegian fjords, the North Atlantic and the Barents Sea showed seasonal variation, with few viruses present in winter, but very large numbers present during the spring.

The implications of the Norwegian findings are enormous, for two reasons. First, viruses might control the numbers of other micro-organisms living in water. The traditional view of the microbial ecosystem is that the number of bacteria in the water is kept in balance by organisms higher up the food chain, especially protozoans, which "graze" on bacteria and keep their numbers in check. It now looks as if the controls come from "below", from the viruses that attack bacteria, called bacteriophages.

The Norwecian researchers calculated that as much as a third of the bacterial population might come under attack from phages every day. Phages can also attack the other members of the microbial community, the algae and protozoa.

The second important implication of the huge numbers of viruses in rivers, lakes and the oceans is that they can ferry genetic materials between organisms. This is an important consideration for genetic engineers who want to release "altered" bacteria into the environment. Viruses move bits of genetic material around by the process of transduction, in which they mistakenly incorporate some of their bacterial host's DNA into their own and then transfer it to their next host. With so many more viruses available to ferry genes around, transduction is probably much more common than previously thought.

Such transfers could help bacteria to adapt to changing environments. On the other hand, phages might also ferry material from genetically engineered micro-organisms. (Extracted from New Scientist, 19 August 1989)

Detecting plant viruses

It has always been a puzzle why one virology laboratory can say that a selection of viruses is similar, yet another equally competent laboratory cannot see the resemblance at all.

Dr. Colin Ward at the Parkville laboratory, Australia, says the picture with potyviruses, the largest and most complex group of plant viruses, has now become a lot clearer.

We know that the antibody reactions are really reflecting structure, and structure is dictated by the complete amino acid sequence. The amino acid sequences of a whole range of viruses has been determined and we have found some parts were common and some were very different. When the "string of beads" (amino acids) that constitute the virus protein folds up into a tertiary shape, then assembles into a virus, its quartenary shape, the common parts are hidden and the variable, unique part is on the surface. Virus specific antibodies should react only with this surface exposed portion of the coat protein. But that unique part can be

removed and degraded by proteases (enzymes present in plants) making it difficult to detect with specific antibodies. Dr. Ward and his colleagues have experimentally removed the variable parts and produced an antibody directed at the central core. So far it has reacted against every potyvirus tried.

The potyvirus group is the largest of 28 groups of plant viruses. About 200 known plant viruses belong to this group.

Potyviruses affect broad acre, horticultural and ornamental crops which makes them commercially very important.

"In addition to virus-specific probes, we are now very close to perfecting a single test which will identify all the potyviruses - a broad spectrum probe or diagnostic reagent that will tell us whether any of this large group of viruses is present in plant tissue or not", he said.

These probes being developed with a Melbourne company, Coselco Mimotopes Pty. Ltd., are targeted at conserved regions of the virus coat protein and genome, and will be useful not only for diagnostic work but also for quarantine purposes. (Source: Bictopic, Vol. 1, No. 1, Spring 1989)

Research instrumentation

Automating batch cell fusion

Hitachi (Japan) has developed a biotechnology technique that speeds up the electrically-induced fusion of incompatible cells. The technology may provide a basis for automating cell fusion and enable mass production of biologically engineered products. The process involves a piece of equipment containing 1,600 microchambers in a 3-inch-wide silicon plate with an electrode at the bottom of each microchamber. The process has a 25 per cent efficiency rate, which is substantially higher than previous efforts at batch cell fusion. (Extracted from High Technology Business, October 1989)

Protein G

Genzyme have announced the release of two products for the isolation and purification of IgG and monoclonal and polyclonal IgG antibodies.

Recombinant Protein G is available with a purity of greater than 90 per cent active protein isolated from streptococci and expressed in E. Coli. Main uses are the purification from serum as fluid and culture supernatants of monoclonal and polyclonal IgG antibodies, Immunoprecipitation of IgG complexes, and as a substrate for conjugation for use as a developing reagent for ELISA, Ria and Western Blot analysis of IgG antibodies.

Also available is an immobilized version of protein G on 4 per cent agarose with a binding capacity for 20 mg of IgG bound/mL of gel with similar results with other species including rabbit, goat, bovine and murine.

Complete data sheets and protocols are available on request. For further information contact Laboratory Supply, 48 52 Sydenham Road, Marrickville NSW 2204. (Source: Australian Journal of Biotechnology, Vol. 3, No. 3, July 1989)

Ultrafermenters

Setric Genie Industriel (SGI) of Toulouse, France, in conjunction with the National Institute of Applied Sciences (INSA), Toulouse, have developed an ultrafermenter for utilization in the food industries such as dairy, brewing, winemaking and yeast companies, etc. It also has application in the pharmaceutical industry for manufacture of vaccines and antibiotics.

The concept of these bioreactors is the integration of a fermenter with tangential filtration, through ceramic membranes, into one single unit. Micro-organisms are cultured in a continuously circulating system which allows a sustained take-off of sterile filtrate. Media levels are constantly adjusted by the automatic feeding of fresh media. The microfiltration membrane retains the micro-organisms in the circulating loop and the ultrafermenter allows concentration of the biomass at the end of a batch culture. The advantages of detoxification, sterile permeate recovery and biomass concentration are all built into the one unit. (Source: Australian Journal of Biotechnology, Vol. 3, No. 3, July 1989)

Glass chromatography columns

A new range of process scale glass chromatography columns from Pharmacia emphasizes ease of use and efficient, hygienic operation in production. BioProcess Glass Columns, available with diameters of 100 mm and 200 mm and heights of 500 mm, 750 mm and 950 mm, have a single screw adaptor that adjusts easily to make even contact with the gel bed. Columns run at 3 bar pressure to extract top performance from modern bioprocessing media, giving separations that are quick, efficient and reliable.

Column design and materials are also compatible with operation under high standards of process hygiene and with a long working life. Materials include calibrated precision, borosilicate glass tubes and high alloy (ASTM S31254) electropolished steel. BioProcess Glass Columns can be autoclaved. (Source: Australian Journal of Biotechnology, Vol. 3, No. 3, July 1989)

Preserving the unpreservable

Biomolecules currently have very short "shelf-lives", and although often isolated at very high cost, they are very difficult to store in fully active form.

A novel approach to biopreservation initiated at the University of Cambridge in the UK, has given rise to a technique known as "undercooling", which may provide a unique solution to many of the problems associated with current methods of storing active biological proteins and cell cultures. The idea has been adopted commercially by a new company on Cambridge's Science Park.

Established procedures such as freeze-drying and cyro-storage in liquid nitrogen kill many animal/plant cells and adversely affect many cell constituents, including proteins such as labile enzymes and hormones. Both methods give disappointingly low levels of post thaw recovery/activity after only short timespans. Ice formation plays a major role here, damaging cell morphology and raising the level of salts which damage biological material. Two other techniques, refrigeration and the use of chemical additives, also have serious limitations, including genetic drift and protein damage respectively.

Working at the University's Department of Botany, Professor Felix Franks was interested in the

tricks used by living organisms to protect their cell water from freezing at sub-zero temperatures. The new break-through exploits the natural capacity of water (under the correct conditions) to remain liquid at temperatures as low as -40°C.

Undercooling avoids freezing by suspending biological matter in a simple carrier fluid - no ice is formed, and cells/biomolecules remain viable and undamaged for extended periods.

Blending for a few seconds gives a stable dispersion of aqueous droplets which can be stored without freezing at an average -20°C. In the illustration an active bacterial culture (Streptococcus cremoris) used in dairy production, is being introduced into the new medium. To recover activity the suspension is simply warmed to ambient temperature, with no costly subculturing required.

The new system is simple and cost effective, and - being especially suitable for microbial cell cultures, as well as enzymes and hormones - is seen as having great potential for the preservation of biotechnology's intermediate products, and for bulk storage and distribution of high value-added biochemicals. In medicine, it represents an uncomplicated way of preserving rare blood components (such as coagulants) and blood cells for much longer periods than those currently available.

Further information on the new process can be obtained from Professor Felix Franks, Pafra Limited, Biopreservation Division, Unit 150, Cambridge Science Park, Milton Road, Cambridge, CB4 4GG, England. Tel: (0223) 420921, fax (0223) 420502. (Source: Australian Journal of Biotechnology, Vol. 3, No. 3, July 1989)

General

New biopolymer discovered

Scientists at the Industrial Research Council's Research Institute for Techniques in Industrial Microbiology (Tokyo) have discovered a new biopolymer that can absorb 500 times its own weight in salt water. Its ability to absorb fresh water is even greater - one gram can absorb one litre. Unlike current synthetic polymers, which have significantly lower absorptive properties for water containing solutes, the biopolymer's absorptive properties remain high.

The researchers isolated this biopolymer from the medium used to grow a strain of Alcaligenes latus. Because the biopolymer is synthesized by bacteria, it may prove cheaper to produce than today's synthetic polymers. (Source: Bio/Technology, Vol. 7, August 1989)

Anti-APO-1 produces programmed cell death

A monoclonal antibody can be used to induce programmed cell death in tumours, according to P. H. Krammer of the German Cancer Research Centre and the University of Heidelberg. Anti-APO-1 might affect normal tissue as well, however, so much more research is needed. Normal mice were infected with cancerous human B-cells. Antibody-secreting cells were then removed from the mice, and the antibodies were isolated. The Anti-APO-1 produced the programmed cell death rather than immune-system mediated death, in which cells swell and burst. The mechanism of the effect is not known. The attachment site is also found on non-cancerous cells. (Extracted from Science News, 29 July 1989)

The enemy with a thousand faces

In the developed countries, one person in six is fated to die of cancer. Some 500,000 Americans alone will succumb to it this year, and 1 million more will discover that it is at work inside them. All the while the incidence of the commonest cancers continues to rise in the world's rich countries.

There is some good news. The incidence of stomach cancer, which accounts for some 5 per cent of all cases, is declining. Nobody knows why, though some suggest that the freshness of refrigerated foods may play a part. The treatments for some rarer cancers have improved enormously.

Decades and billions of dollars spent on research have made little difference to this picture. The biology of cancer is now much better understood but it has led to few effective treatments. Those still come from trial and error.

Most cancer drugs are discovered by accident. Compounds are tested in the blind hope of finding one that works: America's National Cancer Institute (NCI) screens 10,000 each year. Only one potential anti-cancer agent has emerged in the past decade.

The traditional anti-cancer drugs work mostly by interfering with DNA replication. Before a cell can reproduce, it must copy out its genes, written on DNA. Cancerous cells usually divide more frequently than normal ones - so interfering with reproduction in general should hurt the cancer in particular.

The aim of basic research into cancer is to find ways of getting at it directly and so minimizing side-effects. False hopes have been common. Alpha-interferon, a protein made in the body, was touted in the early 1980s as an immune-system booster that would cure all cancers. So far it has been approved for use in the treatment of only three cancers: two rare types of leukaemia (cancer of the blood cells) and Kaposi's sarcoma, which afflicts people with AIDS. No drug developed from a natural product of the body has yet been able to promise cancer patients a normal life, free of the disease.

The emerging fact that cancers are a complicated set of variations on a theme does seem to mean that there will never be a single "magic-bullet" cure. But each time a cancer mechanism is understood, opportunities arise for treatments tailored to disrupting it.

Cancer is always a matter of unrestrained growth. That lack of restraint is caused by damaged genes. Each gene is the stored blueprint for a protein; proteins are the chemicals which do most of the work in cells. When a gene is damaged, things go wrong with the protein and thus with the workings of the cell. Sometimes the cell still manages to make the protein, but with mistakes in its blueprint the protein may work in a different way. At other times the damage is so bad the protein cannot be made at all.

Anything that damages genes can cause cancer. A number of things in the environment can hurt, as can dietary habits - and, of course, smoking. Radiation - including the sun's ultraviolet rays - can also disrupt DNA. According to Sir Walter Bodmer, head of the London-based Imperial Cancer Research Fund (ICRF), genetic damage from such sources triggers off 80 per cent of cancers. There are other ways to get faulty genes. An error

can creep in when DNA is being copied. Or a virus can disrupt the DNA when it stitches its own genes in among the cell's.

There are various ways in which genes can go haywire. The messages that describe proteins are written in a four-letter alphabet. Substituting one letter for another somewhere in the hundreds of millions of characters that make up the genes in a cell sounds trivial. Such alterations cause changes in the gene's product, the protein. Other sorts of damage include moving part of a message from one place to another, or losing a gene altogether.

These errors can lead to cancer in two different ways. They can change a gene so that it makes a protein which spurs the cell on to unrestrained growth. Or they can cripple a gene that is supposed to make a protein which holds the cell in check. The effects are similar. The first class of cancer gene is the oncogene, originally found in viruses that infect chickens and other animals. Virally induced cancers are thought to be rare in humans; but oncogenes do not have to be shipped in with viruses. They can be home-grown, resulting from damage to a normal gene known as a proto-oncogene.

The second class of cancer genes is the suppressor gene. They were brought to light through work on retinoblastoma (RB), a rare childhood cancer of the eye. Two-fifths of its victims have inherited a predisposition to the disease: each of their cells contains only one functioning RB gene. The other is an inherited dud. (Almost all the genes in a cell are found in pairs, one from each parent.) When a cell loses its sole functioning RB gene, it becomes cancerous.

Little is known about the protein described by the RB gene except that it binds to DNA, which suggests that it may regulate other genes. Still it seems almost certain that its role is to keep cell growth under control. When a cell loses both its RB genes, and has no way to make the RB protein, it goes on to multiply inexorably. The idea that cells contain such suppressor mechanisms is not new. Decades ago Dr. Henry Harris, at Oxford University, tried fusing cancer cells with healthy ones. The fused cells stopped growing. The suppressor gene from the healthy cells kept the growth in check.

Suppressor genes and their products have now been found to be missing in a number of cancers. The RB gene is lost in about 40 per cent of bladder cancers, in almost all lung and bone cancers and in breast-cancer tissue. Several other cancers have been shown to have missing genes on particular chromosomes, the cell structures on which DNA is arranged. These missing genes may well be suppressors. Dr. John Minna of the NCI believes that lung cancer may also involve suppressor genes.

The two ways in which genes cause cancer correspond roughly to the two ways in which cell growth is regulated. Some proteins stimulate growth, others inhibit it. The balance between them determines the outcome. Too little inhibition can lead to cancerous growth as surely as too much stimulation does. Oncogenes direct the production of the growth promoters and suppressor genes direct the growth inhibitors. The process of regulation is complicated. On the surface of the cell there are receptor proteins which receive messages from elsewhere and transmit them into the cell. These messages are sent by various routes to the cell's DNA, which then takes appropriate action, either speeding up or slowing down cell growth. The receptors, the message carriers and the mechanisms that control the DNA all rely on proteins. So there are many stages at which a mutated gene can cause cancer.

The sis oncogene produces a growth factor which excites the receptors on the cell surface. Another oncogene, called erbB, which was identified in 1984 by ICRF, Genentech (a Californian biotechnology firm) and the Weizmann Institute in Israel, produces a receptor protein. The normal version of the receptor sits astride the cell's outer membrane. When it comes across a particular growth factor on the outside, it passes on a message inside which makes the cell reproduce. The erbB oncogene, found in avian erythroblastosis virus, produces a stunted receptor, locked into a form which continually sends signals into the cell, thus stimulating reproduction without hindrance.

The protein described by the ras oncogene seems to work at yet another level - that of the G-proteins. These G-proteins are found stuck to the inside face of the cell's membrane, and activate the "secondary messengers" which pass instructions from the perimeter of the cell to the DNA. Further down the growth-signal chain, the products of the fos and myc oncogenes influence molecules in the cell nucleus, affecting the process of growth at the level of DNA.

Dr. Robert Weinberg, one of those who put together the story of retinoblastoma at the Whitehead Institute in Massachusetts, and some colleagues at Cold Spring Harbor, on Long Island, have found oncogenes that work by blocking the effects of suppressor genes. They found proteins from a human cancer-causing virus which stick to the protein described by the RB suppressor gene and stop it from working. By blocking the RB protein they produce much the same effect as would be seen if the RB gene was not there in the first place.

In a network of chemical commands as complex as the one that regulates cell growth, it will often take more than one genetic error to cause a cancer. This explains why cancer is, for the most part, a disease of the old. The longer you live, the more time there is for things to go wrong. It is not often the case that one mutation will cause a cancer. In childhood cancers like retinoblastoma there are two mutations: one inherited, the other acquired later. Adult cancers may have four mutations or more.

The best evidence for this comes from colon cancer. Its progress is easy to follow. Colon cancer usually appears first in a benign form, as an "adenoma". The adenomas may form polyps. Eventually the full-blown malignant carcinoma appears. This progression has been liked with four different mutations. Specific genes on three different chromosomes are lost or damaged and there is also a role for the ras oncogene. A recent study by scientists from Johns Hopkins University in Baltimore, the University of Utah, and the State University of Leiden in Holland, looked at 172 different colon specimens. It found that the ras mutations and deletions from one of the chromosomes were found in all stages of the disease. Deletions from the other two chromosomes, numbers 17 and 18, were usually found in advanced tumours. That suggests a sequence of mutations, all of which have to be present if the disease is to become serious. The evidence is not clear cut, though; some specimens did not show all the genetic alterations, and in some they appeared in different sequences.

The challenge for doctors is to translate limited understanding into treatments. They have come up with several ideas and a handful of new

products to be tested. One promising field is diagnostics. A technique called gene amplification, which has been available for a couple of years, allows the presence of a gene to be ascertained from a small blood sample.

Better diagnosis might improve the outlook for victims of breast cancer by 10-15 percentage points. That may not sound like much; but survival rates after diagnosis of breast cancer have barely crept from 61 per cent in the 1960s to 62 per cent today. Collaborative Research in Lexington, Massachusetts, is developing a genetic probe that can spot erbB-2. There is also a chance of moving beyond diagnosis to treatment. Dr. Bill Gullick of Hammersmith Hospital in London is working on a drug that can counteract the effects of erbB-2. To pass on growth signals from outside the cell, the erbB-2 receptors have to team up in pairs. Develop a chemical that can bloc. their coupling and you can stop transmission of the growth signal.

Dr. Enrique Rozengurt at the ICRF is working on a drug for small-cell lung carcinoma, which accounts for a quarter of all lung cancers. He has focused his studies on a molecule known as bombesin, a powerful promoter of growth secreted in bulk by the lung tumours. Its receptor molecule is like the one associated with G-proteins. Dr. Minna at NCI believes that between them they have found another autocrine loop, like the one described for the sis gene. Large quantites of bombesin are produced by the cancer cell, and then interact with receptors on the surface of the same cell, thereby making the cells divide needlessly. The hunt is now on for a chemical that can block bombesin receptors and thus break the loop. However, even if chemicals are found to block bombesin receptors or the formation of erbB-2 pairs, they might not halt the disease; other genes may be involved. Still, such therapies might be a significant help.

Most of the research effort is concentrated on similar attempts to thwart the oncogenes; researchers find it easier to block an unwanted cellular activity than to replace a lost one. However, for suppressor-gene cancers, doctors are looking at the possibility of gene therapy - replacing defective suppressor genes with healthy ones. The first experiments towards such therapies have just begun under the auspices of America's National Institutes of Health. White blood cells with added genetic markers have been given to patients dying of cancer in order to see how the cells penetrate tumours. Eventually, tumour-fighting genes, rather than innocuous markers, might be introduced. But it will be a long time before gene therapy produces results, if it ever does. The healthy gene must be delivered to almost every tumour cell and an efficient system needs to be developed for getting the gene into the cells.

There is an alternative approach, the body's own defences. The immune system can deal with cancer to a certain extent. With pharmaceutical encouragement, it might become invincible. This was the thinking behind a wave of enthusiasm which greeted cytokine drugs in the early 1980s.

The cytokines are a ubiquitous family of molecules, produced by a wide variety of cells, which play a role in regulating the immune system as well as a host of other bodily functions. They have been found to interact with growth factors and to have much in common with them. Both types of molecule may belong to one big family of cell regulators.

There are plenty of cytokines: about 20 different sorts of alpha-interferon have been picked out. Many work alongside others and their effect together may be quite different from the effect each has alone. So it is impossible to know what will happen when a cell is bombarded with a cocktail of cytokine messages. Unsurprisingly, doctors have run into difficulties when using such drugs on people. Clinical trials of some cytokines have had to be abandoned; they provoked lots of side-effects because their activities were so wide-ranging.

Nevertheless, several other cytokines have followed alpha-interferon through clinical trials. The closest to approval in America are interleukin-2 and colony-stimulating factors. Both were discovered more by luck than by judgment. Interleukin-2 works on only a minority of cancer patients, such as those with melanoma or some cancers of the kidney. It also causes nasty side effects.

Dr. Steven Rosenberg and his colleagues at the NCI have investigated ways to administer the drug. At the moment he is working on tumour-infiltrating lymphocytes (TIL), immune cells that can be isolated from human tumours and grown in interleukin-2 in the laboratory. The cells are then returned to the patient and, according to Dr. Rosenberg, they prove to be highly efficient killers of cancer cells. So far nobody has been able to repeat their findings. A few patients are being treated with TILS and other cytokines.

There are four different colony stimulating factors (CSFs). These aroused interest because they promote the growth of white blood cells (at least in the test-tube). They are now being used to speed the recovery of bone marrow that has been damaged by conventional drug treatment. Patients on such a regimen can be given higher doses.

Cytokine research and oncogene research have different roots; one springs from cell physiology, the other from genetics. Yet they are growing in the same direction. In the mid-1970s scientists discovered a cytokine known as transforming growth factor beta (TGF-beta). An inappropriate name: although it stimulates growth in some cells, it is a powerful inhibitor of growth in others.

Immunologists are also exploring the possibility of cancer vaccines to prod the immune system into action. The trouble is that vaccines usually work by priming the body's immune system to recognize parts of invading viruses, bacteria or any foreign bodies that are found on the surface of the disturbed cells. Oncogene proteins are mostly found inside cells. But research suggests that they may sometimes be brought to the surface. And receptors like the erbB protein are naturally found on the surface. So it may yet be possible to design a cancer vaccine.

Then there are monoclonal antibodies, proteins that seek out and stick to particular molecular structures. In theory they should let scientists aim anti-cancer drugs, poisons and radioactive chemicals directly at tumour cells, thereby avoiding any harm to healthy neighbours. About 20 monoclonal antibodies, developed by various biotechnology and pharmaceutical firms, are being tested on people. Although scientists have been unable to select any tumour specific targets (that may come later when more oncogene proteins are recognized) they can use antibodies which recognize molecules found only in

specific tissues. It also helps that chemicals which bind drug and antibody solidly together have been discovered.

Unfortunately, antibodies are too big to penetrate the central parts of solid tumours easily. They are best at killing off free-floating cells and so come into their own when dealing with leukaemias and other cancers of the blood, or when mopping up cancer cells spreading out from a tumour.

There are other routes to new drugs or better treatments, of less stimulating scientific pedigree, but no less valuable when they produce the goods. New drugs to fight nausea permit the use of higher doses of anti-cancer drugs.

The conclusion must be that some cancers are curable and more will become so. But there will never be a single cure for cancer. The proteins described by cancer genes may share common functional features. Yet the variety of cancer genes that give rise to tumours makes it inconceivable that any one drug could tackle more than a few of the 200 forms of the disease. (Extracted from The Economist, 5 August 1989)

Manipulating genes

It is almost routine now to introduce new genes into plants and animals. For example, genes controlling resistance to disease or to herbicides have been introduced into some plant species.

A more recent approach has been the idea of knocking out the activities of particular genes whose activities may be in some way damaging. An exciting piece of Australian technology, developed in the last two years, seeks to put this approach to practical use. The "gene shears" technique, discovered by the CSIRO Division of Plant Industry, involves molecules that seek out and destroy target RNA molecules. This appears to be a considerable improvement on earlier "antisense RNA" technology where target RNAs were inactivated by attachment but not specific destruction.

Understanding how the "gene shears" molecules work and improving on them is a goal in CSIRO's Division of Biotechnology, through structural and functional studies on the ribozyme molecules and their interaction with other RNAs.

"We have taken both antisense RNAs and ribozyme RNAs, singly and in combination, and have been able to suppress expression of a target gene, in animal cells, in the laboratory", explained Dr. Phil Jennings. As a result, the Division of Biotechnology is now participating with the Plant Industry Division in a much expanded research programme.

The techniques, if they can be perfected, will be extremely useful to medicine and industry as well as in agriculture. (Source: Biotopic, Vol. 1, No. 1, Spring 1989)

D. APPLICATIONS

Pharmaceutical and medical applications

Potential of artificial cells

Artificial cells might be developed to produce insulin or replace human blood cells. Phospholipids from cell membranes can already be used to form liposomes with varying thickness membranes. Artificial cells containing activated charcoal have already been used to clean the blood of some types of blood poisoning. Artificial cells might be loaded with enzymes to replace enzymes that are lacking in people with phenylketonuria (PKU). Artificial cell membranes might even be developed to enclose pancreatic cells to protect them from attack when they are injected into the bodies of diabetics. Human trials could begin at the University of Toronto by 1991. Artificial cells might also be able to deliver drugs. At least 10 firms have now applied to the United States Federal Drug Agency for permission to test liposome drug delivery systems. Such drugs might be worth $2 billion by 1995. (Extracted from New Scientist, 3 June 1989)

Malaria vaccine

A further step towards the development of a malaria vaccine has been reported by researchers at New York University.

In experiments with mice, Professor Ruth Nussenzweig has been able to show that a subset of the white blood cells of the immune system are able to prevent the growth of malaria parasites when in the form known as the sporozoites.

In humans, malarial parasites in the sporozoite form first lodge in the liver, but are then converted into forms that circulate in the red blood cells.

The importance of Nussenzweig's research is that it identifies for the first time a part of one of the protein molecules of the sporozoite coat which appears to provoke the natural immune response in mice.

The work is being supported by Swiss company Hoffmann-La Roche. (Source: European Chemical News, 2 October 1989)

Malaria vaccine setback

Newly discovered heterogeneity in the human malaria agent Plasmodium vivax will add further complexity to the development of an effective malaria vaccine. A key candidate for malaria vaccines has been a nine-amino acid repeating segment of the parasite's major surface protein, the circumsporozoite (CS) antigen; the nonapeptide has generally been found to be conserved among isolates, is repeated often in the CS molecule, and is able to elicit immune responses. However, R. Rosenberg and colleagues at the Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand, report that in a western province of Thailand over 14 per cent of sampled malaria parasites had a different nonapeptide. These novel organisms evade detection by tests based on the standard nonapeptide and make counts of malaria-infected mosquitoes inaccurate; furthermore, no protection against these strains is likely to be provided by a vaccine elicited against the standard nonapeptide. (Abstracted with permission from Science, Vol. 245, p. 903, 1 September 1989 by Ruth Levy Guyer. Copyright 1989 by the AAAS)

Understanding of drug resistance may lead to malaria vaccine

Better malaria drugs could be developed by better understanding how tumour cells and parasites develop drug resistance. Much drug resistance in tumour cells is due to P glycoprotein transporting the anticancer drugs out of the cell. Multidrug

resistance (mdr) genes are also present in Plasmodium falciparum, according to researchers at the Harvard School of Public Health and the Walter & Eliza Hall Institute (Melbourne, Victoria, Australia). Some parasites resistant to chloroquine have multiple copies of the mdr gene. The gene is also similar to a gene that transports pigment in Drosophila, which may help explain why chloroquine affects pigmented tissue in humans (skin and retina). Verapamil can partly overcome mdr in cancer cells, and perhaps can be useful in the treatment of malaria.

Another drug being tested against malaria blocks DNA replication in the parasite, just as some anticancer drugs do. Resistance to the drug apparently involves modifying it so that its active site is no longer active. (Extracted from New Scientist, 29 July 1989)

Influenza cure closer

A team of scientists led by Dr. Peter Colman has brought a cure for influenza that much closer to reality with the development of a novel compound based on knowledge of the three-dimensional structure of a key protein - the enzyme neuraminidase - on the surface of the influenza virus.

CSIRO is collaborating with the Victorian College of Pharmacy and Biota Holdings, an Australian company which owns the technology under a licensing agreement with CSIRO.

The group's work has shown that despite the influenza virus' ability to change constantly, a key portion of the neuraminidase molecule remains the same.

Most drug action is the result of the drug binding to a specific target, often a protein molecule, in the body.

The basis of these discoveries has been CSIRO's division of specialized knowledge in X-ray crystallography.

Once the target was identified, crystallizing the protein was the necessary intermediate step to enable the researchers to see its structure in sufficient detail. This done, drugs were designed to fit precisely into the structure making up the active region of the neuraminidase using computer modelling techniques. These first drugs have been tested by the pharmaceutical company, Glaxo, and have shown sufficient promise to excite the company's interest in further collaboration.

A new wave a pharmaceuticals based on this approach will only be possible, according to Dr. Colman, if there are enough "design"-oriented scientists who know how to match shape with shape, chemists who can tell whether the shapes are stable and easily manufactured, pharmacologists to put theory into practice, and money - $100 million and upwards.

The excitement of being on track to produce what may be the world's first truly effective antiviral drug is the spur. (Source: Biotopic, Vol. 1, No. 1, Spring 1989)

AIDS at bay?

Hopes that AIDS can be beaten soared after the results of yet another trial with Wellcome's zidovudine (AZT) showed that the drug slows down the advance of the disease in HIV-infected people who do not yet suffer from AIDS or AIDS related complex (ARC). The trial, conducted by the USA's National Institute of Allergy and Infectious Diseases (NIAID), showed that the advance of the disease in asymptomatic HIV carriers was slowed down by half if they were treated with AZT. The trial was halted after the results became known and the placebo group was also put on AZT.

The new results come barely two weeks after NIAID announced encouraging results for the treatment of early-ARC patients with AZT. Meanwhile there are fears that people undergoing long-term treatment with AZT may develop a resistant HIV strain.

Clinical trials on a genetically engineered AIDS drug developed by Genentech have started at the US National Cancer Institute. Immunoadhesin is based on part of the CD4 receptor and an antibody which activates killer immune cells. (Source: Chemistry and Industry, 4 September 1989)

AIDS drug price is cut

Burroughs Wellcome Company has announced a 20 per cent reduction in the price of its AZT anti-AIDS drug. While the company says its motivation is mainly economic, it admits pressure from AIDS activist groups played a role.

Effective immediately the company is reducing the wholesale distributor price of "Retrovir" from $1.50 to $1.20 per capsule.

The last price change for the drug, also a 20 per cent reduction, was made in 1987, the year it was approved by Food & Drug Administration. Despite the changes, AZT remains one of the most expensive drugs sold.

With a retail markup of about 30 cents per capsule, it now sells for around $6,600 per year, down from just under $8,000 per year, for the maximum 12-capsule-per-day regimen.

However, Burroughs notes that for many patients, the price may be even lower. Recent trials among asymptomatic HIV-infected patients - those who are infected with the virus but show no symptoms - indicate a 5-capsule-per-day programme yields some benefits.

Such a programme would cost only $6 per day, wholesale, or about $2,200 per year, a 70 per cent reduction in cost of therapy versus 12 capsules per day at the drug's price when it first came out.

In fact, it is the larger market potential represented by asymptomatic patient treatment that the company says led to the price cut.

It is estimated that more than 20,000 people worldwide are now taking AZT, but that at least 100,000 and perhaps several hundred thousand more will take the drug based on the recent trial results.

Critics of the company welcome the price cut, but most say more could be done.

Analysts are of the opinion that Burroughs has already recouped its initial investment in the drug and that production costs, at anywhere from 10 cents to about 50 cents per capsule, are much lower than the new price of $1.30 per capsule. (Source: Chemical Marketing Reporter, 25 September 1989)

AIDS drug doing well in trials

Phase I clinical trials to test the safety of the proposed AIDS drug 2',3' dideoxyinosine (DDI)

"suggest that DDI can induce clinical improvement at doses that cause minimal short-term toxicity", say Robert Yarchoan and colleagues from the National Cancer Institute and Abbott Laboratories. However, they caution, toxicity could still appear at higher doses or in longer term studies. Improved drugs are needed because zidovudine, or AZT, the only drug currently approved by FDA for use against AIDS, is toxic at clinical dosage levels and tends to lose its effectiveness after a time, possibly because the AIDS virus develops resistance to it. In the DDI trials, there was little evidence of effectiveness at the lowest four doses administered, but patients receiving higher doses showed a number of positive physiological and clinical signs. The researchers hope to proceed to Phase II (effectiveness) trials later this year. Bristol-Meyers, the drug's manufacturer, has proposed supplying it free to patients who need it but cannot participate in clinical trials. (Reprinted with permission from Chemical and Engineering News, 31 July 1989. Copyright (1989) American Chemical Society)

Alpha interferon helps AZT treatment

Alpha interferon, already approved for marketing in the United States, may be effective in slowing the development of AIDS, according to small-scale studies. The drug has not been shown to prolong survival of AIDS patients, so it should not be touted as a cure. Despite the promising results of the small-scale trials, AIDS advocacy groups are being more cautious in their evaluation of alpha interferon, unlike their lively approbation of other experimental drugs that show some promise. Results of the latest small-scale trial, published by A. Fauci of NIAID, indicate that alpha interferon and AZT together can treat AIDS and Kaposi's sarcoma. Adding alpha interferon allows AZT doses to be reduced. In a test of alpha interferon and AZT, patients who received both drugs lost 4 per cent of T-4 cells while those who received AZT alone lost 25 per cent of their T-4 cells.

Researchers at Cornell University and the University of California (San Francisco, USA) agree that alpha interferon is underused in treating AIDS. The interferon apparently inhibits replication of the virus inside cells. Alpha interferon is specifically approved for treatment of hairy cell leukaemia, genital warts and Kaposi's sarcoma, but an approved drug can be prescribed for any indication at a doctor's discretion, so it could immediately be used against AIDS. The lukewarm acceptance of alpha interferon may be due to its high cost or its influenza-like side effects. The lower doses used in the newer studies greatly reduce side effects. (Extracted from New York Times, 15 August 1989)

AIDS drugs doubled

The number of AIDS drugs and vaccines being developed has nearly doubled in the last two years, growing from 35 to 67, according to Pharmaceutical Manufacturers Association's latest survey of AIDS medicines in development.

The association also announced that the American Foundation for AIDS Research (AmFAR) has joined with PMA to jointly collect data on emerging treatments for AIDS.

According to PMA's updated survey, 55 companies are developing drugs and vaccines for AIDS compared with 40 companies in 1987. In development by category are: 20 antivirals, 13 cytokines, 11 immunomodulators, 15 anti infectives, seven vaccines, and two others.

A new category - cytokines - has been created to better reflect the most current terminology in this area of medicine, says PMA. Cytokines are naturally occurring proteins that regulate or modify the growth of specific cells.

The vaccines listed in the report are all in clinical tests. In 1987, PMA made an exception to its criteria for listing only medicines in clinical tests because there were no vaccines being tested in people. Fourteen medicines are being tested in combination with "Retrovir", two with "Cytovene" and one with gamma interferon. There was only one drug approved in 1987 - "Retrovir".

While that drug remains the only therapy approved to treat HIV, PMA's latest report lists eight others that have been approved to treat AIDS-related conditions. (Extracted from Chemical Marketing Reporter, 24 July 1989)

Sulfolipids versus AIDS

The United States National Cancer Institute (Bethesda, MD) reported in its journal that some blue-green algae extracts are "remarkably active against the AIDS virus" in in vitro tests. The compounds involved - derived from Lyngbya lagerheimii and Phormidium tenue - are sulphonic acid-containing glycolipids. The NCR scientists say several chemicals derived from blue-green algae have proven to be highly active against the AIDS virus in test tube experiments. They say the discovery means a new class of chemicals can now be studied for effectiveness against the deadly disease.

Tests of the chemicals in humans cannot begin until scientists are able to make them in much larger quantities and assess their impact in animal laboratory studies. But Mr. Michael R. Boyd, head of the NCI research team, says that because of the urgent need to identify new drugs that might have the potential to treat AIDS, the institute has assigned further tests on the chemicals a high priority.

The new chemicals are combinations of sugars and fatty acids called glycolipids. They were derived from algae collected in Hawaii and the Palau Islands in the South Pacific. Dr. Boyd says the glycolipids halt the growth of the AIDS virus, but researchers do not yet understand how. (Source: Chemical Week, 23 August 1989, and Chemical Marketing Reporter, 28 August 1989)

Yeast system for new drugs

A biotechnology company has licensed Phillips Petroleum Company's Pichia pastoris yeast gene expression system to make human pharmaceuticals.

Under the general, non-exclusive licensing agreement, Chiron Corporation, Emeryville, California, USA, will evaluate the production potential of the Phillips-owned yeast strain across its product line.

The company will first research the feasibility of using Pichia to produce its products, potencially including studies for the full range of Chiron's proteins: growth factors, enzymes, vaccines and diagnostic antigens.

Chiron now produces 19 products, 12 of which are in clinical trials or on the market, most of them expressed through various strains of yeast.

The yeast strain has several production advantages over other expression systems such as

bacterial, mammalian cell or even other yeast strains. Several of the organism's specific advantages are:

- As a methylotrophic yeast, it expresses genetic products while growing on a simple medium, in a clean production process without the effluents which require treatment in some other genetic expression systems;

- Pichia secretes into the medium many of the proteins and enzymes it expresses. Secreted genetic products often require less laboratory manipulation than proteins produced and held within a host cell;

- The material secretes few native proteins. Therefore, the recombinant products it secretes may require only a few purification steps;

- Recombinant products from Pichia are biologically active, soluble and demonstrate proper glycosylation and protein folding, making them similar to those same products found in humans;

- A single protein can make up 35 to 40 per cent of the material's total cellular protein. Some foreign genetic materials have been expressed in Pichia at similar high levels;

- The organism has been produced at cell densities above 400 grams per litre. Productivity scales up linearly from laboratory scale to large-scale commercial production levels. (Source: Chemical Marketing Reporter, 11 September 1989)

Anti-plaque enzyme development

Utilizing recombinant DNA technology, Synergen has developed a protein intended to prevent gingivitis, an inflammatory condition of the gums that precedes frank periodontal disease. The company has announced they had signed an agreement with Colgate-Palmolive to evaluate the technology for the prevention of periodontal disease. The agreement calls for Colgate to test compounds developed by Synergen in Colgate's pre-clinical models and to share the results with Synergen.

Research conducted by Synergen has validated the technical feasibility of using recombinant DNA to create novel enzymes that adhere to the surface of teeth and arrest the build-up of dental plaque. Colgate will now focus on investigating this technology in combination with anti-plaque agents as a prophylactic against periodontal disease. Colgate is already working with Vipont Pharmaceutical's sanguinaria ingredient for the prevention of plaque and is scheduled to test market sanguinaria containing toothpaste in Europe in autumn 1989. (Source: Company News Release, July 1989)

Wound healing and dental advances

New biomedical and biomaterial manufacturing technologies are benefiting from scientists' increased understanding of connective tissue proteins, particularly the collagens.

Knowing how these proteins interact with living tissue helps to create new products which are safe, effective and high value added.

Connective tissue proteins are among the most abundant of animal proteins. Because of this, collagen, for intance, features prominently in many manufacturing contexts - the leather industry, and the production of gelatine and sausage casings.

In medicine, knowledge of these proteins is helping to create biomaterials useful in a variety of applications, including dental, ophthalmic and vascular.

In collaboration with the University of Melbourne, and Wallace Biomedical, CSIRO's Division of Biotechnology is working on creating cost-effective biomaterials based on collagen.

Animal trials are already in progress to evaluate suitable materials for wound dressing.

For periodontal use, the team is working on a material which is integrated into the patient, and so does not require subsequent removal as is often the case with synthetic polymers.

As another example, a vascular prosthesis (replacement blood vessel) manufactured from sheep collagen by BioNova NeoTechnics, has been examined after explant from model studies in dogs. Antibody assays indicate that the animal has successfully accepted the prosthesis and augmented its structure with its own tissues.

In addition, monoclonal antibodies to collagen have been developed in the Division in recent years with the help of financial support from the Medical Engineering Research Association (MERA). These are being used to evaluate the in vivo performance of biomaterials. (Source: Biotopic, Vol. 1, No. 1, Spring 1989)

Could "oligos" be the blockbuster drugs of the future?

Oligonucleotides, short stretches of DNA or RNA better known as "oligos" in the biotechnology business, are attracting a good deal of attention, particularly in California. They can be produced easily - if not yet cheaply - on gene synthesizers. Although it is probably at least a decade before they amount to anything, the hope is that they will prove to be the blockbuster drugs of the early twenty-first century.

Most conventional drugs work by attacking proteins linked to a disease or malady.

Unfortunately, this is rather like using a pharmaceutical sledgehammer, with the result that such drugs often produce unwelcome side-effects. So bioscientists are now looking for ways of developing drugs targeted directly at the genes that make those "unhealthy" proteins.

A key question is whether such gene drugs should be aimed at DNA, "raw" RNA or messenger RNA. Among the first wave of "gene drug" companies launched in the United States are two located in California: Gilead, based in Foster City, and Isis, based in San Diego.

Gilead has opted for DNA, while Isis is designing oligos that block RNA in cell nuclei. Isis thinks its approach of tackling RNA, which is concentrated in one place, is best because it is easier than the favoured route of tackling messenger RNA, which tends to be dispersed throughout the cell. But Isis is covering itself: it is also

working on "anti-sense" drugs aimed at messenger RNA. (Source: Biotechnology Bulletin, Vol. 8, No. 6, July 1989)

New approaches to vaccines

Modern molecular biology is making it possible to produce cheap, safe and effective vaccines. But before they can be pronounced safe and become marketable, a number of problems associated with their development must be overcome.

CSIRO is tackling several of these, with some success.

One of the world's first genetically engineered sub-unit viral vaccines for veterinary use is being developed in collaboration with Arthur Webster Pty. Ltd. and the CSIRO Division of Animal Health.

The vaccine is a weapon against infectious bursal disease virus (IBDV), which causes immune deficiency in poultry, making them vulnerable to other infections. While not necessarily fatal, IBDV slows down the growth rate of commercially-raised chickens, extending the time they take to get to marketable weight and causing considerable economic loss.

Much of the work has been based on a scientific understanding of the structure of proteins and genes and how that information can b capitalized upon.

Viral diseases cause millions of dollars damage to the poultry industry each year. The international market for this vaccine is potentially large, because the disease is significant in all regions around the world where poultry is produced. (Source: Biotopic, Vol. No. 1, Spring 1989)

Livestock applications

Vaccine against sheep tapeworm

Coopers Animal Health is developing a genetically engineered vaccine for use against tapeworm in sheep. The tapeworm parasite Taenia ovis causes a disease known as sheep measles because of spotty cysts in the muscles, which make the meat unsuitable for export. Trials in New Zealand have shown the vaccine to be 95 per cent effective. Coopers says the vaccine will be available in two years. Academic, government and industry researchers are considering developing vaccines against other parasitic animal diseases, such as beef measles, pork measles and hydatids, all of which can also affect humans. The sheep measles vaccine is based on research done in 197. at CSIRO showing that proteins released from the tapeworm egg can be effective as a vaccine. Actual production of such a vaccine had to wait for genetic engineering techniques to be developed. mRNA from the parasite eggs was used to produce cDNA for inclusion in E. coli which then produced the necessary antigens for a vaccine. (Extracted from New Scientist, 15 July 1989)

Stirling Diagnostics pioneers plant and fish health monitoring service

A rapid, state-of-the-art disease detection and monitoring service for freshwater and seawater fish and a wide range of plants and cereals is being pioneered by a British aquaculture and agriculture health care company, Stirling Diagnostics Ltd. (SDL). Already the company is monitoring and diagnosing disease in farmed fish, mushrooms, cereals, potatoes and ornamental plants. Among mushroom growers alone, preventable losses from viral and other diseases world-wide are estimated to be in the order of 225 million pounds sterling.

In their purpose-built facility, the company's scientists employ a full range of techniques such as ELISA (enzyme linked immunosorbent assay), PAGE (Poly Acrylamide Gel Electrophoresis), tissue culture and ISEM (electron microscopy), complemented by a series of diagnostic kits which can analyse samples within hours rather than the usual days. (Source: Biotechnology Bulletin, Vol. 8, No. 8, September 1989)

Blind blowflies tackle deadly sheep disease

Scientists at the CSIRO, Australia's national research organization, have released the pupae of genetically manipulated blowfly en masse on the Furneaux Islands, a remote group of islands north of Tasmania. The release is part of a long-term experiment to combat fly strike which can kill sheep. Over the next two years, the scientists will release more than 400 million pupae, which each take about two days to turn into flies.

The female sheep blowfly (Lucilia cuprina) causes fly strike when it lays eggs in areas of the sheep's fleece close to infected sores. Maggots feed on the sores and enlarge the wounds. In Australia, sheep farmers lose up to A$250 million a year because of the disease. Meat production suffers and the wool fibre weakens, reducing the value of the fleece. Untreated sheep die.

The sheep blowfly is now resistant to various insecticides with which farmers have controlled it in the past. Scientists from the division of entomology at the CSIRO have reared a strain of male sheep blowfly that is both partially sterile and contains mutant genes that confer blindness on their female descendants. A rearrangement of the chromosome which confers maleness causes the sterility.

If the partially sterile males mate with a wild female, only 45 per cent of her eggs will hatch. The female line also carries the mutant gene that will cause white eye and yellow eye in future generations. Females with this condition cannot find food and fall prey to predators.

The experiment on the Furneaux Islands will cover 2,000 square kilometres, an area about 50 times as large as that used for any previous release. After about 15 generations, the scientists hope to eradicate the fly from the islands.

Eventually Foster and the project leader, Rod Mahon, hope to release pupae of the flies on Tasmania and on parts of the Australian mainland. Agriculture departments in New Zealand have also shown interest in the work. Another goal is to release adult flies from aircraft. At present, scientists release pupae from ground stations. (Source: New Scientist, 7 October 1989)

Aquaculture opportunities for feed and drug producers

The tremendous expansion in world aquaculture is creating a dynamic new international area of opportunities for feed, chemical, pharmaceutical and other companies. United States, Western European and Asian aquaculture markets are flourishing, while Latin American, African and the Eastern European countries are poised for exceptional growth.

From its modest beginnings in the 1970s, aquaculture, or fish farming, has become the fastest

growing sector of the global feed market. Over 110 companies worldwide are producing aquaculture feeds, but the potential demand far outweighs the current supply of commercial feeds in many significant areas of the world.

Competition is not yet established for much of the global aquaculture feed market, which is expected to grow from an estimated $1.6 billion in 1988 to $6.6 billion in the year 2000. Aquaculture also offers enormous opportunities for producers of feed additives, drugs, vaccines, diagnostics and growth hormones.

By all accounts the global aquaculture industry is booming. It is one of the fastest growing areas in the food industry and the fastest expanding area of all United States agriculture. Worldwide aquaculture production of finfishes, crustaceans and molluscs rose from an estimated 6.6 million tons in 1975 to about 10 million tons in 1988, an increase of over 50 per cent in eight years. By 2000, the world aquaculture industry is likely to harvest over 21 million tons, representing a 100 per cent increase over current output. It is estimated that one quarter of the world's consumption of seafood in the year 2000 will come from aquaculture.

These numbers translate into a burgeoning aquaculture feed market, which has risen from an estimated 1.7 million tons in 1980 to over 3.6 million tons in 1988. Asia and Oceania assume almost half of the market with most of the other half going to farmers in Western Europe and the United States. By 1990, the worldwide aquaculture feed market is expected to exceed 4.3 million tons and be worth over $21 billion. The market is expected to triple in the 1990s, with sales of over 14 million tons by 2000.

To some degree the rapid increase in aquaculture is partly due to the availability of greater acreage, but gains through increased feeding efficiency have greatly contributed to this. Expansion in aquaculture clearly depends on the availability of better food. Major areas within the aquaculture feed industry include markets for fish meal soybean substitutes, fish pigmentations, delivery systems, vitamins and minerals, in-feed medications such as antibiotics, and a range of other feed ingredients and additives.

Feed is a high value item in aquaculture, and top prices are paid for premium products. Fish itself has a higher value item/pound than most other livestock and many aquaculture producers are willing to invest more money/fish pound on better quality feeds than other animal producers. This is especially true in the United States, Western Europe and Japan.

An increasing number of feed firms, not traditionally involved in aquaculture feeds, are now realizing the tremendous opportunities in this area. Vertical operations that include their own research, development and production of aquaculture feed, the management of fish farms and even fish processing plants are becoming more common as businesses take advantage of the profits available in all levels of the aquaculture industry. The industry is luring such diverse investors as chemical, food, tobacco, public utility, oil, insurance, construction, pharmaceutical, biotechnology and crop agriculture firms. But it is important to note that while investors are entering the industry, the markets are still very open, particularly internationally.

To some extent the aquaculture feed market is different from the traditional feed markets because it also touches upon plant agriculture. Many farmers are supplementing or even replacing their crops with aquaculture operations. Also, commercial fishery companies are beginning to enter the aquaculture business as their catches have been levelling off and even declining in recent years. It is likely that in future, companies will be establishing more relations with both plant agriculture firms and commercial fisheries.

Aquaculture is one area where the established feed industry will be developing brand new and broader marketing networks. Feed companies entering the market will be forming new channels of distribution as well as new relationships with firms not traditionally involved with feeds.

It is becoming increasingly imperative that feed firms move quickly to establish market shares while the aquaculture feed business is still relatively young. Nowhere is this more important than in the developing nations, which hold well over 85 per cent of the world's aquaculture. Most aquaculture harvests are in Asia and the Pacific Rim countries.

The aquaculture industry in Asian countries is enormous. There are an estimated 8 million hectares in production for coastal aquaculture activities in Asia. Some 16 Asian nations are responsible for producing about 79 per cent of the world's aquaculture products.

The prospects of expanding export sales of aquaculture feeds will be different for each group of countries. Trade with highly developed Asian nations such as Korea, Taiwan and Japan will differ from trade in still developing nations such as China and India. The demand for aquaculture feeds in Japan, Taiwan and Thailand should increase at a much faster rate than that of China and India, because consumer's diets in the lesser developed countries are still switching from grains to meats. However, due to the enormity of the aquaculture industry in China and India, these countries could prove to be the most important markets for long-term exports of aquaculture feeds.

There is presently little competition in the aquaculture feed market in most of Asia. However, in the future, United States, European and Japanese aquaculture feed exporters are likely to be competing with an ever increasing number of Asia-based small feed firms, who are expected to start producing their own aquaculture feeds.

Also, many Asian Governments attempt to protect their industries by limiting imports, and this may present the greatest challenge to producers who want to export to this region. The markets are growing so rapidly, however, that most firms will want to meet this challenge.

In some cases, large established feed firms will find it advantageous to either form joint ventures with smaller local producers or purchase them outright to gain market share in a particular region.

Aquaculture feed manufacturing in most Asian nations has been severely restricted because of the lack of capital and technological know-how. China, for example, recently purchased several large aquaculture feed processors but failed to bring them on line due to a lack of expertise. In the immediate future, such areas are likely to rely heavily on imports of aquaculture feed, and joint ventures with foreign firms to satisfy their domestic markets.

There is also a problem in developing marketing strategies for these areas because of the broad range of aquaculture systems in operation. Not only does each species of fish have its own nutritional requirements, but farming practices differ among producers of the same species.

These different practices also have unique feed demands. In addition, traditional methods of farming are sometimes so strong that new products are not accepted. The majority of aquaculture producers in developing nations use farm by-products and pond algae to feed their fish and shellfish.

It will take a substantial marketing effort to convince them that the use of costlier commercial pre-mixed aquaculture feeds results in higher productivity and better profits.

Behind Asia, Western Europe occupies the second largest aquaculture feed market. Although much of the aquaculture industry is in mollusc production, it is the trout and salmon markets that are the most important to aquaculture feed manufacturers. Europe has some of the most advanced intensive operations in the world, and the demand for the highest quality feeds is unparalleled. Salmon and trout farming is dominated by Norway.

Business opportunities are exceptional in the rapidly expanding North American feed market. Recent trade agreements, opening up markets between the United States and Canada, could play an important part in the feed industry, particularly in face of the growing economic power of the European Community and its own imminent dismantling of internal trade barriers.

Two of the key areas for development in aquaculture are therapeutics and diagnostics. Aquaculture production can easily be jeopardized by disease, especially in intensive systems where, just like in livestock production, crowding is both a source of stress and can facilitate the spread of infection. Aquaculture producers undergo major economic losses due to disease.

More veterinary medicine companies and other pharmaceutical concerns are turning their attention towards the development of aquaculture therapeutics to meet growing demand. The presence of disease may be the most prohibiting factor in the growth of aquaculture worldwide.

It is no wonder that in 1987 aquaculture was highlighted at the fourth annual United States IR-4/FDA Workshop for Minor Users of New Animal Drugs. Aquaculture is the fastest growing minor species industry in the United States, and most other countries, but aquaculture therapeutics are far less available than for other animals. Tremendous opportunities are available to feed and pharmaceutical companies investing in the R&D of in-feed and water-applied medications for aquaculture.

Leaders in livestock and poultry feed additives see aquaculture as the next wave of growth in the industry. It should be stressed that feed and pharmaceutical firms who are already involved in developing and producing feed additives for livestock and poultry are in a good position to transfer technology to the aquaculture industry. While traditional markets are growing moderately, aquaculture can provide the key to boosting sales.

Today there is a substantial push in the aquaculture industry for more co-operative government policies and procedures to aid in the development of aquaculture medications. Advocates for United States catfish farmers, for example, are uniting to pressure the United States Department of Agriculture to step up programmes designed to license drugs to fight pond bacteria. There is an urgent need for pharmaceutical manufacturers, producers and distributors to become more involved in the drug and chemical registration process so that the aquaculture industry can continue its growth. The principal block to pharmaceutical registrations for aquatic species has been the lack of major species in aquaculture as compared to say mammalian livestock. However, now that aquaculture farming has become such an important economic force in the global food industry, a great amount of R&D activity is beginning among firms competing to capture their own share of the aquaculture therapeutics markets.

Producers also need reagents that would allow for the rapid diagnosis of diseases. Effective on-site diagnostic tests are badly needed to detect diseases at their earliest stage. Over 17 companies worldwide are involved in aquaculture diagnostics.

There is much room for improved products in the area of disease control, especially involving vaccines and substitutes for antibiotics. The widespread problem of disease has been countered with high amounts of antibiotics, which in itself is becoming a health concern to consumers. In Norway, for example, aquaculture farmers applied over 17,000 kg of antibiotics to their cultures in 1985. By 1987, this figure jumped to over 40,000 kg. As a result, antibiotic consumption in the aquaculture industry now exceeds the combined intake of human and veterinarian medicine on the Norwegian mainland.

The greatest problem with the antibiotics explosion in aquaculture is the question of the development and spread of resistance. Marine microbes can develop resistance in the same way as mammalian organisms. The fact that resistance is transferable means it can at a later stage be spread to human pathogens. The antibiotics that are commonly given to fish include sulpha/trimethoprim, furazolidone, oxytetracycline, and oxolinic acid.

One way around the problem of antibiotics could be through the use of vaccines. Vaccines are becoming an integral part of aquaculture, yet there are still dozens of major diseases for which vaccines are greatly needed. In Scandinavia and parts of the United States, for example, 80 per cent of the salmon and trout were vaccinated in 1988, up from only 5 per cent in 1984, but diseases still caused hundreds of thousands of dollars in losses.

The use of vaccines will mean a much larger output from hatcheries for all types of fish and shellfish. Besides increasing survival rates, vaccines can also increase maturation rates and spawning efficiency.

Salmon, trout and catfish are three areas with good potential markets for vaccines since all three species are farmed in industrialized nations where those in aquaculture are on the whole better educated to advanced aquaculture techniques, and are in a better financial position to purchase vaccination programmes. The Japanese market is particularly strong for producers of aquaculture therapeutics.

The vaccines market in developing nations will probably not be significant until the mid-1990s unless firms can establish either a comprehensive

marketing and distribution programme of their own, or form an agreement with state and/or local authorities in specific regions to institute vaccination programmes. The latter option could become more viable as Governments realize the huge benefits aquaculture holds for their economies. Many Governments in industrialized nations have already instituted awareness programmes and are allocating funding for aquaculture.

Shrimp vaccines are liable to hold the largest markets in Asia and Latin America. The trend towards intensive farming in these regions will undoubtedly promote the sale of aquaculture therapeutics. Vaccines are currently being developed that improve the survival to maturation of female shrimp, while increasing spawning efficiency, resulting in greater profitability in the hatchery. Another vaccine prototype being tested improves survival in juvenile shrimp in growout systems.

One of the major challenges to vaccine producers is finding effective delivery systems. More often than not, delivery methods render their general use impractical. Vaccines, particularly immersion formulations, are generally somewhat limited in their effectiveness, but are inexpensive so their use may be cost effective.

In-feed medications represent an especially important area for aquaculture feed manufacturers. Aquaculture farmers generally use a premix cocktail of ingredients that includes vitamins, trace elements, minerals, amino acids and medications to add to aquaculture feed. Some products also contain an appetite stimulant to promote feeding. Medications that are active against a wide range of gram negative organisms, causing bacterial diseases of farm fish and crustaceans, are especially important.

Some companies are attempting to grow algae in quantities large enough to market as natural aquaculture feed additives. In one development, researchers are trying to get algae to produce salmon's pink colour, rather than through chemicals.

Though it is too early to say with any certainty how much impact the use of hormones to enhance growth will have on aquaculture, the potential advantages are enormous. Altered fish may keep eating and growing during the winter months when most normal fish are dormant. If so, the genetic alteration might allow aquaculture farmers to shorten the time it takes to produce full grown fish.

The Asian and Oceanian regions hold the highest potential market for fish growth hormones, but actual sales will most likely be higher in Japan than in the United States and northern countries of Western Europe. A fish hormone that improves aquaculture growth rates is already commercially available, and other hormones are undergoing trials to assess effectiveness and safety.

As the aquaculture industry grows, it is clear that more feed companies will be producing aquaculture feeds. It is perhaps the most open field in the entire feed industry today, with most of the aquaculture feed being supplied by small, private entrepreneurs. The major limitations to growth in this area seem to be marketing barriers in developing nations, but these markets are so large and open to competition that even a foothold in the area today will likely bring immediate substantial rewards, and, more importantly, provide an early jump on future competitors.

This is one area where small and medium size companies can take large market shares in a country or in a particular product line. Because smaller feed companies often have the versatility to tailor their products to individual needs, they are in a good position to do well in the highly specialized aquaculture feed markets. On the other hand, larger firms have the distribution networks to reach a wider market and may, in the long term, be better suited for satisfying worldwide demand. It may be likely that some larger corporations will buy smaller aquaculture feed concerns, rather than convert or build their own operations.

Since aquaculture is becoming more sophisticated, companies that service the industry will probably be establishing more collaborations with universities and biotechnology firms. In some cases, these collaborations will result in joint venture aquaculture farms where the parties involved can directly capitalize on innovative farm management and products.

One thing is certain about the current status of the aquaculture markets: corporations are going to have to move very quickly to assure success. Global aquaculture is growing at a tremendous rate and the industries that service it are only starting to catch up with demand. Chemical, feed and pharmaceutical companies are just beginning to jockey for position in a worldwide aquaculture industry worth billions, and within ten years many of the market shares that are presently wide open will be claimed.

Number of organizations involved in aquaculture products

Product/activity	Companies	Other organizations
Fish feeds	118	19
Fish feed additives	31	10
Vitamins & minerals	12	0
Pigments	4	0
Algae for fish feed	25	15
Fish vaccines	13	9
Fish antibiotics	13	11
Fish disease diagnostics	17	4
Fish growth hormones	8	12
Other genetic manipulations	11	28
Other products and services	12	31

(This article first appeared on 18 September 1989 in the European Chemical News and has been reprinted with permission from the publishers. The article is based on the Technology Management Group report "Emerging Aquaculture Markets - A Worldwide Study on Feeds and Veterinary Products" published in March 1989. The Technology Management Group may be contacted for further information at 25 Science Park, New Haven, CT 06511, USA. Tel. (203) 786 5445, Fax No. (203) 786 5449)

Agricultural applications

Sterile Medflies

FAO's Seibersdorf laboratories in Austria are producing sterile male Mediterranean fruit flies for release in Israel to keep populations in check. The sterile males mate with wild females, who thus produce no offspring. This is intended to eliminate or at least reduce Medfly populations. The laboratory-produced male pupae have brown coats and the females have white coats. They can therefore be separated by a colour-sensitive seed sorting machine.

This sterile insect technique should be effective in areas that are somewhat isolated from immigration from other areas. An earlier test of the technique on the Italian island of Procida resulted in a 99 per cent decline in Medly populations. Earlier elimination of female Medflies could reduce costs of raising the sterile insects. (Extracted from New Scientist, 5 August 1989)

Natural treatment for toxin

Uniroyal Chemical's Gustafson (Dallas, TX, USA) subsidiary and Morinaga (Japan) will jointly develop bacteria that prevent aflatoxin in crops. The bacterium, Bacillus subtilis, occurs naturally in Japanese soil and has been found by Morinaga to inhibit the spread of Aspergillus flavus, a mould that produces aflatoxin in peanuts, walnuts, corn and cottonseed. Morinaga is primarily a research group. The development agreement with Uniroyal was arranged by Sumitomo (Japan), Morinaga's United States agent. Morinaga and Uniroyal will share the antifungal product's development costs estimated at $1.5 million. The bacteria will be field-tested in 1990 and could be introduced by 1993. (Extracted from Chemical Week, 9 August 1989)

Pheromones emerge as specialty insecticides

AgriSense, a joint venture between Dow Corning Corporation and Provesta Corporation, reports that pheromones secreted by insects to communicate with one another hold growing potential for insect control and promise a vast market for environmentally-safe insecticides tailored to specific pests.

Pheromones are straight-chain hydrocarbons secreted by insects, usually to mate or warn of danger. They do not actually kill insects, but they can be used to disrupt mating and keep insects away from crops. The chemicals were discovered in the 1950s and first tested in the 1970s.

A spokesman for the firm sees the overall market for pheromones as vast, but expects it to break down into a myriad of niche markets for specialty insecticides. Pheromones cannot be patented and many firms are studying the market in the United States, Japan and Europe. AgriSense is currently developing pheromones to use against the Pink Bull Worm in Southwestern USA and the Great Berry Moth in Northeastern USA and the Niagara Peninsula in Canada. Two weeks ago, the firm purchased another pheromone manufacturer, Biological Control Systems Ltd. in the United Kingdom and renamed it AgriSense-BCS Ltd. (Source: Chemical Marketing Reporter, 21 August 1989)

Australian fungus controls American grasshopper

North American grasshoppers face a deadly visitor from Australia. It is Entomophaga praxibuli, a soil fungus that literally eats grasshoppers alive and then forces them to spread its spores after they die. Researchers introduced the fungus this summer to open pastureland in North Dakota in an attempt to control the grasshoppers. If the test proves successful, farmers may use the fungus to control the pests throughout the United States and Canada, where they cost an estimated $400 million per year in lost forage.

Raymond Carruthers, an entomologist for the United States Department of Agriculture (USDA) in Ithaca, New York, says that various species of Entomophaga are found in pastures across the continent, and that E. grylli is an effective control for some species. However, E. praxibuli has several advantages over indigenous species in its ability to attack the grasshoppers.

The fungus lives in the soil and spreads itself by sending up a tube with a spore at its end. It uses hydrostatic pressure to shoot this spore through the air. When a spore lands on a grasshopper it uses enzymes and mechanical force to break through the skin, then lives and reproduces inside the insect. The growing fungus "digests" the grasshopper as it grows.

One of the most remarkable characteristics of this type of fungus is the way that it controls the grasshopper's behaviour. When the insect is near to death, the grasshopper crawls up to the end of a blade of grass or the stalk of a plant, grips it, and dies. The fungus then sends out new tubes through the dead insect's skin, which shoot out spores to infect other grasshoppers.

The only way that a grasshopper can rid itself of these fungi is to raise its body temperature by basking in the sun. For instance, a grasshopper infected with E. grylli will be able to cure itself if it can raise its body temperature to 40°C and maintain this for between six and eight hours.

Carruthers says that the Australian variety, E. praxibuli, will be able to withstand higher temperatures than its American counterparts, so that even a basking grasshopper would not be safe. He adds that E. praxibuli will infect several species of grasshopper that American fungi do not attack. These advantages led researchers to import the Australian fungus, under quarantine, to the laboratory at USDA in 1984. (Source: New Scientist, 26 August 1989)

Genetically altered cucumbers to be tested

The United States Department of Agriculture (USDA) has given approval to a Cornell researcher to field-test cucumbers genetically altered to tolerate the cucumber mosaic virus. It will be the first USDA-permitted field test of a transgenic organism in New York and the first for such a test with cucumbers. Dennis Gonsalves, a plant pathologist at the New York State Agricultural Experiment Station in Geneva, developed the resistant vegetable by splicing a gene from the virus into the plant's DNA. USDA says the experiment, which has already been conducted in a greenhouse setting, began in August 1989 and will continue until frost begins. The mosaic virus causes distorted leaves on plants and reduces both crop yield and quality. (Reprinted with permission from Chemical and Engineering News, 28 August 1989, p. 21. Copyright (1989) American Chemical Society)

Advanced engineered potatoes

Plant Genetics, a subsidiary of Calgene (Davis, CA, USA), may have a way to increase the yield of United States potato farms and reduce the use of pesticides. The company says that field trials with genetically engineered Russet Burbank potato plants show resistance to potato viruses X and Y, and precisely duplicate greenhouse results. The two viruses reduced United States potato crop yields by 10 per cent/year, Calgene says. Currently there is no effective way to control the X and Y viruses. Russet Burbank potatoes account for more than 40 per cent of North American commercial potato production, according to the company, which estimates the value of the United States crop at

$2 billion/year. (Source: Chemical Week, 30 August 1989)

Building a better tomato

Calgene (Davis, CA, USA) and Cambell Soup (Camden, NJ, USA) have successfully completed field trials for tomatoes engineered with a gene that reduces polygalacturonase (PG), a naturally occurring enzyme that causes the breakdown of the fruit cell walls. Called antisense tomatoes, the fruits display increased total solid content, viscosity and consistency, with reduced rotting. The companies say they will file an application with the Food and Drug Administration to market antisense-PG tomatoes by year end. (Source: Chemical Week, 13 September 1989)

Industrial microbiology

How to make microbes make antibiotics

Microbes produce antibiotics only when they have begun to deplete their supply of nutrients and begun to flag. When the key nutrient limiting their growth runs out completely, even the production of antibiotics fails and the culture dies. So there is only a comparatively short window during the life of a culture when it makes its valuable product.

Processing developers anxious to enlarge the window have devised a way of pumping a slow feed of nutrients into the bioreactor once the microbes begin to produce antibiotics. The idea was to keep the organisms assimilating the substrate at a steady but low rate, the correct level for their production of antibiotics.

The trouble is that one cannot measure on-line how fast the microbes are taking up the substrate, so engineers had to arrive at optimal feeding rates by trial and error. Later, computers came into control the process, taking the rate at which the microbes produce the waste product carbon dioxide as an indirect measure of the rate at which they take up the substrate. Computers continually adjust the feed rate on the basis of the rate of the output of carbon dioxide, measured on a mass spectrometer.

If the culture is fed indefinitely, one of two things terminates the process. Either the bioreactor fills up and threatens to overflow, or the culture becomes so dense that the bioreactor cannot supply enough oxygen and the culture dies. To avoid this, technologists developed the cyclic fed batch culture. Under this system, the bioreactor fills up as the feed flows steadily in, and a portion of the culture is removed. As the feed then slowly refills the vessel, the emptying is repeated. Engineers quickly discovered that yields in CFBC were superior to those in simple batch culture, where nothing is added or removed. The reason for this is the subject of much investigation but probably arises from the fact that the supply of nutrients into the bioreactor is so slow that it actually controls the rate at which the organisms grow. They can grow only as fast as nutrients are fed to them. When the bioreactor is nearly full the availability of nutrient to each cell is low, so the culture can grow only slowly. Once some of the volume has been emptied out, there is effectively more nutrient per cell coming into the system and the microbes grow faster. Thus at every "emptying" the growth rate takes a jump. The accompanying burst in antibiotic production presumably happens because the rate at which the microbes assimilate the substrate makes the same jump. In a natural environment this situation signals to the organism that a competitor for the substrate has arrived on the scene. So CFBC stimulates the production of antibiotic by fooling the organism into thinking that it needs to attack some unseen adversary. (Source: New Scientist, 7 October 1989)

E. Coli produces Aqualsyn I

Japan Tobacco (Tokyo, Japan), in conjunction with researchers at the University of Tokyo, has developed a production method for making Aqualsyn I that is ten times as efficient as conventional methods. Aqualsyn I is an alkaline protein decomposing enzyme with high activity at elevated temperatures that is naturally produced by a thermophillic bacteria. The bacteria is used as an additive for detergents and as a biological reagent, but must be cultured at 65°C at fairly low output levels. Japan Tobacco succeeded in implanting the gene for the enzyme onto E. Coli DNA to create a low-cost means of mass producing the enzyme. The E. coli have produced Aqualsyn I proteins with a molecular weight of 38,000. (Extracted from New Technology Japan, July 1989)

Yeast to colour fish and egg yolks

A yeast might be used to produce the pigment that turns salmon flesh pink, according to E. Johnson of the University of Wisconsin. Salmon raised in captivity have white flesh, but the pink flesh of wild ocean salmon brings a higher price. Fish farmers often use the carotenoid pigment astaxanthin, but this can cost $200/lb, according to D. Stuiber of the University of Wisconsin (Madison, USA). Demand may soon outstrip supply for the pigment, but the yeast Phaffia rhodozyma can be manipulated to produce ten times as much of the pigment as normal, according to Johnson. Yeast-derived pigment might cost $50-100/lb. Trout readily assimilate the pigment. Poultry farmers might use the pigment to enhance the colour of egg yolks. (Extracted from Chemical Week, 2 August 1989)

Vinegar production from waste dates

Waste dates are highly rich in sugars, which offer the possibilities of preparing alcoholic solutions by fermentation under anaerobic conditions which will later be the acetification wort for the production of vinegar. The sugar content of date juice of 160g/litre gives a solution of sugar to ethanol equal to 56.6 per cent.

The date palm (Phoenix dactilifera L.) is the main culture in the south of Algeria. The number of palms is estimated to be 7 million, producing 170,000 tons of fruit. Although several varieties of dates are used for local consumption and others are exported, more than 10,000 tons are useless for this purpose which constitutes a considerable waste. This quantity could reach 30 per cent of production. Those dates which are useless commercially (deformed, unripe or dates damaged by parasites) could possibly be made use of by the elaboration of new products, such as sugars, jam, juice, wine or yeast. Dr. A. Touzi and Dr. N. Boughnou of the Laboratory of Industrial Microbiology, Algiers, are working on producing vinegar biologically after double fermentation and were able to achieve a satisfactory acetification corresponding to the norm established by the Permanent International Vinegar Committee (1979) and the WHO/FAO Commission (1982).

Further information may be obtained from Drs. Touzi and Boughnou, Laboratory of Industrial Microbiology, c/o Haut Commissariat à la Recherche, 2 Bd. Frantz Fanon, B.P. 1017, Algiers, Algeria.

Environmental applications

Biodegradable packaging plastic from Battelle

Battelle in Frankfurt, Federal Republic of Germany, has developed a new, totally biodegradable material specially designed for packaging, which it says is suitable for use in one-way boxes or blister packs. The starch-based material apparently has extremely promising properties: it is transparent and flexible, and in water or wet soil micro-organisms can degrade it within days to carbon dioxide and water.

Minor additives make the special starch, on which the material is based, easy to process. Among the applications foreseen by Battelle are the envelopes around cigarette packets, inserts in chocolate boxes, sanitary products, and gardening and agricultural materials and tools. Battelle also anticipates that the material will win a significant share of the protective packaging market, currently dominated by polystyrene.

Some 1.5 million tons of packaging materials are used each year in Europe and Battelle estimates that between 50,000 and 100,000 tons of these materials could be replaced by the new material. The development of production technology for the new biomaterial is expected to take a further two years, at a cost of around DM2 million, and Battelle is seeking industrial partners. Details from: Dr. Renate Gross-Lannert or Dr. Rainer Frische, Battelle Europe, Am Romerhof 35, D-6000 Frankfurt 90, Federal Republic of Germany, or on (69) 79 08 22 14. (Source: Biotechnology Bulletin, Vol. 8, No. 6, July 1989)

Additives to degrade common polymers

St. Lawrence Starch (Mississauga, ON) has developed surface modified starch additives to make common polymers biodegradable. Standard starch is not suitable for the purpose, but modifying the starch so that its surface is hydrophobic and reducing its moisture content enables it to be processed in polymer melts at over 160°C. It can be used to make polyethylene, polypropylene, polyurethane and polystyrene biodegradable. Interest in the technology has increased due to the rapid proliferation of laws restricting the use of nondegradable plastics. Degradable plastics are generally degraded by bacteria, fungi or actinomycetes, either by mechanical or chemical action. The Ecostar modified starch is available as a white powder for adding to plastics. It can be based on cornstarch or potato starch. The starch can be attacked by micro-organisms, thus weakening the mechanical strength of the plastic and greatly increasing the surface area of the plastic to expose antioxidants to metal salts in soil, thus creating peroxides that further degrade the plastic. Ecostar Plus additive also includes accelerators to enhance degradation of plastics for uses such as agricultural mulch. (Extracted from Plastics Engineering, July 1989)

PCB degrading gene cloned

Researchers at the Fermentation Research Institute (Tsukuba City, Ibaraki, Japan) have cloned a gene capable of biodegrading polychlorinated biphenyls (PCBs) from bacterial chromosomal DNA. The genes were originally taken from several soil-resident bacteria that are capable of surviving with PCBs as the sole source of carbon nutrients. The bacteria decompose the PCB into chlorobenzoate. The researchers plan to use the results of their research to breed chlorobenzoate-eating bacteria strains that also consume PCBs (Extracted from New Technology Japan, September 1989)

Biodegradable plastic

Environmental concern is leaving its mark on the plastics industry as the plastics industry leaves less of a mark on the environment. By 1992, one third of all plastic used in bags and films in Europe is expected to be biodegradable, compared with only 9 per cent now, according to a recent report.*

Most biodegradable plastics technologies add an agent to the plastic which causes its disintegration through biological processes or light. Most biodegradable plastics contain starch as an additive.

The major application for biodegradable plastics in western Europe at the moment is in carrier bags, with a market worth $7.3 million in 1988, and expected to reach $27 million by 1992. Plastic containers will then, however, be the largest market for such plastics, at $50 million, up from $3 million in 1988. Mulch film, now the second largest application, with consumption of $3.1 million worth of biodegradable plastic in 1988 is expected to grow to $8.1 million in 1992. Garbage bags will account for $6.3 million in 1992, from just $642,000 in 1988. West European production of biodegradable plastics is expected to grow to 21 million tons per year by 1992, from 4.6 million tons last year.

The markets for biodegradable plastics are expected to differ widely in size between western European countries, though European Community legislation may reduce these differences. The United Kingdom, however, is expected to do rather poorly in biodegradable plastics even in 1992, with a market of only $2.3 million. Source: Chemistry and Industry, 4 September 1989)

Protective enzymes

Researchers at Texas Agricultural and Mechanical University (College Station) and the University of Guelph (Guelph, ON) say they have discovered an enzyme produced by bacteria common in soil that breaks down the toxins in some chemical weapons and pesticides by attacking certain chemical bonds. When the genetic code for the enzyme was transferred from the bacteria to a group of embryonic fruit flies, researchers report that the resulting insects had as much as 20 times greater pesticide resistance than ordinary adult flies. The goal is to allow beneficial insects to be more resistant to pesticides and to develop treatments to accelerate the breakdown of pesticides in the environment. The research team maintains that extreme care is being taken to prevent the transfer of the enzyme code to wild populations. (Source: Chemical Week, 27 September 1989)

Biodegradable plastic

Pertec, the research arm of Italy's Feruzzi, has developed what it describes as a "second generation" biodegradable plastic which contains over 50 per cent cereal starch, petroleum-based non-toxic synthetic polymers of molecular weight lower than polyethylene and hydrophiles. The

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* The European market for biodegradable plastics, $3,400, Frost & Sullivan, 4 Grosvenor Gardens, London SW1W 0DH.

company estimates the time for biodegradation as from one to six months for a flexible film and several years for a hard plastic film. (Source: European Chemical News, 2 October 1989)

General Electric speeds up PCB degradation

Natural degradation of polychlorinated biphenyls (PCBs) by bacterial decay can be accelerated by more than 70 per cent, according to research scientists at General Electric in Schenectady, New York.

Dr. Stephen Hamilton, the environmental sience manager, claims to have increased the activity of the bacteria by the addition of a nutrient medium consisting of nitrogen, phosphorus and trace metals. The process dechlorinates the PCBs, facilitating their eventual destruction. Hamilton says the process is important because it attacks the more highly chlorinated PCBs which have caused the most environmental concern.

The dechlorination was demonstrated on sediment samples taken from rivers across the United States. Hamilton suggests the results show bioremediation as a promising approach to the problems of removing PCBs from waterways. In addition, GE has been able to fine-tune culture mediums to attack specific types of PCBs.

PCBs are degraded naturally by anaerobic and aerobic bacteria. Dechlorination takes place slowly in anaerobic conditions. This releases compounds, which are more easily destroyed by aerobic bacteria, when washed out from sediments to an environment where oxygen is present. (Source: European Chemical News, 2 October 1989)

E. PATENTS AND INTELLECTUAL PROPERTY RIGHTS

Improvement of plant breeders' rights

A Study Committee of the National Council for Agricultural Research in the Netherlands (NRLO) in June 1989 published its second report on plant breeders' rights and patent rights in relation to plant genetic engineering. As an alternative to the pending patent legislation by the European Communities which would extend patent protection to living organisms, they suggest to extend plant breeders' rights. The desired improvements relate to both the extension and strengthening of plant breeders' rights. The majority of the improvements forms already part of the present proposals for the revision of the UPOV Convention (International Union for the Protection of New Varieties of Plants). All types of varieties of all cultivated plants should be made eligible for protection under the plant breeders' rights system. Until now the testing authorities have hesitated to make the step from the present restricted lists to such an open-ended system.

It is suggested to clarify in the plant breeders' rights legislation that the expression "material of a variety" includes all material from which the variety with its typical characters can be reproduced, i.e. whole plants and parts of plants such as protoplasts, cells, cell aggregates, cell lines, plant tissues, specific organs, artificial seeds etc. The farmers exemption, that is the right of the grower to multiply a protected variety for use on his own premises, should be restricted to multiplications for non commercial purposes only, according to this proposal.

The report also favours a system of dependency, comparable to that existing in the patent rights system. Both the planned revision of the UPOV Convention and the new EEC Draft Council Regulation on Community Breeders' Rights contain proposals to introduce a system of dependency in plant breeders' rights. While the use of new varieties in breeding programmes in general will remain free, just as it is today, the breeders' rights would be extended to specific "derived varieties". According to the report, a "derived variety" should be a variety which has undergone some genetic modification. Since it will become more and more easy to create a new variety by selection for or introduction of an identifiable piece of DNA, these changes would leave the breeder of the original variety without remuneration although he has done the major breeding work. The introduction of a dependency system for genetic modifications of protected varieties would remedy such a situation. No developing country has signed the UPOV Convention yet. (Source: Biotechnology and Development Monitor, No. 1, September 1989)

USPTO's new rules

The US Patent and Trademark Office (PTO) has proposed new rules that most biotechnology patent applicants submit sequence data on computer disks - following a rigidly defined format.

If adopted, the proposed rules would govern applications containing any DNA sequence longer than 10 bases, or any peptide longer than four amino acids. The rules would affect any patent application that "discloses" or "contains" any such sequence, regardless of whether the sequence is claimed or crucial to the invention. The sequence data must be set off in a separate section, and the printed version would have to be duplicated exactly (as confirmed by a statement made under penalty of perjury) on a 5.25- or 3.5-inch disk in IBM or Macintosh format.

As stated in the PTO notice, "The format proposed herein is based on the Genbank data format and forms currently in use. Submission of sequence data using the current Genbank format and forms is generally acceptable ...". Right now, however, Genbank requires only ASCII (American Standard Code for Information Interchange) sequences. It specifies no particular format.

To achieve the PTO format, most inventors will have to revise their data, inserting numbers and splicing together DNA and amino-acid sequences exactly as the PTO specifies. The paper version must be printed in a fixed-width font, where the letter "I" takes up the same width as the "M". Typeset fonts (such as the one the PTO used in its example) will be prohibited. On the disk, "hard returns" will be prohibited (word processors vary widely in their treatment of these characters: some use hard returns only to mark the ends of paragraphs; others insert a hard return at the end of every line).

If an application violates even a single provision, it can be delayed for months while the inventor and attorney straighten it out - at considerable expense.

To make matters even more worrisome, the PTO proposal is based on software that is not yet available. The hoped for program, called Author-In, is being developed at Intelligenetics (Mountain View, CA), the contractor that now operates Genbank. If Author-In works as envisioned, a scientist will be able to feed in a file of sequence data, which the program would then rearrange to fit the PTO's format - prompting the operator for each additional datum the PTO requires.

The new rules were scheduled to assume the force of law on 1 January 1990 regardless of whether

inventors and attorneys were ready to comply. (Extracted from Bio/Technology, Vol. 7, August 1989)

Mycogen files for patents on biotoxins

Mycogen Corporation says that company scientists have discovered novel strains of the bacteria Bacillus thuringiensis that are toxic to plant parasitic nematodes.

Mycogen scientists have developed a test that is capable of identifying Bt biotoxins effective against these pests. Patents have been filed covering the discoveries.

The biotoxins discovered by Mycogen will most likely reach commercial markets in plants genetically engineered to be resistant to the pests.

The most common control measures for plant parasitic nematodes are traditional plant breeding and chemical nematicides. However, traditional methods of breeding nematode resistant plants involve long and complicated processes.

Chemical nematicides can be toxic to mammals and other wildlife and have been implicated in groundwater contamination. In addition, nematodes have built up resistance to many chemical nematicides.

Earlier this year, Mycogen researchers discovered several novel strains of Bt toxic to parasitic nematodes in livestock. This was the first evidence that Bt toxins have animal health applications. (Source: Chemical Marketing Reporter, 11 September 1989)

Genetics Institute wins US patents

Massachusetts-based Genetics Institute is claiming a strong position in Factor VIII and macrophage colony stimulating factor (M-CSF) development, with the granting of two US patents.

The first patent covers materials used to manufacture the hormone M-CSF via recombinant DNA technology. M-CSF is a protein that stimulates the production and functional activities of the monocyte and macrophage white blood cells, which play an important role in defence against infections.

A further patent covering the manufacturing process itself is expected shortly. The company is currently carrying out clinical trials of M-CSF in cancer patients and in bone marrow transplant recipients.

The second patent claims a class of variants of the blood clotting protein Factor VIII, as well as DNA methods for their manufacture. These modified proteins are much smaller and potentially may be manufactured more efficiently than full-length Factor VIII, claims the company. They could offer a less expensive product for haemophilia treatment. (Source: European Chemical News, 2 October 1989)

Patent suit disclosed

Cetus Corp. announced on 3 August that a complaint had been filed by E.I. DuPont de Nemours & Co. asking that DuPont be declared not liable to Cetus under two patents covering GeneAmp polymerase chain reaction (PCR) technology. The complaint alleged that the patents are invalid and not infringed by DuPont, but did not state any basis for the allegations.

Cetus is commercializing its GeneAmp PCR technology in the human diagnostics field through an arrangement with Hoffman-La Roche Inc. In the research instrumentation business, the company has a joint venture with Perkin-Elmer Corp. Forensic and other applications of the technology are also being developed by Cetus. (Source: Biotechnology Bulletin, Vol. 8, No. 8, September 1989)

No patents on animals please, we're European

Last June, the European Patent Office in Munich rejected an application for a patent on a strain of mouse. The American patent office had granted a patent on the same mice last year. The difference in the decisions highlights an important legal and ideological split between Europe and the US that may have profound effects on the development of biotechnology.

The strain of mouse concerned was transgenic: it carried a gene that scientists had added to its natural genome. Companies that produce such animals (or plants) want to be able to patent them. The organisms are the products of what is usually a long and expensive programme of research and development. The companies argue that the organisms are the fruits of invention. They point out that the American patent office ruled that "everything under the sun" can be patented, so long as it is a matter of rewarding invention. If European authorities rule out patents for transgenic animals, much of the associated research and development could move elsewhere.

In 1988, however, the World Intellectual Property Organization (WIPO) issued an expert opinion which put a new slant on the issue. WIPO is the UN body charged with administering the web of treaties on patents and copyright that protects authors and inventors throughout the world. Its committee, charged with "harmonizing" international laws for the protection of inventions, decided that the European convention excluded from patent protection "plant or animal varieties or essentially biological processes for the production of plants and animals". The one exception was "microbiological processes or the products thereof".

This statement complicated the already complex legal issue of what constitutes an animal.

The mice for which the EPO refused to award a patent are called "oncomice": they contain genes, called oncogenes, which cause them to develop various cancers. They are valuable to scientists studying the genetic control of cancer. Last year, the American patent office awarded a patent, number 4 736 866, on the mice to their inventors, Philip Leder, of Harvard Medical School in Boston, and Timothy Stewart, now at the biotechnology company, Genentech, San Francisco. (Extracted from New Scientist, 26 August 1989)

RAFI Communiqué - May/June 1989

FARMERS' RIGHTS
The Informal Innovation System at GATT (TRIPS) and in intellectual property negotiations in the context of new biotechnologies

(This article, prepared by the Rural Advancement Fund International, stresses the importance of intellectual property rights of developing country plant breeders)

Introduction

Some nations are beginning to reformulate their patent systems in the light of the rise of biotechnology and the corporate desire to own and control life. In various countries, the patenting of

animals, plants, micro-organisms, genes and specific characteristics is being codified into law. Such patenting laws will give monopoly-like rights of ownership and control to their holders and thus function as a subsidy given by society to industry.

Major industrialized countries want a uniform system of patents covering life forms recognized by all. Patents awarded in one country, but not recognized in others, are of limited value. Thus, the US argues that the absence of these patent-subsidies constitutes a kind of non-tariff trade barrier. They argue that any nation not adopting appropriate legislation is really engaging in unfair trade practices.

Patent systems are generally geared towards recognizing the "Western model" of innovation. But a more informal, communal system of innovation has existed for centuries in Third World countries in agriculture. There, Third World farmers continue to produce very valuable genetic materials - a plethora of diverse crop varieties.

The Third World has genuine economic clout. Biotechnology and modern plant breeding rely on the genes found in the Third World. But these genes are not "raw materials" in the traditional sense, because they have already been selected, nurtured, improved and developed by Third World farmers. And this process continues even today. These materials reflect the ingenuity, inventiveness and genius of the people. But traditional patent systems are biased towards the style of innovation common to the North.

Northern enterprises recognize that the biological diversity of the South is worth billions of dollars in commercially-viable products. As access to Third World germplasm is being negotiated in the UN Environment Programme (UNEP) in Nairobi and the Food and Agriculture Organization (FAO) in Rome, patenting systems which will determine who owns, controls and benefits from this germplasm are being formulated at the General Agreement on Tariffs and Trade (GATT), the World Intellectual Property Organization (WIPO) and at the Union for the Protection of New Varieties of Plants (UPOV) in Geneva.

The South could be victimized by these proceedings. But proposals are being advanced to recognize and reward Third World innovation. These proposals would give power and meaning to the concept of "farmers' rights" and the "informal innovation system". Much is at stake, including billions of dollars of annual royalty payments.

"The seriousness is underscored by the fact that, with the exception of sunflowers, no major crop plant is native to North America, and we are completely at the mercy of foreign nations, particularly developing countries, for genetic diversity" (Richard E. Lyng, US Secretary of Agriculture). 1/

The Constructive Strategy: The case for Farmers' Rights

Farmers' Rights arose in the FAO Commission on Plant Genetic Resources in 1987 and has been juxtaposed, ever since, to Plant Breeders' Rights (a term for seed patenting).

The South contends that Farmers' Rights are the practical and moral equivalent of Breeders' Rights and that the North must recognize these rights in a substantive way. In effect, developing countries argue that they will withdraw their objections to Breeders' Rights (the UPOV Convention) if the North will recognize Farmers' Rights through a tax-based payment to the FAO International Fund for Plant Genetic Resources. The North believes that a simple "thank you" will suffice to recognize "Farmers' Rights".

In February 1989, a round-table on technology licensing co-sponsored by the International Centre for Insect Physiology and Ecology (ICIPE) and the African Academy of Sciences, advanced the Farmers' Rights concept considerably by broadening the discussion to all forms of innovation and posing a non-Western model of inventiveness called the "informal innovation system". 2/

In April 1989, the Ethiopian delegation 3/ to the Third FAO Commission on Plant Genetic Resources carried the expanded concept through that debate and won agreement from the FAO Legal Department to provide a study for the next session in 1991 or sooner. 4/

The basic features of the informal innovation system position are that:

1. Farmer landraces, plants in use for medicinal purposes, other biological products and processes in use, and other innovations in use (including those relevant to industrial patents, trade marks, design or copyright) are the result of human ingenuity and represent immediate inventions (or discoveries);

2. Most of these inventions/discoveries are not the product of academic or commercial research but arise from "informal" (often co-operative) efforts which are as purposeful and creative as any similar efforts in more formal or "Western" models of innovation;

3. Crop plant collectors gather present-day, improved germplasm (not the material of ten thousand years ago). Botanists collect both medicinal plants and landraces and the knowledge (or "intellectual property") of those who have bred, discovered and protected the genetic material. In each case, the present intellectual integrity of the informal innovation system is compromised by the existing model of intellectual property rights which offers no recognition or compensation.

Although the informal innovation system is capable of meeting all the conceptual criteria for intellectual property rights required by current conventions, the Western model is biased towards individualized and juridical app'ication procedures which are not sympathetic to the style of inventiveness common, in particular, to rural societies. Therefore, current conventions make the systematic exploitation of Third World intellectual integrity inevitable.

However, as Northern Governments and industry move to legislate a certain form of intellectual property protection anchored to trade relations (GATT); and as they amend existing conventions (WIPO and UPOV) to permit the patenting of biological products and processes (much of which is derived from informal innovators), there is an opportunity to fundamentally restructure these conventions to recognize and recompense (indirectly through intergovernmental programmes) Third World innovators.

Negotiators in GATT, WIPO and UPOV as well as those reviewing Farmers' Rights in FAO and a proposed Treaty on Biological Diversity in UNEP, must reopen their discussions in order to incorporate fully the informal innovation system.

Should inclusion prove cumbersome, two alternative steps might be considered:

1. A tax on all commercialized biological material, in the North, surrendered to an intergovernmental fund (for the conservation and utilization of biological diversity in the South) roughly equal to a normal royalty charge (several billions of dollars per annum);

2. Automatic Licensing Rights (without royalties) to all Third World countries for all patents based upon any materials derived from the South.

This strategy would by no means exclude the normal application of sovereign rights over national property and it would serve to complement the protection afforded by the UNESCO Convention on the Means of Preventing the Illicit Import, Export and Transfer of Ownership of Cultural Property (1970). In fact, the full implications of the UNESCO Convention bear closer scrutiny with regard to its application covering living material. 5/

The context

Whereas property rights apply to physical objects, intellectual property applies to ideas. Intellectual property includes patents, trade marks, copyright, design and breeders' rights. The extent of "rights" granted over an idea depends upon the type of idea. Copyright gives rights to the author for her/his lifetime but only protects the form of expression of the idea - not the idea itself. Industrial patents give rights to the idea for a limited time period.

Even within patents there are a range of systems of rights. Inventors' certificates and automatic licensing, for example, require that the idea be made available to all who ask for it at a fixed royalty rate. There is no exclusive monopoly over the idea. Most recent patent laws, however, grant exclusive monopoly rights over the idea so that the inventor can both obtain a royalty and determine the terms of sale or the conditions under which the invention will be used. This affords much greater control in the market-place.

Intellectual property is recognized to be a form of social subsidy for research wherein the Government intervenes in the "free" market to create an artificial monopoly for a private interest. The level of societal subsidy is the royalty - the difference between the market value of the invention without the patent and the price charged with the patent. The extent of subsidy is further augmented by the degree of social support for the higher education of the inventors since inventors obviously build upon earlier developments and rarely finance the full costs of their own schooling.

Intellectual property criteria

As the intellectual property system of the nineteenth century is a product of the industrial revolution and the inability of normal property law to protect the ideas of mechanical inventors, plant breeders' rights is a product of the twentieth century development of Mendelian genetics and the inability of intellectual property systems to protect the ideas of breeders. And, farmers' rights (the informal innovation system) is a product of the era of biotechnology and the inability of other systems, in the context of new biotechnologies, to protect the ideas of informal innovators.

Plant breeders could not meet the stringent criteria once required for industrial patents. They could not offer society an "inventive step" and the normal criteria for both "utility" and "non-obviousness" were too subjective to be applied to living material. Without an inventory of the Garden of Eden, it was impossible to prove novelty or disprove chance discoveries. The old mechanical system just did not seem to work.

Nevertheless, breeders maintained that they had "ideas" that were socially useful and that these ideas could be too readily copied in the "Xerox machine" of a farmers' field. A whole new intellectual property system was fashioned which essentially granted breeders the same rights as inventors, but without many of the obligations.

Today, informal innovators also claim, also legitimately, that they have "ideas" which also have social value which are also unprotected. Once again, crop landraces (sometimes called "primitive" varieties) and medicinal plants may not meet the full existing criteria of earlier intellectual property systems, but they do meet the standards of "ideas", "usefulness" and "non-obviousness" that have been at the core of the development of patent-like régimes.

It is, therefore, timely to:

1. Either amend the existing conventions (especially the WIPO Convention) to include farmers' rights; or

2. Create a new convention exclusively for farmers' rights; or

3. Develop an alternative system of recognition and financial reward for informal innovators.

The destructive strategy: The Western patenting system

Although concepts of intellectual property protection in the Western world date back to the ancient Greeks, the modern struggle between those supporting and those opposing monopoly control over innovations properly dates to the England of 1623 and ends at the Vienna World's Fair 250 years later (1873). 6/ The formal capitulation, however, took place in Paris 10 years later with the signing of the Paris Convention creating the industrial patent system.

The battle over patents is long and complex. In the half-century prior to the Vienna Fair, opponents in the UK, Holland, Switzerland, Italy and Germany bitterly attacked the concept of monopoly and turned back or prevented patent laws and regulations. In the prevailing era of "free trade", patents were regarded as "barriers to trade" similar to tariffs.

The anti-patent movement collapsed abruptly in 1873 in the face of economic depression and rising nationalism and because of a compromise proposed by advocates allowing for the use of a "compulsory licence" if an invention were improperly worked or if the royalty charges were usurious. 7/

In the intervening century since the Paris Union, the Convention has been redrafted on six occasions with a seventh now under way. On each occasion, the interests of the major industrial concerns have been strengthened and the rights of society have been weakened. The duration of patent protection and the scope of protectable inventions has expanded. The strength of the actual monopoly has also been increased. In fact the whole relationship and debate has been reversed:

- Where compulsory licences were once seen as the compromise to control monopoly, recent industry and government papers describe such

licences as offensive barriers to rightful monopoly. (In GATT, the code words are "relaxing of restrictions"); 8/

- Where food, medicine and other goods vital to national security were commonly regarded as too important to be patented, failure to provide national protection now leads to harsh trade reprisals for countries such as Brazil and South Korea; 9/

- Where "life" was seen as beyond the rights of inventors, failure to offer life patenting may, today, lead to economic embargoes; 10/

- Whereas patents were originally seen as a non-tariff barrier to free trade, the present GATT round would interpret the absence of patent protection as a trade barrier; 11/

- In a GATT round where agricultural subsidies are under attack, the most vociferous opponent of farm subsidies (the United States) is demanding patent subsidies for farm-based biological products and processes.

In summary, a Western model for private sector industrial technological innovation is now to be imposed over the entire world, over all living and non-living material, regardless of the original understanding and objectives of patent treaties or the rights of sovereign nations to determine their own development and security requirements.

Indeed, if proposed changes to GATT and WIPO are successful, the only forms of human innovation (for physical products and processes) that will not be patentable will be those of informal innovators in the Third World. Long after foods, medicines and items of national security are subject to exclusive monopolies, only the improved germplasm of the Third World will be deemed (by the North) to be "too important" or "too inconvenient" to be patented.

On TRIPS and TRAPS

At the outset of the Uruguay round of GATT negotiations, the United States and Japan insisted that failure to subsidize foreign inventions should be seen as a barrier to international trade and as actionable grievances under GATT rules. Thus began "TRIPS" (Trade-Related Intellectual Property rights discussions) and a major "trap" for the Third World. American embassies abroad approached Governments with memoranda intended to show the losses of revenue created by the "failure" of some States to match US and Japanese categories of patentable material. Of particular concern was the "failure" of several States to provide product patents for pharmaceuticals. However, the memoranda urged Governments to allow product patents on everything including food. 12/

Accompanying the memoranda was a graph from the US International Trade Commission (USITC) showing losses for 1986 for 193 US-based companies (US $23.8 billion). Other USITC estimates ranged from a low of $43 billion to a high of $102 billion supposedly lost. 13/ The US TRIPS negotiator told RAFI that while the range of figures relates to all countries violating US intellectual property standards, Third World transgressors "are at the top of the list". Further, the official made it clear that "biotechnology is very much part of the negotiation" and that the US position on the type or level of life to be regarded to be patentable is "no exclusion". Finally, the negotiator confirmed that the USITC figures are only for American corporate "losses" and that similar figures should be expected for Western Europe and also Japan. 14/ Other researchers, including trade consultant Jacques Gorlin, confirm that hard data from other trading blocs is not available but that the sums involved, at least for Europe, should be similar to those for the United States. 15/

Both the GATT secretariat (Dunkel) and the South Commission have acknowledged that biotechnology protection is part of the GATT debate.

It is not yet clear if GATT will fully succumb to US/Japanese pressure. Many European States see dangers for WIPO and UPOV in the proposal. Many States recognize that surrendering to pressure now means granting the US and Japan the de facto right to determine what (if anything) of life is patentable for the world community.

Biological products and processes account for approximately 40 per cent of the world economy. Should all this, over several decades, become patentable - and were it patented in the same ratio as non-living materials - the world would experience an approximate 40 per cent increase in royalty charges. This, however, drastically underestimates the real impact for three reasons: (1) by definition, biological materials in the form of food, medicines, clothing and shelter are more important to life and the lives of poor people especially; and (2) biological materials are already making inroads into areas previously occupied by industrial products such as energy, construction, chemicals, etc.; and (3) despite the diversity of flora and fauna, the greatest economic power resides in no more than 12-30 plants and only a half-dozen animals. The genetic uniformity of these species may increase the effectiveness of gene patents.

Surendra J. Patel, Senior Consultant to the UN University and former Director of Technology Transfer at UNCTAD, eloquently describes the actual impact of the patent system on the Third World. 16/ Patel notes that less than 1 per cent of all world patents are granted to Third World nationals and that the overwhelming majority of all patents taken out in the Third World are not actually "worked" (manufactured) in these countries. Despite this, GATT would force the South to subscribe to its new régime.

TRIPS negotiations reopened in Geneva and Paris in early July 1989. Even aggressive US delegates, however, expected the final decision to run into 1990. For the Third World, the best defence may be a strong offence - Farmers' Rights and the concept of the Informal Innovation System.

Major "offenders" 17/ as defined by the US Trade Representative

Argentina	Japan
Australia	Malaysia
Brazil	Mexico
Canada	New Zealand
Chile	Nigeria
China	Norway
Colombia	Pakistan
Egypt	Philippines
European Community	Portugal
Federal Republic of Germany	Spain
Finland	Sweden
France	Switzerland
Greece	Taiwan
Gulf Council	Thailand
India	Turkey
Indonesia	United Kingdom
Italy	Venezuela
	Yugoslavia

Comparing Intellectual Property Systems

WIPO: Industrial Patents	UPOV: Breeders' Rights	FAO: Farmers' Rights
Objective		
To create a system that would "protect" the ideas of industrial inventors where normal property law criteria could not work.	To create a system that would "protect" the ideas of plant breeders where normal intellectual property criteria could not work.	To create a system to "protect" the ideas of Community innovators where normal patent/PBR criteria cannot apply.
General principles		
Inventors are entitled to exclusive monopoly protection for a fixed time if they can demonstrate novelty, utility and non-obviousness (NUN). In return, society demands that the invention be described, deposited and worked.	Breeders are entitled to exclusive monopoly protection for a fixed time if they can demonstrate distinctiveness, uniformity and stability (DUS). In return demands variety be available for research and that it be worked.	Community innovators are entitled to exclusive monopoly protection for a fixed time if they can demonstrate the NUN patent criteria. Society requires the material to be described, deposited and worked.
Non-patentable inventions		
Originally, inventions relevant to national security; foods, pharmaceutical and chemicals; biological products and processes; anything contrary to decency or the public interest.	Originally, hybrids and end-products or material discovered rather than developed.	Presumably, any material contrary to the national interest.
Inventive step		
Beginning with an "idea", the inventor must demonstrate an advance in science adding to Society's knowledge.	Since the breeder's idea failed to provide Society with an inventive step, PBR requires that the variety differ from others by an "important characteristic" which implied an agronomic quality but has since come to mean important to meet the criteria of "distinctiveness" only.	Community innovators begin with an "idea" which rarely includes an inventive step. Like breeders, however, their landrace varieties have a collective distinctiveness which can be described.
Absolute world novelty		
Patent must be provably unique from any prior invention patented or otherwise found anywhere in the world.	Although variety criteria is the same, breeders concede that they cannot prove world novelty so test is against other protected varieties only and onus of proof is on society not on breeder.	Community can probably claim world novelty better than breeders.
Utility		
Patented inventions must serve a useful purpose.	Breeders have been unable to distinguish between "new" and "improved" and have fallen back upon the "important characteristic" approach to distinctiveness.	Landrace varieties would not be grown if they were not useful to society.
Non-obviousness		
Other workers skilled in the science must not find the invention an obvious extrapolation of another invention. There must be a new idea.	Breeders have found this difficult to prove and have relied, again, upon the important "characteristics" criteria as now interpreted.	This, in the case of landrace varieties, is also difficult for community innovators - though no more difficult than for other breeders.
Discoveries		
Recent reinterpretations suggest patentable.	Products of nature are patented although national laws vary on rules and practices.	National sovereignty laws would make discoveries ineligible for protection.

Scientific exemption		
Invention must be deposited and disclosed via a written description but scientists are not guaranteed access to the invention for research.	Variety may be used as an original source of variation for further varieties. Variety must be deposited but need not be fully described.	Landrace varieties could only be used for research on the basis of contractual agreement. Deposit is achieved through gene banks and descriptions are provided from gene bank data.
Farmers' exemption		
It is illegal for farmers to save seed for another season or to trade/sell seed to neighbours.	Farmers may save and trade seed within limits.	Farmers may save and trade seed within limits.
Generic protection		
Broad protection, possibly for a species or genera or for specific characteristics (regardless of species) is possible.	Protection is limited to a specific variety.	Beyond the landrace variety, any material derived or adapted from that variety is also part of the right of the innovator.
Enforcement		
Obligation of patent holder in the civil courts.	Two thirds of field varieties sold as certified seed leaving enforcement the responsibility and cost of the State.	Enforcement would be part of the contractual arrangement with gene banks and national seed certification systems.

FOOTNOTES

1/ In a letter dated 11 March 1987, addressed to Mr. James C. Miller, III, Director of the Office of Management and Budget concerning a proposition that would have user fees for access to US gene banks.

2/ Draft Report of the Conference of the African Academy of Sciences and the International Centre for Insect Physiology and Ecology (ICIPE), Nairobi, 1-3 February 1989.

3/ Note on Farmers' Rights in the context of other discussions related to an informal innovation system - Delegation of Ethiopia, FAO Commission on Plant Genetic Resources, Third Session, 17-21 April 1989, Rome, Italy. (Document was presented by Dr. Melaku Worede with copies available to interested delegations and observers.)

4/ FAO Commission on Plant Genetic Resources, Third Session, 17-21 April 1989, draft report.

5/ For further discussion of this point, see Development Dialogue 1983: 1-2 "The Law of the Seed - Another Development and Plant Genetic Resources", pages 46-52.

6/ Much of the historical information in these paragraphs is drawn from: Department of Consumer and Corporate Affairs (Government of Canada), Working Paper on Patent Law Revision, June 1976, particularly pages iii-v and 1-4.

7/ See, for example, Paul Beck von Mannagetta, Das neue österreichische Patentrecht (Vienna: Holder, 1897), p. 17, Franz Wirth, Die Patent-Reform (Frankfurt a. M., 1875, (p. 69, note 14, p. 102.

8/ South Commission on the Uruguay Round (Mexico City, 8 August 1988), Trade related Intellectual Property Rights.

9/ Request that all categories of inventions including express reference to "food" and "pharmaceutical products" was contained in an undated note to selected delegations presented by US Government officials regarding the GATT-TRIPS Negotiations. RAFI has a copy of the memorandum.

10/ Specific reference to patenting in biotechnology is made in the proposed (undated) text prepared by Dunkel (Director-General, GATT), titled: "Trade-related aspects of intellectual property rights and trade in counterfeit goods (TRIPS)", circulated in early 1989.

11/ Ibid.

12/ RAFI was handed a copy of the untitled memo by a GATT negotiator in Geneva on 24 April 1989, although we had been told of the contents of the memo by news reporters in Oslo on 6 April. The existence of the memo was common knowledge and reported in the press in Norway.

13/ Surenda J. Patel, "Trade-Related Aspects of Intellectual Property Rights in the Uruguay Round of Multilateral Trade Negotiations", prepared at the request of the Commonwealth Secretariat, October 1988, p. 16. Patel reports that the ICC reckons their figure to approximate 2 per cent of total world trade but notes that 2 per cent would be closer to US$42 billion in 1986.

14/ From a telephone discussion with C. Michael Hathaway, Senior Deputy General Counsel, Office of the Trade Representative, on 9 June 1989.

15/ From a telephone conversation on 14 June 1989 with Mr. Gorlin in Washington, D.C. Mr. Gorlin was recommended to RAFI by C. Michael Hathaway.

16/ Notes: "193 TNE" refers to the 193 US enterprises that reported royalty losses to their Government in 1986. "USITC" refers to the United States International Trade Commission and its low and high estimates of "losses" for 1986. "ICC" is the International Chamber of Commerce which has made its own estimate of world royalty "losses".

17/ Thomas G. Donlan, "Son of Gephardt - Will Super 301 Trigger Trade Wars?" table on page 17, Barron's, 8 May 1989.

Now available from ICDA Seeds Campaign: Patenting Life Forms in Europe, proceedings from an international conference sponsored by ICDA Seeds Campaign and GRAEL at the European Parliament in February 1989. This publication contains the full text of 18 interventions by policy-makers and public interest groups on the subject of life patenting.

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- RR1 (Beresford), Brandon, Manitoba, R7A 5Y1, Canada/204-483-3955/Telex No. 7601055RAFIUC.
- RAFI/IIZ, Wipplingerstr. 32, A-1010 Vienna, Austria/222/53 347 86-0/Telex No. 111010 TZST-A ATT.IIZ/RAFI.

F. BIOINFORMATICS

Biotechnology in Japan

Although many books have been written on the US biotechnology industry, the English-language literature providing information on Japanese companies working with biotechnology is scant. This book 1/ is an attempt to bridge that gap by providing up-to-date analysis of the Japanese biotechnology industry and information on Japanese companies working with the new technology.

As the Japanese strengthen their biotechnology efforts, opportunities for forming strategic alliances with these companies are opening up. This volume cites examples of such alliances, identifying instances of joint ventures, research contracts, and marketing and licensing agreements involving Japanese companies and Western firms during the last few years.

The authors point out that an understanding of the elements of the US biotechnology industry does not assure an understanding of the Japanese industry. In this area, the two countries are vastly different. Thus, in addition to the analysis and data presented, the roles of Government, industry academia and Japanese culture are explained and the strengths and weaknesses of each of these elements of technology and development are described. The book concludes with a chapter comparing and contrasting biotechnology in the US and in Japan.

Biotechnology separations

Sorptive separation techniques, including adsorption, ion exchange and liquid chromatography on solid supports, appear in almost every product separation or purification scheme dealing with fermentation or biochemical feedstreams. The major objective of this book 2/ is to place these different methods in perspective, relative to each other, so that selection of the appropriate technique or combination of techniques can be readily made. Emphasis has been placed on laboratory evaluation methods, scale-up and industrial applications, but the author has tried to include enough theory for the interested reader to pursue selectivity and kinetic consideration for these procedures.

A brief sketch of the nature of the biochemical feedstream and all the processes which might be involved in isolating the desired products from that feedstream opens the book and subsequent chapters cover adsorptive separation, ion exchange procedures and column chromatography procedures. Adsorptive separation, the oldest of the sorptive techniques is often regarded as strictly for the removal of unwanted impurities or colour bodies, but closer examination indicates there are many applications in which adsorption is useful in isolating biochemical products. The chapter on ion exchange procedures builds on what has gone before by demonstrating the effects of the additional sorptive specificity associated with exchange of ions. Column chromatography processes cover the use of sorptive materials to create an environment that allows the separate recovery of two or more solutes.

Ecologists urge case-by-case risk assessments for GEOs

A group of seven environmental biologists issued a report to the Ecological Society of America (ECA) on the planned introduction of genetically engineered (transgenic) organisms. 3/ The authors state that the capability of making precise genetic changes may reduce certain unintended consequences, but that precise genetic characterization of transplanted genes "does not ensure that all the ecologically important aspects of the phenotype can be predicted for the environments into which an organism will be introduced".

Examples of potential ecological effects of transgenic organisms noted in the report are:

- The creation of modified plants capable of escaping cultivated fields and invading sensitive ecosystems;
- The acquisition by weeds of herbicide resistance;
- Biological pesticides with a broad host range that infect beneficial as well as targeted pests;
- Disruption of biotic communities and alteration of nutrient cycles by the introduction of certain plants and micro-organisms.

The report recommends that the ecological assessment of transgenic organisms consider a multiple set of attributes pertaining to the genetic alteration, the parent organism, and the environment for which the product is being designed. In addition it states that assessment of risks should be done on a case-by-case basis with testing that moves in stages from the laboratory to the greenhouse. Assuming these preliminary studies reveal no unacceptable risks, the report recommends proceeding to "carefully planned small-scale field trials that include evaluation of both intended and unintended effects on other species in the ecosystem". (Source: GeneWATCH, Vol. 5, No. 6)

1/ BIOTECHNOLOGY JAPAN. By Mark D. Dibner and R. Steven White. Cloth 7.5 by 9.5 inches. 313 pages. McGraw-Hill Book Company, 11 West 19th Street, New York, N.Y. 10011. $180.00.

2/ SEPARATION AND PURIFICATION TECHNIQUES IN BIOTECHNOLOGY. By Frederick J. Dechow. Cloth 6.5 by 9.5 inches. 490 pages. Noyes Data Corporation, Mill Road at Grand Avenue, Park Ridge, N.J. 07656. $72.00.

3/ Ecology 70 (2): 101-112, April 1989.

Biotechnology revolution and the third world

The biotechnology revolution presents an immense challenge for developing countries and international organizations to take appropriate policy measures to harness the development potential of new technologies and to ward off their adverse effects. The eighteen contributions in this volume by distinguished experts critically examine the nature of these challenges and suggest policy imperatives. Part one highlights the potential of biotechnologies for developing countries in different areas. Part two deals with various issues of concern to the third world arising from the emerging trends in global biotechnology industry. Part three proposes the policy options and the strategies for the international community. By IRS. New Delhi, Research and Information System for the Non-Aligned and Other Developing Countries, 1988, 451 pp., Rs 250.

Enzyme systems for lignocellulose degradation (Edited by M. P. Coughlan of the Department of Biochemistry, University College, Galway, Ireland and published by Elsevier Science Publishers Ltd., Crown House, Linton Road, Barking, Essex 1911 8JU, UK, priced at 56 pounds sterling.)

Vast quantities of lignocellulosic materials, i.e. biomass, are available for exploitation as potential sources of food, fuels and chemical feedstocks. As the term "lignocellulose" implies, such materials are comprised, in the main, of cellulose, hemicellulose and lignin. Thus, exploitation of the potential of biomass requires that each of these major polymers be utilized, perhaps by conversion to their simpler constituents and then to more valuable end products.

For a variety of reasons, biological conversion is preferred over chemical conversion procedures. Obviously, such processes must be efficient. Thus, it is clear that one must have a thorough understanding of the enzyme systems required for the hydrolysis of each of the major components in question and of the micro-organisms (fungi and bacteria) that produce these enzyme systems.

This was essentially the subject matter of the Galway Workshop, in which 28 pre-circulated papers relating to the Commission of the European Communities' COST 84-bis programme on lignocellulose by-product utilization were presented briefly and discussed at length by representatives from most of the EEC countries, Switzerland, Finland, the USA and Canada.

As the title indicates, the topics covered included procedures for optimizing the production of fungal and bacterial cellulose-, hemicellulose- and lignin-degrading enzyme systems; the biochemical and molecular biological aspects of such systems that allow for a greater understanding now and the promise of greater productivity in the future; the problems associated with the recalcitrance of crystalline cellulose and how this may be overcome; the utilization of the hemicellulose fraction of fodder by ruminants and non-ruminants; the applications of the enzyme systems in question and/or of the organisms that produce them in feed and fodder (silage) preparation, fuel (e.g. ethanol) production, xylitol production, and in general industrial (e.g. pulp and paper manufacture) usage; and the economics of lignocellulose utilization and the influence of the various end products on the economic feasibility of particular processes.

The European Community Directorate of Science Research and Development some time ago instituted a number of concerted action programmes charged with the responsibility of promoting co-operation in scientific and technical research (hence the acronym COST). COST 84-bis, one such programme, co-ordinates ongoing multidisciplinary research activities, within the Community and other contributing countries, on the use of lignocellulose-containing by-products and other plant residues for animal feeding and industrial purposes. This it does by the holding of regular committee meetings at which representatives of each of the member States and other contributing countries participate; by providing funding for the exchange of personnel between laboratories engaged in relevant research; by assisting the setting up and operation of centres of excellence in specific analytical techniques to which investigators may send/bring samples for analysis; and by the provision of funding for the holding of workshops at regular intervals. The theme of these workshops varies from one meeting to another so that, over a period of four or five years, each of the major salient aspects of lignocellulose research is the subject matter of intense discussion by a select group of investigators relevant to the topic in question. The workshops held to date include: "Degradation of lignocellulosics in ruminants and in industrial processes" (Lelystad, The Netherlands - March 1986); "Treatment of Lignocellolosics by white-rot fungi" (Braunschweig, Federal Republic of Germany - October 1986); "Evaluation of straws in ruminant feeding" (Theix, France - June 1987); "Evaluation and characterization of lignocellulose for animal feed and industrial use" (Aberdeen, United Kingdom - June 1988).

Research on the origin, preparation and use of lignocellulosic materials is being out in many parts of Europe. Much of this research is funded, at Community level, in a number of programmes. These include: the Energy Programme (Joule) treating, inter alia, biomass as an energy source; the Raw Materials Programme, involving lignocellulosics as a renewable raw material; the ECLAIR Programme, dealing with lignocellulosics as part of the effort of intensifying collaboration between agriculture and industry; the Agricultural Research Programme which deals with straw as an agricultural by-product; and the Biotechnology Programme which funds, or funds to a limited extent, work on the genetic engineering of lignin-degrading micro-organisms.

Thus, research on lignocellulosics is dispersed over a large number of application-oriented programmes, while, simultaneously, the basic substrate-related questions requiring investigation are the same in all programmes.

The Concerted Action COST 84 with its key broad orientation towards the use of lignocellulosic waste materials can serve as a meeting ground for research scientists in the various application-oriented projects to discuss common basic research problems as well as the more applied aspects of the use of waste materials. The short summary and the recommendations of this workshop should be seen against this background:

1. The scarcity of oil as a raw material, and as an energy source, in the more or less distant future, and the preservation and restoration of the quality of the environment, will lead to an increased and more complete use of lignocellulosics. This is already the subject of considerable research effort.

2. As many of the potential future uses of lignocellulosics are presently economically unprofitable, the necessary research effort will not

be furnished by industry but will have to be supported from public funds.

3. Research should be basic and multi-disciplinary, combining biochemistry, microbiology, molecular biology, protein engineering and others so as to gain an insight into the basic structure of lignocellulosic materials and how they can be degraded or otherwise utilized.

Europe now to have access to NTIS data

The vast store of research and technology data that the National Technical Information Service has on file is now available to scientists and others in Western Europe through an agreement signed with ILI, a UK specialist publishing house. ILI has installed a microfiche library of the more than 2 million NTIS reports at its headquarters in Ascot, near London. Clients can purchase printed copies of specific items following a search of the microfiche data base that ILI undertakes free of charge. Most reports, many in the area of chemical technology and process engineering, have never before been published outside the US, notes Richard Boden, ILI's publishing manager. NTIS, an arm of the US Commerce Department, was set up 44 years ago to collect and sell Government research reports. More recently it has been compiling technical information from Japanese and West European sources. (Reprinted with permission from Chemical Engineering News, 24 July 1989, p. 19. Copyright (1989) American Chemical Society)

Bionet service terminates

Bionet, a computer network for molecular biologists and biochemists, is shutting down at the end of September. A decision by the US National Institute of Health not to renew the grant that has supported the service for the past five years prompted the planned shutdown.

Bionet is run by IntelliGenetics, Inc., of Mountain View, California, as a non-profit resource for the scientific community. By the original conditions of the NIH grant, the company was supposed to do molecular biology research - applying its computer system to performing evolutionary comparisons of DNA or protein sequences, for example - in addition to providing computer services for researchers who subscribed to the service.

The principal demand is for performing DNA or protein sequence comparisons. The first thing molecular biologists want to do when they sequence a new protein or nucleic acid is to see if it resembles other known sequences. Bionet is about the only place where all the protein and DNA data bases are available in one place with the necessary software for doing the comparisons. (Abstracted with permission from Science, Vol. 245, p. 126, 14 July 1989, By J.L.M. Copyright 1989 by the AAAS)

Spotlight on Brazil: Tropical Data Base

The Tropical Data Base (Base de Dados Tropical, BDT), is an information centre, created to be a link between culture collections and their users. It has data on the holdings of culture collections, research programmes and projects, and a directory of experts involved with basic and applied microbiology.

With support from FINEP (Federal Government agency) and the State Government of Sao Paulo, the following activities have been carried out since 1982:

- Publication of the National Catalogue of Strains (eds. 1984, 1986, 1989);
- National survey on culture collections and existing human resources;
- Computer communication;
- Training programme.

The collection, analysis and dissemination of data for the national catalogue has led to major progress in the data quality of Brazilian collections. Each individual collection has revised its holdings and all who have been directly or indirectly involved have become aware of the importance in establishing a national network of culture collections.

The survey was fundamental to the establishment of national policies and has shown the importance of long-term support for culture collections. It has also been used in the establishment of the training programme and in increasing international co-operation in this field. A steering committee has been created by the Federal Government in order to assess the development of the national culture collection programme. At present, the Federal Government is funding 12 selected collections.

Aside from the National Catalogue, all information is also available online through a local network called STM-400, belonging to the Ministry of Communications. This system stores information on different data bases and also has all communication facilities, such as electronic mail, teleconferences and bulletin board.

Through this system, BDT has made the following information available:

- National Catalogue of Strains;
- Information on the culture collections included in the catalogue;
- News, such as training courses, publications, congresses.

The BDT has been linked to the MSDN network since March 1987. This has led to the recognition by international organizations of the potential value of the BDT in this field. Electronic mail facilities have greatly helped in establishing links with scientists internationally and, specifically, in the organization of training courses in which international consultants have participated. Since 1986, five training courses and six seminars have been held. The exchange of information and experience with culture collections from abroad also led to collaborative projects.

All work carried out by the BDT has been significantly aided by the existence of the Tropical Culture Collection (Colecao de Culturas Tropical, CCT). It holds strains of bacteria, fungi and yeasts, including type and reference, strains and many industrially-useful organisms.

The CCT is now setting up a screening programme for the isolation of micro-organisms of industrial, economic and biotechnological interest. In the near future it plans to set up sub-collections of isolates from tropical environments such as rain forests and dry lands.

Through these activities, the demand for cultures and specialized services is steadily increasing. The BDT will expand its activities in the future, both as an information centre of microbiological reources and in developing software of interest to culture collections. Further

international co-operation will be sought, not only with developed nations, but also with developing countries, making the experience we have gained of microbiological data collection, analysis and dissemination available.

It order to become a part of the scientific and industrial community of the world today, it is necessary to have access to up-to-date information, both from one's own country and from abroad. It is evident that this exchange never occurs on an equal basis due to economic problems in developing countries which result in inadequate public infra-structure, lack of training and experience, and lower demand for specialized services. These problems delay the emergence of a critical and demanding market for the information services which are needed. Even so, knowledge of one's own situation - both scientific and technical - is essential for the future development of a nation. We believe the BDT is making a significant contribution in the microbiological area, helped by our international contacts and facilitated by the MSDN services.

For further information on the BDT's activities please contact: Vanderlei P. Canhos, BDT/FTPT, Rua Latino Coelho 1301, C.P. 1889, 13.085 Campinas, SP, Brazil. Telex: 4909975092 CDT UI.

The C.A.B. International Mycological Institute's Culture Collection Data Base

The Culture Collection Database is maintained on C.A.B. International's VAX 8350/6310 Cluster computer. In addition to catalogue data, information on growth requirements, preservation methods, enzymes, secondary metabolites, physiological tests and special features are included. Searches can be carried out on the data base, for which a charge may be made. Information on strains held can be obtained in the period between printing catalogues from the data base.

Since transferring onto C.A.B. International VAX computer there is increased capacity for additional information being entered and facilities for more rapid searching and retrieval. The data base or parts of it can also be made available on floppy discs, on tape, or other machine-readable forms, for personal use. Direct online access is also to be provided.

The catalogue data will also form a part of various national and international data bases concerned with microbial strains. The CMI is working closely with initiatives being taken in the UK and the EEC, and is now operating as the UK Node for MINE (Microbial Information Network Europe), the CEC-sponsored integrated catalogue project for culture collections, which began in 1986.

MiCIS

The MiCIS data base (the Microbial Culture Information Service), originally based at the Laboratory of the Government Chemist, UK, has now relocated at the Information Centre for European Culture Collections in Braunschweig, Federal Republic of Germany. The data base holds strain data from all UK National Culture Collections and access to MiCIS is either direct via the (International) Packet Switch System (I)PSS or via a gateway link ghrough MSDN, the Microbial Strain Data Network. It is planned that the MiCIS data base will become part of the centralized European data base of MINE, the Microbial Information Network Europe. Further information from: Information Centre for European Culture Collections, Mascheroder Weg 1b, D-3300 Braunschweig, Federal Republic of Germany. Tel.: National (0531) 618715, International +49 531 618715. Fax: (0531) 618718 (via DSM). Contacts: Dr. Eva-Beate Jorzig, Petra Reinecke.

Microbial Information Network Europe (MINE)

Microbial Information Network Europe (MINE) is sponsored by the EEC Biotechnology Action Programme, and is an integrated catalogue project, incorporating a European network of microbial culture collection data banks. The objective is to improve awareness of strains available and facilitate ordering. All participating national nodes and individual collections will be able to access MINE online free of charge. Access for potential customers will initially be free through national nodes.

Present European partners acting as national nodes are as follows: Belgium, the Belgian Co-ordinated Collection of Micro-organisms, Belgian Science Policy Office (Brussels); Federal Republic of Germany, Deutsche Sammlung von Mikroorganismen (Braunschweig); Greece, Dairy Department, Agricultural University of Athens (Botanikos, Athens); Italy, Department of Plant Biology, University of Perugia (Perugia); The Netherlands, Centraalbureau voor Schimmelcultures (Baarn); Portugal, the Gulbenkian Institute of Science (Oeiras); Spain, Department of Microbiology, Faculty of Biological Sciences, University of Valencia (Burjasot, Valencia); United Kingdom, C.A.B. International Mycological Institute (Kew).

The UK Node at CMI has been working in co-operation with MiCIS and data of all major UK Culture Collections from both the LGC Computer and the CABI VAX cluster will be integrated via the Information Centre for European Culture Collections, now based at Braunschweig, Federal Republic of Germany.

The MINE project under the CEC BAP programme will be completed at the end of 1989, by which time all data will be integrated into a centralized European data base, in preparation for the service to go online from 1990 under the CEC BRIDGE programme. Plans are being made to extend the data held to full strain data.

C.A.B. library

The CMI library houses a unique collection of literature in the fields of pure and applied mycology: fungal taxonomy and systematics, plant pathology (including bacterial and viral diseases), medical and veterinary mycology, and more recently biodegradation, biodeterioration and related aspects of fungal biotechnology. Its holdings represent a considerable localized resource for anyone working in these areas of research.

The library receives approximately 1,000 current serial titles on a regular basis from countries world wide; this includes many less accessible journals and reports as well as the major periodicals in its subject area, in addition to other non-current titles. These are further supplemented by a large and varied collection of reprints and photocopies: about 135,000 items, including that of the Biodeterioration Centre (formerly at the University of Aston). Books and a significant conference proceedings collection represent a further 4,000 volumes. The adjacent libraries of the Royal Botanic Gardens form a complementary source of literature.

Visitors are welcome to use the resources and facilities available at the CMI library, but are advised to contact the librarian beforehand to make appropriate arrangements.

The library can supply photocopies from the originals of many items abstracted and indexed in the Institute's secondary publications detailed in this catalogue. Requests should comply with the conditions laid down in UK copyright regulations. Charges (including first class/airmail delivery): 6 pounds sterling/$US 10.00 per item of up to 15 pages, plus 0.40 pounds sterling/$US 0.60 per additional page. Orders should be prepaid (in pounds sterling or United States dollars) to avoid delay; frequent users of the service should inquire about our deposit account scheme.

Requests for photocopies and further details should be directed to: Document Delivery Service, C.A.B. International, Library Services Centre, Silwood Park, Buckhurst Road, Ascot, Berks SL5 7TA, UK.

CAB ABSTRACTS online

The contents of the more than 50 C.A.B. International abstract journals, including the CMI abstract journals have, since 1973, been contained in the CAB ABSTRACTS data base. The data base containing more than 2 million records is available for online searching either as a complete file or as separate sub-files corresponding to each abstract journal. Online searching is a highly cost-effective way of carrying out literature searches, and provides users with a printout of bibliographic records, the majority with informative abstracts, on their specific subject.

The CAB ABSTRACTS data base is publicly available via a number of major online hosts and is easily accessed from most countries using low cost data communication networks. A standard terminal with an acoustic coupler or modem is all that is needed to connect the user through the local telephone system to the online network. A word processor or personal computer with an appropriate telecommunications interface may also be used.

Charges for online access comprise three components: the telecommunications charges; the online host connect time charge; and a citation charge for each record output from the data base. Search costs will depend on the search strategy, more often than not extremely simple, and the number of records printed out. A typical search taking between five and 10 minutes and printing out 20 records will cost approximately $US 15,000. Most online hosts provide passwords free of charge and invoice monthly for usage.

Downloading, i.e. capturing information in computer-readable form, from the CAB ABSTRACTS data base is permitted for:

(a) Temporary storage of search output retrieved online for the purposes of editing, reformatting or printing at no additional charge.

(b) Long-term storage and re-use of data using the "download" facility on ESA-IRS or DIMDI where a downloading charge has been incorporated into the royalty charges. Downloading from other hosts is permitted subject to acceptance of written conditions and payment of the appropriate fees.

For full details of the downloading terms and conditions, please write to the Machine Readable Products Manager, CABI, Wallingford, Oxon OX10 8DE, UK.

G. MEETINGS

1 February 1990 London, UK.	Management of Biotech Opportunities - A New Realism for the Process Industries. Further information from Society of Chemical Industries, 14/15 Belgrave Square, London SW1X 8PS, UK.
9-10 April 1990 Nottingham University, UK.	Extracellular Microbial Products and Bio-deterioration. Further information from Dr. Joan Kelly, CMI, Ferry Lane, Kew, Surrey TW9 3AP, UK.
22-27 April 1990 Spindleruv Mlyn, Czechoslovakia.	7th International Workshop on the Molecular Genetics of the Mouse. Further information from Jiri Forejt, Institute of Molecular Genetics, Czechoslovak Academy of Sciences, 14220 Prague 4, CSSR.
6-9 May 1990 Seoul, Korea.	2nd International Biotechnology Conference: Asian-Oceanian Biotechnology Conference. Further information from the Organizing Committee, 2nd International Biotechnology Conference, Nam Seoul, P.O. Box 33, Seoul 151, Republic of Korea.
22-26 May 1990 Munich, FRG.	IFAT '90 - The World's Largest Specialized Fair for Waste Disposal.
2-6 July 1990 Laurceston, Tasmania, Australia.	Tasmania '90 - Australian Society for Microbiology - Annual Scientific Meeting. Further information from the Australian Biotechnology Association, 1 Lorraine Street, Hampton, Victoria 3188, Australia.
11-13 September 1990 University of Reading, Reading, UK.	Second International Conference on Separations for Biotechnology. Further information from Prof. D. L. Pyle, Biotechnology Group, Department of Food Science and Technology, Reading University, Reading RG6 2AP, UK.
24-27 September 1990 University of Leeds, Leeds, UK.	Biotech UK. Further information from Prof. J. D. Bu'Lock, University of Manchester, Manchester M13 9PL, UK.
10-13 December 1990 Ashok Hotel, New Delhi, India.	Biotek India '90. Second International Exhibition and Conference on Biotechnology. Further information from CONVEX, Applied Technology Services Pvt., Ltd., 14P Bassant Lok, Vasant Vihar, New Delhi 110 057, India.

H. SPECIAL ARTICLES

Safety, biotechnology and the problem of international trade-offs

Introduction
by
Dr. M. Levin
and Dr. R. Wachbroit*

Risk analysis has become an increasingly important component in the development, regulation and promotion of biotechnology. While many countries, including the developing ones, are aware of the many benefits that biotechnology promises, the complex issues concerning the special risks in the environmental application of this technology are not well understood, especially when it comes to the international management of biotechnology risks.

To some extent the United States may appear to be a model. Not only does the US have an elaborate regulatory system, there have been almost 200 field tests of biotechnology products in the US with no adverse effects noted to date. In no other country has this scale of testing been approached. This article will examine the regulatory structure of the US in terms of its ability to ensure the safe development of the biotechnology industry. The article then proceeds to examine the special problems that arise when safety concerns take on an international dimension. The fundamental problem regarding safety begins with the realization that risks cannot be reduced to zero. Hence, determining safety requires making "trade-offs". Different countries might be drawn to make different trade-offs because of their differing national agendas and priorities. How should these different trade-offs be reconciled? How ought the information and expertise needed for risk assessment be co-ordinated and made available, especially when the safety of developing countries is involved? The article includes an assessment of the current international organizations, activities and procedures for handling environmental biosafety issues. The article concludes with a number of specific recommendations to improve international co-operation leading to the development of safe methods for testing and utilizing engineered organisms in environmental situations.

Risk analysis

The overall process of risk analysis has two components: risk assessment and risk management. Risk assessment is the determination of the probability or likelihood of harm. The assessment process consists of the collection and analysis of the appropriate data that lead to an estimation of likelihood of harms. Risk management focuses on the actions that should be taken, given these risks. The risk management process begins with risk assessment but it also takes into account a number of other factors including the benefits of the product (e.g., less use of hazardous chemicals in the case of a biological pesticide) and the social implications of the risky activity (e.g., the impact of the use of Bovine Growth Hormone on the structure of the agriculture industry). Political factors must also be considered. 1/ Managing risk requires striking a balance between all of these factors. Since many of these factors will often suggest different responses, proper risk management - i.e., safety - involves the necessity of making trade offs.

Risk communication

Recent events have demonstrated the importance of risk communication. 2/, 3/ A number of authors have emphasized the need for the early involvement of the lay public and the need to clearly communicate risk information. 4/, 5/, 6/

Some commentators have suggested that all risk analyses share at least five elements that strongly affect the ability of experts to communicate risks to the public. These elements include (1) the path by which information reaches the audience (the path to the public is not direct); (2) the limited value of experts when the process becomes highly politicized; (3) the extent to which the local community believes it is affected; (4) the role of the mass media; and (5) the technical or cultural background of the audience. Technical audiences are more responsive to data developed using defined sets of principles and data. The boundaries are kept narrow and there is a high degree of reliance on statistical methods. Non-technically oriented audiences are more interested in broad problem definitions and analyses.

Because of the involvement of life forms and the interaction with the environment, biotechnology risk analyses rely more heavily on probability estimates than other technology assessments. Consequently they must incorporate a greater degree of uncertainty into the analysis. The differences in the background and perspective of the recipients of risk analyses information will affect the evaluation of the results and the management decisions. The role of risk communication in establishing meaningful communication between assessor and those potentially affected becomes especially critical. Drawing these groups together to reach agreement also requires strong co-ordination efforts among those conducting risk assessments as well as attention to the means of communication.

Co-ordination within the US

Background

In order to understand the efforts to co-ordinate biotechnology risk management in the US, it is important to understand how the regulatory framework is structured. Three agencies are involved, each of which is required to comply with a general statute for environmental protection and each of which has a specific mission. A co-ordinating committee has been formed to harmonize activities between agencies, which has published a framework for regulation and a list of applicable statutes. 7/

Each of the three agencies is responsible for compliance with the National Environmental Policy Act (NEPA) which is binding on all US Federal agencies. NEPA attempts to ensure that Federal actions are environmentally sound. In essence it requires each agency to evaluate the possible environmental outcomes of its proposed actions and look for a balance between benefits and possible adverse impacts. The agencies must conduct and document a thorough review of all pertinent available information, including alternatives, and seek public comment.

Each agency is also guided by its particular legislation. All of the relevant legislation is based in part on safety. Safety has been viewed from a number of perspectives. For example, safety can be viewed from the standpoint of workers in general, from the standpoint of particular categories of workers (e.g., laboratory or factory employees), from the point of the potential

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impact of industrial emissions on the environment, or from the standpoint of public health. Each of these standpoints has provided the basis for specific statutes. Implementing these statutes led to the establishment of the federal regulatory agencies. There are no statutes specifically dealing with the safety of biotechnology products.

The first effort to deal with the safety of biotechnology (molecular biology, as it was then called) was not the result of law-making but grew out of concerns voiced by the scientists involved. The protocol was developed and administered by the National Institutes of Health, resulting in its Recombinant Advisory Committee and the well-known RAC guidelines. 8/, 9/ The RAC guidelines focused on laboratory worker safety. They functioned with a great deal of success by stressing containment. In the initial version of these guidelines, any type of release of genetically engineered organisms into the environment was completely prohibited.

Although only federally funded molecular biological research was covered, non-federally funded researchers were expected to comply on a voluntary basis, which they did. An outcome of this procedure was the creation of Institutional Biosafety Committees (IBCs). These committees were established at all research and at most industrial facilities involved in molecular biology. They provide a first line of review of safety requirements for specific research projects. Although they were developed to aid the RAC by providing local review of some applications for rDNA research, they currently review most of rDNA research requiring review in the US.

Specific agencies

With the scaling up of molecular biology to industrial levels, safety emerged as an industrial issue. The safety of workers other than laboratory employees, of the environment and of agricultural products as well as the safety of the public health in general became involved. Because of their stated missions, three agencies - the Food and Drug Administration (FDA), the Environmental Protection Agency (USEPA) and the Department of Agriculture (USDA) - became heavily involved in biotechnology regulation.

The FDA has a large role in regulating biotechnology products because of the Food, Drug and Cosmetics Act and the Public Health Services Act. The agency has a mandate to ensure efficacy and safety of food and pharmaceutical products. The FDA's criteria for product evaluation focuses on purity, lack of adverse effects and efficacy. It has been estimated that the FDA has already ruled on thousands of biotechnology products, although not many of them have any potential ecological impact. FDA's environmental concerns and responsibilities result from the requirement to comply with NEPA.

The USEPA is the primary agency responsible for ecological and related public health issues. EPA administers seven environmental statutes. It regulates biotechnology under two of them, the Toxic Substances Control Act (TSCA) and the Federal Fungicide and Rodenticide Act (FIFRA). These two acts are best described as "gateway legislation" since they are invoked before new products are released to the environment. Unlike other EPA statutes which are oriented towards abatement, TSCA and FIFRA are oriented towards prevention. FIFRA covers all pesticidal products and is clearly applicable to biotechnology products. New chemicals or new uses for existing chemicals trigger TSCA. Recombinant DNA is considered a new chemical in order to invoke TSCA, and the new life form resulting from the genetic recombination is therefore included in what TSCA covers. The EPA reviews are considered the equivalent of NEPA reviews.

The USDA has the responsibility of enhancing production and for assuring the safety and nutritional quality of food and fibre. The agency's primary environmental concerns are the safety of crop plants and cattle. The USDA has three divisions that deal with biotechnology. The Agricultural Research Service deals with research issues and has formed an equivalent to the NIH RAC to review proposals. It is also instituting an information service as part of its National Biological Impact Assessment Programme and has an office that serves to co-ordinate activities within the agency. The agency's Food Service and Inspection Service functions to ensure the safety and wholesome characteristics of all food products. Through the Animal and Plant Health Inspection Service the agency meets its responsibilities for licensing veterinary biological material and for issuing permits for the transport of biological material. The USDA has formed the Biotechnology, Biologics and Environmental Protection Division (BBEPD) with responsibility for all biotechnology products. As a result of NEPA the USDA has the responsibility for ensuring safe ecological utilization of engineered crops, cattle and veterinary products.

The international situation

The US regulatory structure reflects the growing concern in the US for developing a safe biotechnology industry. The concern and enthusiasm for biotechnology is certainly not confined to the US. Various other nations engaged in or planning to engage in biotechnology research and development have produced regulatory structures that are distinctly different from the USA's. Nevertheless, regardless of the quality of these national regulations and safety measures, there are several reasons for focusing international attention on the issue of biotechnology safety.

First of all, genetically engineered organisms do not respect national borders. A common public fear is that a harmful micro-organism might be released into the environment. Such organisms cannot be "recalled", and, if they successfully adapt to the environment, they will increase exponentially. An exponential increase of a harmful engineered organism would soon pose a threat to neighbouring countries. And there is no practical way of securing borders against micro-organisms.

In one respect this concern is like the international concern over nuclear energy. As the Chernobyl disaster made vivid, a nuclear accident in one country can have widespread effects in others. But there is an important difference between nuclear energy and biotechnology: although both may be linked to weapons development, for the most part nuclear power is an expensive and complex technology, requiring sophisticated installations. This provides de facto international regulation of nuclear power. In contrast, biotechnology is not a secret technology; and the technology has become so easy that students in some US high schools perform recombinant DNA experiments as part of their course work.

This suggests a second reason for focusing international attention on the issue of biotechnology safety. While many scientists believe

that the possibility of harmful genetically engineered micro-organisms running amok is low, this belief is based on experienced researchers following safe laboratory practices. The easy availability of this technology raises the possibility that some work with genetically engineered organisms might not be done with as much preparation and care as many scientists assume is the case.

Problems facing international biotechnology regulation

There are three main issues facing international regulation in biotechnology.

The first, and perhaps the most obvious issue is the issue of authority. When disagreements about trade-offs occur within a country, the political structure of that country will typically identify an authority that sets a procedure by which disagreements are resolved into a national policy. A good example in the US is the establishment of the Council on Environmental Quality. The Council was established to review environmental issues and recommend a course of action to the President. The recommendations led to the passage of the NEPA. Resolving disagreements between nations is a different matter, for in so far as we acknowledge national sovereignty, there is no supernational authority.

The issue of authority is not at all peculiar to biotechnology regulation. Every kind of international arrangement - from specific trade agreements to military treaties to the establishment of common manufacturing standards - faces this issue. Our discussion of biotechnological risk has little to say on this issue. The issue of authority is a general issue, requiring a more general discussion.

Our discussion focuses on the other two issues. In order to understand these issues, we need to say more about what a trade-off problem involves.

A trade-off problem starts with the general assumption that we cannot completely eliminate risk. We can lower the risks involved in many situations, but this is always at a price. We might install more safety devices or double and triple check possible sources of harm, but at some point we must stop. The possible increase in safety does not warrant further cost. It may not be worth any further expense of time, money, or energy to make a small probability of harm even smaller. This point can be called the "trade-off solution".

Trade-off problems are notorious for admitting of more than one "solution". Or, to put it more accurately, people can rationally disagree over the acceptability of particular solutions. Much of this disagreement is due to the role values play in identifying an acceptable level of risk since reasonable people can disagree within a limited range on the significance of these values.

The role values play in trade-off problems takes two forms. Values enter by their identifying certain losses as costs or harms. Is the loss of a particular species a cost or harm? Surely not unless (the preservation of) the species is of some value. Values also enter by partly fixing a weighting on the factors being balanced. How important is the environment, high technology or economic progress?

This leads to the second issue facing international regulation in biotechnology: while disagreements over these values can certainly occur locally, the range of the disagreement is greater when we consider decision-makers coming from different cultures or countries. For example, one country might value a particular species of animal more highly than its neighbouring countries do because of the role that animal plays in its history, folklore, myths, etc. Plainly, that country will have sharp disagreements with its neighbours concerning the appropriate trade-offs and levels of safety if these animals are at significant risk.

Trade-off solutions are also obviously a function of the available information and its interpretation. This suggests two ways people could disagree on a trade-off solution even though they agree on values. (1) There could be a disagreement because one party does not have all the relevant data available. In a sense this is a trivial disagreement since it can be resolved, at least theoretically, by making available all the relevant data. (2) Even if all the relevant data is available, there could be a disagreement in interpreting the data. After all, experts do disagree on the assessment of technological risks.

These two types of disagreements can clearly arise in the international arena. The first type of disagreement - disagreements arising because not all parties are aware of the relevant data - can be an especially important problem for developing nations that lack the appropriate expertise in identifying and collecting the information. Nevertheless, while this may be an important practical problem, the situation is quite clear theoretically: all parties have a responsibility to ensure that all the relevant information is made available. The second type of disagreement - disagreements arising because the experts disagree - can be an important problem especially if the opposing experts happen to fall into different cultures. For example, consider a case where the experts of nation A are mainly ecologists and the experts of nation B are mainly evolutionary biologists. Even as a theoretical matter, the resolution of this type of disagreement is not at all clear.

Prospects for international regulation

Most developed countries have been developing biotechnology regulations internally. There have been a number of attempts on an international level to reach agreement on a framework for product evaluation and on requirements for field testing. Developing countries may be able to benefit from these efforts, but in each case one must make certain that the particular country's or region's needs are being met. These needs will affect the type and stringency of the regulatory framework. This requires considering the economic, cultural and social aspects of the particular country as well as the scientific issues such as the specifics of the product and how it might affect the ecological balance. International co-operation is essential not only because many of the products will be marketed on a global scale but also because viable organisms released to the environment will not respect political boundaries.

International co operation in environmental issues has been accepted as necessary in a number of areas. The United Nations Environment Programme, International Union for the Conservation of Nature and Natural Resources (IUCN) and the World Wildlife Fund have recently signed a memorandum establishing a monitoring centre to be called the World Conservation Monitoring Centre, and each of the three partners have pledged financial support.

Similarly, the Food and Agriculture Organization published an international code of conduct in 1986 on the distribution and use of pesticides which not only describes the shared responsibilities but also discusses the need for a co-operative effort and for generally accepted practices. Nevertheless, concerns have been raised about the status of regulations in developing countries. 10/

As demonstrated by the difficulties encountered in field testing a recombinant Rinderpest vaccine in Africa, progress in generating products which have the potential to boost the standard of living and aid agriculture is markedly slowed in the absence of clear regulatory pathways. Thus, the lack of an internal regulatory framework within developing countries and the lack of agreements between developing countries may well result in an even slower development and application of biotechnology products.

With these thoughts in mind, one can ask if the regulatory procedures of the US, the regulatory procedures of any developed country, or the agreements between developed countries are satisfactory models for developing countries. The well-documented problems within the US concerning co-ordinating the individual agencies and the eight unauthorized releases points out the difficulties within one country. Even within national boundaries differences of public opinion can occur to produce resistance to field tests and products: tests in different parts of the US have encountered different reactions. While the Organization for Economic Co-operation and Development guidelines may be accepted this year, they are the result of a series of meetings that began in 1983. This delay points to the problems associated with gaining international agreement for guidelines.

Nevertheless, there have been many public meetings, debates within expert panels, government reports, presentations at meetings of scientific societies and publications in scholarly journals. There is thus an extensive knowledge base which should include many if not all of the important issues concerning safety and environmental biotechnology. The time, effort and cost of reaching the current plateau in biotechnology regulation need not be duplicated by developing countries.

The large differences between developing countries in geography, training of regulatory officials, presence of a regulatory infrastructure, cultural background and available expertise in required disciplines points to future difficulties in developing appropriate regulatory procedures.

However, the documents of the OECD, the guidelines generated by the developed countries, and the proposed scientific rationales for evaluating the safety of biotechnology products produced by scientific societies and organizations 11/, 12/, 13/, 14/, 15/ form a valuable starting point in meeting some of these difficulties. These materials, further refined as a result of international or regional meetings, could lead to a general and basic document describing both principles and procedures (Basic Principles and Procedures Document) for estimating potential ecological effects of engineered organisms on a national and regional basis. The document should be sufficiently comprehensive to enable a country to identify principles and to select procedures so that it could conduct a risk assessment which would be sensitive to its cultural, social and economic values. While the document could not contain binding requirements, the principles of assessing risk and of estimating benefits would be clearly defined. The only requirement on sovereign States is that they conduct the risk-benefit process in a manner appropriate to their country and region.

A second important value of the document would be to demystify the science underlying biotechnology. The process of producing risk assessment principles would require a thorough review of the debates, conclusions, guidelines and safety research on a world-wide scale. Thus, experts in biotechnology as well as involved government officials could become familiar with the safety issues. It could also provide a basis for public education.

Developing countries could greatly benefit from the activities of the developed countries by taking advantage of electronic access to ecologically oriented data banks 16/, 17/ and by using artificial intelligence systems. Both of these tools are being developed to aid the evaluation of safety regarding the marketing and releasing of genetically engineered products. These tools would help resolve another issue - the lack of a large cadre of well-trained scientists in many developing countries. Expert panels can be formed to evaluate individual proposals. However, these panels require a pool of expertise which is unavailable in most countries. This shortage of trained personnel is affecting the US regulatory process, leading to a reliance on government staff scientists and on *ad hoc* communication with experts. The need for a large panel would be diminished if the principles involved and the data needed were clearly identified at an early stage in the assessment. A BPPD would have the effect of limiting the breadth of the expert panel. If the data needed are clearly defined in advance, one could select experts from closely related fields and rely on them to develop information in the fields required by the case at hand.

The development and utilization of a BPPD, along with the identification and linking of the appropriate electronic data bases, would have an effect on another important aspect of the utilization of biotechnology products. Public resistance to field tests and product utilization is directly related to the amount of information available to the public and how it is presented. Compliance by investigators is directly related to the amount of information available to them that justifies the need for the regulations and indicates how best to comply. Establishing a mechanism for conducting workshops aimed at informing the public and the regulated community about the risk assessment process would have a positive effect on compliance. The existence of a data bank would provide access to authoritative sources and ensure completeness of the data acquisition effort. This information could be used for public education as well as for decision making.

Thus, the BPPD would have a positive effect on the development of internal and regional biotechnology regulations, it would provide a basis for public education and involvement, and it might decrease the requirement for specific experts. The international scope of the process needed to develop the document would take full advantage of all of the regulatory debate that has taken place thus far. The result could be a document acceptable by all participants because it has a sound scientific base and public support.

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